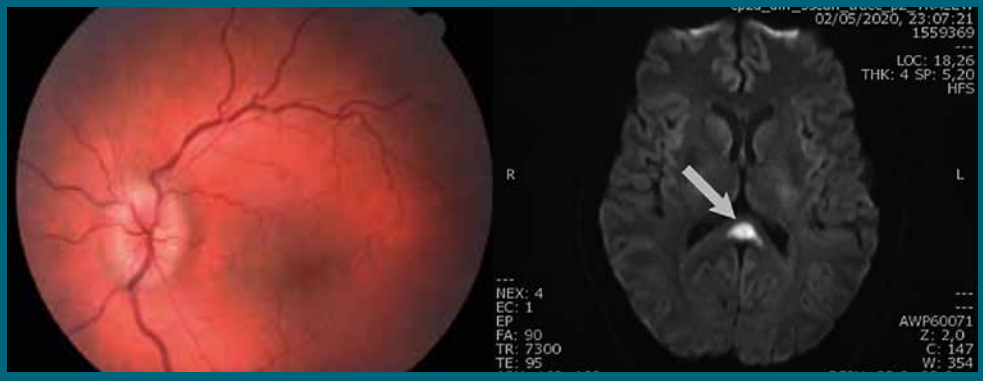
Oftalmología Clínica y Experimental

Publicación científica del Consejo Argentino de Oftalmología • ISSN 1851-2658 • Volumen 13 • Número 3 • Septiembre 2020



Dengue y visión: ojos y cerebro

Retinopatía diabética y teleoftalmología

Inyecciones intravítreas en la Argentina

Aceite de silicona intracraneal

OCE 13.3

NUEVO

RÁPIDO ALIVIO DE LOS SÍNTOMAS DE OJO SECO[1]

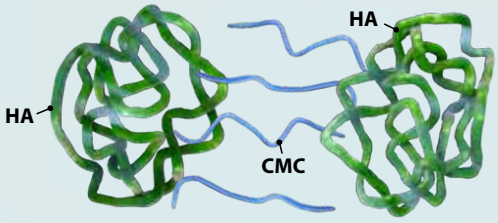
Refresh FUSION®

Combinación exclusiva de

CARBOXIMETILCELULOSA + ÁCIDO HIALURÓNICO*

para todo tipo de pacientes, incluyendo pacientes post quirúrgicos (Lasik) y usuarios de lentes de contacto[2]

La matriz permite que cada polímero (CMC+HA*) conserve sus propias características y genere una sinergia logrando[1,4-7]:



- Aumentar el tiempo de retención en la superficie ocular.
- Rápida reepitelización corneal. Protección de larga duración de la superficie ocular.
- Mejorar el tiempo de permanencia durante y entre parpadeo (Un parpadeo más cómodo).

Doctor/a,
Escaneando el código QR usted podrá consultar el prospecto de ***Refresh Fusion***

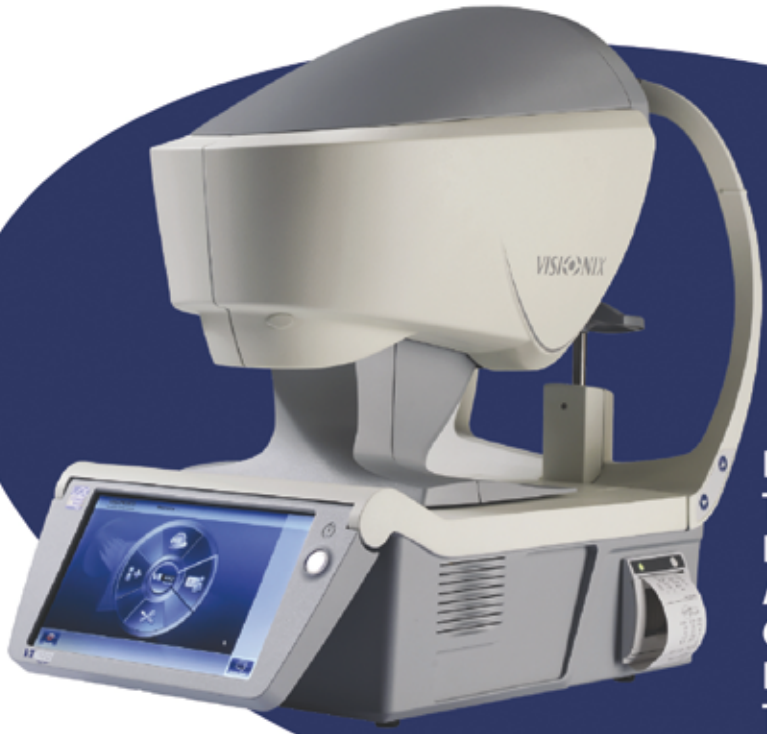
Allergan™
an AbbVie company

* Excipiente

Referencias: 1. Simmons. P.A. .et al..Clinical Ophthalmology. 2015: 9:665-675. **2.** Prospecto Refresh Fusion **3.** Aragona P, Papa V, Micali A, Santocono M, Milazzo G. Long term treatment with sodium hyaluronate-containing artificial tears reduces ocular surface damage in patients with dry eye. Br J Ophthalmol. 2002;8612] :181-184. **4.** She, Y. et al. Journal of Ocular Pharmacology and therapeutics, 2015; 31(9)525-530. **5.** Hunt et al. In: Drug delivery systems, fundamentals and techniques, 1987. Garrett et al. Invest Ophthalmol Vis Sci 2007. **6.** Garrett et al. Curr Eye Res 2008 **7.** Zheng et al. Cornea 2013. 3. Lee et al. Cornea 2011

AR-REF-2050018 - Mayo 2020

Plataforma Multidiagnóstica
VX-120/130



7 estudios en 90seg

Refractometría
Tonometría
Paquimetría
Aberrometría
Queratometría
Pupilometría
Topografía corneal
de cara anterior y posterior*
Cámara Multi-Scheimpflug

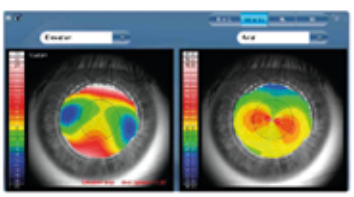
VISIONIX

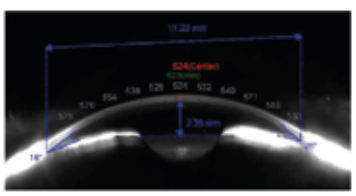
- Refracción diurna y nocturna
- Topografía con 24 anillos de Placido (Mapa Axial, Mapa tangencial, Mapa de Elevación, Mapa de refracción)
- Paquimetría central y periférica
- Punto más delgado de la córnea
- Ángulo Irido Corneal y Ángulo Kappa
- Profundidad de la cámara anterior
- Visualización de las opacidades de cristalino
- Presión intraocular corregida
- Queratometría (K1, K2, promedio, cilindro y eje)
- Toricidad corneal (diferencia en dioptrías entre las curvaturas de los meridianos principales y del eje), índice de simetría, Gradiente de Curvatura Apical, Queratometría Apical, Factor-P , Excentricidad
- Aberrometría (Análisis de Zernike ocular y corneal de Alto orden, Bajo orden, total, RMS; Mapas de aberraciones, Función de dispersión de puntos [PSF], Función de transferencia de modulación [MTF], Simulación de la agudeza visual)

*** Modelo VX-130. Impresora interna no disponible**

- ✔ OPERADOR INDEPENDIENTE
- ✔ CENTRADO AUTOMÁTICO
- ✔ AUTO ENFOQUE
- ✔ AUTO MEDICIÓN
- ✔ CONEXIÓN WIFI
- ✔ REPORTES DE IMPRESIÓN

TOTALMENTE CUSTOMIZABLES





www.3boptic.com
(341) 452 7400
(11) 4304 6475
ventas@3boptic.com
/3boptic

3B OPTIC INSTRUMENTS

AstaTec

MELAG
competence in hygiene

Vacuklav 41B+ Evolution

Clase B

- 9 minutos para ciclo desenvuelto
- Prevacio fraccionado para instrumental hueco (handpiece)
- Ciclos para desenvueltos, pouch, doble bolsa, textiles y priones
- Capacidad 18 litros
- Opciones para documentación en red o Stickers

En la actualidad, los autoclaves se dividen por clases: N/S/B

Los más desarrollados son los clase B. Esta clasificación garantiza la esterilización de elementos huecos (ej pieza de mano facoemulsificador), material dentro de cajas perforadas y priones, mediante el proceso de PREVACIO FRACCIONADO y que superen el test de Helix.

Este test evalúa la penetración del vapor en las cavidades con valores de presión y temperatura según normas internacionales.

Estos equipos disponen de capacidad de carga (18 litros, 25 diámetro x 35 fondo) pudiendo realizar ciclos para todas las necesidades de instrumental. Dispone de programas para desenvueltos, pauch, doble bolsa, textiles y priones.

La velocidad de esterilización para material desenvuelto ronda los 9 a 12 minutos, siendo un excelente tiempo en función a su capacidad de carga.

Vacuklav 31 B+

Clase B

- 12 min ciclo desenvuelto
- Prevacio fraccionado para instrumental hueco (handpiece)
- Ciclos para desenvueltos, pouch, doble bolsa, textiles y priones
- Capacidad 17 litros
- Opciones para documentación en red o Stickers

www.melag.com/es/productos/autoclaves/clase-profesional/vacuklav-31-b

Quality – made in Germany

(011) 4545-6661
info@asta-tec.com
www.asta-tec.com

astatec_sa
Astatec
AstaTec S.A.

ZEISS
Business Partner

iLUX®

HOW IT WORKS

LA OPORTUNIDAD DEL OJO SECO

Los procedimientos en el consultorio se están convirtiendo en el segmento de más rápido crecimiento en el tratamiento del ojo seco: casi 8 de cada 10 médicos consideran esto como una oportunidad para hacer crecer su práctica.[1]

INGRESAR A PACIENTES EN UN SISTEMA DE CUIDADO DEL OJO SECO

Como los pacientes a menudo ignoran los síntomas, mejorar el cuidado del ojo seco comienza con un diagnóstico. Pregunte a sus pacientes si usan lágrimas artificiales y con qué frecuencia. Cuanto antes comience la conversación sobre el ojo seco, más éxito tendrá.

SEE IT

Observe las Glándulas de Meibomio bloqueadas a través de la lente de aumento.

HEAT IT

Presione el botón para convertir la luz LED en energía térmica localizada.

TREAT IT

Tenga control total de la presión mientras comprime suavemente el párpado.

PERSONALIZE IT

Seleccione solo las áreas que necesitan tratamiento.

RESULTADOS ESPERADOS

- El tratamiento en ambos ojos lleva aproximadamente de 8 a 12 minutos
- El tiempo de ruptura de la película lagrimal se prolongó un 71% en una semana y un 90% más en un mes después del tratamiento[2]
- Las Glándulas de Meibomio producen tres veces más meibum en una semana después del tratamiento y cuatro veces más un mes después del tratamiento[2]

1. Ipsos Alcon Dry Eyes Brand Research 10 Oct2016 (v1.0)
2. Comparison of a Handheld Infrared Heating and Compression Device. (v1.0)

AR-ILU-1900013

Alcon
VE BRILLANTEMENTE

*Euromonitor, 2018. Valor de venta retail en la categoría de marca de lentes progresivas. Armazon: Oliver Peoples Sheldrake 0OV5036. Essilor, Varilux y Varilux Comfort Max son marcas registradas de Essilor International, 2020. COD VX119.

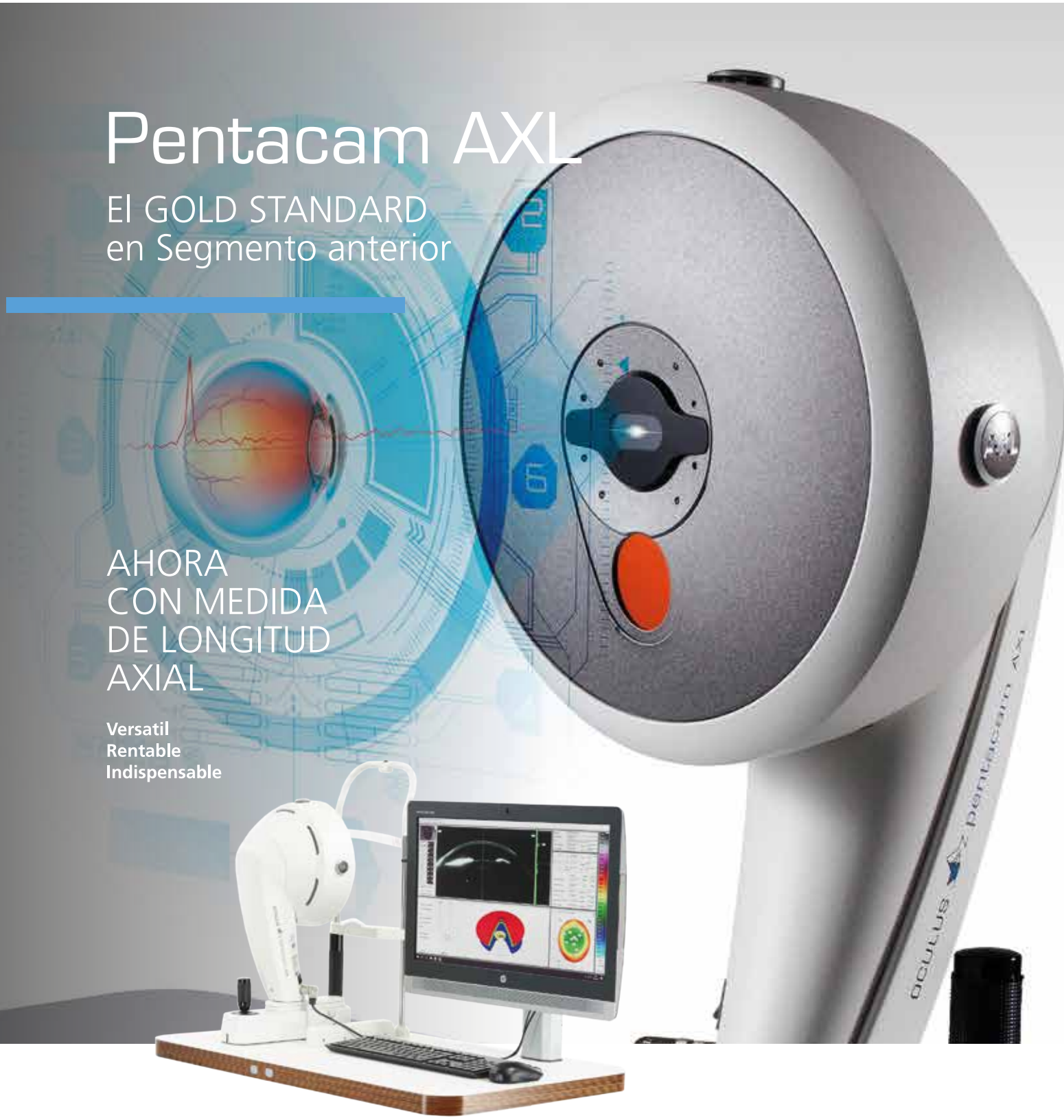
OCULUS®

Pentacam AXL

El GOLD STANDARD en Segmento anterior

AHORA CON MEDIDA DE LONGITUD AXIAL

Versatil
Rentable
Indispensable



ESCANEA EL CODIGO PARA MAS INFORMACION

Jean Jaures 419 nro.11 / Ciudad Autónoma de Buenos Aires
Tel (011) 4866 4484 / 6116 / 4441

omnisrl.com.ar OMNI SRL OMNI.srl

OMNI
PASION POR LA TECNOLOGIA

Canon

Internacional
ÓPTICA & OFTALMOLOGÍA
25

Cámara *CR-2 PLUS*

Xephilio *OCT-A1*

Representante Exclusivo para la Argentina

Tel +54.11.4384-6031 (int. 120) | internacional.com.ar/oftalmologia
info@internacional.com.ar

Publicación científica del Consejo Argentino de Oftalmología ISSN 1851-2658

Oftalmología Clínica y Experimental

Volumen 13 • Número 3 • Septiembre de 2020

Sumario

Oftalmología Clínica y Experimental

La revista **Oftalmología Clínica y Experimental** (ISSN 1851-2658) tiene una frecuencia trimestral (cuatro números por año). Su objetivo es brindar acceso a material científico en español, en portugués y en inglés. Contiene trabajos originales de investigación clínico-quirúrgica y básica, comunicaciones breves, informe de casos y series, revisiones sistemáticas, apuntes en medicina basada en la evidencia, bioestadística y prevención de la ceguera, comentarios de resúmenes destacados para la práctica oftalmológica presentados en congresos y reuniones de la especialidad y referencias a publicaciones de otras revistas. Se estimula el envío de correspondencia para la sección de cartas de lectores abierta a todos los profesionales que deseen expresar sus comentarios sobre los trabajos publicados y observaciones preliminares importantes para la práctica oftalmológica. Los trabajos recibidos son evaluados por profesionales (árbitros o revisores) con conocimiento del tema tratado de acuerdo con normas internacionales. La revista cuenta con un sistema de autoevaluación para contabilizar créditos de educación permanente. Los artículos podrán ser localizados e identificados a través de los buscadores usuales de la web abierta y bases de datos regionales.
El Comité Editorial de la revista adhiere a los principios establecidos por el Internacional Committee of Medical Journal Editors y se ajusta a los principios de la Declaración de Helsinki y a los principios de cuidados de animales para experimentación de la Association for Research in Vision and Ophthalmology (ARVO).

Equipo

Domicilio editorial: Consejo Argentino de Oftalmología, Tte. Gral. J. D. Perón 1479, PB, 1037AAO Buenos Aires, Argentina. Teléfono: (54-11) 4374-5400 líneas rotativas. Correspondencia al editor: secretaria@oftalmologos.org.ar

Número de propiedad intelectual 69974236.

Impresión: Galtprinting, Ayolas 494, C1159AAB Buenos Aires, Argentina

www.oftalmologos.org.ar/oce/

ISSN 1851-2658

Ocular inflammatory manifestations induced by dengue virus infection

Marcelo Rudzinski[a, b] and Adriana E. Echeverría[a, c]

[a] *Catedra de Oftalmología, Universidad Católica de las Misiones, Posadas, Misiones, Argentina.*

[b] *Consejo Nacional de Investigaciones Científicas y Técnicas, (CONICET), Argentina.*

[c] *Hospital de agudos Ramón Madariaga, Parque de la Salud, Posadas, Misiones, Argentina.*

Received: July 7th, 2020.
Accepted: July 26th, 2020.

Corresponding author
Dr. Marcelo Rudzinski
Universidad Católica de Misiones
Av. Jauretche 1036
3300 Posadas, Misiones
Argentina
(376) 446-9697
rudzinski-investigacion@ucami.edu.ar

Oftalmol Clin Exp (ISSN 1851-2658)
2020; 13(3): 113-126.

Aknowledgements
We would like to thank graphic designer Fabian Goya for helping with the figures.

Abstract

Dengue infection can produce a wide clinical spectrum of inflammatory manifestations in the eye. Ocular manifestations during the critical period of the disease are more frequently associated with vascular damage induced by the viral protein NS1. Sight-threatening retinal conditions in that period include posterior uveitis and dengue maculopathy. Retinal hemorrhages, edema, vasculitis and exudative retinal detachment are the most frequent presentations of posterior uveitis. SD-OCT and OCTA are tools capable to locate the affected retinal layers and capillary plexus involved in the retinopathy. Although infrequent, neuroophthalmological manifestations are an important cause of visual disturbance, inducing ophthalmological inter-consults in hospitalized patients. Available treatments include supportive measures, systemic corticosteroids and intravenous immunoglobulin. There is an urgent need for clinical studies to test drugs known to restore vascular permeability as well as new antiviral drug candidates.
Keywords: dengue, ocular manifestations, 2020 epidemic.

Manifestaciones inflamatorias oculares inducidas por el virus del dengue

Resumen

La infección por dengue produce un amplio espectro de manifestaciones inflamatorias oculares. Las

que ocurren durante el período crítico de la enfermedad están asociadas con daño vascular inducido por la proteína viral NS1. Las manifestaciones retinales que pone en riesgo la visión del paciente durante este período son las uveítis posteriores y la maculopatía por dengue. Hemorragias, edema y vasculitis retinal junto con el desprendimiento exudativo de retina son las manifestaciones oculares más frecuentes de la uveítis posterior. La tomografía de coherencia óptica de dominio espectral (SD-OCT) y la angiografía tomográfica de coherencia óptica (OCTA) son herramientas útiles, capaces de localizar los plexos capilares afectados en esta retinopatía infecciosa. Aunque infrecuentes (respecto del total de pacientes infectados) las manifestaciones neurooftalmológicas son causa de consulta oftalmológica por síntomas visuales e interconsultas de pacientes hospitalizados. Los tratamientos disponibles incluyen medidas de soporte y asistencia general, corticoides sistémicos y tratamiento con inmunoglobulina intravenosa. Existe una urgente necesidad de ensayos clínicos orientados a testear drogas con conocida actividad estabilizadora de la permeabilidad vascular retinal así también como de drogas antivirales.
Palabras clave: dengue, infecciones oculares.

Manifestações inflamatórias oculares induzidas pelo vírus do dengue

Resumo

A infeção por dengue produz um amplo espectro de manifestações inflamatórias oculares. As que acontecem durante o período crítico da doença estão associadas com dano vascular induzido pela proteína viral NS1. As manifestações retinianas que põem em risco a visão do paciente durante esse período são as uveítes posteriores e a maculopatia por dengue. Hemorragias, edema e vasculite retiniana junto com o desprendimento exudativo de retina são as manifestações oculares mais frequentes da uveíte posterior. A tomografia de coerência óptica de domínio espectral (SD-OCT) e a angiografia tomográfica de coerência óptica (OCTA) são ferramentas úteis, capazes de localizar os plexos capilares afetados nesta retinopatia infeciosa. Embora infrequentes (em relação ao total de pacientes infetados) as manifestações neurooftalmológicas são causa de consulta oftalmológica por sintomas visuais e interconsultas de pacientes hospitalizados. Os tratamentos disponíveis incluem medidas de suporte e assistência geral, corticoides sistêmicos e tratamento com imunoglobulina intravenosa. Existe uma urgente necessidade de ensaios clínicos orientados a testar drogas com conhecida atividade estabilizadora da permeabilidade vascular retiniana como também de drogas antivirais.
Palavras chave: dengue, infeções oculares.

Introduction

Dengue virus (DENV) belongs to the *Flaviviridae* virus family. It is an arbovirus, an arthropod borne virus[1], meaning that the virus is transmitted by an arthropod.

The mosquito *Aedes aegypti* is its main vector in urban settings and *Aedes albopictus* in rural and rainforest areas. The recent expansion of *Aedes aegypti* distribution in the world resulted in a 30 fold increase in the incidence of dengue disease in the last decades[2-3].

DENVs are a group of positive mono-catenary RNA viruses that are antigenically related and grouped according to the human serum response (serotype) in DENV-1 to DENV-4. The genome is an 11 Kb RNA strand with 10 genes coding 3 structural proteins and 7 nonstructural proteins. Protein M and Protein E are the main proteins of the envelope. Protein C forms the capsid. The nonstructural proteins are NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5[1].

Dengue is found in tropical and sub-tropical climates worldwide, mostly in urban and semi-urban areas. The global incidence of dengue has grown dramatically in recent decades. There are 100-400 million of estimated infections each year. The largest number of dengue cases ever reported globally was in 2019. The American region alone reported 3.1 million cases, with more than 25,000 classified as severe[2]. According to the National Health Ministry, Argentina has more than 92.229 dengue suspected cases since week 31 of 2019 (end of July 2019)[4]. Of those patients, 56492 are confirmed dengue cases. The propaga-

tion of the disease from the north of the country during the first trimester of 2020, resulted in the worst known epidemy of dengue in Argentina. Current prevalent serotypes in Argentina are DENV-1 in the northwest, DENV1- and DENV-4 in the center and DENV-1, DEN-2 and DENV-4 in the northeast of the country. The three serotypes (DENV-1, DENV-2 and DENV-4) were also detected in Buenos Aires province[4].

Each serotype comprises several genotypes that have specific geographical distributions[5]. Five genotypes for DENV-1, 6 for DEN-2, 5 for DENV-3 and 4 genotypes for DNV-4. Infection by any of the serotypes generates a humoral immune response. Antibodies providing protection against all serotypes are called heterotypic antibodies and their protection lasts approximately 3 months. Specific antibodies against the infective serotype (homotypic antibodies) provide homotypic protection which was believed to be lifelong[6]. However, in a recent review of samples from patients in Nicaragua (obtained between epidemic outbreaks 2005 to 2012) homotypic reinfections were found within the same serotype for DENV-1, DENV-2 and DENV-3 serotypes[7]. Analysis of samples from patients reinfected in a large outbreak in Peru 2010-2011 also showed homotypic reinfection of patients with a DENV-2 American-Asian genotype different from the infecting DENV-2 Asian genotype that primarily infected the patients in 1995[8]. Together the data destroyed the dogma: one-time infection by a homologous DENV serotype.

Pathophysiology

The DENV NS1 protein is a complex multifunction protein involved in capsid assembly, host immune system evasion and vascular leakage. DENV NS1 has been shown to circulate as a soluble protein at high levels (1-2 μg/ml), correlating with DENV viremia[9].

The hallmark of severe dengue is increased vascular permeability. Collapse of the vascular lumen as well as increase endothelial markers were shown in small vessels while no signs of endothelial cell (EC) necrosis or EC DENV infection accompanied the above mentioned changes[10]. Vessel hyperpermeability was suggested to be either a direct effect of DENV NS1 on the glycocalyx[11] or a consequence of the function of several cytokines released by PBMC[12] after the activation of Toll-like-receptor-4 TLR4[13]. It was shown that DENV-NS1 can activate sialidases, cathepsin L and heparinases thus triggering the degradation of sialic acid and heparan sulfate at the glycocalyx[14]. DENV NS1 was shown to induce hyperpermeability in all tested human endothelial cells, with maximal effect on pulmonary endothelial cells[15]. The vascular leakage is apparently mediated by the specific interaction and subsequent internalization of NS1 in endothelial cells. Recently, the decrease of EC barrier integrity was associated with the activation of the p38MAPK pathway and it could be restored after the treatment with a p38MAPK inhibitor[16].

Humoral immune response

Antibodies typically protect humans from viruses in 3 ways: A) neutralization (antibody blocks virus interaction with host cell), B) opsonization (antibody coats virus and typically targets it for uptake by macrophages and neutrophils), C) antibody-dependent cellular cytotoxicity (ADCC, where the antibody mediates the destruction of infected cells).

In severe dengue, antibodies play a different detrimental function for the host. Severe dengue most commonly occurs among patients with secondary DENV infections and infants with primary infections. The most widely cited hypothesis for the pathogenesis of severe dengue in a second infection setting is called antibody-dependent enhancement (ADE)[17]. Human serological studies, as well as animal and in vitro models support the ADE hypothesis. Although the exact mechanisms are not clear, ADE is the process in which DENV complexed with non-neutralizing antibodies can enter into a greater proportion of cells of the mononuclear lineage, such as monocytes, macrophages and dendritic cells, thus increasing the quantity of infected cells and consequently increasing virus production. In

dengue, non-neutralizing heterotypic IgG anti-DENV antibodies produced during first DENV infection can form antibody-DENV complexes in the second infection that can allow uptake of DENV by mononuclear cells. DENV then replicates in these macrophages thereby increasing viral production. The uptake of the heterotypic antibody-virion complex occurs after the docking of the immune complex to the Fcγ-R of a mononuclear cell expressed on its surface[18]. Recently, dengue viral load at presentation and the odds of severe disease were highest among patients with low to intermediate pre-infection antibody titers and lowest among those with the highest antibody titers[19].

The role of antibodies against NS1 is still matter of discussion. On the one hand, passive transfer of anti-DENV-NS1 antibodies to mice has proven to avoid lethal encephalitis[20]. Antibodies that bind sNS1 in circulation were shown to neutralise its vasoactive effects, as demonstrated in a mouse model of NS1-induced vascular leakage[12]. On the other hand, human antibodies against NS1 may react against human endothelial cells[21], platelet antigens[22] and anticoagulation factors[23]. Human antibodies against NS1 can also consequently produce vascular leakage, thrombocytopenia and coagulopathy, possibly as a consequence of NS1 mimicry effect.

Clinical symptoms

In 2009, the WHO changed the definition of dengue infection. Symptomatic dengue can present as undifferentiated fever, dengue and severe dengue. Asymptomatic dengue could represent at least approximately 10% of infected patients[24]. The main symptom in dengue is fever, usually higher than 38°C, reaching in many patients 40°C and lasting 3-7 days. Myalgia, joint pain, retroocular pain, sore throat and facial erythema could also be present. Dengue can present with alarming signs: abdominal pain, persistent vomiting, clinically evident fluid accumulation, mucosal bleeding, lethargy or restlessness, liver enlargement > 2 cm, increased hemoconcentration concurrent with platelet decline[25]. Alarming signs indicate the need for patient hospitalization to avoid severe complications. Severe dengue can present as severe plasma leakage, severe bleeding or severe organ involvement[25].

After the mosquito bite there is a period of up to 7 days of incubation without clinical symptoms. The febrile period lasts between 4-7 days and is followed by the critical period. This period lasts approximately 2 days and is characterized by defervescence (decrease in body temperature), hemoconcentration and decrease of platelet count. The recovery phase is the last period and is characterized by the return of plasma to the vasculature with near normal hematocrit values.

Diagnosis of dengue infection

Approximately 24 to 48 h before the febrile period there is already detectable viremia which lasts till the start of the critical period. During viremia either RNA or antigen detection methods could be used for the diagnosis of Dengue infection. The CDC and the WHO recommend RT-PCR for the diagnosis of dengue disease, during this period. After the febrile period, the diagnosis is based on the detection of specific IgM and IgG antibodies[1, 25].

Ocular manifestations of dengue

Anterior manifestations

Subconjunctival hemorrhages are the most frequent ocular sign reported by patients with dengue infection. Up to 37,3% of patients with thrombocytopenia presented it during the critical period[26]. Diffuse epithelial keratitis as well as stromal keratitis has been reported in patients with acute dengue infection[27]. Necrotizing scleritis was observed in a Japanese patient without precedent autoimmune diseases who became infected with dengue virus during holidays in the Philippines[28]. The patient's scleritis was controlled with methylprednisolone pulse-therapy. There were no further recurrences after treatment, but the patient developed scleral thinning over the following years.

Table 1. Uveitis caused by dengue virus infection. Clinical presentations reported frequencies and response to treatment.

Uveitis	Clinical presentation	Frequency	Response to treatment
Anterior	Unilateral or bilateral Predominantly non-granulomatous	Frequent after the recovery period, up to 5 months	Good response to topical corticosteroids
Intermediate	Associated with dengue maculopathy	Rare	Insufficient data
Posterior	Retinal vasculitis	Frequent	Good response to systemic corticosteroids Final visual acuity varies according to lesion in the outer retinal layers
	Exudative retinal detachment	Frequent	
	Multifocal chorioretinitis	Less frequent	
	Acute posterior multifocal placoid pigment epitheliopathy (APMPPE)		
	Choroiditis		
	Acute zonal occult outer retinopathy (AZOOR)		
	Neuroretinitis (macular star)	Rare	

Other anterior manifestation of dengue infection is acute angle closure glaucoma (AAG). AAG associated with dengue can present with unilateral or bilateral involvement[29]. This entity may be associated with extensive choroidal effusions[30] or as a consequence of an iris plateau configuration[31].

Patients presenting with ocular pain, eye redness and photophobia few weeks or months after acute dengue fever are frequently diagnosed with presumed dengue associated anterior uveitis[32]. Anterior uveitis (AU) is less frequently diagnosed during acute disease[33]. AU can present as unilateral or bilateral uveitis, more frequently as non-granulomatous uveitis[34]. The etiological mechanism seems to be an autoimmune reaction following dengue infection since the patients respond to topical or periocular corticosteroids.

Posterior manifestations

Intermediate uveitis is an infrequent presentation of dengue infection. In a series of 65 eyes of patients with visual complains associated with dengue infection only 8 had intermediate uveitis[35]. Approximately 11% of patients who experience dengue maculopathy, a frequent clinical presentation of dengue infection, also have signs of intermediate uveitis[36].

Posterior uveitis (PU) is a common complication of dengue infection. PU by dengue is one of the three more frequent aetiologies of posterior uveitis in Singapore[37]. Clinical presentations of PU in dengue comprise vascular retinitis, exudative retinal detachment, chorioretinitis and neuroretinitis (Table 1). In a study that included 41 patients, 15 of 65 eyes with posterior ocular manifestations had retinal vasculitis[38]. Other retinal signs associated with retinal vasculitis are intraretinal hemorrhages and exudative retinal detachment[39-40]. Exudative retinal detachment was observed in 13 of those 15 previously mentioned eyes with severe retinal vasculitis in the study published by Theo SC. In severe cases of retinal vasculitis retinal ischemia may be present due to microvascular occlusion[41]. When the macular retinal detachment has fibrinous material a pseudophypopion can be observed as that reported in two patients from Malaysia[42].

Multifocal areas of chorioretinitis with retinal vasculitis, retinal hemorrhages and exudates were described by Tabbara K in 2 patients from Saudi Arabia[43].The patients had leukopenia and throm-

bocytopenia with high titers of IgM anti-dengue. The healing of the lesions left discrete atrophic chorioretinal scars with nummular shapes. Chorioretinal lesions during dengue infection may display features in the spectrum of acute posterior multifocal placoid pigment epitheliopathy (APMPPE)[44] or choroiditis[45]. Multifocal chorioretinal lesions resembling APMPPE were described in a patient who developed dengue fever after visiting the Caribbean islands. The OCT revealed disruption of the ellipsoid layers and RPE. The healing of the lesion left discrete chorioretinal scars[44]. Severe decrease in visual acuity and persistent scotoma in patients with dengue infection were associated with disruption of the outer neurosensory retina involving the outer limiting membrane, the myoid and ellipsoid zone as well as the outer segments of the photoreceptors, findings similar to those described in acute zonal occult outer retinopathy, AZOOR[46-47].

Concomitant inflammation of the optic nerve and macula can manifest as neuroretinitis. A classical presentation of neuroretinitis with vitritis, papillitis, exudates forming a macular star was reported in a Brazilian patient with acute dengue fever[48].

Two reports of blinding panophthalmitis in patients with severe dengue were recently described[49-50]. In both cases, the patients were admitted to hospital. They developed panophthalmitis due to secondary bacterial infection (Staphylococcus epidermidis and Bacillus Cereus). Both patients survived but the infected eyes were eviscerated.

Clinical spectrum of dengue maculopathy

Dengue maculopathy is the most frequent cause of visual complains in patients with dengue infection. Approximately 10% of infected patients admitted to hospitals will develop dengue maculopathy (DM)[51] or complain of blurry vision[52]. Main visual symptoms are blurry vision and or scotomata[51]. Decrease of visual acuity (VA) typically appears during the critical period, but it can also present up to 30 days after the febrile period. Other less frequent symptoms are myodesopsia and metamorphopsia. The decrease in VA at the time of diagnosis is mild to moderate in most patients. Approximately 69% of patients had a VA of 20/200 or better according to Teoh *et al*[35]. Bilateral involvement is very frequent but usually asymmetrical[35-36]. The triad of photopsia, myodesopsia and blurry vision was highly predictive of retinal hemorrhages[52].

According to its pathogenesis and ordered by frequency: macular edema, macular retinal detachment + severe vasculitis, macular hemorrhage and foveolitis are the most frequent clinical presentations of DM[42]. In a small case series, Chan *et al* found that macular hemorrhages were the most frequent cause of decreased visual acuity followed by retinal vasculitis and macular retinal detachment[33].

Three different patterns were described in DM using standard optical coherence tomography (OCT): diffuse retinal edema, cystoid retinal edema and foveolitis (Table 2). The latter is characterized by a thickening and hyperreflectivity of the subfoveal outer retinal layers[38].

The use of OCT angiography (OCTA) in patients with foveolitis and outer maculopathy shows flow deficit of the superficial retinal capillary plexus in 43,75% of the patients. Areas with flow deficit in the deep retinal capillary plexus were present in all patients. None of the eyes showed presence of choriocapillaris flow deficit areas[53].

Recently a new clinical presentation involving the macular neuroretina during dengue disease was described. Acute macular neuroretinopathy (AMN) is characterized by ischemia of the retinal deep capillary plexus (DCP)[54]. Clinically, retinal exudation can present around the foveal area. Macular retinopathy can be accompanied by vitritis and by optic nerve inflammation. Fluorescein angiography may show vascular leakage in the macular area and optic disc staining in the late phase. The OCTA displays involvement of the different vascular retinal plexus but only the deep retinal capillary plexus are associated with the disruption of the IS/OS junction of the retina, a typical finding in optical coherence tomography (OCT) of AMN patients[55].

Other reported immediately after macular complication dengue infection is choroidal neovascularization[56]. Veloso *et al* described the case of a 54-year-old female patient complaining of decreased visual acuity in her left eye two weeks after dengue fever.

Table 2. Dengue maculopathy: clinical presentations and findings on fluorescein angiography (FA), optical coherence tomography (OCT) and OCT-angiography (OCTA).

Dengue maculopathy	Clinical presentation	Fluorescein-angiography (FA)	OCT pattern	OCT-A pattern
Macular edema	Diffuse macular edema	Late hyper-fluorescence. Diffuse fluorescein leakage	Diffuse retinal thickening (DRT), around central/ paracentral fovea. Loss of foveal dimple	Flow deficit in the superficial capillary plexus
	Cystoid macular edema	Hyper-fluorescence due to leakage in cystoid retinal spaces in middle and late stages	Cystoid fluid spaces in the middle layers of the retina	
Exudative retinal detachment (ERD) + severe vasculitis	ERD + vasculitis Vitritis	Perifoveal fluorescein leakage and hyper-fluorescence in middle and late stages	Subretinal fluid, cystoid macular edema may also be present	Not described for dengue
Macular hemorrhage	Macular hemorrhage	Hypo-fluorescence due to fluorescence blocking in the macular area	Accumulation of fluid of medium reflectivity at the retina affecting the normal layers architecture	Not described for dengue
Foveolitis	White yellowish dots in the fovea Mild vitritis	Perivascular foveal leakage and blockage of arteriolar fluorescence	Hyper-reflectivity at the outer plexiform and outer nuclear layers	Flow deficit in the superficial and deep capillary plexus
Acute macular neuroretinopathy (AMN)	Exhudation around vessels of macular area	Fluorescein vascular leakage around the macular vessels. Optic disc staining in late phase	Disruption of the IS/OS junction in the outer retina	Flow deficit in the 3 capillary plexus, low VA is associated with flow deficit of the deep capillary plexus

A diagnosis of classic CNV was made with FA and confirmed with SD-OCT. The patient was treated with ranibizumab intravitreal injections reaching a BCVA of 20/20 after the treatment.

Neuro-ophthalmological manifestations

Approximately 97% of patients with dengue fever will complain of headaches[57]. Neurological signs upon dengue infection are reported in only 1% to 5% of patients[58] and neuro-ophthalmic manifestations are rare or infrequent[59]. Nevertheless, in the clinical history of 2 out of the 3 patients described below, who sought ophthalmic consultation during the 2020 epidemic in Misiones, the primary ocular manifestation was neuro ophthalmological. Encephalitis and dengue encephalopathy are the most frequent neurological manifestations, followed by Guillain-Barré syndrome and nerve palsies. Abducens nerve palsies (VI nerve palsy) is a frequent form of nerve palsies associated with dengue infection. Abducens palsies as well as the above mentioned neurological manifestations are more frequent during the critical period[60-62]. Optic neuritis was reported to occur in 0.1% to 1.5% of patients with dengue infection[35]. It could present as either inflammation of the optic disc or as retrobulbar optic neuritis[63-64]. Recently, Lana-Peixoto *et al* reported two cases of neuromyelitis optica spectrum disorder (NMOSD) in patients positive for serum AQP4-antibody suggesting that dengue infection may trigger seropositive NMOSD[65].

Treatment

Good resolution of anterior mild inflammatory manifestations may be achieved with topical corticosteroids such as in mild to moderate anterior uveitis[66]. Local periocular treatment (sub-Tenon's triamcinolone injection) can be used in severe forms of unilateral anterior uveitis and mild cases of dengue retinopathy. The use of intravitreal triamcinolone can be considered in patients with unilateral maculopathy[36].

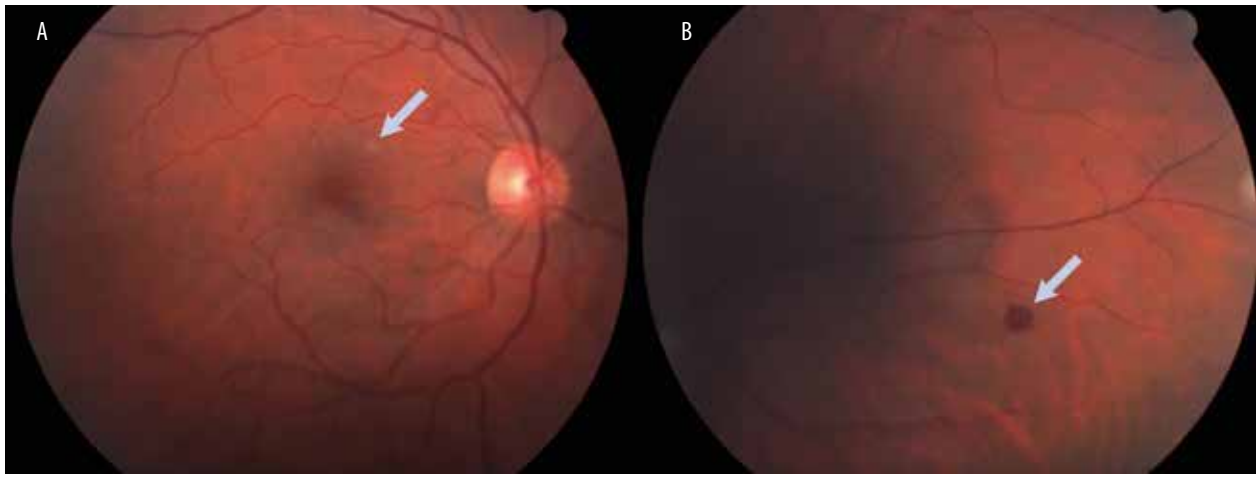


Figure 1. (A) Small yellowish retinal lesion in the inferior area of the macula outside the fovea (arrow). (B) Retinal hemorrhage in the nasal area of the right eye (arrow).

Systemics corticosteroids are needed in severe scleritis and in posterior manifestations where immune mediated mechanisms are suspected (retinal vasculitis, AMN and foveolitis). In patients whose visual acuity was lower than 20/100, methylprednisolone pulse therapy (1 g/day) was efficient in the treatment of severe posterior uveitis and optic neuritis. Pulse therapy should be followed by oral prednisone with slow tapering.

There are few reports of severe PU and dengue maculopathy patients with VA lower than 0.1 treated with intravenous Immunoglobulin (0,4 g/kg/ day) for 3 days. Visual acuity was restored to 0.5 after 15 days of treatment[67].

Despite the fact that anti-VEGF therapy had shown to restore vascular permeability in macular edema associated with retinal vasculopathy, there are no reports regarding its use in dengue maculopathy except for choroidal neovascularization[56]. The use of such well-known agents could be hypothetically useful, specially in macular edema caused by dengue infection.

Ocular findings in patients examined during the 2020 dengue epidemic

Case 1 (retroorbital pain-normal vision)

A 42 years old man seeks consultation due to retroocular pain. He has been diagnosed dengue fever by a medical doctor specialized in tropical medicine. He suffered high fever, asthenia and myalgia for 5 days. He is in the recovery phase but still complains of bilateral retroocular pain. A diagnosis of dengue is suspected based on the symptoms and a positive antigen NS1 ELISA test. His best corrected visual acuity (BCVA) was 20/20 in both eyes. The patient had normal pupillary reflexes and ocular movements. There were no anterior signs of ocular inflammation. Intraocular pressure was 16 mmHg in both eyes. There were scattered retinal hemorrhages outside the posterior pole in both eyes (Fig. 1). A small, yellow, well-defined deep retinal dot like those described in foveolitis was observed in the superior part of the macula, outside the fovea, in the right eye (Fig. 1). The patient received no treatment and was controlled 15 days later dengue disease was confirmed by the presence of anti DENV positive IgM and IgG results. Resolution of the hemorrhages and the macular spot was confirmed after 3 months of the initial examination.

Case 2 (severe unilateral decrease in visual acuity)

A 38-year-old male patient seeks ophthalmic consultation as an outpatient in a private clinic. He complains of decrease in visual acuity in the left eye for the last 3 days accompanied by pain when moving the eye. Three weeks before he had 4-day episode of fever, malaise and headaches. He also

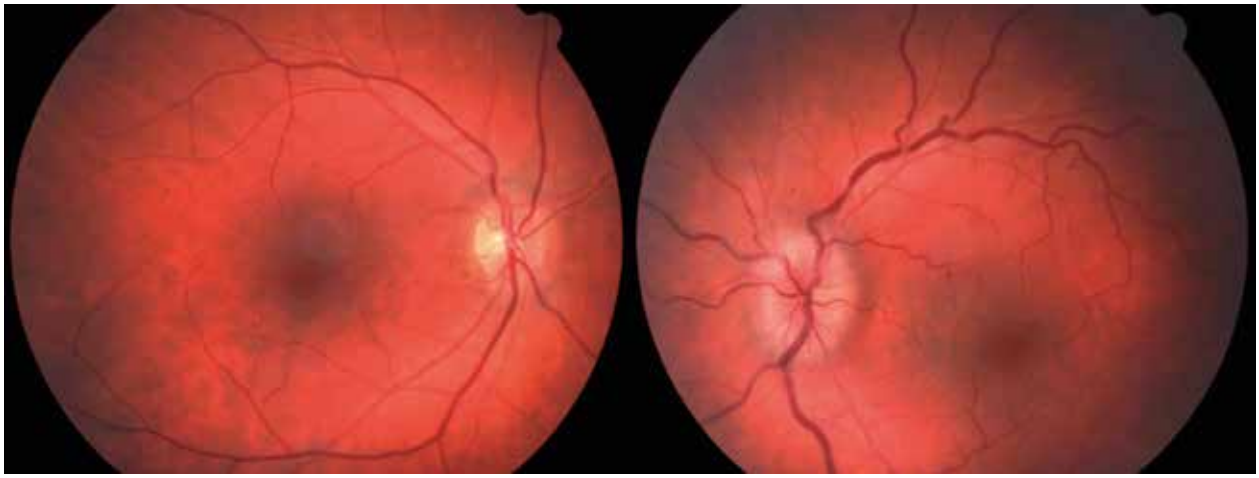


Figure 2. Images of the right and left posterior fundus of the eye. The right optic disc and macular area appears normal. The left optic disc has diffused borders with exudative changes that together with the clinical presentation of the patient led to the diagnosis of left optic neuritis.

referred a history of relatives with dengue infection. BCVA was 20/20 in the right eye and counting fingers on the left eye. There was a RAPD in the left eye and severe decrease in the chromatic vision. The anterior biomicroscopy was normal as well as the intraocular pressure in both eyes. The fundus of the eye revealed a left optic disc with diffuse borders and inflammation (Fig. 2). There were no signs of retinopathy. The right eye fundus was normal. Routine lab exams (hematocrit, ESD, kidney and liver function assays) as well as an MRI with gadolinium of the CNS and serology for dengue, syphilis and toxoplasma gondii were ordered. The patient did not want to receive corticosteroid pulsetherapy in a hospital, due to the COVID-19 pandemic, so he started oral meprednisone 1mg/kg/day as an outpatient. The CNS MRI results, and the routine lab exams were normal. VDRL and serology for syphilis were negative. A positive IgM and IgG anti-DENV was detected. Serology for toxoplasma gondii indicated a chronic infection, a regular finding in an adult patient from Misiones. The patient visual acuity started to improve daily. After 4 weeks of treatment the patient attained 20/20 vision on the left eye and his visual fields were normal.

Case 3 (abducens nerve palsies)

A 42 years old man seek consultation at the emergency room. He complained of dysesthesia in his lower extremities, dysarthria and diplopia for the last 48 h. He had fever, myalgia and gastrointestinal symptoms for the last 10 days. He explains that due to the SARS-Cov2 pandemic intercurrence he received telephonic assessment and was prescribed paracetamol. The clinician that examined him in the emergency room ordered routine blood laboratory test (hematocrit, WBC count, ESR, PCR, liver and kidney function laboratory tests), a Central Nervous System CAT-scan without gadolinium and an ophthalmologic examination. The CNS CAT-scan was normal. The ophthalmic examination revealed: BCVA of 20/20 in both eyes and a 30-degree esotropia in the left eye. Limited abduction of the left eye was confirmed and a left abducens nerve palsy was diagnosed. Due to his poor general health status (fever, tremors and asthenia) the patient was admitted to the hospital. A fundus examination showed performed revealing retinal exudates along the temporal vessel in the right eye and a small macular hemorrhage in the left eye. The neurologists that examined the patient ordered a CNS MRI with gadolinium and an angio-MRI. The exams revealed an acute ischemic event at the knee of the corpus callosum and also in the left cerebellum (Fig. 3). Due to the patient's signs and symptoms and the SARS-Cov-2 pandemic + dengue epidemic intercurrence, the patient was isolated and nasopharyngeal and blood samples were obtained. Seventy-two hours later the

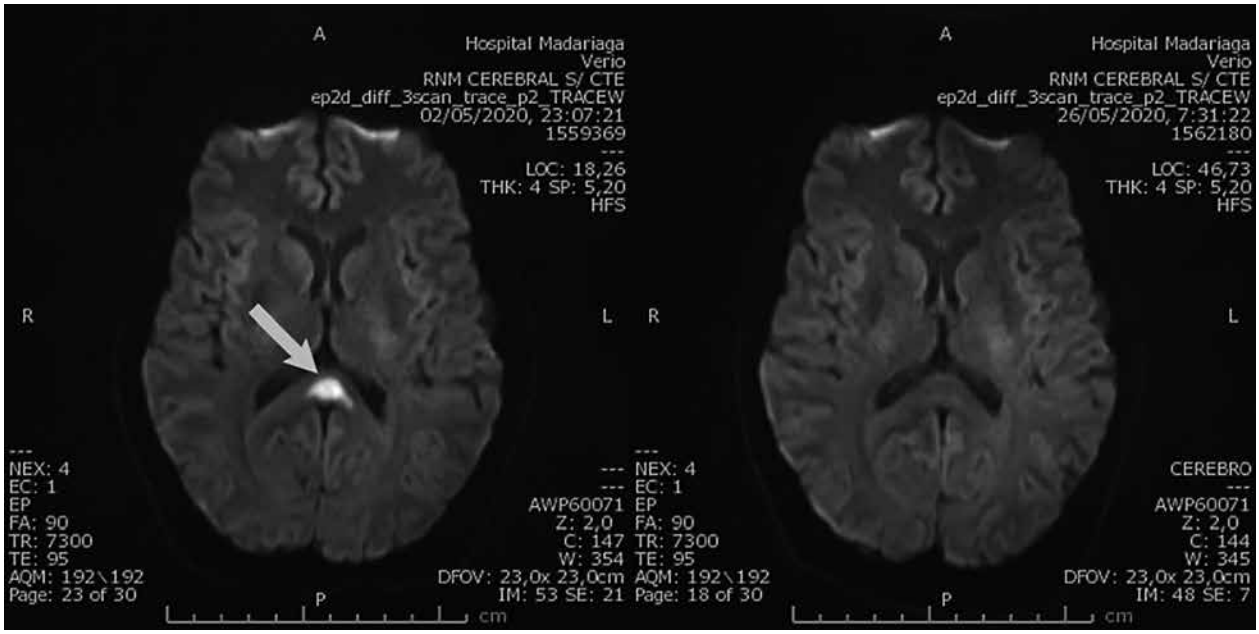


Figure 3. Central Nervous System MRI with gadolinium showing lesion in the central splenium of the corpus callosum in the diffusion-weighted imaging (image on the right). After two weeks the lesion in the corpus callosum disappeared (image on the left).

SARS-Cov-2 PCR result was negative and the NS1 for dengue was positive. No specific treatment was administered during the days of hospital admission. The neurological symptoms and ocular motor paresis improved without specific treatment. The diagnosis of dengue disease was confirmed with IgM and IgG positive serology. A diagnosis of reversible splenial syndrome (RESLES) was made based on signs and symptoms manifested by the patient, MRI images and the evolution of the patient. Although RESLES was recently described in a patient with dengue infection, this is the first case were RESLES is described with angiopathic changes in the retina.

Discussion

The ocular clinical spectrum caused by dengue infection is not random. It is influenced by the degree of vascular endothelial damage induced by the virus as well as the inflammation induced by the immune response of the host. A predominance of retinal hemorrhages and perivascular exudates in the fundus examination are an indicative of endothelial cell damage, the presence of retinal vasculitis and optic neuritis are more likely associated with a significative humoral immune response. Mechanistically it seems that early in the evolution of the disease (symptomatic and critical period), ocular and neuro-ophthalmological manifestations may be related to direct viral effects, immune mediated or due to systemic or metabolic complications (thrombocytopenia, leukopenia or hypoalbuminemia), while post-recovery and late manifestations are mainly immune mediated.

The posterior exudative and hemorrhagic manifestations are also influenced by the depth of the retinal capillary plexus disrupted. The more superficial the retinal capillary plexus affected the more superficial the exudation in the retina, resembling Purtscher-like retinopathy[68]. On the other hand, posterior deep manifestations such as foveolitis or AMN indicate the involvement of deep retinal capillary plexus. Knowledge of the retinal plexus involved is important because the alteration of deep retinal plexus is associated with disruption of the ellipsoid and interdigitation zone of the outer retina and a consequent

persistent decreased visual acuity and scotoma as described in AMN[55]. Together, the results indicate a relevant role of OCTA in the diagnosis of the retinopathy upon dengue infection.

Endothelial damage and vascular leakage are the main pathogenetic mechanism during the first two weeks of the disease while immunological mechanism may persist for few months. After an extensive search in the online clinical databases only one publication of chronic uveitis was associated with dengue infection. Recently, however, in a population based cohort study dengue infection was associated with the development of a higher frequency of autoimmune diseases. The list of diseases included known etiology for anterior uveitis (Reiter's syndrome) and posterior or diffuse uveitis (systemic vasculitis) as well as optic neuritis (multiple sclerosis)[69].

Despite our limited experience with the disease, the review of dengue epidemics, including the 2020 dengue epidemic in Misiones, taught us valuable lessons: 1) patients with dengue infection may be visually asymptomatic but still present retinal changes, while the disease is not affecting the fovea. Also, afebrile or asymptomatic dengue infected patients may develop exudative or inflammatory ocular manifestations, so dengue infection should be ruled-out if clinical ocular signs are compatible with dengue diagnosis. 2) The use of new technologies such as SD-OCT and OCTA can help in the diagnosis of the retinopathy and follow up of patients. 3) Neuro-ophthalmological signs may not be that infrequent as described. Two out of the 3 patients that seek ophthalmologic examination and were examined by the authors, had neuro-ophthalmological manifestations. 4) Immune mediated ocular manifestations such as anterior uveitis, retinal vasculitis and optic neuritis may appear few weeks or months later after the critical period of the disease. 5) The treatment of posterior uveitis and dengue maculopathy has been limited to corticosteroids and intravenous immunoglobulin. Clinical studies using agents known to restore vascular permeability such as bevacizumab, ranibizumab and aflibercept can be projected to evaluate its clinical use in dengue maculopathy as additional treatments.

References

1. Carballal G, Oubiña JR. *Virología médica*. Buenos Aires: Corpus, 2015.

2. World Health Organization. *Dengue and severe dengue* [online]. Geneve: WHO, June 2020 (Fact sheets). Available: https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue.

3. Guzman MG, Gubler DJ, Izquierdo A *et al*. Dengue infection. *Nature Rev Dis Primers* 2016; 2: 16055.

4. Argentina. Ministerio de Salud. Dirección Nacional de Epidemiología e Información Estratégica. Vigilancia de dengue y otros arbovirus. *Boletín Integrado de Vigilancia Epidemiológica* 2020; 502: 6-19.

5. Acosta EG, Bartenschlager R. Paradoxical role of antibodies in dengue virus infections: considerations for prophylactic vaccine development. *Expert Rev Vaccines* 2016; 15: 467-482.

6. Wilken L, Rimmelzwaan GF. Adaptative immunity to dengue virus: slippery slope or solid ground for rational vaccine design? *Pathogens* 2020; 9: 470.

7. Waggoner JJ, Balmaseda A, Gresh L *et al*. Homotypic dengue virus reinfections in Nicaraguan children. *J Infect Dis* 2016; 214: 986-993.

8. Forshey BM, Stoddard ST, Morrison AC. Dengue viruses and lifelong immunity: reevaluating the conventional wisdom. *J Infect Dis* 2016; 214: 979-981.

9. Libraty DH, Young PR, Pickering D *et al*. High circulating levels of the dengue virus nonstructural protein NS1 early in dengue illness correlate with the development of dengue hemorrhagic fever. *J Infect Dis* 2002; 186: 1165-1168.

10. Sahaphong S, Riengrojpitak S, Bhamarapravati N, Chirachariyavej T. Electron microscopic study of the vascular endothelial cell in dengue hemorrhagic fever. *Southeast Asian J Trop Med Public Health* 1980; 11: 194-204.

11. Liao B, Tang Y, Hu F *et al*. Serum levels of soluble vascular cell adhesion molecules may correlate with the severity of dengue virus-1 infection in adults. *Emerg Microbes Infect* 2015; 4: e24.

12. Beatty PR, Puerta-Guardo H, Killingbeck SS *et al*. Dengue virus NS1 triggers endothelial permea-

bility and vascular leak that is prevented by NS1 vaccination. *Sci Transl Med* 2015; 7: 304: 304ra141.
13. Modhiran N, Watterson D, Muller DA *et al*. Dengue virus NS1 protein activates cells via Toll-like receptor 4 and disrupts endothelial cell monolayer integrity. *Sci Transl Med* 2015; 7: 304ra142.
14. Puerta-Guardo H, Glasner DR, Harris E. Dengue virus NS1 disrupts the endothelial glycocalyx, leading to hyperpermeability. *PLoS Pathog* 2016; 12: e1005738.
15. Puerta-Guardo H, Glasner DR, Espinosa DA *et al*. Flavivirus NS1 triggers tissue-specific vascular endothelial dysfunction reflecting disease tropism. *Cell Rep*-2019; 26: 1598-1613.e8.
16. Barbachano-Guerrero A, Endy TP, King CA *et al*. Dengue virus non-structural protein 1 activates the p38 MAPK pathway to decrease barrier integrity in primary human endothelial cells. *J Gen Virol* 2020; 101: 484-496.
17. Guzman MG, Alvarez M, Halstead SB. Secondary infection as a risk factor for dengue hemorrhagic fever/dengue shock syndrome: an historical perspective and role of antibody-dependent enhancement of infection. *Arch Virol* 2013; 158: 1445-1459.
18. Katzelnick LC, Gresh L, Halloran ME *et al*. Antibody-dependent enhancement of severe dengue disease in humans. *Science* 2017; 358: 929-932.
19. Waggoner JJ, Katzelnick LC, Burger-Calderon R *et al*. Antibody-dependent enhancement of severe disease is mediated by serum viral load in pediatric dengue virus infections. *J Infect Dis* 2020; 221: 1846-1854.
20. Henchal EA, Henchal LS, Schlesinger JJ *et al*. Synergistic interactions of anti-NS1 monoclonal antibodies protect passively immunized mice from lethal challenge with dengue 2 virus. *J Gen Virol* 1988; 69: 2101-2107.
21. Falconar AK. The dengue virus nonstructural-1 protein (NS1) generates antibodies to common epitopes on human blood clotting, integrin/adhesin proteins and binds to human endothelial cells: potential implications in haemorrhagic fever pathogenesis. *Arch Virol* 1997; 142: 897-916.
22. Wan SW, Yang YW, Chu YT *et al*. Anti-dengue virus nonstructural protein 1 antibodies contribute to platelet phagocytosis by macrophages. *Thromb Haemost* 2016; 115: 646-656.
23. Chuang YC, Lin YS, Liu HS, Yeh TM. Molecular mimicry between dengue virus and coagulation factors induces antibodies to inhibit thrombin activity and enhance fibrinolysis. *J Virol* 2014; 88: 13759-13768.
24. Tan W, Liew JWK, Selvarajoo S *et al*. Inapparent dengue in a community living among dengue-positive Aedes mosquitoes and in a hospital in Klang Valley, Malaysia. *Acta Trop* 2020; 204: 105330.
25. Centers for Disease Control and Prevention. *Dengue: with or without warning signs* [online]. Atlanta: Centers for Disease Control and Prevention. Available: https://www.cdc.gov/dengue/training/cme/ccm/page47831.html
26. Kapoor HK, Bhai S, Jhon M, Xavier J. Ocular manifestations of dengue fever in an East Indian epidemic. *Can J Ophthalmol* 2006; 41: 741-746.
27. Chhavi N, Venkatesh C, Soundararajan P, Gunasekaran D. Unusual ocular manifestations of dengue fever in a young girl. *Indian J Pediatr* 2013; 80: 522-523.
28. Kamoi K, Mochizuki M, Ohno-Matsui K. Dengue fever-associated necrotizing scleritis: a case report with long-term follow-up. *Medicine (Baltimore)* 2018; 32: e11875.
29. Pierre Filho JTP, Carvalho Filho JP, Pierre ETL. Bilateral acute angle closure glaucoma in a patient with dengue fever: case report. *Arq Bras Oftalmol* 2008; 71: 265-268.
30. Saranappa SBS, Sowbhagya HN. Panophthalmitis in dengue fever. *Indian Pediatr* 2012; 49: 760.
31. Levaggi ND, Lucas AN, Barletta JAE. Bilateral acute angle closure in a patient with dengue fever: a case report. *Arq Bras Oftalmol* 2017; 80: 266-267.
32. Antlanger M, Shaw SJ, Kurup SK. Presumed dengue-associated immune-mediated uveitis. *Can J Ophthalmol* 2011; 46: 92-93.
33. Chan DPL, Teoh SCB, Tan CDH *et al*. Eye Institute Dengue-Related Ophthalmic Complications Workgroup. Ophthalmic complications of dengue. *Emerg Infect Dis* 2006; 12: 285-289.
34. Gupta A, Srinivasan R, Setia S *et al*. Uveitis following dengue fever. *Eye (Lond)* 2009; 23: 873-876.
35. Teoh SC, Chan DP, Nah GK *et al*. A re-look at ocular complications in dengue fever and dengue haemorrhagic fever. *Dengue Bull* 2006; 30: 184-190.

36. Bacsal KE, Chee SP, Cheng CL, Flores JVP. Dengue-associated maculopathy. *Arch Ophthalmol* 2007; 125: 501-510.
37. Siak J, Jansen A, Waduthantri S *et al*. The pattern of uveitis among Chinese, Malays, and Indians in Singapore. *Ocul Immunol Inflamm* 2017; 25: S81-S93.
38. Teoh SC, Chee CK, Laude A *et al*. Eye Institute Dengue-related Ophthalmic Complications Workgroup. Optical coherence tomography patterns as predictors of visual outcome in dengue-related maculopathy. *Retina* 2010; 30: 390-398.
39. Siqueira RC, Vitral NP, Campos WR *et al*. Ocular manifestations in dengue fever. *Ocul Immunol Inflamm* 2002; 12: 323-327.
40. Lim WK, Mathur R, Koh A *et al*. Ocular manifestations of dengue fever. *Ophthalmology* 2004; 111: 2057-2064.
41. Koundanya VV, Chowdhary N, Agarwal M, Katre P. Secondary dengue retinitis with associated occlusive retinal vasculitis. *J Ophthalmic Inflamm Infect* 2019; 9: 7.
42. Ng CWK, Tai PY, Mohamed SO. Dengue maculopathy associated with choroidopathy and pseudohypopyon: a case series. *Ocul Immunol Inflamm* 2018; 26: 666-670.
43. Tabbara K. Dengue retinochoroiditis. *Ann Saudi Med* 2012; 32: 530-533.
44. Goldhart R, Patel H, Davis JL. Acute posterior multifocal placoid pigment epitheliopathy following dengue fever: a new association for an old disease. *Ocul Immunol Inflamm* 2016; 24: 610-614.
45. Yadav HM, Majumder PD, Biswas J. Dengue associated choroiditis: a rare entity. *J Ophthalmic Inflamm Infect* 2017; 7: 14.
46. Fang PP, Pfau M, Holz FG, Finger RP. Persistent visual loss in dengue fever due to outer retinal damage. *Clin Exp Ophthalmol* 2017; 45: 747-749.
47. Oliver GF, Carr JM, Smith JR. Emerging infectious uveitis: Chikungunya, dengue, Zika and Ebola: A review. *Clin Exp Ophthalmol* 2019; 47: 372-380.
48. de Amorim Garcia CA, Gomes AHB, de Oliveira AGF. Bilateral stellar neuroretinitis in a patient with dengue fever. *Eye (Lond)* 2006; 20: 1382-1383.
49. Arya D, Das S, Shah G, Gandhi A. Panophthalmitis associated with scleral necrosis in dengue hemorrhagic fever. *Indian J Ophthalmol* 2019; 67: 1775-1777.
50. Kamal R, Shah D, Sharma S *et al*. Culture-positive unilateral panophthalmitis in a serology-positive case of dengue hemorrhagic fever. *Indian J Ophthalmol* 2018; 66: 1017-1019.
51. Su DHW, Bacsal K, Chee SP *et al*. Dengue Maculopathy Study Group. Prevalence of dengue maculopathy in patients hospitalized for dengue fever. *Ophthalmology* 2007; 114: 1743-1747.
52. Seet RCS, Quek AML, Lim ECH. Symptoms and risk factors of ocular complications following dengue infection. *J Clin Virol* 2007; 38: 101-105.
53. Agarwal A, Aggarwal K, Dogra M *et al*. OCTA Study Group. Dengue-induced inflammatory, ischemic foveolitis and outer maculopathy: a swept-source imaging evaluation. *Ophthalmol Retina* 2019; 3: 170-177.
54. Li M, Zhang X, Ji Y *et al*. Acute macular neuroretinopathy in dengue fever: short-term prospectively followed up case series. *JAMA Ophthalmol* 2015; 133: 1329-1333.
55. Aggarwal K, Agarwal A, Katoch D *et al*. Optical coherence tomography angiography features of acute macular neuroretinopathy in dengue fever. *Indian J Ophthalmol* 2017; 65: 1235-1238.
56. Veloso CE, Schmidt-Erfurth U, Nehemy MB. Choroidal neovascularization induced by immunogenic alteration of the retinal pigment epithelium in dengue fever. *Case Rep Ophthalmol* 2015; 6: 18-23.
57. Domingues RB, Kuster GW, Onuki de Castro FL *et al*. Headache features in patients with dengue virus infection. *Cephalalgia* 2006; 26: 879-882.
58. Carod-Artal FJ, Wichmann O, Farrar J, Gascón J. Neurological complications of dengue virus infection. *Lancet Nuerol* 2013; 12: 906-919.
59. Somkijrungroj T, Kongwattananon W. Ocular manifestations of dengue. *Curr Opin Ophthalmol* 2019; 30: 500-505.
60. Shivanthan MC, Ratnayake EC, Wijesiriwardena BC *et al*. Paralytic squint due to abducens

nerve palsy: a rare consequence of dengue fever. *BMC Infect Dis* 2012; 16: 156.
61. Mishra A, Shukla S, Aggarwal S, Chaudhary B. Lateral rectus palsy in a case of dengue fever. *Med J Armed Forces India* 2015; 71 (suppl.1): S101-S103.
62. Mazliha M, Boo YL, Chin PW. Isolated unilateral sixth cranial nerve palsy: a rare presentation of dengue fever. *Malays Fam Physician* 2016; 11: 25-26.
63. Preechawat P, Poonyathalang A. Bilateral optic neuritis after dengue viral infection. *J Neuroophthalmol* 2005; 25: 51-52.
64. Boo YL, Lim SY, Chin PW, Hoo FK. Bilateral optic neuritis with maculopathy: a rare manifestation of dengue fever. *Malays Fam Physician* 2017; 12: 32-34.
65. Lana-Peixoto MA, Pedrosa D, Talim N *et al*. Neuromyelitis optica spectrum disorder associated with dengue virus infection. *J Neuroimmunol* 2018; 318: 53-55.
66. Ng AW, Teoh SC. Dengue eye diseases. *Surv Ophthalmol* 2015; 60: 106-114.
67. Chang PEJ, Cheng CL, Asok K *et al*. Visual disturbances in dengue fever: an answer at last? *Singapore Med J* 2007; 48: e71-e73.
68. Lima LH, Vianello S, Pimentel S *et al*. Dengue fever presenting as purtscher-like retinopathy. *Ocul Immunol Inflamm* 2018; 26: 660-665.
69. Li HM, Huang YK, Su YC, Kao CH. Increased risk of autoimmune diseases in dengue patients: a population-based cohort study. *J Infect* 2018; 77: 212-219.

Assessing potential barriers and facilitators in preparation for implementing a diabetic retinopathy tele-screening program in Argentina

Tomás Ortiz Basso[a], Ariel Paladini[b]

[a] *Hospital Italiano de Buenos Aires, Argentina.*

[b] *Dirección de Atención Primaria y Gestión Sanitaria, Ministerio de Salud de La Pampa, Santa Rosa, Argentina.*

Received: July 28th, 2020.
Accepted: August 4th, 2020.

Corresponding author
Dr. Tomás Ortiz Basso
Centro Oftalmológico
Escalante 67
Santa Rosa, La Pampa, Argentina
+54 (02954) 423397
tomasortizbasso@gmail.com

Oftalmol Clin Exp (ISSN 1851-2658)
2020; 13(3): 127-134.

Acknowledgments
We acknowledge the support of La Pampa Health Ministry, Ana Lia Fite for her valuable help with the language.

Abstract

Objective: Tele-screening programs against blindness have proved to be effective in many countries. However, there are lots of difficulties that could directly influence their execution, and scaling them up could be a hard challenge. This study aims to identify barriers and facilitators for implementing a DR tele-screening program in a rural area of Argentina.
Methods: A qualitative research study was performed. Unstructured interviews with the healthcare team were made and a Consolidated Framework for Implementation Research to assess details of the program was carried out.
Results: Main enablers are simple examination, good organizational structure, and political decision to implement the program. Principal barriers are work overload, initial high costs, and cultural rejection.
Conclusion: Barriers and facilitators should be assessed before implementing a DR Tele-Screening Program. It is recommended to gain political support and face cultural barriers before the implementation.
Keywords: telemedicine, vision screening, diabetic retinopathy, glaucoma, blindness, Argentina, La Pampa (province).

Evaluando posibles barreras y facilitadores para implementar un programa de *tele-screening* de retinopatía diabética en la Argentina

Resumen

Objetivo: Los programas de *tele-screening* han demostrado ser eficaces para disminuir la ceguera en muchos países de mundo. Sin embargo, existen muchas dificultades que influyen directamente en su ejecución. El objetivo de este estudio fue identificar barreras y facilitadores para implementar un programa de *tele-screening* de retinopatía diabética en una zona rural de Argentina.
Métodos: Se realizó un estudio cualitativo a través de entrevistas no estructuradas con el equipo de atención médica de la provincia de La Pampa. Para identificar barreras y facilitadores del programa se conformó un marco consolidado para la investigación de implementación.
Resultados: Los principales facilitadores hallados fueron: contar con un examen de retina simple, tener una estructura de atención médica organizada y buscar la decisión política de implementar el programa. Dentro de las mayores barreras se encuentran: la sobrecarga laboral, los altos costos iniciales y el rechazo cultural hacia la teleoftalmología.
Conclusión: Antes de implementar un programa de *tele-screening* se deben evaluar los posibles obstáculos y facilitadores que conlleva. Se recomienda obtener apoyo político y hacer frente a las barreras culturales antes de su implementación.

Palabras clave: telemedicina, tamizaje masivo, retinopatía diabética, glaucoma, ceguera, Argentina, La Pampa (provincia).

Avaliando possíveis barreiras e facilitadores para a implementação de um programa de *tele-screening* de retinopatia diabética na Argentina

Resumo

Objetivo: Os programas de *tele-screening* tem demostrado ser eficientes para diminuir a cegueira em muitos países do mundo. Porém, existem muitas dificuldades que influenciam diretamente em sua execução. O objetivo deste estudo foi identificar barreiras e facilitadores para a implementação de um programa de *tele-screening* de retinopatia diabética em uma zona rural da Argentina.
Métodos: realizou-se um estudo qualitativo através de entrevistas não estruturadas com a equipe de atenção médica da província de La Pampa. Para identificar barreiras e facilitadores do programa se formou um quadro consolidado para a pesquisa de implementação.
Resultados: Os principais facilitadores encontrados foram: contar com um exame de retina simples, ter uma estrutura de atenção médica organizada e buscar a decisão política para a implementação do programa. Dentro das maiores barreiras foram encontradas: a sobrecarga de trabalho, os altos custos iniciais e a rejeição cultural para a teleoftalmologia.
Conclusão: Antes de implementar um programa de *tele-screening* devem-se avaliar os possíveis obstáculos e facilitadores que implica. Recomenda-se obter apoio político e fazer frente as barreiras culturais antes de sua implementação.

Palavras clave: telemedicina, programas de rastreamento, retinopatia diabética, glaucoma, cegueira, Argentina, La Pampa (província).

Introduction

Diabetic retinopathy (DR) is the leading cause of blindness in working age people and it is estimated that its prevalence will triplicate by 2050[1-2]. Main cohort studies estimate that 3% to 10% of diabetic patients have vision-threatening DR[3]. It is known that severely visually impaired people represent high sanitary costs[4]. If global prevention measures are not taken, society could be hardly stricken either in terms of public health and financial costs[5].

Blindness caused by diabetes can be reduced up to a 50% with a proper medical treatment[6]. To achieve this, an early diagnosis is of vital importance. The American Diabetes Association recommends an annual eye examination, however, only a third of the population adheres to this advice[7-8]. Poor adherence is associated with lack of information, lack of access or geographical restrictions[9].

Currently, in Argentina inequalities in health system access are frequent. Scanty human resources, reduced incomes, long distances, and system centralization are the main causes of this situation.

Within this context, telemedicine stands as a cutting-edge short cut to solve this problem[10]. It represents an improvement in the access to sanitary system for many patients, mainly elderly people, chronic patients or those detached from health care centers[11].

DR tele-screening programs have been developed all around the world[12-13]. However, although there is enough evidence to support these programs, their outcomes in different contexts are unknown. There are many factors that may influence the effectiveness and accomplishment of scientific innovations in daily practice[14]. Therefore, in recent years, implementation research studies have been emerging, aiming to characterize and contextualize an intervention, trying to improve the quality and effectiveness in real world[14].

The Consolidate Framework for Implementation Research (CFIR) was developed, to understand the reasons why the process may or may not be successful. It is divided into 5 constructs: intervention characteristics, inner setting, outer setting, individual characteristics and process, each of which should be thoroughly evaluated before the implementation of any program[15].

The purpose of this study is to describe the use of the CFIR to identify barriers and facilitators for the implementation of a DR tele-screening program in Argentina.

Methods

Study design

To identify barriers and enablers for the implementation of a DR tele-screening program, we conducted a qualitative study. The CFIR constructs were fulfilled based on personal interviews to ophthalmologists, endocrinologists, primary care practice leadership, clinicians, nurses, informatic and administrative staff.

Unstructured interviews were conducted. They aimed at understanding the perspectives that interviewees had regarding their lives, experiences, or situations. Heads and leaders of each field were selected for the interviews. Interviewees were professionals with more than 10 years of expertise in their fields. Interviews were conducted a year before the implementation began. They were performed in a Health Ministry office and in the hospitals where the interviewees worked. Several face to face interviews were performed. Each one lasted between 1 and 4 hours. The interviewers were the 2 authors of this paper. Main outcomes of each interview were registered. The authors of this paper discussed and analyzed barriers and enablers after each interview.

This study adhered to the tents of the Declaration of Helsinki and Institutional Review Board approval was obtained.

DR tele-screening program (Fig. 1)

The program will take place in rural communities of La Pampa (Argentina) with no ophthalmologist on a permanent basis, so patients need to travel long distances. The program will be equipped with a non-mydriatic retinal camera (*Digital Retinography System [DRS]*, CenterVue SpA, Padova, Italy) to take two images from each eye, a rebound tonometer (*Icare ic100,* Icare Finland Oy, Vantaa, Finland) and a visual acuity chart. A nurse will be trained to operate this equipment and will have a standardized operating procedures manual.

The population of each community will be identified by the informatic department through the "diabetes diagnosis" in the electronic records. Then, each primary care team will confirm the diagnosis of each patient, before the tele-screening team visits the community.

People in each community will be informed about the program development through phone calls and public announcements. Diabetic patients will be assessed by a nurse in each community health care center. The images will be encrypted and uploaded in the electronic history, ensuring patients' identities. Images com-

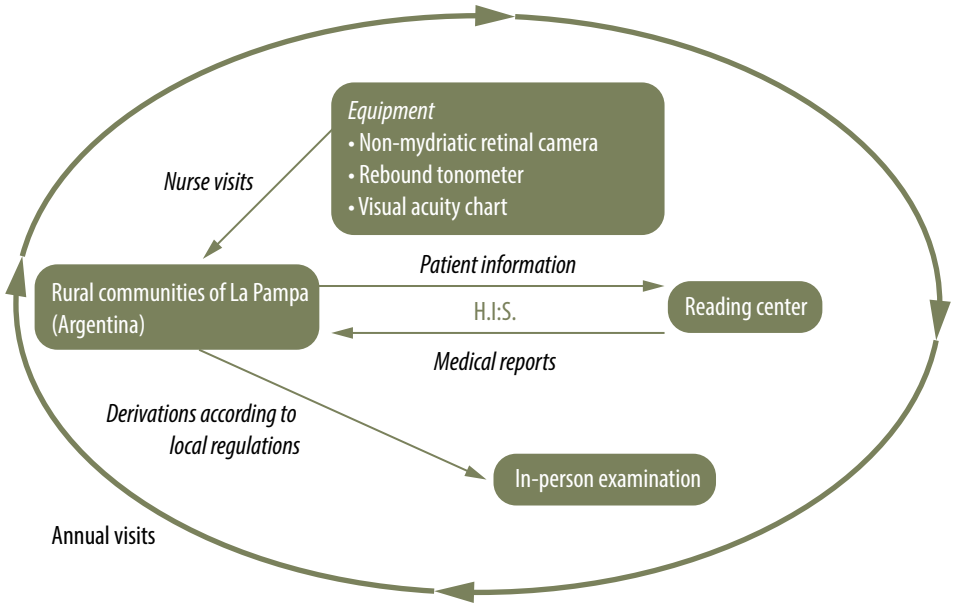


Figure 1. Diabetic Retinopathy Tele-Screening Program. Annual visits plan for each rural community. H.I.S: Health Information System.

ply with Digital Imaging and Communications on Medicine (DICOM) standards[16].

Ophthalmologists will evaluate images from a central reading center and classify them according to the International Clinical Diabetic Retinopathy Study scale[17]. Medical reports will read as follows: 1) normal, perform an annual examination; 2) mild retinopathy, perform an annual examination; 3) moderate retinopathy, visit an ophthalmologist during the next 6 weeks; 4) severe retinopathy, visit an ophthalmologist during the next 7 days. Patients who need an ophthalmologist appointment will be transferred to the central hospital. The health system will oversee patients' derivations according to local regulations.

Outcomes definitions

A description of the 5 constructs of the CFIR was performed: 1) intervention characteristics: refers to the particular characteristics that would made the program successful, including evidence strength, relative advantage, adaptability, trialability, complexity, cost; 2) inner setting: describes the possible interaction between internal components of the program, including structural characteristics, networks, culture, implementation climate; 3) outer setting: possible interactions between external factors and the program, including patients' needs and resource, peer pressure, external policies; 4) individual characteristics: analyzes the possible actions and behaviors of the participating individuals, including knowledge and beliefs about the intervention; 5) process: actions and activities that should take place to have an effective program, including planning, executing and evaluating[18].

Data were compiled, and descriptive statistics were calculated by using Microsoft Excel for Office 365 (Microsoft Corporation, Redmond, WA).

Results

Consolidated Framework for Implementation Research (Fig. 2)

Intervention characteristics

Reviewing the literature, similar programs have been found, implemented all around the world, and some of them have proved to be cost-effec-

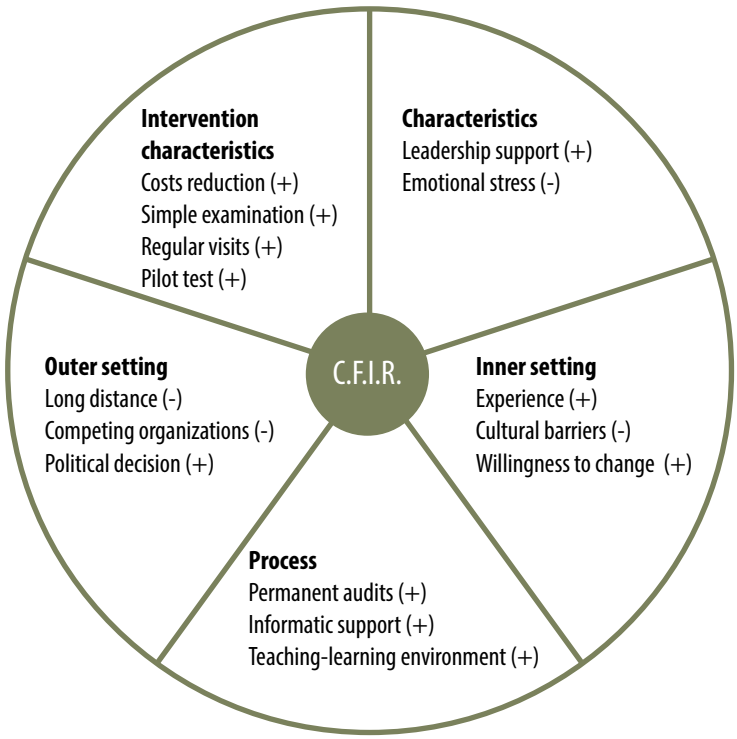


Figure 2. Main enablers and barriers of the Program, according with the CFIR constructs. CFIR: Consolidated Framework for Implementation Research; (+) enabler; (-) barrier.

tive[19]. Alternative solutions were evaluated, such as an ophthalmologist travelling around the different communities. This will result in higher costs and will be significantly stressful and more time demanding.

This program is the simplest way to tackle the proposed problem, a diabetic patient undergoes a quick eye examination without pupil mydriasis in his own town, and in one week's time he receives the report. Through image digitization, sub-processes reduction and continuous audits, complexity threats that may lead to loss reports or data misinterpretation, would be avoided.

The program will have core components such as a protocol, a schedule of visits and audits. The program aims at adapting to the needs and environment of each community. This "adaptable periphery" becomes more versatile depending on the members of each team and on each team's cycle (members on holidays, local epidemics, economy, or politics).

The program has been tested in Rancul, a rural town where the population showed great interest in the proposal. During two visits, 58 type 1 and 2 diabetic mellitus people were checked. In this pilot test, 61.5% of the population had had a previous fundus examination performed, and only 15.3% had had it assessed in the past year. DR was found in 38.4% of the patients. This test allowed researchers to assess and improve the implementation logistics, analyze possible problems and to strategically anticipate contingencies.

Even though equipment acquisition may represent a barrier at the beginning, in the end it would be cost-effective, as only 10% to 30% of participants would undergo a second assessment[20]. The costs of complementary studies and

treatments for people without medical insurance will be covered by the Government.

Outer setting

Rural populations must travel long distances to access an eye examination. At present, some ophthalmologists go around the province. However, they do not reach all the communities and do not do it regularly, this generally results in late treatments. This program will allow early diagnosis, avoiding time loss and increasing effectiveness.

As many ophthalmologists could feel threatened by the program, meetings were organized to explain that the program gives relevance, hierarchy and organizes appointment management. Thus, ophthalmologists will participate and work for the program as part of the solution.

Political will to implement the program is the main facilitator, so guidelines should aim at keeping it active in time. Complementary studies and treatments, the journeys, and the lodging, will conform to present requirements of the system.

Inner setting

La Pampa Health Ministry has experience with a similar program, that takes a mammograph to different communities. This experience has helped healthcare teams develop a scaffold of working methodology.

Rural communities share a solidary fellowship culture, within which everyone tries to collaborate with each other. Healthcare centers are settled within small rural communities and the heath staff is clearly aware of the populations needs. They complain about the lack of eye doctors' visits along the year.

Endocrinologists, who receive patients from these towns, also complain about the lack of possibilities for their patients to have an eye examination regularly. Besides, those who finally have access to it, rarely return with the results.

Characteristics of individuals

New procedures sometimes result in doubts, mistakes, and loss of time, that may lead to emotional exhaustion within the teamwork. The strategy is to make everyone feel as key participants of the program, so they will be more motivated and will strive to adapt to it. Group support is essential during this stage. Social events among teams should be organized to construct knowledge, to foster brainstorming and peer acknowledgement.

Feedback and achievement recognition will be forwarded with an analysis of the situation in each community.

Process

All the communities of the area will be visited during the first year and previous meetings should be held with each team to reach consensus about needs. Each teamwork will be trained according to the diabetic patient's healthcare recommendations and on the program methodology. Trainings will include presential interactive instruction and e-learning tools management. A continuous teaching-learning environment will we carried out in all the implementing process.

Meanwhile, diabetic patients and their relatives, will be contacted and informed about the importance of a regular health check-up to prevent further complications.

The program will use the informatic system to have quick access to all information related to the intervention. Audits will be carried out for patient's follow-up, to foster feedback to teamwork and to improve the quality of the program.

Discusion

One of the main facilitators for implementing a RD tele-screening program was the government´s support. Other programs have proved that without federal appropriations or research grants, the sustainability and the scaling-up,

were not possible[21]. So, having the government support from the start is the key piece to put it into practice.

It is vital that all the stakeholders of the program recognize the advantages of its implementation. If they perceive the benefit it will be surely successful[22]. Stakeholders, admitted that by applying this technology they will improve patient's quality of life, decrease the risk of blindness and save economic resources.

A program must have a core component and an adaptable periphery. The more flexible the intervention is, the more effective the program will be[22]. The proposed program has a central component that stakeholders must follow, but it will be adapted to the local conditions. Flexibility is the key for a successful program implementation.

A pilot test was performed in a small community, which has a strong positive association with effective implementation. It is highly recommended to test the intervention in small scale first, in order to adjust details before going on[22].

Understanding population needs is one of the main issues, since programs which focus on population requirements are more likely to be successful[23]. Primary healthcare staff are aware about the imperative need of an ophthalmologist for their community, and this program fulfills this need.

It is important to evaluate competing organization before implementing a program[22]. In a highly competitive market, peers could feel threatened by the program and may boycott it. It is important to make them understand that the program, far for threatening their practice is directed to enhance primary health care and secondary prevention actions. This will foster the relationship between care levels, improving the quality of health service[24].

Culture also influences the program dynamics and stands as one of the most critical barriers. Introducing a cultural-sensitive model would improve the program integration[25]. This program will take advantage of the cultural setting, as health teams are part of the community, more commitment and a strong emotional component will be added.

It is important to identify the implementation climate, in order to evaluate the attitude towards change and the receptivity for change in working habits. The primary care team of each community involved in our program is open for innovation because they understand that these initiatives will favor the population's welfare. It is of great importance to achieve empathy among team members so they can adapt easily and give priority to the model. Setting a learning friendly environment, with constant feedback, is essential to maintain motivation over time.

Careful planning is basic for effective implementation. So, a one-year program schedule was stablished, and training activities were organized for the staff before the start. Quality of execution should be measure all through the program. In this way we enforce the program sustainability.

One limitation of our study is that we did not interviewed people from the rural community. However, we interviewed health care professionals, who indirectly gave us information about the rural community´s needs. Another is that interviews were not recorded, and a detail presentation could not be done, however the information was registered and taken into account in the program design.

Conclusion

This study proved that one of the main enablers for the implementation of a DR tele-screening program is government´s support, and that the principal barriers to overcome are the cultural interactions. Foundations to scale-up to other similar regions and to implement similar programs were settled down.

References

1. International Diabetes Federation. *IDF Diabetes atlas*. 9th ed. Brussels: IDF, 2019. Available in: https://www.diabetesatlas.org [cited: July 2020].

2. Kempen JH, O'Colmain BJ, Leske MC *et al.* The prevalence of diabetic retinopathy among adults in the United States. *Arch Ophthalmol* 2004; 122: 552-563.

3. Saaddine JB, Honeycutt AA, Narayan KMV *et al*. Projection of diabetic retinopathy and other major eye diseases among people with diabetes mellitus: United States, 2005-2050. *Arch Ophthalmol* 2008; 126: 1740-1747.

4. Romero-Aroca P, de la Riva-Fernandez S, Valls-Mateu A *et al*. Cost of diabetic retinopathy and macular oedema in a population, an eight year follow up. *BMC Ophthalmol* 2016; 16: 136.

5. Panton UH, Bagger M, Barquera S. Projected diabetes prevalence and related costs in three North American urban centres (2015-2040). *Public Health* 2018; 157: 43-49.

6. Ferris FL 3rd. How effective are treatments for diabetic retinopathy? *JAMA* 1993; 269: 1290-1291.

7. Fong DS, Aiello L, Gardner TW *et al*. Diabetic retinopathy. *Diabetes Care* 2003; 26 (Sup 1): S99-S102.

8. Sloan FA, Yashkin AP, Chen Y. Gaps in receipt of regular eye examinations among medicare beneficiaries diagnosed with diabetes or chronic eye diseases. *Ophthalmology* 2014; 121: 2452-2460.

9. Moss SE, Klein R, Klein BEK. Factors associated with having eye examinations in persons with diabetes. *Arch Fam Med* 1995; 4: 529-534.

10. Rathi S, Tsui E, Mehta N *et al*. The current state of teleophthalmology in the United States. *Ophthalmology* 2017; 124: 1729-1734.

11. Rodríguez Cabrera K, Vélez Ospina JA. Impacto de las TIC en el nivel de innovación en América Latina y el Caribe: estimaciones econométricas a nivel de un panel. *Redes.com: revista de estudios para el desarrollo social de la comunicación* 2014; 9: 341-360.

12. Kirkizlar E, Serban N, Sisson JA *et al*. Evaluation of telemedicine for screening of diabetic retinopathy in the Veterans Health Administration. *Ophthalmology* 2013; 120: 2604-2610.

13. Zanotto BS, Etges APB da S, Siqueira AC *et al*. Avaliação econômica de um serviço de telemedicina para ampliação da atenção primária à saúde no Rio Grande do Sul: o microcusteio do projeto TeleOftalmo. *Cien Saude Colet* 2020; 25: 1349-1360.

14. Suárez-Obando F, Gómez-Restrepo C, Castro-Díaz SM. Ciencias de la implementación: de la evidencia a la práctica. *Acta Med Colomb* 2018; 43: 207-216.

15. Kirk MA, Kelley C, Yankey N *et al*. A systematic review of the use of the Consolidated Framework for Implementation Research. *Implement Sci* 2016; 11: 72.

16. Digital Imaging and Communications in Medicine (DICOM). Arlington, VA: DICOM Secreariat, Available in: https://www.dicomstandard.org/

17. Wilkinson CP, Ferris FL 3rd, Klein RE *et al*. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. *Ophthalmology* 2003; 110: 1677-1182.

18. The Consolidated Framework for Implementation Research [en línea]. Ann Arbor, MI: CFIR Research Team-Center for Clinical Management Research. Available in: https://cfirguide.org/ [cited: July 2020].

19. Sharafeldin N, Kawaguchi A, Sundaram A *et al*. Review of economic evaluations of teleophthalmology as a screening strategy for chronic eye disease in adults. *Br J Ophthalmol* 2018; 102: 1485.1491.

20. Andonegui J, Serrano L, Eguzkiza A *et al*. Diabetic retinopathy screening using tele-ophthalmology in a primary care setting. *J Telemed Telecare* 2010; 16: 429-432.

21. Liu Y, Torres Diaz A, Benkert R. Scaling up teleophthalmology for diabetic eye screening: opportunities for widespread implementation in the USA. *Curr Diab Rep* 2019; 19: 74.

22. Greenhalgh T, Robert G, Macfarlane F *et al*. Diffusion of innovations in service organizations: systematic review and recommendations. *Milbank Q* 2004; 82: 581-629.

23. Shortell SM, Marsteller JA, Lin M *et al*. The role of perceived team effectiveness in improving chronic illness care. *Med Care* 2004; 42: 1040-1048.

24. Rodríguez Villa S, Alonso Álvarez C, de Dios Del Valle R *et al*. Análisis de un programa de teleoftalmología para el cribado de retinopatía diabética en área rural tras cinco años. *Arch Soc Esp Oftalmol* 2016; 91: 426-430.

25. Gershon RRM, Stone PW, Bakken S, Larson E. Measurement of organizational culture and climate in healthcare. *J Nurs Adm* 2004; 34: 33-40.

Practice patterns for intravitreal injections in Argentina: results from a national survey of the Argentine Council of Ophthalmology

Nicolás Crim[a*], Evangelina Espósito[a*], M. Fernanda Barros-Centeno[a], M. Eugenia González-Castellanos[a], Carla D. Guantay[a], Alejandro González-Castellanos[a], Dana Martínez[a], Mariano Irós[b], Pablo Daponte[c], Julio A. Urrets-Zavalía[a].

[a] *Servicio de Oftalmología, Clínica Universitaria Reina Fabiola, Universidad Católica de Córdoba, Argentina.*

[b] *Instituto de Microcirugía Ocular Córdoba, Argentina.*

[c] *Centro Integral de Salud Visual, Buenos Aires, Argentina.*

** Nicolás Crim and Evangelina Espósito contributed equally to this paper.*

Received: July 2nd, 2020.
Accepted: August 4th, 2020.

Corresponding author
Dr. Julio A. Urrets-Zavalía
Servicio de Oftalmología
Clínica Universitaria Reina Fabiola
Universidad Católica de Córdoba
Jacinto Ríos 554, piso 7
(5000) Córdoba, Argentina.
+54 351 4142121
julioaurrets@gmail.com

Oftalmol Clin Exp (ISSN 1851-2658)
2020; 13(3): 135-144.

Abstract

Objective: To assess current practices of intravitreal injections (IVI) and related complications among ophthalmologists in Argentina.
Methods: In 2016, an anonymous web-based 39-question survey was designed using Google Forms tool and made accessible to 5,436 affiliated ophthalmologists to the Argentine Council of Ophthalmology currently practicing in Argentina. The questionnaire inquired on demographic information concerning the treating physician (age, gender, subspecialty practice, etc.), the procedure (number of IVI/month, treated disease, injected drugs, facility, technique/instrumentation (antisepsis, lid speculum, sterile gloves, and mask) and complications.
Results: 438 (8.05%) ophthalmologists responded the survey, 87.7% of whom perform IVI; 66.4% were middle-aged physicians, and 20.3% Retina specialists. The most frequently treated disease is age-related macular degeneration, followed by diabetic macular edema. Off-label drugs are used by 54.4%. IVI are performed in the OR by 82.8%. Povidone-iodine is used by 97.7%, a sterile lid spec-

ulum 89%, sterile gloves 92.7%, a mask in 88%. Complications during the procedure were reported by 18.7% of respondents, being conjunctival hemorrhage the commonest (93.1%). Post injection complications were reported by 25.8% of respondents, and these complications included ocular hypertension and endophthalmitis.
Conclusions: Surveyed-based estimates about usual practices of ophthalmologists in Argentina performing IVI and some of the related complications were obtained. Disparities in current practices of IVI were frequent. The majority of respondents agreed in performing injections in the OR, the use of topical povidone-iodine and lid speculum. Performing more than 20 injections per month, practicing Retina/Vitreous subspecialty and not using a lid speculum, were more frequently associated with endophthalmitis.
Key words: intravitreal injection; endophthalmitis; anti-angiogenic drugs.

Inyecciones intravítreas en Argentina: resultados de la encuesta nacional del Consejo Argentino de Oftalmología

Resumen

Objetivos: Evaluar las prácticas habituales en inyecciones intravítreas, y complicaciones asociadas, entre los oftalmólogos de Argentina.
Métodos: En 2016, una encuesta anónima de 39 preguntas utilizando la plataforma Google Forms, se ofreció a 5.436 médicos oftalmólogos afiliados al Consejo Argentino de Oftalmología que ejercen en Argentina. Las preguntas indagaban sobre información relacionada al médico tratante (edad, género, subespecialidad, etc.), el procedimiento (número de IVI/mes, enfermedad preferentemente tratada, espacio físico donde realizan las inyecciones, drogas inyectadas, técnica/instrumentación (antisepsia, uso de blefaróstato, guantes estériles y máscara), y las complicaciones durante y posteriores a la inyección.
Resultados: 438 (8,05%) médicos oftalmólogos respondieron la encuesta, 87,7% de los cuales realizan inyecciones intravítreas. La mayoría de ellos tenían una edad entre 30 a 50 años. Sólo el 20,3% eran especialistas en Retina. La enfermedad más frecuentemente tratada es la degeneración macular relacionada a la edad, seguida por el edema macular diabético. El 54,4% utiliza drogas "fuera de etiqueta". Las inyecciones intravítreas son realizadas en el quirófano por el 82,8%. El 97,7% de los encuestados utiliza iodopovidona, el 89% blefaróstato estéril, el 92,7% guantes estériles, y el 88% cubreboca. El 18,7% reportó complicaciones durante el procedimiento, siendo la hemorragia conjuntival la más frecuentemente reportada (93,1%). El 25,8% de los encuestados comunicó complicaciones post inyección, las que incluyeron hipertensión ocular y endoftalmitis.
Conclusiones: En este estudio basado en una encuesta se obtuvieron por primera vez aspectos vinculados a las prácticas usuales y complicaciones relacionadas de médicos oftalmólogos de Argentina que realizan inyecciones intravítreas. Con frecuencia se observaron disparidades en dichas prácticas. La mayoría de los encuestados coincidieron en realizar las IVI en quirófano, en utilizar iodopovidona y blefaróstato. La realización de más de 20 inyecciones por mes, practicar la subespecialidad de Retina/Vítreo y el no usar blefaróstato se asociaron más frecuentemente a endoftalmitis.
Palabras clave: inyección intravítrea; endoftalmitis; drogas antiangiogénicas.

Injeções intravítreas na Argentina: resultados de uma pesquisa do Conselho Argentino de Oftalmologia

Resumo

Objetivos: Avaliar as práticas habituais em injeções intravítreas e complicações associadas, entre os oftalmologistas de Argentina.
Métodos: Em 2016, uma pesquisa anónima de 39 perguntas utilizando a plataforma Google Forms, se ofereceu a 5.436 médicos oftalmologistas afiliados ao *Consejo Argentino de Oftalmologia* que exercem na Argentina. As perguntas indagavam sobre informação relacionada a médico tratante (idade, género, subespecialidade, etc.), o procedimento (número de IVI/mês, doença preferentemente tratada, espaço físico onde se realizaram as injeções, drogas injetadas, técnica/instrumentação (antissepsia, uso de blefaróstato, luvas esterilizadas

e máscara), e as complicações durante e posteriores a injeção.
Resultados: 438 (8,05%) médicos oftalmologistas responderam à pesquisa, 87,7% dos quais realizam injeções intravítreas. A maioria deles tinha uma idade entre 30 e 50 anos. Apenas 20,3% eram especialistas em Retina. A doença mais frequentemente tratada é a degeneração macular relacionada à idade, seguida pelo edema macular diabético. 54,4% utiliza drogas "fora de etiqueta". As injeções intravítreas são realizadas no bloco operatório por 82,8%. 97,7% dos entrevistados utiliza iodopovidona, 89% blefaróstato estéril, 92,7% luvas esterilizadas, 88% máscara.18,7% reportou complicações durante o procedimento, sendo a hemorragia conjuntival a mais frequentemente reportada (93,1%). 25,8% dos entrevistados comunicou complicações pós-injeção, que incluíram hipertensão ocular e endoftalmite.
Conclusões: Neste estudo baseado em uma pesquisa se obtiveram por primeira vez aspectos vinculados as práticas usuais e complicações relacionadas de médicos oftalmologistas de Argentina que realizam injeções intravítreas. Com frequência se observaram disparidades nas práticas. A maioria dos entrevistados coincidiram em realizar as IVI em bloco operatório, em utilizar iodopovidona e blefaróstato. A realização de mais de 20 injeções por mês, praticar a subespecialidade de Retina/Vítreo e não usar blefaróstato foram associados mais frequentemente a endoftalmite.
Palavras chave: injeção intravítrea; endoftalmite; drogas anti-antigênicas.

Introduction

Intravitreal injections (IVI) have expanded importantly as a therapeutic delivery option over the past 13 years, resulting from the introduction of novel drug therapies to treat several potentially blinding diseases, and constitute at present a routine procedure, with millions of IVI performed throughout the world. Technically, they do not entail important difficulties to their execution, but a bad or careless technique may lead to a devastating functional and anatomical result. Despite its widespread use, some severe complications may result from IVI such as elevation of intraocular pressure, cataract, intraocular haemorrhage, retinal detachment, and endophthalmitis[1-2]. However, there is no consensus about recommendations regarding the optimal protocol about security measures for patients[3-4].

In Argentina a national registry for IVI does not exist, and no formal guidelines or recommendations are available concerning best practices for this therapeutic procedure.

The aim of this study was to evaluate through a survey current practices among ophthalmologists performing IVI throughout Argentina, and possible resulting complications.

Material and methods

This is a transversal and observational study consisting in a cross-sectional survey. In July 2015, an anonymous web-based questionnaire was sent by the Argentine Council of Ophthalmology to 5,436 ophthalmologists practicing in Argentina. The study and questionnaire were approved by the Ethics Committee of both the University Clinic Reina Fabiola and the Argentine Council of Ophthalmology.

Survey: a 39-question survey was designed using the Google Forms tool (Google LLC, Mountain View, CA, U.S.A.). An internet link to get access to the survey and an explanatory letter were sent by e-mail the same day to each member of the Argentine Council of Ophthalmology, and the survey remained opened to participants for 30 consecutive days. During this period, several reminder flyers concerning the purposes and importance of the survey were sent by e-mail to all members.

The questionnaire inquired on:

1. Demographic information related to the treating physician that included age, gender, province/state in Argentina of current ophthalmology practice, specific training in IVI during residency, post-residency training in Retina, subspecialty practice (if any), national or international retina society membership).

2. Specific questions about the procedure, such as informed consent for patients, mean number

Table 1. Subspecialty area that occupies most of respondents' practicing time.

Subspecialty	% (n)
General Ophthalmology	41.32% (181)
Anterior Segment	28.31% (124)
Retina / Vitreous	20.32% (89)
Paediatric Ophthalmology	4.11% (18)
Uveitis	2.51% (11)
Refractive Surgery	0.68% (3)
Orbit and Lacrimal System	0.68% (3)
Ocular Oncology	0.46% (2)
Plastic and Cosmetic Surgery	0.23% (1)
Ocular Surface	0.23% (1)
Other	1.14% (3)

of IVI per month, predominant treated disease, most frequently injected drug, pre-injection preparation of patient, facility for IVI (office or operating room), reasons for facility choice, technique and instrumentation (positioning of patient during injection-seated or lying flat on her/his back, antisepsis, anesthesia, use of lid speculum, use of sterile gloves, use of mask by physician and patient), post-injection use of antibiotics, complications during and after injection, and occurrence of endophthalmitis.

Statistical analysis: Results are presented mainly with descriptive statistics using SPSS software 25.0 (IBM Corp., Armonk, New York, USA). Data from the survey were analyzed in terms of frequency of responses for each question. The Chi-squared test was used to investigate differences between the frequencies. A p value of <0.05 was considered statistically significant.

Results

A total of 438 (8.05%) ophthalmologists participated in the survey, 87.7% (384) of whom perform IVI. The majority of them (66.4%, n=291) ranged between 30 and 50 years old, 29.9% (131) were more than 50 years old, and only 3.6% (16) were less than 30 years old. Also, the majority of the respondents (68.7%, n=301), were males.

An informed consent was obtained from patients before treatment by 88% (338) of respondents; 65.7% of them (222) used an informed consent specific for IVI approved by the Argentine Council of Ophthalmology, 17.1% (23) used a general non-specific informed consent, and 17.1% (23) an informed consent designed by themselves. Among those respondents who do not provide an informed consent to patients, 50% (23) ignore that an informed consent is available for this specific purpose, and the other 50% believe that it is not necessary.

Almost half of our respondents practice General Ophthalmology (41.3%), followed by Anterior Segment (28.3%) and Retina/Vitreous (20.3%) specialists (Table 1).

Less than half of the respondents, 40.6% (178) have a fellowship or post-residency training in retina. From the total respondents 20,78% (91) do not perform this subspecialty despite having a post-residency training in retina, and 2.74 % (12) have most of the time dedicated to retina without undergone specific training. However, 51.1% (224) received specific training in IVI during their residency program. The posterior segment specialists (Retina and vitreous, Uveitis, Oncology) are 22.83% (100).

Concerning the number of IVI procedures performed per month, 12.33% (54) of respondents do not perform IVI, 39.7% (174) perform less than five injections, 37.7% (165) 5 to 20 IVI, and 10.3% (45) more than 20 IVI per month.

When we asked about the sort of diseases treated the most popular answer was neovascular age-related macular degeneration (nAMD) (33.9%), followed by diabetic macular edema (DME) (29.7%), macular edema complicating a retinal vein occlusion (RVO) (15.5%), neovascular myopic maculopathy (8.7%), pseudophakic macular edema (4.1%), and central serous chorioretinopathy (3.9%).

Follow-up schedule among respondents was as follows: 76.6% (294) control their patients 24 hours after injection, 16.4% (63) during the

week post injection, and 7% (27) do not control at all until the next injection.

Injected drugs

Anti-angiogenic drugs are the most common substances injected (98.7%, n=379), followed by corticosteroids (37.5%, n=144), antibiotics (24.7%, n=95), oncologic drugs (2.9%, n=11), and ocriplasmin (2.6%, n=11).

Off-label drugs are used by 54.4% (209) respondents, and drugs approved by the Food and Drug Administration (FDA) from the U.S.A. and the National Administration of Drugs, Food, and Medical Technology (ANMAT) from Argentina by 45.6% (175). Among respondents that use off-label drugs, 58.6% (122) use prefilled syringes, and 41.4% (86) take each dose of drug from the vial at the moment of injection. There is no statistical difference in the chosen drug between posterior segments specialists and non-specialists (p 0.79).

Preparation of the patient prior to injection

Preparation of the patient includes to administer drops, and to drape the patient before the procedure. Patients are prepared prior to injection by the performing ophthalmologist in 84.1% (323), 5.2% (20) occasionally, and 10.7% (41) never prepare their patients by themselves.

Facility

IVI are performed in the operating room (OR) by 82.8% (318) of respondents, and in the office by 17.2% (66). For those that use the OR, their reasons were: presumed less possibility of a legal issue that might occur in case of complications or unfavourable results 60% (191), presumed less risk for endophthalmitis 56.6% (180), to enhance significance of the procedure 51.6% (164), to better handle complications 42.8% (136), comfort 30.8% (98), and economic convenience for the physician 21% (67). Reasons for performing the injection in the office were as follows: safety 53% (35), less expensive for the patient 50% (33), comfort 50% (33), simplicity 45.4% (30), scientific support 39.4% (26), and for better work flow 39.4% (26). The OR is preferred by 76% (76) of posterior segment specialists and 85% (242) of non-specialists (p 0.03).

Technique and instrumentation

Positioning of the patient: IVI is performed with patients lying face up by 91.9% (353) of respondents, and only a minority (8.1%, n=31), performs injections with the patient in a seated position. There was no statistical difference between retina specialist and other sub specialists in the positioning choice of patient (p 0.4).

Antisepsis: Povidone-iodine is used by 97.7% (335) respondents, 70.1% (235) of whom use a 5% concentration, 19.7% (66) a 10% concentration, and 10.2% (34) use less than 5% concentration. Several applications of povidone-iodine drops spaced by a few minutes each is the preference of 57.9% (194) respondents, and only one drop of povidone-iodine immediately before injection is used by 42.1% (141).

Anesthesia: Topical anesthesia in the form of repeated conjunctival instillations is used by 89% (309) of respondents. Topical application of anesthetic drug with a cotton swab at the site of injection is preferred by 9.2% (32), and periocular injection by 1.7% (6) of respondents.

Lid speculum: A lid speculum is used by the vast majority of respondents (93%, n=357), and a high proportion (89%, n=342) uses a sterile lid speculum for each procedure.

Sterile gloves: 92.7% (356) use sterile gloves and 7.3% (28) do not.

Mask: 88% (338) of the respondents use a mask, and only 12% do not; 24% (92) of the respondents put a mask over the patient´s mouth and nose, and 76% (292) do not.

Pressure with a cotton swab over the site of injection immediately after the injection to prevent reflux or conjunctival hemorrhage is performed by 85.9% (330) of respondents.

Complications during the procedure

Complications during the procedure were reported by 18.7% (72) of respondents. For those

Table 2. Post intravitreal injection complications report.

Endophthalmitis	54.5%	(54)
Ocular hypertension	51.5%	(51)
Uveitis	19.2%	(19)
Cataract	9.1%	(9)
Posterior vitreous detachment	8.1%	(8)
Retinal tear	4.0%	(4)
Retinal detachment	3.0%	(3)

reporting complications, they occur rarely in 91.7% (66) respondents, and frequently in only 8.3% (6). Regarding the sort of complication, the question allowed more than one answer and the most popular complication was conjunctival hemorrhage, reported by 93.05% (67) of respondents, followed by lens injury (26.4%, 19), vitreous hemorrhage (15.3%, 11), and retinal injury (5.6%, 4). Complications during procedure are more likely to occur with non-specialists, and this is statistically significant, p-value < 0.001. The age group of the performing physician was not relevant.

Post injection prophylactic antibiotic treatment

Post injection topical antibiotics are frequently indicated, either alone or associated with a corticosteroid, by the vast majority of respondents (94.5%, n=363/384), moxifloxacin the most frequently topical antibiotic indicated (51%, n=185), followed by gatifloxacin (37.7%, n=137), ciprofloxacin (8.3%, n=30), tobramycin (2.8%, n=10), and erythromycin (0.3%, n=1).

Systemic antibiotics are used by a small proportion of respondents (4.4%, n=17/384), and the most frequently systemic antibiotic used is ciprofloxacin (58.8%, n=10), followed by levofloxacin (23.5%, n=4), and azithromycin (17.7%, n=3). There is no statistical difference in the prophylactic antibiotic treatment between posterior segments specialists and non-specialists.

Post injection complications

One or more complications observed at least once were reported by 25.8% (99/384) of respondents, being ocular hypertension, endophthalmitis, and uveitis the most frequently reported (Table 2). They were referred as rare by all respondents (99) and resolved favorably in 88.9% (88). Eighty six percent (332) of the responders never had endophthalmitis as a complication of IVI. Post injection complications are more likely to occur with non-specialists, and this is statistically significant, p-value < 0.00001. The age group of the performing physician was not relevant.

Endophthalmitis

When analysing answers concerning any endophthalmitis versus never endophthalmitis, no statistical difference was found among respondents that had received a retina training, injection performed in OR or office, patient positioning, iodopovidone concentration, use of lid speculum, sterile gloves, use of mask or topical or systemic antibiotics after injection (p >0.05). However, a significant statistical difference was found when a mask was used by patients (p 0.03).

Discussion

Practices concerning IVI, especially in those tending to prevent endophthalmitis, may vary substantially between nations, and between areas in a same country, possibly as the result of lack of scientific evidence from randomized clinical trials and specific guidelines drawn from them[5].

In Argentina, there is no registry concerning the distribution of ophthalmologists among the different subspecialty areas, but it is assumed that the majority of them practices Comprehensive Ophthalmology and one or more subspecialty, and only a few practices strictly one subspecialty. It is surprising that almost half of our respondents performing IVI practice Comprehensive Ophthalmology, and only 20% are Retina/Vitreous specialists. Moreover, complications

were more likely to occur among those who never received subspecialty vitreo-retinal training. This may raise some concerns referred not only to the specific training that General Ophthalmologists could have for IVI, but also concerning deep knowledge and adequate criteria to treat vitreoretinal diseases necessitating an IVI and adequate follow-up of treated patients. This work shows that complications during and after the procedure are more likely to occur without a specific posterior segment training. It would be interesting to assess if surgical training might be a protective factor. In a study from two hospitals in northwest England, Michelotti *et al* concluded that trained nurses would be a safe resource to perform IVI when retinal specialists are lacking[6]. Nevertheless, information about general ophthalmologists performing IVI is scarce. In Germany, patients regularly consult the general ophthalmologist for monitoring but, when needed, they are referred to the specialized injecting ophthalmologist for IVI, and both professionals are satisfied with the situation and the care provided to the patient[7].

Another prominent aspect of this survey is the disappointing small amount of survey respondents. Only 8% answered, in contrast with the 34% recently reported by Hanumunthadu *et al*. in the UK[8]. This issue maybe related with the fact that non-respondents do not perform IVI's, or a limited interest in surveys, as surveys evaluating physicians´ practices are very uncommon in Argentina. In the last Argentine Council of Ophthalmology's survey about post-surgical endophthalmitis, only 6% of polled ophthalmologists responded[9].

Many aspects of IVI practices are controversial, and differences in those practices are observed among countries around the world. Moreover, there are no major randomized clinical trials evaluating best practices for IVI. In 2014, Avery *et al*. published updated consensus guidelines for IVI technique and monitoring, including the deferral of an injection in an eye with external infection, the reduction of aerosolized droplets from the oral cavity of the patient and treating physician, and the use of topical application of povidone-iodine to the ocular surface and lid border prior to injection[10]. However, substantial variability is accepted, especially concerning the facility (OR) vs office-clinical room), and the use of topical antibiotics, a mask for the patient and/or the physician, a lid speculum, sterile gloves, among others[10].

Infectious endophthalmitis is an uncommon but potentially devastating complication of IVI. Its incidence following IVI of anti-VEGF agents has been reported to range between 0.02% to 0.3% per injection, with a cumulative rate per patient receiving multiple injections[11]. For the time being, most ophthalmic surgeons use povidone-iodine as the preferred and established method of antisepsis in the preparation for ocular procedures, and remains the gold standard for endophthalmitis prophylaxis[12]. Topical povidone-iodine for antiseptic preparation of the ocular surface and lid borders prior to an IVI is preferred by the vast majority of ophthalmologists in our survey, and also by others[4]. Endophthalmitis rates after IVI where povidone-iodine was used in the antiseptic preparation have been reported to occur in 0.03% to 0.06%[11, 13]. Recently, it has been reported that topical administration of 5% povidone iodine over 30 seconds can be considered a safe approach for antisepsis preceding IVI[5]. In contrast, in cases where povidone-iodine is not used the risk of post IVI endophthalmitis appears to be higher[14]. In those patients with presumed iodine allergy or severe ocular surface irritation secondary to povidone-iodine instillation, chlorhexidine could be a possible alternative. In one multicenter study by Merani *et al*, antisepsis prior to IVI provided by aqueous chlorhexidine 0.05% and 0.1% was evaluated in 40,535 IVI by 7 different retina specialists from 3 centers, with an endophthalmitis rate of 0.0074% (1 in 13,512) per injection, comparing favorably with previous studies that evaluated povidone-iodine[15].

Topical antibiotics have not proven to decrease the rate of endophthalmitis and increase the chances of antibiotic resistance and overall cost of the procedure[16-17]. Moreover, there is some evidence that they could increase endophthal-

mitis rate, possibly by altering the conjunctival normal flora and inducing resistance as the consequence of repeated exposure to antibiotics[16, 18-20]. Topical antibiotics are used by 70.9% of international members of the American Society of Retina Specialists (ASRS) compared to 21.8% of U.S.A. members, according to the 2013 ASRS survey[21]. The use of topical antibiotics was reported by 83% of our surveyed ophthalmologists.

Argentina, as a middle-income country, has many economic limitations and the use of off-label drugs is a great choice, given that the efficacy an potential risks are comparable to FDA-approved drugs, and the costs much less[22]. Interestingly, near half of the ophthalmologists use FDA-approved drugs, mostly for legal issues fear, or sometimes because they are provided by the public health services[23].

Among our respondents, the OR is the place of choice to perform IVI (82%) due to increased standard of practice, fear of complications or legal issues. IVI are predominantly performed in a clinical facility in U.S.A., but the OR appears to be the preference of many ophthalmologists from different European countries. In a study from Tabandeh *et al* comparing 8,647 IVI performed by an American surgeon in a clinical setting, and 3,063 IVI performed by an Italian surgeon in an OR, endophthalmitis was observed to occur in 0.035% of clinic setting´s injections and in 0.065% of those performed in the OR, a difference with no statistical significance[24]. Furthermore, the 2013 survey of the ASRS addressing questions to both U.S.A. and international members, it was concluded that the OR facility was largely preferred for IVI by international members (57.3% vs 1.8% of U.S.A. members)[21].

Lid speculum, either sterile or non-sterile, is widely used, although bimanual lid retraction and fixation seems to provide more comfort for the patient[25]. Lid speculum provides a wider exposed area without the risk of a brisk eyelid closure, keeping the physician with both hands free. Nevertheless, the lack of use of lid speculum does not seem to represent an additional risk for endophthalmitis[26].

Experts recommend to minimize talking during IVI, and to wear face masks[5]. In our survey, we found that the use of mask by the injecting physician is common, but the patient´s mouth and nose are not covered during the procedure.

Infectious endophthalmitis is an uncommon but potentially devastating complication of IVI. Its incidence following IVI of anti VEGF agents has been reported to range between 0.02% to 0.3% per injection, with a cumulative rate per patient receiving multiple injections[11]. In our survey, post injection complications were reported by 25.8% of respondents, among whom endophthalmitis was referred by 86%. Risk factors for endophthalmitis were: to perform more than 20 injections per month, to inject with the patient in a seated position, to practice the subspecialty Retina/Vitreous, to not prepare themselves the patient prior to injection, to not use a lid speculum, to not use sterile gloves, and to have complications during the procedure. When endophthalmitis occurred, a favorable outcome resulted in only 11.1% of cases.

Conclusions

Although participation of argentine ophthalmologists in our survey was poor, the findings provided for the first time surveyed-based estimates of usual practices of ophthalmologists in Argentina performing IVI. Only 20% of respondents were Retina specialists. Post-injections complications were more likely to occur among ophthalmologists never having received subspecialty vitreo-retinal training. The majority of respondents agreed in performing injections in the OR, the use of topical povidone-iodine for antiseptic preparation of the ocular surface and lid borders prior to injection, the use of a lid speculum, and the post-injection prescription of topical antibiotics. Performing more than 20 injections per month, practicing Retina/Vitreous subspecialty and not using a lid speculum, among others, were more frequently associated with endophthalmitis.

Acknowledgments: To the Consejo Argentino de Oftalmología (CAO) for the support, and to

Mr. Fernando Guzmán from the Communication Area of the CAO, for his assistance in the web design and distribution of the survey.

References

1. Kim HD, Kim SH, Cho IH *et al*. Effects of repeated intravitreal bevacizumab injections on the inner retinal function in neovascular age-related macular degeneration. *Acta Ophthalmol* 2013; 91: e154-e156.
2. Kim SJ. Intravitreal injections and endophthalmitis. *Int Ophthalmol Clin* 2015; 55: 1-10.
3. Zerbib J, Bourhis A, Cornut PL *et al*. Prise en charge de la DMLA exsudative en France en 2015. *J Fr Ophtalmol* 2017; 40: 723-730.
4. Loewenstein I, Goldstein M, Moisseiev J, Moisseiev E. Accuracy and precision of intravitreal injections of anti-vascular endothelial growth factor agents in real life: what is actually in the syringe? *Retina* 2019; 39: 1385-1391.
5. Grzybowski A, Told R, Sacu S *et al*. 2018 update on intravitreal Injections: Euretina Expert Consensus recommendations. *Ophthalmologica* 2018; 239: 181-193.
6. Michelotti MM, Abugreen S, Kelly SP *et al*. Transformational change: nurses substituting for ophthalmologists for intravitreal injections: a quality-improvement report. *Clin Ophthalmol* 2014; 8: 755-761.
7. Wachtlin J, Ringwald A, Maulhardt T *et al*. Cooperation of German ophthalmologists in routine care of patients with neovascular age-related macular degeneration: results of the non-interventional BRIDGE study. *Graefes Arch Clin Exp Ophthalmol* 2016; 254: 1529-1536.
8. Hanumunthadu D, Nowak VA, Hassan F *et al*. Variations in treatment delivery for patients with neovascular AMD in the UK: results from an Ophthalmology Trainee Clinical Research Network Study. *Ophthalmol Ther* 2017; 6: 295-300.
9. Crim N, Espósito E, Martínez D *et al*. Prevención de endoftalmitis posquirúrgica en Argentina: encuesta nacional del Consejo Argentino de Oftalmología 2014. *Oftalmol Clin Exp* 2017; 10: 1-11.
10. Avery RL, Bakri SJ, Blumenkranz MS *et al*. Intravitreal injection technique and monitoring: updated guidelines of an expert panel. *Retina* 2014; 34 Suppl 12: S1-S18.
11. Fileta JB, Scott IU, Flynn HW Jr. Meta-analysis of infectious endophthalmitis after intravitreal injection of anti-vascular endothelial growth factor agents. *Ophthalmic Surg Lasers Imaging Retina* 2014; 45: 143-149.
12. Ahmed Y, Scott IU, Pathengay A *et al*. Povidone-iodine for endophthalmitis prophylaxis. *Am J Ophthalmol* 2014; 157: 503-504.
13. Merani R, Hunyor AP. Endophthalmitis following intravitreal anti-vascular endothelial growth factor (VEGF) injection: a comprehensive review. *Int J Retina Vitreous* 2015; 1: 9.
14. Modjtahedi BS, van Zyl T, Pandya HK *et al*. Endophthalmitis after intravitreal injections in patients with self-reported Iodine allergy. *Am J Ophthalmol* 2016; 170: 68-74.
15. Merani R, McPherson ZE, Luckie AP *et al*. Aqueous chlorhexidine for intravitreal injection antisepsis: a case series and review of the literature. *Ophthalmology* 2016; 123: 2588-2594.
16. Schwartz SG, Flynn HW, Grzybowski A. Controversies in topical antibiotics use with intravitreal injections. *Curr Pharm Des* 2015; 21: 4703-4706.
17. Hunyor AP, Merani R, Darbar A *et al*. Topical antibiotics and intravitreal injections. *Acta Ophthalmol* 2018; 96: 435-441.
18. Bhavsar AR, Stockdale CR, Ferris FL 3rd *et al*. Diabetic Retinophaty Clinical Research Network. Update on risk of endophthalmitis after intravitreal drug injections and potential impact of elimination of topical antibiotics. *Arch Ophthalmol* 2012; 130: 809-810.
19. Dossarps D, Bron AM, Koehrer P *et al*. FRCR net. Endophthalmitis after intravitreal injections: incidence, presentation, management, and visual outcome. *Am J Ophthalmol* 2015; 160: 17-25 e1.
20. Menchini F, Toneatto G, Miele A *et al*. Antibiotic prophylaxis for preventing endophthalmitis after intravitreal injection: a systematic review. *Eye (Lond)* 2018; 32: 1423-1431.
21. Stone TW, Mittra RA. ASRS 2013 preferences and trends membership survey: Chicago, IL.

American Society of Retina Specialists, 2013.
22. Singh SR, Dogra A, Stewart M *et al*. Intravitreal ziv-aflibercept: clinical effects and economic impact. *Asia Pac J Ophthalmol (Phila)* 2017; 6: 561-568.
23. Rosenfeld PJ, Windsor MA, Feuer WJ *et al*. Estimating medicare and patient savings from the use of bevacizumab for the treatment of exudative age-related macular degeneration. *Am J Ophthalmol* 2018; 191: 135-139.
24. Tabandeh H, Boscia F, Sborgia A *et al*. Endophthalmitis associated with intravitreal injections: office-based setting and operating room setting. *Retina* 2014; 34: 18-23.
25. Alattas K. Patients' tolerance of bimanual lid retraction versus a metal speculum for intravitreal injections. *Clin Ophthalmol* 2016; 10: 1719-1721.
26. Shah CP, Garg SJ, Vander JF *et al*. Post-Injection Endophthalmitis (PIE) Study Team. Outcomes and risk factors associated with endophthalmitis after intravitreal injection of anti-vascular endothelial growth factor agents. *Ophthalmology* 2011; 118: 2028-2034.

Comparación entre viscoelástico y solución salina balanceada para implantar lente intraocular

Diana Patricia Villalba Hoyos[a], Álvaro Noguera Cruz[b], Jorge Acosta Reyes[c], Juan Pablo Quiceno Franco[a]

[a] *Centro Visual Moderno, Manizales, Colombia.*

[b] *Oftalmólogo especialista en glaucoma, práctica privada, Manizales, Colombia.*

[c] *Departamento de Salud Pública, Universidad del Norte, Barranquilla, Colombia.*

Recibido: 13 de abril de 2020.
Aceptado: 31 de julio de 2020.

Correspondencia
Dra. Diana Patricia Villalba Hoyos
Centro Visual Moderno
Sede Vizcaya
Carrera 23A, # 67-09
Manizales, Caldas, Colombia
+57 03(6) 893-3240
dianapatrica22@gmail.com

Oftalmol Clin Exp (ISSN 1851-2658)
2020; 13(3): 145-154.

Resumen

Objetivo: Comparar resultados quirúrgicos entre los pacientes a quienes se les colocó viscoelástico oftálmico y en los que se usó solución salina balanceada para mantener la cámara anterior durante la implantación de la lente intraocular después de facoemulsificación.
Métodos: Se realizó un estudio clínico retrospectivo de casos-controles en 20 pacientes a quienes se mantuvo la cámara anterior con viscoelástico (grupo A) y en 26 (grupo B) con solución salina balanceada. Se evaluaron características prequirúrgicas en la población y aspectos quirúrgicos (porcentaje y tiempo de facoemulsificación, tiempo quirúrgico y facilidad de implantación de la lente intraocular). Se realizaron mediciones de paquimetría central, presión intraocular y biomicroscopía del segmento anterior a las 24 horas, a la semana y al mes de la cirugía. También se determinó el equivalente esférico, agudeza visual mejor corregida (AVmc), cambio refractivo miópico y grado de opacidad capsular posterior al mes de la cirugía. Los resultados se compararon para variables cuantitativas a través de una prueba U de Mann Whitney y para variables cualitativas la significancia estadística por medio del Chi-cuadrado o prueba exacta de Fisher (significancia $p< 0.05$).
Resultados: El tiempo quirúrgico fue menor en el grupo B (p=0,003). Al mes de la cirugía los pacientes del grupo A presentaron una mediana de AVmc

de 0,19 LogMAR y los del grupo B de 0,10 LogMAR (p=0,296). Ningún paciente presentó hipertensión ocular postoperatoria.
Conclusión: El tiempo quirúrgico disminuyó con la hidroimplantacion y ambas técnicas fueron seguras para la salud visual del paciente.
Palabras clave: hidroimplantación, viscoelástico, facoemulsificación, cataratas, técnica quirúrgica.

Comparison between viscoelastic devices and balanced saline in intraocular lens implantation

Abstract

Objective: To compare surgical outcomes between patients on whom ophthalmic viscoelastic devices or balanced saline solution was used to maintain the anterior chamber during intraocular lens implantation after phacoemulsification.
Methods: A retrospective case-control clinical trial was performed with the participation of 20 patients whose anterior chambers were maintained with viscoelastics (Group A) and 26 patients (Group B) on whom balanced saline solution was used for this purpose. Preoperative features of the population, as well as surgical aspects (percentage and time of phacoemulsification, surgical time and ease of intraocular lens implantation), were evaluated. Postoperative measurements made were: central pachymetry, intraocular pressure and anterior segment biomicroscopy 24 hours, one week and one month postoperatively. In addition, spherical equivalent, best spectacle-corrected visual acuity (BCVA), myopic refractive change and posterior capsule opacity one month after surgery were obtained. Results were compared using the Mann-Whitney U-test for quantitative variables and for the statistical significance of quantitative variables, the Chi-square or Fisher's exact test was used (significance $p < 0.05$).
Results: The surgical time was lower in Group B ($p = 0.003$). One month after surgery patients of group A had a median BCBA of 0.19 LogMAR while in those of group B it was 0.10 LogMAR ($p = 0.296$). None of the patients had postoperative ocular hypertension.
Conclusion: The surgical time lowered with hydroimplantation, and both techniques were safe for the patient's visual health.
Keywords: hydroimplantation, viscoelastics, phacoemulsification, cataracts, surgical technique.

Comparação entre viscoelástico e solução salina balanceada em implante de lentes intraoculares

Resumo

Objetivo: Comparar resultados cirúrgicos entre os pacientes a quem foi colocado viscoelástico oftálmico e nos que se usou solução salina balanceada para manter a câmara anterior durante a implantação da lente intraocular depois de facoemulsificação.
Métodos: Realizou-se um estudo clínico retrospectivo de casos-controle em 20 pacientes para quem se manteve a câmara anterior com viscoelástico (grupo A) e em 26 (grupo B) com solução salina balanceada. Avaliaram-se características pré-cirúrgicas na população e aspectos cirúrgicos (porcentagem e tempo de facoemulsificação, tempo cirúrgico e facilidade de implantação da lente intraocular). Realizaram-se medições de paquimetria central, pressão intraocular e biomicroscopia do segmento anterior às 24 horas, uma semana depois e um mês logo da cirurgia. Também se determinou o equivalente esférico, acuidade visual melhor corrigida (AVmc), mudança do erro refrativo miópico e grau de opacidade capsular posterior um mês depois da cirurgia. Os resultados foram comparados com variáveis quantitativas através de uma prova U de Mann Whitney e com variáveis qualitativas à significância estatística através do Chi-quadrado ou prova exata de Fisher (significância $p< 0.05$).
Resultados: O tempo cirúrgico foi menor no grupo B (p=0,003). Ao mês da cirurgia os pacientes do grupo A apresentaram uma média de AVmc de 0,19 LogMAR e os do grupo B de 0,10 LogMAR (p=0,296). Nenhum paciente apresentou hipertensão ocular pós-operatória.
Conclusão: O tempo cirúrgico diminui com a hidroimplantação e ambas as técnicas foram seguras para a saúde visual do paciente.

Palavras chave: hidroimplantação, viscoelástico, facoemulsificação, cataratas, técnica cirúrgica.

Introducción

Hasta ahora el único tratamiento curativo de las cataratas es el quirúrgico que ha mostrado ser altamente coste efectivo[1-2]. Según la Organización Mundial de la Salud, en el mundo hay aproximadamente 285 millones de personas con discapacidad visual, de las cuales 39 millones son ciegas y 246 millones presentan baja visión[3]. En términos mundiales, los errores de refracción no corregidos constituyen la causa más importante de discapacidad visual, pero en los países de ingresos medios y bajos las cataratas siguen siendo la principal causa de ceguera[3]. En un estudio realizado en el Departamento de Santander, Colombia, la prevalencia de ceguera fue de 1,79%, afectando prioritariamente a la población pobre y rural siendo la catarata la responsable del 67.61% de los casos[4]. La facoemulsificación es una técnica muy utilizada en la actualidad para la operación de cataratas. Su aparición se remonta a los inicios de los años 60[5] y mostró su mayor potencial a los inicios de los años 80 con la aprobación de las lentes intraoculares pleglables[6]. Aunque es una de las técnicas quirúrgicas más seguras y precisas de la oftalmología moderna, existen riesgos de complicaciones y muchas de estas están asociadas al aumento de la presión intraocular que puede estar relacionada con la cantidad de material viscoelástico retenido al final de la cirugía[7]. Las propiedades viscosas y elásticas de dispositivos viscoelásticos oftálmicos tienen numerosos beneficios en la cirugía de cataratas: no sólo pueden crear y mantener el espacio en el compartimiento anterior, sino que también pueden proteger y lubricar el endotelio corneal y desplazar y estabilizar el tejido[8]. Sin embargo, después de la implantación de la lente, es obligatorio eliminar completamente el viscoelástico de la cámara anterior y detrás de la óptica de la lente intraocular. Si se deja en el ojo, el viscoelástico puede inducir un aumento postoperatorio de la presión intraocular (PIO)[9]. Además, si el cirujano no retira de la bolsa capsular el viscoelástico, puede ocurrir un síndrome de distensión del saco capsular[10]. Muchos cirujanos rehúyen la colocación de la punta de faco detrás de la óptica de la lente intraocular durante la limpieza de la corteza debido al riesgo de ruptura capsular posterior. Además, la incisión de pequeño tamaño hace que sea difícil eliminar completamente el viscoelástico detrás de la lente intraocular. Por lo tanto, se ha empezado a implantar lentes intraoculares acrílicas plegables sin viscoelástico usando una técnica que se llama hidroimplantación, donde se utiliza solución salina balanceada para mantener la cámara anterior durante la implantación de la lente, técnica que describió Harshul Tak en la India[11].

En la actualidad ya son varios los cirujanos de catarata en el mundo que están utilizando este procedimiento, sin embargo se desconoce —según la revisión exhaustiva de las bases de datos disponibles en internet— que hasta la fecha se hayan realizado estudios en Colombia para evaluar sus resultados; por tal motivo se hizo imprescindible recabar información en nuestro medio y como principal objetivo de este estudio establecer si existen diferencias entre el uso de viscoelástico oftálmico y la solución salina balanceada para mantener la cámara anterior durante la implantación de la lente intraocular después de facoemulsificación en pacientes operados en el Centro Visual Moderno de Manizales, Colombia.

Métodos

Diseño de estudio

Estudio clínico retrospectivo de casos-controles para la comparación de dos intervenciones con el fin de mantener la cámara anterior durante el implante de la lente intraocular. Grupo A: mantenimiento con viscoelástico. Grupo B: con solución salina balanceada. Los grupos fueron conformados de acuerdo con la selección de oftalmólogo tratante, no se utilizó ningún método aleatorio y la recolección de los datos se hizo de forma retrospectiva. El proyecto fue aprobado por el comité de ética de la Universidad del Norte, de Colombia, y se realizó cumpliendo con la declaración de Helsinki.

Participantes y variables a estudiar

Población accesible: pacientes operados de catarata por técnica de facoemulsificación más implante de lente intraocular (un ojo por cada paciente) en el Centro Visual Moderno de Manizales, Colombia, que cumplieran con los criterios de inclusión y exclusión, que se indican:

Criterios de inclusión: edad entre 40 y 80 años, catarata senil superior NO2 o NC2 (*The lens opacities classification system III*).

Criterios de exclusión: profundidad de cámara anterior menor 2 mm, patología corneal, catarata complicada, glaucoma, pseudoexfoliación, miopía severa, historia previa de queratomileusis *in situ* asistida por láser (LASIK), tiempo quirúrgico total de más de 30 minutos, tiempo de faco total de más de 90 segundos, ruptura de cápsula posterior durante el procedimiento, conversión a extracción extracapsular de catarata.

Muestra: no probabilístico, por conveniencia. La muestra fue de 46 pacientes, dos grupos, el grupo A lo conformaron 20 pacientes a quienes se le mantuvo la cámara anterior con viscoelástico para el implante de lente intraocular y el grupo B lo conformaron 26 pacientes en los que se mantuvo la cámara anterior con solución salina balanceada.

En este estudio se tomaron los datos de las historias clínicas: para los pacientes estudiados que tenían cirugía de catarata en ambos ojos se tomó el ojo que cumpliera con los criterios de inclusión del estudio y si los dos cumplían, se registró el último ojo operado (sin tener en cuenta que técnica se había empleado para el otro ojo). Por lo cual, nos centramos sólo en el ojo escogido para el estudio y para otros pacientes que sólo se habían operado de un ojo se escogió éste, siempre y cuando también cumpliera con los criterios de inclusión, de lo contrario eran excluidos del presente estudio.

Variables: en el preoperatorio se investigó sexo, ojo operado, antecedente de hipertensión arterial, diabetes mellitus, retinopatía diabética proliferativa o no proliferativa, vitrectomía vía pars plana, equivalente esférico (dioptrías), agudeza visual mejor corregida en LogMAR (autorrefractómetro Huvitz, modelo 7000 verificado por el mismo optometrista con retinoscopía utilizando un Foropter Nidek modelo RT-600), paquimetría central en micras (Palm Scan modelo P 2000), profundidad de cámara anterior en milímetros (regla biométrica Palm Scan modelo P 2000), presión intraocular en mmHg (tonómetro de Goldmann), clasificación Van Herick de cámara anterior[12]. Grado de opacidad y color del núcleo del cristalino preoperatorio, grado de opacidad de la corteza del cristalino, grado de opacidad subcapsular posterior del cristalino (sistema LOCS III)[13]. En el intraoperatorio de determinó: tiempo quirúrgico (min), tiempo de facoemulsificación (seg), porcentaje de facoemulsificación, sustancia utilizada para la implantación de la lente intraocular (viscoelastico/solución salina balanceada). El primer día, a la semana y al mes postoperatorio se estudió paquimetría central, presión intraocular, grado de inyección conjuntiva bulbar (normal 0, inyección leve 1, inyección moderada 2, inyección severa 3), presencia o ausencia de dispersión de pigmento retroquerático, precipitados retroqueráticos, edema epitelial microquístico, estrías en la membrana de Descemet, estrías de la Descemet que comprometen el eje visual, discoria pupilar, ectopía pupilar, iridodonesis, edema estromal, eje visual comprometido por el edema estromal, características del edema corneal (focal/difuso) clasificación Van Herick de cámara anterior, efecto Tyndall en cámara anterior (< 1 cel/campo: grado 0, 2-15 cel/campo: grado 1+, 16-25 cel/campo: grado 2+, 26-50 cel/campo: grado 3+ , > 50 cel/campo: grado 4+)[14], presencia o ausencia de lente intraocular en cámara posterior, lente intraocular subluxada, lente intraocular luxada a cámara anterior, lente intraocular centrada. Además se determinó el equivalente esférico, agudeza visual mejor corregida, cambio refractivo miópico (diferencia de equivalente esférico superior a 1.5 dioptrías) y grado de opacidad capsular posterior (0-4) en el primer mes postoperatorio.

Evaluación estadística

La fuente de información fueron las historias clínicas sistematizadas y para la técnica de recolección se utilizó el auto-diligenciamiento del instrumento. Los datos se consignaron en un cues-

tionario estructurado con el programa Excel. Las variables cualitativas fueron codificadas para el procesamiento. La información se importó al programa IBM SPSS Statistics versión 22.0®. Previo a la construcción de la base de datos se revisó nuevamente el cuestionario a fin de evitar errores. Para verificar que los datos consignados en la base de datos fueran los correctos, los cotejó una persona distinta a la que había introducido los datos; también se eligieron al azar 20 registros y se verificaron los datos consignados para confirmar la concordancia de los mismos. Para la presentación y análisis de los resultados se emplearon para el componente descriptivo tablas univariadas, bivariadas y gráficos de conformidad con los objetivos específicos; las tablas se construyeron de acuerdo con el tipo de tabla y la naturaleza de las variables analizadas. El análisis descriptivo se efectuó para las variables cualitativas por medio de porcentajes y para las variables cuantitativas, mediana con el rango intercuartílico o la media y su desviación estándar. Al establecer diferencias entre los dos grupos de estudio los resultados se compararon: para variables cuantitativas a través de una prueba de U de Mann Whitney y para variables cualitativas, la significancia estadística por medio del Chi-cuadrado o prueba exacta de Fisher y su *p*, aceptándose la significancia, cuando *p* es < de 0.05.

Técnica quirúrgica y tratamientos postoperatorios

Los pacientes escogidos para el estudio fueron operados por un solo cirujano quien realizó la misma preparación (independientemente del tipo de catarata y por estar familiarizado con ambas técnicas; para el implante de la lente intraocular en algunas jornadas usó solución salina balanceada y en otras, viscoelástico). Hizo bloqueo peribulbar previa asepsia y antisepsia con povidona yodada al 10% en párpados y aplicación de colirio de brimonidina al 0,2%, moxifloxacino 0.5% y benoxinato clorhidrato (oxibuprocaína clorhidrato) al 0,4%. Realizó bloqueo usando 8 cc (4 cc peribulbar superior y 4 cc peribulbar inferior) obtenidos de la siguiente preparación: una ampolla de hialuronidasa + 50 cc de roxicaína simple al 2% de esta dilución se obtienen 4 cc que se mezclan con 4 cc de bupibacaína 0.25%. Posterior al bloqueo, el paciente se deja con un vendaje ocular con ligera compresión por 10 minutos y se traslada a la sala de operaciones (microscopio Moller Wedel). Posición decúbito supino, cabecera a 0 grados, campos quirúrgicos previa asepsia y antisepsia, povidona yodada al 10% para párpados y al 5% para aplicación ocular; se retira ésta con solución salina balanceada y se procede a realizar las paracentesis corneales periféricas en el meridiano de las 3 y 9 con cuchillete 15 grados. Se realiza incisión principal súpero-temporal con cuchillete 2.75 mm. Se hace tinción de cápsula anterior de cristalino con azul tripán y retiro de éste con solución salina balanceada. Se practica técnica del escudo maleable (*soft shell*)[25] con viscoelástico dispersivo de baja viscosidad (hialuronato de sodio al 3% + HPMC al 2% y luego un viscoelástico cohesivo: hialuronato de sodio al 1%. Se procede a la capsulorrexis circular continua con pinza utrata y con cánula de Gimbel y se practica hidrodisección e hidrodelaminación utilizando solución salina balanceada. Se rota el núcleo y se extrae con el sistema de facoemulsificación utilizando un equipo Alcon Accurus 800CS con la técnica de faco-chop. Se irrigan y aspiran restos corticales y en este momento la técnica cambia si en el paciente se quiere implantar el lio manteniendo la cámara con viscoelástico o si se usará hidroimplantación. En el primer caso coloca viscoelástico en cámara anterior hasta el grado que se expanda cámara y saco capsular y procede a implantar el LIO plegable. En el segundo caso luego de irrigar y aspirar la corteza se deja insertada la cánula de irrigación en cámara anterior y se procede a la implantación de la LIO hasta comprobar que esté en saco capsular. Independientemente de cuál sea la técnica utilizada, se coloca cloruro de acetil colina 1% en cámara anterior para miosis pupilar y se procede a aspirar restos de viscoelástico. Se practica sutura en incisión principal con nylon 10-0 y se hidratan incisiones.

El paciente sale de cirugía con fórmula de prednisolona 1% por un mes a dosis reductivas, moxifloxacino 0.5% por 10 días y acetaminofén 1 gramo cada 8 horas por cinco días. Se coloca parche ocular por 4 horas.

Tabla 1. Tiempo quirúrgico y agudeza visual mejor corregida primer mes postoperatorio con el rango intercuartílico (RIC) y valor de P.

	Grupo A n:20	**Grupo B n:26**	**Valor de P**
Tiempo quirúrgico (min)	27,00 (RIC: 25,00-29,00)	25,00 (RIC:20,00-25,00)	0,003
Agudeza visual mejor corregida primer mes postoperatorio (LogMAR)	0,19 (RIC:0,00-0,25)	0,10 (RIC:0,00-0,17)	0,296

Tabla 2. Media de la paquimetría central en los tiempos estudiados (µm), desvió estándar (σ), rango intercuartílico (RIC) y valor de P.

Paquimetría central (µm)	**Grupo A n=20**	**Grupo B n=26**	**Valor de P**
Preoperatoria	530 (σ 34,51) (RIC: 528-548)	543(σ 33,16) (RIC: 516-560)	0,244
Primer día del postoperatorio	742(σ 122) (RIC: 632-816)	731 (σ 65) (RIC: 691-763)	0,912
Primera semana del postoperatorio	583 (σ 67,23) (RIC: 542-617)	571 (σ37,8) (RIC:530-607	0,698
Primer mes del postoperatorio	541 (σ 40,95) (RIC: 516-563)	547 (σ 34,89) (RIC: 522-562)	0,868

Resultados

Los pacientes pertenecientes al grupo A tenían una media de edad de 69,85 y los del grupo B tenían una media de edad de 68,73 años (p=0,673). Esto nos muestra dos grupos homogéneos estadísticamente en cuanto a edad. Predominó el sexo femenino en ambos grupos (13 mujeres en el grupo A y 14 en el B). El ojo derecho fue el más operado (OD: 26 pacientes y OI: 20 pacientes). El antecedente de HTA fue encontrado en un 60% en el grupo A y un 58,70% en el grupo B. El antecedente de diabetes mellitus para el grupo A fue de 10% y el grupo B, 23,10%. Ningún paciente de ambos grupos tenía antecedente de retinopatía diabética (proliferativa o no proliferativa) ni vitrectomía por pars plana. Se encontró una mediana de equivalente esférico prequirúrgico para el grupo A de -0.50 dioptrías y para el grupo B de 0.00 dioptrías, y al mes posquirúrgico de -0,31 dioptrías grupo A y -0,87 dioptrías grupo B (p=0,292). El tiempo quirúrgico fue menor en el grupo B (p=0.003) (tabla 1). La mediana de agudeza visual mejor corregida prequirúrgica para el grupo A fue de 0,70 LogMAR y para el grupo B, 0,65 LogMAR. En los dos grupos la agudeza visual mejoró en el primer mes postoperatorio en comparación con el preoperatorio, los pacientes pertenecientes al grupo A tenían una mediana de agudeza visual mejor corregida primer mes post operatorio de 0,19 LogMAR, y los del grupo B 0,10 LogMAR (p 0,296) (tabla 2).

La profundidad de cámara anterior prequirúrgica fue para el grupo A de 3,05 mm y grupo B de 3,09 mm. En cuanto al grado de opacidad del cristalino en ambos grupos predominó N04NC4, 40% grupo A y 50% grupo B. El grado de opacidad de la corteza del cristalino predominante para ambos grupos fue C2, 70% grupo A y 53.8% grupo B. El grado de opacidad subscapular posterior predominante en ambos grupos fue SP1, 95% grupo A y 84.6% grupo B. La mediana de tiempo de faco para el grupo A fue de 27.5 segundos y grupo B 29 segundos. La mediana del porcentaje de faco para el grupo A fue de 28.50% y el grupo B 32.50%. Un 25% en el grupo A y una 26.9% en el grupo B presentó leve inyección de conjuntiva bulbar el primer día posquirúrgico. Esta variable estuvo ausente en los demás tiempos evaluados para los dos grupos. Un solo paciente del grupo

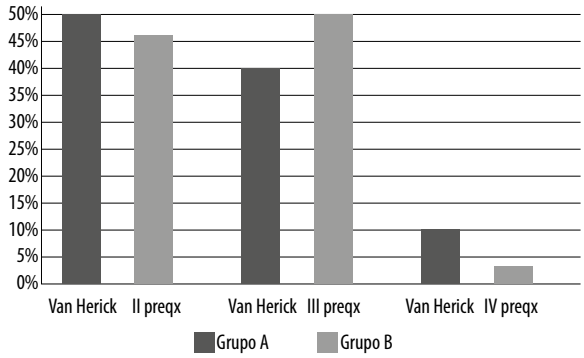


Figura 1. Van Herick prequirúrgico.

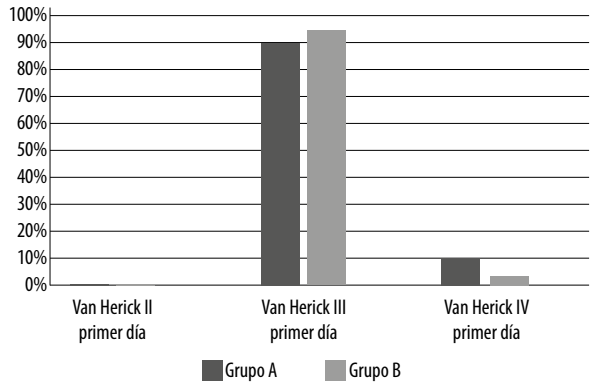


Figura 2. Van Herick primer día postoperatorio.

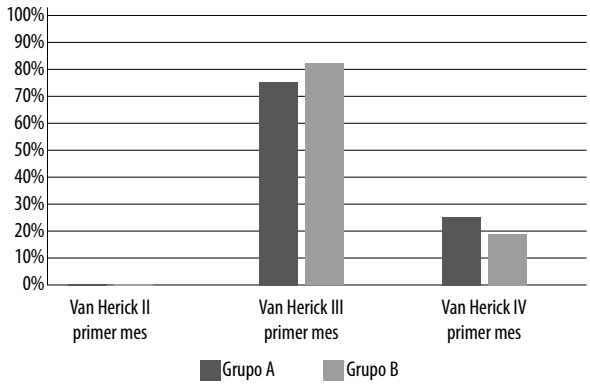


Figura 3. Van Herick primer mes post quirúrgico.

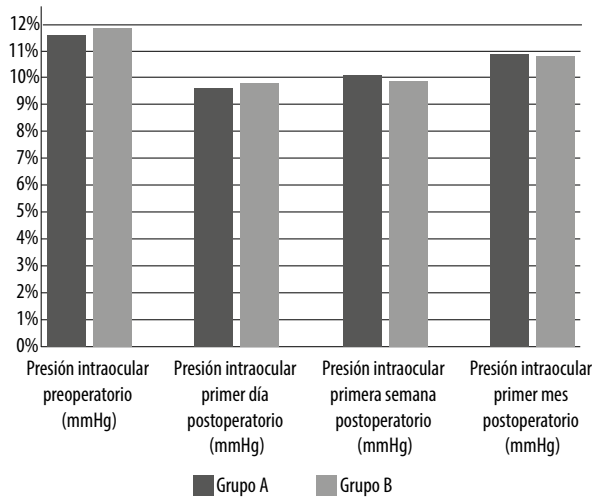


Figura 4. Presión intraocular (mmHg) en todos los tiempos evaluados.

de solución salina balanceada presentó precipitados retroqueráticos el primer día postoperatorio. Un solo paciente del grupo de viscoelastico presentó edema epitelial microquístico el primer día posquirúrgico (p=0.435) no encontrando este signo en los demás tiempos evaluados en ambos grupos. En los dos grupos se notó un aumento de la paquimetría el primer día posquirúrgico (fig. 1). Ningún paciente de ambos grupos presentó hipertensión ocular el primer día, a la semana o al mes de operado (fig. 4). La presencia de Tyndall en cámara anterior se observó en ambos grupos en un bajo porcentaje el primer día postoperatorio (grado 1: grupo A 15% y grupo B 3.8%; grado 2: grupo A 5% y grupo B 3.8%; grado 3: grupo A 0% y grupo B 15,4%) persistiendo hasta la semana también en un bajo porcentaje en el grupo A y no en el grupo B (grado 1 y 2 en 5% del grupo A y grado 0 un 100% en grupo B). En ambos grupos se encontró un aumento del Van Herick de cámara anterior posquirúrgico que se mantuvo en el transcurso del tiempo (figs. 2 y 3). En el primer día posquirúrgico el porcentaje de pacientes con edema estromal para el grupo A fue de 65% y grupo B 42.3%, en todos los casos fue difuso y comprometía el eje visual; en los demás tiempos evaluados el edema estromal estaba ausente. El ciento por ciento de pacientes del grupo A y 80.8% del grupo B presentó estrías en la membrana de Descemet el primer día posqui-

rúrgico (valor de p=0,059), un sólo paciente del grupo de solución salina balanceada tuvo estrías en la Descemet a la semana postoperatorio, este hallazgo no fue encontrado en los demás tiempos evaluados para ambos grupos. Se encontró cambio refractivo miópico en 9,1% del grupo A y 20,0% en el grupo B al mes postoperatorio (p=0,614). Para todos los tiempos posquirúrgicos estudiados en ambos grupos no se encontró dispersión de pigmento retroquerático, la facilidad de implantación de la LIO fue buena; no hubo discoria pupilar, ectopia pupilar, iridodonesis, lentes subluxadas, luxadas a cámara anterior. Todas los lentes de encontraban centradas en cámara posterior y al mes pop en ambos grupos todos los pacientes tuvieron opacidad grado 1 de cápsula posterior.

Discusión

Al comparar en este estudio a los pacientes que se les colocó viscoelástico oftálmico y en los que se usó solución salina balanceada para mantener la cámara anterior durante la implantación de la lente intraocular después de la facoemulsificación, se demostró que el tiempo quirúrgico es menor con el uso de solución salina balanceada en comparación con el uso de viscoelástico, siendo este el hallazgo con mayor significancia estadística (tabla 1). Tal hallazgo complementa lo encontrado por Ho Young Lee en Seúl, Corea[15]. En este estudio la agudeza visual de todos los pacientes mejoró al mes posquirúrgico comparada con el preoperatorio, no encontrando diferencias significativas entre los dos grupos estudiados (tabla 1). En los dos grupos se notó un aumento de la paquimetría el primer día posquirúrgico (tabla 2), no hubo diferencia significativa entre ambos, aunque en este estudio no se realizó recuento de células endoteliales. Este hallazgo es un dato indirecto del funcionamiento del endotelio tal como confirma lo encontrado en un estudio realizado en Europa con 60 ojos en donde se concluyó que la facoemulsificación conduce a modificaciones endoteliales[16]. Ningún paciente de ambos grupos presentó hipertensión ocular en los tiempos estudiados, tal hecho afirma lo encontrado en un estudio en la India en el 2013 en donde se concluyó que el único factor de riesgo que se relaciona con alta PIO es el antecedente de glaucoma[17]. En Pakistán se comparó la presión intraocular (PIO) postoperatoria entre la implantación de la lente intraocular usando hidroxipropilmetilcelulosa (HPMC) al 2% y la implantación de LIO por técnica de hidroimplantación después de facoemulsificación y llegaron a la conclusión de que en comparación con el uso de HPMC para la implantación de LIO, la hidroimplantación resultó en aumento insignificante de la PIO postoperatoria en 24 horas[18].

Según un estudio realizado en Francia luego de cirugía de catarata, ya sea extracapsular o por facoemulsificación, puede haber un pico de hipertensión ocular las primeras 5 horas de la cirugía con disminución de ésta a partir de las 18 horas posquirúrgicas[19]; sin embargo en este estudio no se investigó la presión a las 5 horas posquirúrgicas por lo que no se pudo confirmar este fenómeno, pero si se observó el descenso leve de la PIO a las 24 horas y en los demás tiempos estudiados.

En Pakistán y en Corea se realizaron estudios similares en donde se comparó la presión intraocular postoperatoria entre la implantación de la lente intraocular usando viscoelástico y la implantación de lente intraocular por técnica de hidroimplantación después de facoemulsificación. Encontraron elevación significativa de la PIO en el grupo de viscoelástico a las 24 horas postoperatorio no hallada en el grupo de hidroimplantación con descenso posterior de ésta al transcurrir el tiempo en ambos grupos[20-21], tal hallazgo no fue encontrado en el presente trabajo sin embargo puede estar relacionado con la completa remoción de viscoelástico que suele hacer el cirujano; que puede verse reflejado en el mayor tiempo quirúrgico encontrado para el grupo de viscoelástico en comparación con el grupo de solución salina balanceada, lo cual fue estadísticamente significativo (p>0,003). Además el uso de aplicación de colirio de brimonidina al 0,2% antes de la cirugía pudo prevenir a todos los pacientes este pico de hipertensión ocular, esto afirma lo reportado en un estudio en donde inmediatamente después de la facoemulsificación

se encontró que los hipotensores disminuyeron la presión intraocular de manera significativa a las 6 y a las 24 horas después de la cirugía[22].

La presencia de Tyndall en cámara anterior se observó en ambos grupos en un bajo porcentaje el primer día postoperatorio persistiendo hasta la semana también en un bajo porcentaje en el grupo de viscoelástico y no en el de solución salina balanceada. No se encontraron diferencias significativas entre los dos grupos estudiados, sin embargo tal hallazgo comprueba lo hallado por Petel y colaboradores en Estados Unidos quienes encontraron uveítis posquirúrgica en una de cada 400 cirugías de catarata[23]. En ambos grupos se encontró un aumento del Van Herick de cámara anterior posquirúrgico que se mantuvo en el transcurso del tiempo, lo que confirma lo registrado en la literatura: la remoción del cristalino aumenta la profundidad de la cámara anterior[24]. Llama la atención en este estudio que en el primer día posquirúrgico el porcentaje de edema estromal y estrías en la membrana de Descemet era mayor en los pacientes de viscoelástico que en los de solución salina balanceada, aunque no fue estadísticamente significativo (valor de p=0,059). No se han reportado hasta la fecha en las bases de datos bibliográficas estudios en donde se hayan analizado estrías en la Descemet entre dos grupos similares.

Con respecto al resto de variables estudiadas tampoco existen diferencias significativas postoperatorias entre el uso de viscoelástico oftálmico y la solución salina, evolucionando ambos grupos satisfactoriamente al mes postoperatorio. Si bien en este estudio no se han realizado mediciones directas de recuento endotelial y el seguimiento ha sido corto, los resultados sobre seguridad coinciden con los anteriormente publicados por Bianchi en su estudio sobre complicaciones intraoperatorias en procedimientos de facoemulsificación realizados sin la utilización de sustancias viscoelásticas[26].

Conclusión

En el presente estudio se encontró que la única diferencia estadísticamente significativa entre el uso de viscoelástico oftálmico y la solución salina balanceada para mantener la cámara anterior durante la implantación de la lente intraocular después de facoemulsificación es el tiempo quirúrgico que disminuye con la hidroimplantación y que ambas técnicas son seguras para la salud visual del paciente. Se hace necesario realizar otros estudios en donde se analicen otras variables tales como recuento de células endoteliales con el uso de las dos técnicas.

Referencias

1. O'Day DM. Management of cataract in adults: quick reference guide for clinicians. The Cataract Management Guideline Panel of the Agency for Health Care Policy and Research. *Arch Ophthalmol* 1993; 111: 453-459.

2. Desai P, Reidy A, Minassian DC *et al*. Gains from cataract surgery: visual function and quality of life. *Br J Ophthalmol* 1996; 80: 868-873.

3. Organización Mundial de la Salud. Ceguera y discapacidad visual [en línea], 11 oct. 2018. Disponible en: http://www.who.int/mediacentre/factsheets/fs282/es/

4. Galvis Ramírez V, Rey Serrano JJ, Rodríguez Villamizar LA. Prevalencia de ceguera en el Departamento de Santander, Colombia. *MedUNAB* 2009; 12: 66-73.

5. Pandey SK, Milverton EJ, Maloof AJ. A tribute to Charles David Kelman MD: ophthalmologist, inventor and pioneer of phacoemulsification surgery. *Clin Exp Ophthalmol* 2004; 32: 529-533.

6. Davis G. The evolution of cataract surgery. *Missouri Medicine* 2016; 113: 58-62.

7. Vajpayee RB, Verma K, Sinha R *et al.* Comparative evaluation of efficacy and safety of ophthalmic viscosurgical devices in phacoemulsification [ISRCTN34957881]. *BMC Ophthalmol* 2005; 5: 17.

8. Van den Bruel A, Gailly J, Devriese S *et al.* The protective effect of ophthalmic viscoelastic devices on endothelial cell loss during cataract surgery: a meta-analysis using mixed treatment comparisons. *Br J Ophthalmol* 2011; 95: 5-10.

9. Grzybowski A, Kanclerz P. Early postope-

rative intraocular pressure elevation following cataract surgery. *Curr Opin Ophthalmol* 2019; 30: 56-62.
10. Meier FM, Sarra GM, Stürmer JP. Hydrops des Kapselsacks nach Implantation faltbarer Acryllinsen [Capsular bag distention after implantation of foldable acrylic lenses]. *Klin Monbl Augenheilkd*. 2004; 221: 315-318.
11. Tak H. Hydroimplantation: foldable intraocular lens implantation without an ophthalmic viscosurgical device. *J Cataract Refract Surg* 2010; 36: 377-379.
12. Wilke R, Wagner B. *Van Herick's method for the estimation of the chamber angle*. Jena: Carl Zeiss Meditec (Publication no. 1276-334).
13. Chylack LT Jr, Wolfe JK, Singer DM *et al*. The lens opacities classification system III. The Longitudinal Study of Cataract Study Group. *Arch Ophthalmol* 1993; 111: 831-836.
14. Jabs DA, Nussenblatt RB, Rosenbaum JT. Standardization of uveitis nomenclature for reporting clinical data: results of the first International Workshop. *Am J Ophthalmol* 2005; 140: 509-516.
15. Lee HY, Choy YJ, Park JS. Comparison of OVD and BSS for maintaining the anterior chamber during IOL implantation. *Korean J Ophthalmol* 2011; 25: 15-21.
16. Chiotoroiu S, Pandelescu M, Epure C, Stefaniu I. Studiu comparativ al modificarilor endoteliale in chirurgia cataractei prin doua tehnici de facoemulsificare [Comparative study of endothelial changes in cataract surgery with phacoemulsification technique]. *Oftalmologia* 2008; 52: 95-99.
17. Coban-Karatas M, Sizmaz S, Altan-Yaycioglu R et al. Risk factors for intraocular pressure rise following phacoemulsification. *Indian J Ophthalmol* 2013; 61: 115-118.
18. Zia S, Iqbal Y, Ashraf KM, Mirza A. Intraocular pressure after IOL implantation with hydroxypropylmethylcellulose 2% vs hydro-implantation. *Pak J Ophthalmol* 2013; 29: 12-15.
19. Chahory S, Clerc B, Guez J, Sanaa M. Intraocular pressure development after cataract surgery: a prospective study in 50 dogs (1998-2000). *Vet Ophthalmol* 2003; 6: 105-112.
20. Zia S, Iqbal Y, Masood K, Mirza A. Intraocular Pressure after IOL Implantation with Hydroxypropylmethylcellulose 2% vs Hydro-implantation. *Pak J Ophthalmol*. 2013; 29(1):12-15.
21. Lee HY, Choy YJ, Park JS. Comparison of OVD and BSS for maintaining the anterior chamber during IOL implantation. *Korean J Ophthalmol* 2011; 25: 15-21.
22. Unal M, Yücel I. Effect of bimatoprost on intraocular pressure after cataract surgery. *Can J Ophthalmol* 2008; 43: 712-716.
23. Coban-Karatas M, Sizmaz S, Altan-Yaycioglu R, et al. Risk factors for intraocular pressure rise following phacoemulsification. *Indian J Ophthalmol* 2013; 61: 115-118.
24. Uçakhan OO, Ozkan M, Kanpolat A. Anterior chamber parameters measured by the Pentacam CES after uneventful phacoemulsification in normotensive eyes. *Acta Ophthalmol* 2009; 87: 544-548.
25. Arshinoff SA, Norman R. Tri-soft shell technique. *J Cataract Refract Surg* 2013; 39: 1196-1203.
26. Bianchi GR. ¿Faco sin visco y sin complicaciones?: estudio de complicaciones intraoperatorias. *Oftalmol Clin Exp* 2018; 11: 103-113.

Test de sobrecarga hídrica en pacientes con glaucoma en estadio avanzado-terminal

Eva de los Ángeles Medina, Marcos A. Geria, Javier F. Casiraghi

Sección Glaucoma, División Oftalmología, Hospital de Clínicas José de San Martín, Universidad de Buenos Aires, Argentina

Recibido: 10 de enero de 2020.
Aceptado: 29 de julio de 2020.

Correspondencia
Dra. Eva de los Ángeles Medina
Av. Córdoba 2351
(1120) Buenos Aires
+54-9-11-44305222
medinaeva@yahoo.com.ar

Oftalmol Clin Exp (ISSN 1851-2658)
2020; 13(3): 155-159.

Resumen

Objetivo: Evaluar los efectos del test de sobrecarga hídrica (TSH) sobre la presión intraocular (PIO) en pacientes con glaucoma de ángulo abierto en estado avanzado-terminal.
Método: Estudio clínico prospectivo en pacientes con glaucoma avanzado-terminal de ángulo abierto (con y sin cirugía previa de glaucoma, con y sin medicación), que realizaron el TSH (1 litro de agua administrado en 5 minutos) evaluando la PIO basal y a los 15, 30 y 45 minutos posteriores.
Resultados: los valores de PIO fueron (media y desvío estándar): *basal*: 12,61 ± 2,02 mmHg; *minuto 15*: 14,53 ± 3,17 mmHg; *minuto 30*: 16,15 ± 3,26 mmHg, y *minuto 45*: 14,84 ± 2,79 mmHG. Al comparar los resultados, se encontró una diferencia estadísticamente significativa al minuto 30 respecto de los valores basales (p=0,013).
Conclusión: Ingerir 1000 ml de agua en 5 minutos incrementa la PIO en pacientes con glaucoma avanzado-terminal. Otros estudios deberán evaluar la relevancia de estos hechos en situaciones similares, como son ecografías renovesicales, prostáticas y ginecológicas.
Palabras clave: test de sobrecarga hídrica, glaucoma, presión intraocular, cirugía de glaucoma.

Water load testing in patients with advance/end stage glaucoma

Abstract

Objective: To evaluate the effects of the water load test (WLT) on intraocular pressure (IOP) in

open-angle glaucoma patients with advanced/end-stage disease.
Method: Prospective clinical study conducted in patients with advanced/end-stage open-angle glaucoma (with and without prior glaucoma surgery, with and without medication) who underwent the WLT (1 liter of water administered over 5 minutes) and whose IOP at baseline and 15, 30 and 45 minutes after administration was measured.
Results: IOP values obtained were the following (mean and standard deviation): *Baseline:* 12.61 ± 2.02 mmHg; *Minute 15*: 14.53 ± 3.17 mmHg; *Minute 30*: 16.15 ± 3.26 mmHg, and *Minute 45*: 14.84 ± 2.79 mmHg. Comparison of the results evidenced a statistically significant difference at minute 30 vs. baseline values (p= 0.013).
Conclusion: Drinking 1000 ml of water over a period of 5 minutes increases IOP in patients with advanced/end-stage glaucoma. Further studies should evaluate the significance of these facts when patients have to undergo similar situations, such as kidney-bladder, prostate and gynecologic ultrasounds.
Keywords: water load test, glaucoma, intraocular pressure, glaucoma surgery.

Test de sobrecarga hídrica em pacientes com glaucoma avançado-terminal

Resumo

Objetivo: Avaliar os efeitos do teste de sobrecarga hídrica (TSH) na pressão intraocular (PIO) em pacientes com glaucoma de ângulo aberto em estado avançado-terminal.
Método: Estudo clínico prospectivo em pacientes com glaucoma avançado-terminal de angulo aberto (com e sem cirurgia de glaucoma anterior, com e sem medicação), que realizaram o TSH (1 litro de água administrado em 5 minutos) avaliando a PIO basal e aos 15, 30 e 45 minutos posteriores.
Resultados: os valores de PIO foram (média e desvio padrão): *basal*: 12,61 ± 2,02 mmHg; *minuto 15*: 14,53 ± 3,17 mmHg; *minuto 30*: 16,15 ± 3,26 mmHg, e *minuto 45*: 14,84 ± 2,79 mmHg. Ao comparar os resultados, se encontrou uma diferença estatisticamente significativa ao minuto 30, respeito dos valores basais (p=0,013).
Conclusão: Ingerir 1000 ml de água em 5 minutos incrementa a PIO em pacientes com glaucoma avançado-terminal. Outros estudos deverão avaliar a relevância destes fatos em situações semelhantes, como são ecografias renovesicais, prostáticas e ginecológicas.
Palavras chave: teste de sobrecarga hídrica, glaucoma, pressão intraocular, cirurgia de glaucoma.

Introducción

El test de sobrecarga hídrica (TSH) se comenzó a difundir en los comienzos de la década del 50 con la publicación de Leydhecker[1], que posteriormente confirman otros autores como una de las pruebas utilizadas para evaluar pacientes con glaucoma[2-4]. También desde hace muchas décadas se tiene conocimiento de la importancia de la ingesta de líquidos y la diuresis sobre la presión intraocular (PIO)[5]. Aunque se puso en duda su utilidad[6], actualmente sigue estando vigente en la evaluación de pacientes con glaucoma que fueron sometidos a diferentes tratamientos farmacológicos y quirúrgicos según recientes publicaciones[7-16].

Además otorga información indirecta del funcionamiento del trabeculado.

Por lo tanto, el objetivo del presente estudio ha sido evaluar el efecto del test de sobrecarga hídrica en la PIO en pacientes con glaucoma de ángulo abierto en estado avanzado-terminal.

Materiales y métodos

Diseño del estudio

Se realizó un estudio clínico prospectivo entre 2012 y 2014 en el Hospital de Clínicas José de San Martín de la ciudad de Buenos Aires, Argentina, que fue aprobado por el comité de ética del hospital de realización y fue diseñado y realizado siguiendo los lineamientos de la Declaración de Helsinki y, tras habérselo explicado a los pacientes, se obtuvo de cada uno su consentimiento informado para participar del estudio. Se incluyeron pacientes mayores de 18 años de edad de ambos sexos, con una agudeza visual de 1 a 4

décimas (1/10 a 4/10), que asistieron al servicio de glaucoma del hospital en el período mencionado, que tuvieran glaucoma de ángulo abierto y que estuvieran o no operados de glaucoma con y sin medicación.

Se constató por campo visual y evaluación del nervio óptico que el glaucoma se encontrara en estadio avanzado terminal según lo establecido por los criterios de daño de Hodapp-Parrish-Anderson (MD menor a -12 dB, n puntos p-5% mayor a 27 [50%], n puntos menor 1%:14 y en 5 grados centrales: cualquier punto 0 dB y en ambos hemicampos puntos igual o menor a 15dB) y una excavación papilar de 08 o peor.

Se excluyó a todo paciente con glaucoma de ángulo estrecho o cerrado que cursaran infecciones activas de la superficie ocular, alteraciones corneales, dificultad para colaborar en la tonometría de aplanación, insuficiencia renal, insuficiencia cardíaca y los que rechazaron el consentimiento informado.

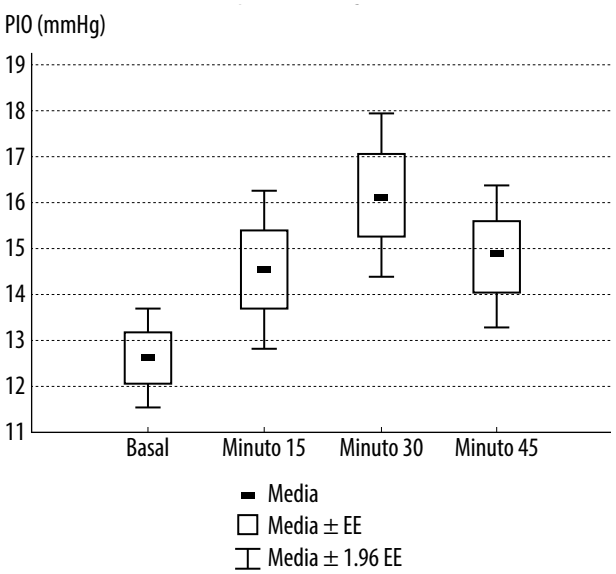


Figura 1. Variación de la presión intraocular evaluada antes y luego de la ingesta de un litro de agua a diferentes tiempos en 26 ojos.

Procedimiento de realización del TSH

El TSH consistió en: ingesta durante 5 minutos de 1.000 ml de agua potable previo ayuno total de al menos cuatro horas. Se realizó el registro de la PIO previo a la toma de agua (toma basal) y luego a distintos momentos: a los 15, 30 y 45 minutos. La toma de PIO la realizó siempre el mismo médico, con el mismo tonómetro de aplanación de Goldmann Haag Streit cuya calibración fue previamente controlada y con el paciente sentado frente a la lámpara de hendidura.

Evaluación estadística

Los datos se volcaron en una base de datos (tipo Excel) y luego se analizaron empleando el paquete estadístico: SPSS 16 BY SPSS INC (1989-2007). Se determinaron las distribuciones de frecuencia y las estadísticas descriptivas adecuadas para cada variable según su escala de medición y distribución. Se realizó el análisis de variancia (ANOVA) a mediciones repetidas para evaluar la existencia de diferencias estadísticamente significativas considerando: F = 6,35 y P = 0,001. Para establecer en qué momento aparecieron estas diferencias se compararon los pares de promedios entre sí (test de Bonferroni).

Resultados

Se incluyeron en total 26 ojos con glaucoma de ángulo abierto. Se dividieron los ojos en dos grupos: uno con solo gotas =18 ojos (17 con máxima medicación, es decir 3 drogas y un ojo con dos drogas) y otro con 8 ojos operados de glaucoma (un ojo solo tenía cirugía previa, un ojo recibía dos drogas y los 6 restantes recibían máxima medicación).

Los promedios de presión intraocular a lo largo de la prueba de sobrecarga hídrica se muestran en la figura 1.

Los valores de PIO encontrados a los diferentes tiempos fueron (media y desvío estándar): *basal*: 12,61 ± 2,02 mmHg;

minuto15: 14,53 ± 3,17 mmHg;

minuto 30:16,15 ± 3,26 mmHg y

minuto 45: 14,84 ± 2,79 mmHg.

Tras analizar los resultados, se detectó que la PIO al minuto 30 se incrementaba en forma esta-

dísticamente significativa respecto de los valores basales (p=0,013). Con un intervalo de confianza del 95% para las diferencias entre los promedios de PIO basal y 30 minutos, que varió entre 0,6 y 6,408 mmHg.

Discusión

De acuerdo con los resultados presentados, se ha encontrado que tras realizar el TSH con la ingesta rápida de 1 litro de agua, se genera un aumento de la PIO estadísticamente significativo a la media hora en un grupo de pacientes con glaucoma avanzado en estadío terminal. Esta prueba tiene gran vigencia actualmente dado que a pesar de los adelantos tecnológicos es de simple realización y de bajo costo. Su principal utilidad es que permite el seguimiento de pacientes con glaucoma pero no es de provecho para su diagnóstico por su baja sensibilidad (15,6%) a pesar de ser altamente específico (96,7%)[19]. Pueden existir variantes en su realización, dependiendo de la cantidad de líquido administrado (800 o 1000 ml)[15] o el tiempo entre medida y medida de PIO. Por ejemplo, Danesh-Meyers y colaboradores en su trabajo extendieron el tiempo de ingesta (15') y de mediciones de la PIO hasta 60 minutos, mostrando que la presión desciende a medida que transcurre el tiempo y que los picos son menores en pacientes operados de trabeculectomía con mitomicina C, comparado con los expuestos a terapéutica médica[20].

En nuestro trabajo el descenso de la PIO se evidenció ya después de los 30 minutos. Cabe destacar que habitualmente se realizan diferentes prácticas médicas diagnósticas en estudios complementarios, donde se requiere una ingesta de abundante líquido en un breve período de tiempo, como en las ecografías reno-vesicales, prostáticas y ginecológicas. Como se ha visto en este estudio, esto podría determinar el aumento de la PIO en pacientes con glaucoma avanzado. Hay estudios que han evaluado mediante el TSH el compromiso del campo visual en pacientes con glaucoma avanzado-terminal[16-22]. Estos son datos de este trabajo que deberían compartirse con otras especialidades, como clínica médica y diagnóstico por imágenes, y también con los propios pacientes, explicándoles que deben evitar la ingesta de mucho líquido en poco tiempo.

Teniendo en cuenta el mecanismo de acción del TSH, se podrían haber comparado las dos poblaciones de casos evaluados (de operados y no operados), ya que hay publicaciones que hablan sobre el diferente resultado del test en pacientes operados, aunque ese no fue el objetivo primario del presente estudio y puede ser interesante evaluarlo a futuro, en un diseño experimental específicamente armado para tal fin.

Conclusiones

Tras ingerir 1 litro de agua en 5 minutos se incrementa la PIO en pacientes con glaucoma avanzado-terminal. Teniendo en cuenta el delicado estado visual de estos pacientes y la necesidad de una presión intraocular baja y estable, sería aconsejable explicarles que deben evitar la ingesta abundante de líquido en cortos períodos de tiempo y tener presente su potencial riesgo ante situaciones médicas de práctica frecuente y difundida, como lo son la realización de ecografías u otros métodos de diagnóstico complementarios que requieran de una abundante ingesta de líquidos. Del mismo modo, para confirmar estos resultados será necesario realizar un futuro estudio con mayor número de casos.

Referencias

1. Leydhecker W. The water-drinking test. *Br J Ophthalmol* 1950; 34: 457-479.

2. Leydhecker W. Comparative provocative tests in glaucoma. *Br J Ophthalmol* 1950; 34: 535-544.

3. Campbell DA, Gloster J, Tonks EL. Some observations on the water drinking test in glaucomatous and non-glaucomatous subjects. *Br J Ophthalmol* 1955; 39: 193-203.

4. Winder AF, Siddiqui AA, Donovan HC. Ocular hypertension and systemic responses to the water-drinking test. *Br J Ophthalmol* 1978; 62: 414-419.

5. Campbell DA. Diuretics and the eye. *Br Med J* 1961; 2: 467-474.
6. Roth JA. Inadequate diagnostic value of the water-drinking test. *Br J Ophthalmol* 1974; 58: 55-61.
7. Susanna R Jr, Clement C, Goldberg I, Hatanaka M. Applications of the water drinking test in glaucoma management. *Clin Exp Ophthalmol* 2017; 45: 625-631.
8. Özyol P, Özyol E, Baldemir E. Intraocular pressure dynamics with prostaglandin analogs: a clinical application of the water-drinking test. *Clin Ophthalmol* 2016; 10: 1351-1356.
9. Muñoz CR, Macias JH, Hartleben C. Reproducibilidad de la prueba de sobrecarga hídrica. *Arch Soc Esp Oftalmol* 2015; 90: 517-521.
10. Razeghinejad MR, Tajbakhsh Z, Nowroozzadeh MH, Masoumpour M. Water drinking test: intraocular pressure changes after tube surgery and trabeculectomy. *J Ophthalmic Vis Res* 2017; 12: 390-396.
11. Razeghinejad MR, Tajbakhsh Z, Nowroozzadeh MH *et al*. The water-drinking test revisited: an analysis of test results in subjects with glaucoma. *Semin Ophthalmol* 2018; 33: 517-524.
12. Prata TS, Dias DT. The water-driking test and glaucoma progression: considerations regarding the test usefulness as an independent risk assessment tool. *J Glaucoma* 2018; 27: e25-e26.
13. De Moraes CG, Susanna R Jr, Sakata LM, Hatanaka M. Predictive value of the water drinking test and the risk of glaucomatous visual field progression. *J Glaucoma* 2017; 26: 767-773.
14. Scoralick ALB, Gracitelli CPB, Dias DT *et al*. Lack of association between provocative test-based intraocular pressure parameters and functional loss in treated glaucoma patients. *Arq Bras Oftalmol* 2019; 82: 176-182.
15. Mursch-Edlmayr AS, Luft N, Podkowinski D *et al*. Differences in optic nerve head blood flow regulation in normal tension glaucoma patients and healthy controls as assessed with laser speckle flowgraphy during the water drinking test. *J Glaucoma* 2019; 28: 649-654.
16. The Advanced Glaucoma Intervention Study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration. *Am J Ophthalmol* 2000; 130: 429-440.
17. Brubaker RF. Targeting outflow facility in glaucoma management. *Surv Ophthalmol* 2003; 48 Sup. 1: S17-S20.
18. Susanna R Jr, Vessani RM, Sakata L *et al*. The relation between intraocular pressure peak in the water drinking test and visual field progression in glaucoma. *Br J Ophthalmol* 2005; 89: 1298-1301.
19. Cronemberger S, Nassim C, Vieira Filho HM *et al*. Provocative tests, functional exams and daily curve of intraocular pressure in glaucoma suspects *Vision Pan-America* 2012; 11: 80-84.
20. Danesh-Meyer HV, Papchenko T, Tan YW, Gamble GD. Medically controlled glaucoma patients show greater increase in intraocular pressure than surgically controlled patients with the water drinking test. *Ophthalmology* 2008; 115: 1556-1570.
21. Mansouri K, Medeiros FA, Marchase N *et al*. Assessment of choroidal thickness and volume during the water drinking test by swept-source optical coherence tomography. *Ophthalmology* 2013; 120: 2508-2516.
22. Susanna R Jr, Clement C, Goldberg I, Hatanaka M. Applications of the water drinking test in glaucoma management. *Clin Exp Ophthalmol* 2017; 45: 625-631.

Silicone oil chiasmal syndrome: an atypical vitreoretinal complication

Macarena Clementi[a], Andrés Bastien[c], Pedro Lylyk[d, e], María Belén Nallino[f], Haydée Martínez[b], Muhammad Tariq Bhatti[g], Javier Casiraghi[b]

[a] *Hospital Central de San Isidro "Dr. Melchor Ángel Posse", Acassuso (Buenos Aires) Argentina.*

[b] *Hospital de Clínicas "José de San Martín", Buenos Aires, Argentina.*

[c] *Hospital Italiano de Buenos Aires, Argentina.*

[d] *Equipo de Neurocirugía Endovascular Radiología Intervencionista (ENERI), Buenos Aires, Argentina.*

[e] *Clínica La Sagrada Familia, Buenos Aires, Argentina.*

[f] *Diagnóstico Médico Oroño, Rosario (Santa Fe), Argentina.*

[g] *Departments of Ophthalmology and Neurology, Mayo Clinic College of Medicine, Rochester, Minnesota, USA.*

Received: April 13rd, 2020.
Accepted: July 21st, 2020.

Corresponding author
Macarena Clementi, MD
Av. Santa Fe 431
(B1641) Acassuso, Buenos Aires province
Argentina
+54 9-11 5856-2206
dramacarenaclementi@gmail.com

Oftalmol Clin Exp (ISSN 1851-2658)
2020; 13(3): 160-165.

Acknowledgement
Special thanks to Antonio Carrizo MD (Hospital Italiano of Buenos Aires), and Adriana Ojeda MD (Diagnóstico Médico Oroño, Rosario).
Conflict of interest statement and disclosure of any funding received for this work: this work was performed with the fund from the authors and they don't have conflict of interest to declare.

Abstract

Purpose: Present a case-based rare post-vitrectomy complication secondary to silicone oil (SO) migration through the visual pathway, to the central nervous system (CNS).
Case report: A 75-year-old woman consulted for acute decreased visual acuity (VA) in her left eye (OS), with history of stable glaucoma but IOP peaks in her right eye and no light perception after vitrectomy with SO 14 months prior. She had bilateral disc cupping and visual field loss compatible with a chiasmal syndrome. Magnetic resonance images showed SO in the visual pathway with progression to the intracranial subarachnoid space and into the ventricles, recovering VA and visual field (VF) in contralateral eye (OS) after the combined antiinflamatory corticotherapy and the ocular SO extraction in the right eye in order to discontinue the leakage inside the CNS.
Conclusions: Silicone oil optic neuropathy may be more frequent than diagnosed. It is therefore advisable to perform urgent neuroimaging studies in

patients with optic disk risk factors (cupping, congenital anomalies) associated to otherwise unexplained visual incoveniences in the fellow eye after a successful vitrectomy, since a neurosurgery could be avoided.
Keywords: chiasmal syndrome; silicone oil; silicone oil migration; vitrectomy; vitreoretinal surgical complications

Síndrome quiasmático por aceite de silicón: complicación atípica de cirugía vitreorretinal

Resumen

Objetivos: Presentar una rara complicación pos-vitrectomía a propósito de un caso con migración de aceite de silicón a través de la vía óptica hacia el sistema nervioso central (SNC).
Reporte de caso: Paciente de 75 años, femenina, consulta por disminución de agudeza visual (AV) en su ojo izquierdo (OI), con antecedentes de glaucoma estable, pero picos de hipertensión ocular y visión no luz pos-vitrectomía con colocación de aceite de silicón (AS) 14 meses previos. Presentaba excavación papilar y alteración del campo visual (CV) bilateral, compatible con un síndrome quiasmático. Las imágenes de resonancia magnética mostraron aceite de silicón en la vía óptica que progresó al espacio subaracnoideo intracraneal y luego hacia los ventrículos cerebrales. Recuperó su AV y CV en el ojo contralateral (OI) luego del tratamiento combinado de corticoterapia antiinflamatoria y extracción del AS intraocular del ojo derecho (OD), con el objeto de discontinuar la fuga al SNC.
Conclusión: La neuropatía óptica por aceite de silicón puede ser más frecuente de lo que se piensa, por lo que se recomienda realizar estudios de neuroimágenes urgentes en pacientes con discos ópticos de riesgo (excavados, anomalías congénitas) y molestias visuales en el ojo contralateral al operado, a pesar de una vitrectomía exitosa, ya que se puede evitar una intervención neuroquirúrgica.
Palabras clave: síndrome quiasmático; aceite de silicón; migración de aceite de silicón; complicaciones de cirugía vitreorretinal; vitrectomías.

Síndrome quiasmática por aceite de silicone: complicação atípica de cirurgia vitreorretinal

Resumo

Objetivos: Apresentar uma rara complicação pós-vitrectomia a propósito de um caso com migração de aceite de silicone através da via óptica para o sistema nervoso central (SNC).
Reporte de caso: Paciente de 75 anos, feminina, consulta por diminuição de acuidade visual (AV) em seu olho esquerdo (OI), com antecedentes de glaucoma estável, mas picos de hipertensão ocular e visão não luz pós-vitrectomia com colocação de aceite de silicone (AS) 14 meses prévios. Apresentava escavação papilar e alteração do campo visual (CV) bilateral, compatível com uma síndrome quiasmática. As imagens de ressonância magnética mostraram aceite de silicone na via óptica que progrediu ao espaço subaracnóidea intracraniana e logo para os ventrículos cerebrais. Recuperou sua AV e CV no olho contralateral (OI) logo do tratamento combinado de corticoterapia antiinflamatória e extração do AS intraocular do olho direito (OD), com o objetivo de descontinuar a fuga para o SNC.
Conclusão: a neuropatia óptica por aceite de silicone pode ser mais frequente do que se pensa, pelo que é recomendado realizar estudos de neuroimagens urgentes em pacientes com discos ópticos de risco (escavados, anomalias congênitas) e desconforto visual no olho contralateral ao operado, apesar de uma vitrectomia com sucesso, já que é possível evitar uma intervenção neurocirúrgica.
Palavras chave: síndrome quiasmática; aceite de silicone; migração de aceite de silicone; complicações de cirurgia vitreorretinal; vitrectomias.

Introduction

The silicone oil (SO) was introduced in 1962 for the treatment of retinal detachment by Cibis *et al*. and is selected according to the vitreoretinal pathology and the technique[1]. It has been described that is well tolerated for up to 6 months.

Later, complications were reported, such as emulsification, keratopathy, cataract formation, high IOP, closure of inferior iridectomies, migration to the subconjunctival space[2], and to the upper eyelid causing ptosis and rarely, retinal toxicity[3-5].

We report a case herein, where not only we describe silicone optic neuropathy as an atypical complication of vitreoretinal surgery, but also how the diagnosis was arisen after recognizing a chiasmal syndrome, and neuroimages were opportunely done and analyzed in order to treat promptly avoiding devastating visual consequences, and also neurosurgical intervention.

Case report

A 75-year-old woman consulted for acute decreased visual acuity (VA) (20/40) in her left eye (OS). She had history of glaucoma diagnosed 20 years ago, trabeculoplasty and cataract surgery in both eyes (10 years ago) and vitreoretinal surgery with SO 1000 centistokes (cs), followed by ocular hypertension in right eye (OD) (40 mmHg) with very poor visual recovery (no light perception), 14 months prior to consultation.

Her IOP was normal (OD 15 mmHg, OS 9 mmHg); with bilateral relative afferent pupillary defect (RAPD), most accentuated in OD, and color vision was impaired OS with the Ishihara color plates. The fundoscopy showed bilateral glaucomatous atrophy, (megalopapillae with 0.9 cup-disk excavation) and generalized pallor, more in the temporal area of the disk, with applicated retina in OD (Fig. 1).

An Octopus G1X visual field (VF) showed amaurosis in OD and inferior-nasal remanent in OS (Fig. 1).

Differential diagnoses of optic neuropathies were considered rapidly: giant cell arteritis was ruled out (normal Erythrocyte Sedimentation Rate and C-Reactive Protein test, normal temporal arteries ultrasonography); and also rheumatology lab routine was done arousing negative results.

A brain magnetic resonance image (MRI) study ruled out a sellar tumor, but the findings were the most unusual: Fluid-Attenuated Inversion Recovery (FLAIR), T1 and T2 scans showed hyperintense material in the right optic nerve as chiasmal region, and this material showed to be hypointense in T1 images with fat suppression and gadolinium (both characteristics of the silicone oil); in the right eye and optic chiasm (Fig. 2a-b).

After 1 month of observation and corticotherapy (4 intramuscular dexamethasone injections separated for 7 days), a surgery was performed to extract the intraocular SO from OD. After that, the MRI findings showed migration of this substance to the cerebral subarachnoid space (Fig. 2c), and a notorious increase in OS VA to 20/20 as well as her VF recovery, from a week after the initial treatment (only superior arcuate scotomatous defect, related with her previous glaucomatous disease) and still stable after a year-follow-up.

Discussion

After an extensive literature review, we can say that intracranial (subarachnoid and intraventricular) migration of SO from the vitreous cavity of the eye is a rare phenomenon, with approximately 25 cases reported in the literature[6], firstly reported in 1983 by Ni *et al.*, intravitreal SO has been demonstrated in pathological specimens in the retrolaminar optic nerve causing visual loss due to an optic neuropathy[7].

In this article we report a new case with a chiasmal syndrome presentation (worsening in VA, temporal hemianopia and infero-nasal remanent, pupillary reflex and color vision impairment, as well as optic disk pallor).

As Boren *et al.* described, the retrolaminar migration of intraocular SO can be presumed to be related to the dimension of the optic disk (big disks), high IOP, and the determining fact of a vitreoretinal surgery with SO, which stimulates the leakage through the lamina cribosa[6].

Another case described the same pattern that also affects the retrochiasmal optic tract[8] and Eckle *et al.* also report a similar case: a 66 year-old-man that had a vitreoretinal surgery secondary to retinal detachment in OS with the introduction of SO with atrophic and glaucomatous optic disk[9]. The patient suffered a VF defect in the fellow eye (although VA was 20/20) in association with chi-

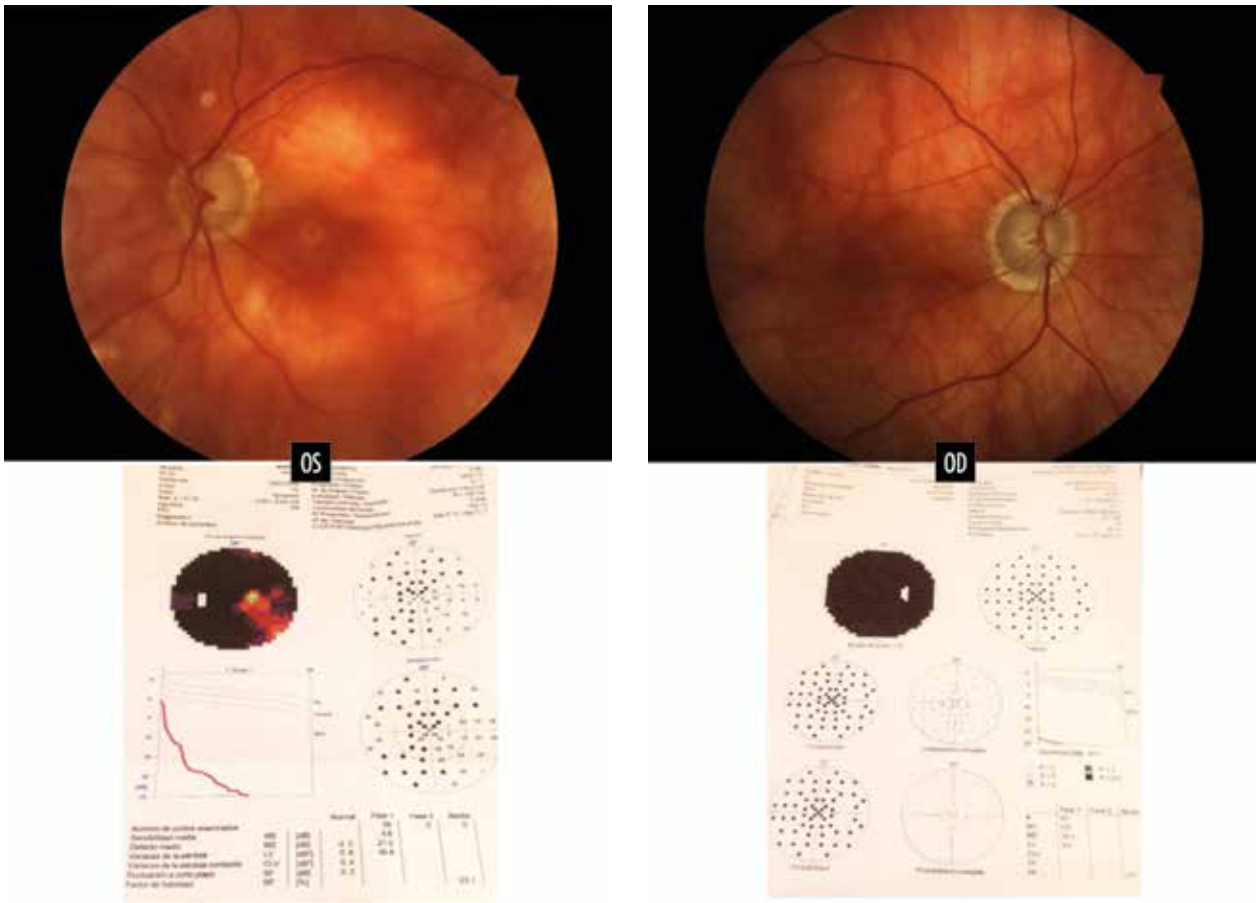


Figure 1. Retinography and VF OS and OD.

asmal migration of intraocular SO, and resulted in neurosurgery (which was the *principal difference* with the present case who recovered with systemic corticosteroids): left optic nerve sheath fenestration, with posterior suction of the SO and irrigation. And VF was recovered after surgery.

The pathophysiology is also uncertain. Possibly, the SO penetrates the subarachnoid space through the laminar holes and dehiscences (demonstrated on behalf optical coherence tomography [OCT] in glaucomatous eyes), or through the space where the vessels penetrate the optic nerve (both central retinal artery and central retinal vein). This route was also proposed as an explanation for cases of Terson's syndrome, as well as the pseudo-Schnabel's degeneration, where the lamina cribosa reflects the infiltration of silicone vacuoles. The Schnabel's degeneration itself is the ischemic necrosis of the retrolaminar optic nerve in acute glaucoma creating cystic spaces; that filled with vitreous humor create a reflection in this location. Carol L. Shields *et al*. in 1989 explains why many retinal detachments are successfully operated, but have poor vision, remarking the idea that "in glaucomatous eyes, intraocular SO appears to have a worrisome potential for posterior migration into the central nervous system (CNS)"[10].

OCT images can actually help us to recognize a possible infiltration of this substance in the retina, since it's been described that there could be seen different findings such as thinning of the ganglion cell layer and microcystic changes in the inner nuclear layer of the retina, even thought not specific for SO, since it could also be seen in other eti-

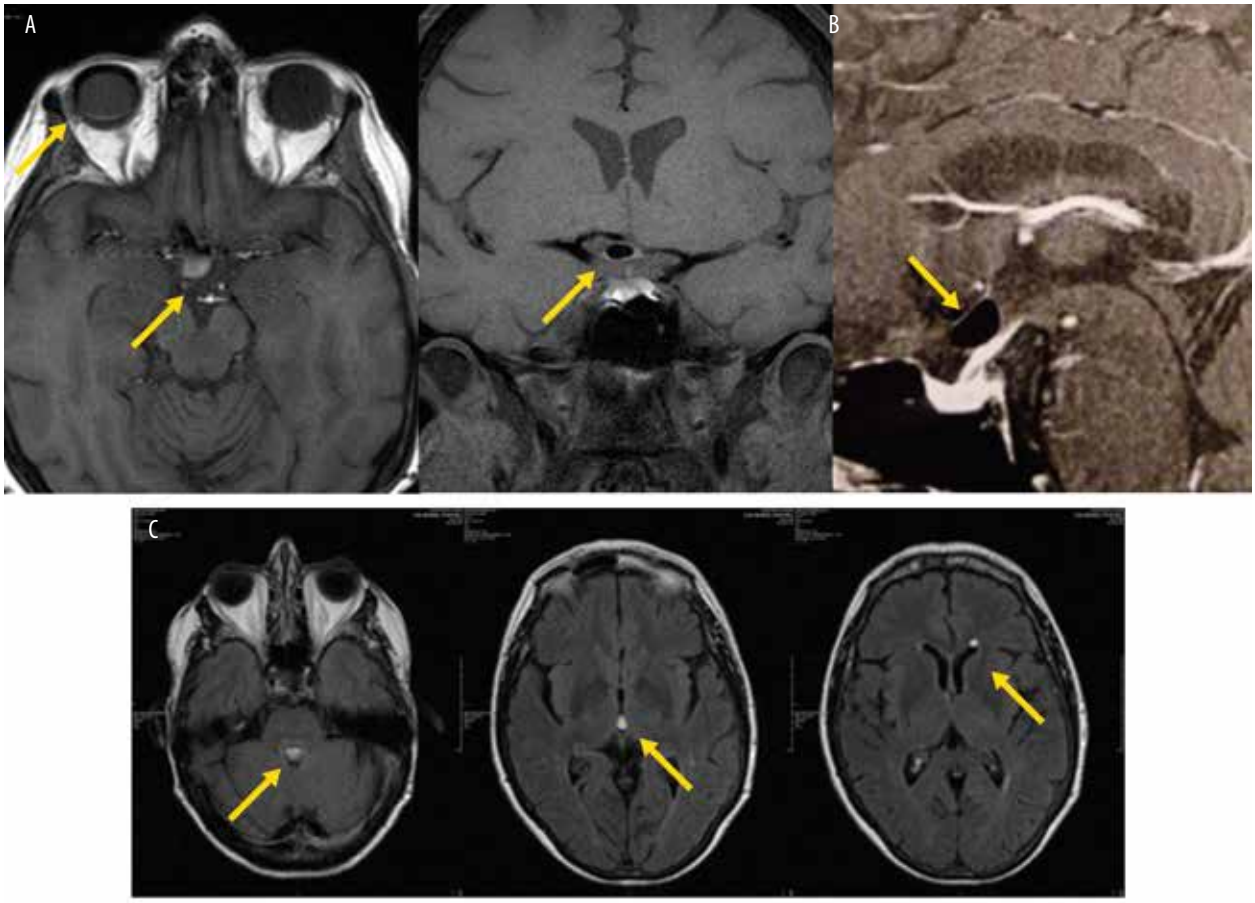


Figure 2. Brain MRI. (A) Axial T1-weighted image showing SO in right vitreous cavity, optic nerve and chiasm. (B) Coronal and sagittal T1-weighted, fat suppressed and gadolinium images showing SO inside the chiasm. (C) Axial T1-weighted images with the SO in fourth, third and lateral ventricles. Arrows indicate the location of silicone oil.

ologies such as Leber's hereditary optic neuropathy and multiple sclerosis-associated optic neuritis[11-12]. However, neuroimaging would be crucial in this case for the specific detection of the infiltration of SO in the CNS. Pathognomonic imaging findings should be taken into consideration, mostly when differentiating from blood, and in cases where there is the precedent of a retinal detachment surgery. Blood can be determined as 30-60 Hounsfield units (HU) and SO on average of 82 HU in computed tomography (CT) images. The appearance of intraocular SO has been described to be hyper-intense relative to contralateral humoral vitreous on T1 weighted and hyper-, hypo- or iso-intense on T2 -weighted MRI sequences, these variations probably due to the different viscosities of the oil (more viscosity will be more hypo-intense on T2 scans), and therefore since our patient received 1000 cs SO, it appeared more hyperintense in T2 scans, with respect to 5000 cs SO tamponades[13]. Several MRI protocols are used to determine SO detection and include short T1 inversion recovery (STIR: single tau inversion recovery sequence) or FAT-SAT which suppress the signal originating from fat leaving the water signal unaffected, and T1 and T2-turbo spin echo (TSE) sequences. Silicone has a different relaxation time than the one of tissue-fat, which at 1.5 Tesla has a radiofrequency approximately 440 Hz lower than the frequency of water[14]. In our case, neuroimaging interpretation

was the key to determining the etiology, fat-supression generated hypointense signal (T1 FAT-SAT). *We suggest the best protocol for the detection of silicone oil is fat-suppression fast T1 and T2 weighted MRI images with gadolinium.*

How long should the SO remain in the operated eye is still unclear, especially in patients with high postoperative IOP as well as pre-existing glaucoma, and with optic disk risk factors such as: megalopapillae, optic pit, morning glory. These should be considered for the management of these patients before and after vitrectomy. Nevertheless, there is much more to be studied to understand the pathophysiology of our patient, as well as the characteristics of the SO used in the surgical procedure. Although Hruby Paul *et al.* described headaches secondary to intraventricular SO successfully managed with ventriculoperitoneal shunt[15-16], amongst other authors, it's almost innocuous to the CNS[17], with no significant complications described to the actual moment.

In conclusion, silicone oil optic neuropathy may be more frequent than diagnosed. It is therefore advisable not only to perform a detailed ophthalmologic exam, but also neuroimaging studies in patients with otherwise *unexplained VA or VF loss after successful vitrectomy in the contralateral eye.*

References

1. Cibis PA, Becker B, Okun E, Canaan S. The use of liquid silicone in retinal detachment surgery. *Arch Ophthalmol* 1962; 68: 590–599.

2. De Bernardo M, Iaccarino G, Russo V, Rosa N. Echographic evaluation of a subconjunctival cystic lesion. *Case Rep Ophthalmol Med* 2017; 2017: 5401850.

3. Quintyn JC, Genevois O, Ranty ML, Retout A. Silicone oil migration in the eyelid after vitrectomy for retinal detachment. *Am J Ophthalmol* 2003; 136: 540-542.

4. Deguchi Y, Maeno T, Hori Y *et al.* Migration of intraocular silicone oil from the vitreous cavity into the upper eyelid causing ptosis. *Case Rep Ophthalmol* 2014; 5: 226-230.

5. Dehghani A, Rezaei L, Tavallali A, Dastborhan Z, et al. Upper eyelid silicone oil migration after sutureless 23-gauge vitrectomy. *Adv Biomed Res* 2017; 6: 58.

6. Boren RA, Cloy CD, Gupta AS *et al.* Retrolaminar migration of intraocular silicone oil. *J Neuroophthalmol* 2016; 36: 439-447.

7. Ni C, Wang WJ, Albert DM, Schepens CL. Intravitreous silicone injection: histopathologic findings in a human eye after 12 years. *Arch Ophthalmol* 1983; 101: 1399-1401.

8. Bobba S, Fox OJK, Lee MB *et al.* Contiguous silicone oil migration from the vitreous cavity to the optic tract. *J Neuroophthalmol* 2017; 37: 464-465.

9. Eckle D, Kampik A, Hintschich C *et al.* Visual field defect in association with chiasmal migration of intraocular silicone oil. *Br J Ophthalmol* 2005; 89: 918-920.

10. Shields CL, Eagle RC Jr. Pseudo-Schnabel's cavernous degeneration of the optic nerve secondary to intraocular silicone oil. *Arch Ophthalmol* 1989; 107: 714-717.

11. Caramoy A, Droege KM, Kirchhof B, Fauser S. Retinal layers measurements in healthy eyes and in eyes receiving silicone oil-based endotamponade. *Acta Ophthalmol* 2014; 92: e292-e297.

12. Shalchi Z, Mahroo OA, Shunmugam M *et al.* Spectral domain optical coherence tomography findings in long-term silicone oil-related visual loss. *Retina* 2015; 35: 555-563.

13. Herrick RC, Hayman LA, Maturi RK *et al.* Optimal imaging protocol after intraocular silicone oil tamponade. *AJNR Am J Neuroradiol* 1998; 19: 101-108.

14. Kiilgaard JF, Milea D, Løgager V, la Cour M. Cerebral migration of intraocular silicone oil: an MRI study. *Acta Ophthalmol* 2011; 89: 522-525.

15. Hruby PM, Poley PR, Terp PA *et al.* Headaches secondary to intraventricular silicone oil successfully managed with ventriculoperitoneal shunt. *Retin Cases Brief Rep* 2013; 7: 288-290.

16. Grzybowski A, Pieczynski J, Ascaso FJ. Neuronal complications of intravitreal silicone oil: an updated review. *Acta Ophthalmol* 2014; 92: 201-204.

17. Papp A, Tóth J, Kerényi T *et al.* Silicone oil in the subarachnoidal space: a possible route to the brain? *Pathol Res Pract* 2004; 200: 247-252.

Absceso corneal de evolución tórpida

Diego Desio[a, b], Patricio Grayeb[b], Fernando Pellegrino[b], Diego Ramírez Arduh[a], Gabriela Esperanza[a], Norma Apestey[b], Paula Anauati[b], Federico Guisasola[b]

[a] *Centro de la Visión, Paraná, Entre Ríos, Argentina.*

[b] *Hospital Oftalmológico Santa Lucía, Buenos Aires.*

Recibido: 2 de julio de 2020.
Aprobado: 2 de agosto de 2020.

Correspondencia
Dr. Diego D. Desio
Malvinas 91
(3100) Paraná, Entre Ríos.
+54 0343 423 2405
diegodesio@hotmail.com

Oftalmol Clin Exp (ISSN 1851-2658)
2020; 13(3): 166-172.

Resumen

Objetivo: Presentar un caso clínico complejo de queratitis infecciosa de difícil tratamiento.
Caso clínico: Paciente de 35 años de edad de sexo femenino con absceso corneal avanzado de evolución tórpida en ojo derecho. Tras toma de muestras (raspado corneal para examen directo, microbiológico, cultivo y antibiograma) y tratamiento empírico con colirios fortificados, se requirió realizar recubrimiento conjuntival y trasplantes de córnea en cuatro ocasiones, además de una cirugía de cataratas 8 meses luego del último trasplante, hasta lograr la resolución de la infección. Se identificaron como agentes causales: *Staphylococcus aureus*, hongos universales y *Acanthamoeba spp*.
Conclusión: Ante la evolución errática en queratitis infecciosa, se debe sospechar su origen polimicrobiano y utilizar todos los recursos terapéuticos y clínico-quirúrgicos para su resolución. Se subraya la importancia de intentar la identificación del agente causal para realizar un tratamiento específico.
Palabras clave: absceso corneal, queratitis infecciosa, recubrimiento conjuntival, injerto corneal.

Corneal abscess of torpid evolution

Abstract

Objective: To report a complex clinical case of difficult-to-treat infectious keratitis.

Clinical case: Thirty-five-year-old female patient with an advanced corneal abscess of torpid evolution in her right eye. After sample collection (corneal scraping for direct and microbiological examination, culture and antibiogram) and empirical treatment with fortified eye drops, conjunctival flaps and corneal grafts were required on four occasions, in addition to cataract surgery 8 months after the last graft, until resolution of the infection was achieved. The causative agents identified were: *Staphylococcus aureus*, universal fungi and *Acanthamoeba spp*.

Conclusion: When faced with a case of infectious keratitis of erratic evolution, a polymicrobial origin should be suspected and all the therapeutic and clinico-surgical resources should be used for its resolution. The importance of trying to identify the causative agent involved in order to administer specific therapy is hereby stressed.

Keywords: corneal abscess, infectious keratitis, conjunctival flap, corneal graft.

Abscesso de córnea de evolução tórpida

Resumo

Objetivo: Apresentar um caso clínico complexo de ceratite infecciosa de difícil tratamento.

Caso clínico: Paciente de 35 anos de idade de sexo feminino com abscesso de córnea avançado de evolução tórpida em olho direito. Após colheita de amostras (raspagem da córnea para exame direto, microbiológico, cultura e antibiograma) e tratamento empírico com colírios fortificados, foi preciso realizar revestimento conjuntival e transplantes de córnea em quatro ocasiões, além de uma cirurgia de cataratas 8 meses logo do último transplante, até obter a resolução da infeção. Identificaram-se como agentes causais: *Staphylococcus aureus*, fungos universais e *Acanthamoeba spp*.

Conclusão: Frente à evolução inestável em ceratite infecciosa, se deve suspeitar sua origem polimicrobiano e utilizar todos os recursos terapêuticos e clínico-cirúrgicos para sua resolução. Se salienta a importância de intentar a identificação do agente causal para realizar um tratamento específico.

Palavras chave: abscesso de córnea, ceratite infecciosa, revestimento conjuntival, enxerto corneal.

Introducción

La afectación de la córnea por agentes infecciosos puede tener efectos devastadores para la visión, pudiendo afectar la transparencia e incluso la estructura corneal, debilitándola hasta su perforación[1]. Generalmente las queratitis infecciosas severas suelen producirse en ojos con factores predisponentes, como pueden ser diferentes enfermedades crónicas de superficie ocular[2-3], antecedentes de cirugías corneales o que hayan atravesado la córnea[4] o en pacientes usuarios de lentes de contacto[5-6]. También resulta importante el antecedente de traumatismo ocular y cualquier situación que pueda generar una ruptura del epitelio o altere la homeostasis del sistema de defensa ocular[3].

En lo que respecta a sus agentes causales, las más frecuentes son las queratitis bacterianas, que representan entre el 65% y el 90% de las infecciones corneales, y en su mayoría son producidas por especies cocos Gram positivos (80%)[7-9]. Las infecciones fúngicas representan entre el 10% y el 15% en países en vías de desarrollo[10-11]. La incidencia de nuevas queratitis por HSV (enfermedad tanto epitelial como estromal) es de 18 a 25 por 100.000 con tasas de recurrencia estimadas en 50% a los 5 años y más de 60% a los 20 años[12-13]. Dentro de las queratitis por parásitos, las amebas del género *Acanthamoeba* son agentes causales de una infección corneal grave y difícil de diagnosticar con una prevalencia estimada de 1-9 en cien mil[14-15]. Un porcentaje variable (3%-21%) de los casos es polimicrobiano, combinando distintas bacterias, hongos o amebas[6-9, 11].

Por lo tanto, el objetivo de este trabajo es presentar un caso clínico de un paciente con un absceso de córnea de difícil manejo y describir su evolución clínica, diagnósticos etiológicos en contexto polimicrobiano y su tratamiento clínico-quirúrgico.

Caso clínico

Se presenta a la consulta una paciente de sexo femenino de 35 años de edad que refiere dolor ocular derecho de un mes de evolución. El ante-

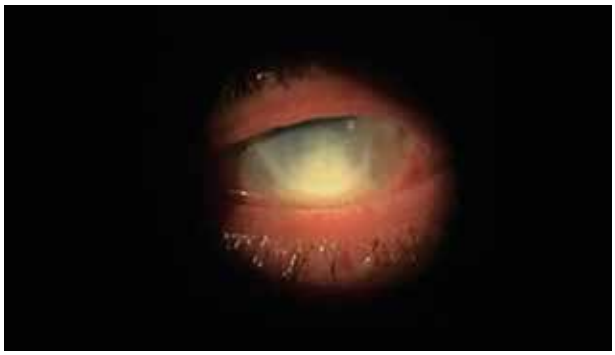


Figura 1. Infiltrado corneal anular con afectación de la cámara anterior.

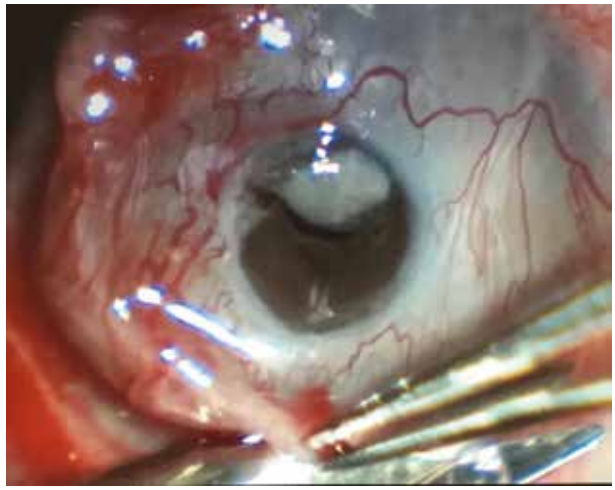


Figura 2. Perforación corneal. Nótese el recubrimiento conjuntival previamente realizado.

cedente asociado era que en el trabajo (oficinista) le entró una "basurita" en el ojo derecho. Concurrió a varias consultas oftalmológicas donde le indicaron múltiples colirios/ungüentos (ciprofloxacina 0.3%, moxifloxacina 0.5%, eritromicina 1% ungüento, ganciclovir 0.15%, atropina 1%) durante 30 días, sin haber notado mejoría. Anteriormente sus controles oftalmológicos habían sido normales, según refirió.

En la evaluación oftalmológica, la agudeza visual del ojo izquierdo era normal (10/10) sin corrección y tenía visión bulto en el ojo afectado, donde se observaba la presencia de un absceso corneal de forma anular central mayor a 6 milímetros con gran adelgazamiento del estroma corneal central y compromiso de cámara anterior (fig. 1). Ante este aspecto, como posibles diagnósticos diferenciales se postularon los siguientes: infección por *Pseudomonas*, *Acanthamoeba*, micosis, herpes y abuso de anestésicos. La paciente negó el uso de anestésicos tópicos y de lentes de contacto (ni con graduación, ni cosméticos).

Se realizó toma de muestras mediante raspado corneal para examen de directo y de estudio microbiológico (cultivo y antibiograma) y comenzar con tratamiento de colirios fortificados de vancomicina 50 mg/ml y ceftazidima 50 mg/ml cada hora y ganciclovir 0.15% cada 4 horas. A las 72 horas, el directo y cultivo fueron negativos y, debido a la mala evolución del cuadro, se decidió realizar recubrimiento conjuntival y tenoniano bipediculado.

Se mantuvieron antibióticos fortificados tópicos por 2 meses y luego controles frecuentes. A los 6 meses del recubrimiento conjuntival se presentó de urgencia por molestias y se diagnosticó perforación corneal central (fig. 2). Se decidió realizar un injerto corneal en caliente de 7.50 mm de diámetro. Se tomaron muestras por raspado corneal para directo y cultivo que informó presencia de estafilococo *aureus* sensible a vancomicina. Se reinició tratamiento con colirios fortificados de vancomicina 50 mg/ml y ceftazidima 50 mg/ml cada dos horas, que luego se fueron disminuyendo gradualmente hasta mantener en tres veces por día. Se utilizó también prednisolona acetato 10 mg/ml cada seis horas y atropina 1% cada doce horas.

A mes del injerto, comenzó en la córnea receptora un infiltrado anular que avanzó centrípetamente. Su evolución terminó en una nueva perforación, en el sector de la unión donante receptor, a nivel inferior (fig. 3). Se indicó un segundo injerto corneal en caliente, esta vez de 8.00 mm de diámetro. Se tomaron nuevas muestras para análisis microbiológico y PCR para hongos. Ante la sospecha de una coinfección corneal por hongos se inició, junto con el tratamiento previo, una

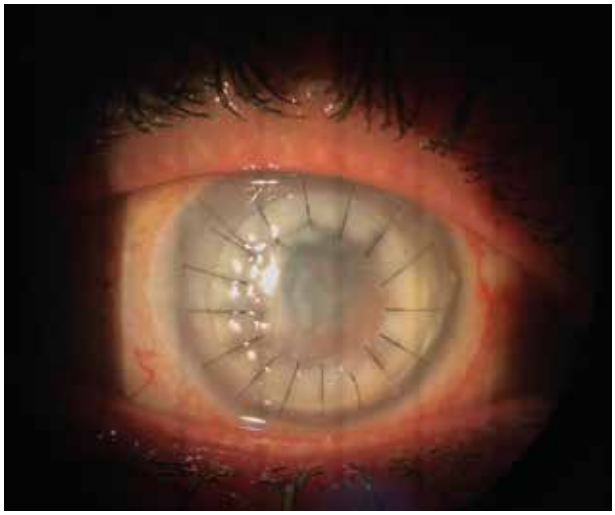


Figura 3. Infiltración corneal sobre injerto corneal y en la zona de unión, en el primer transplante realizado.

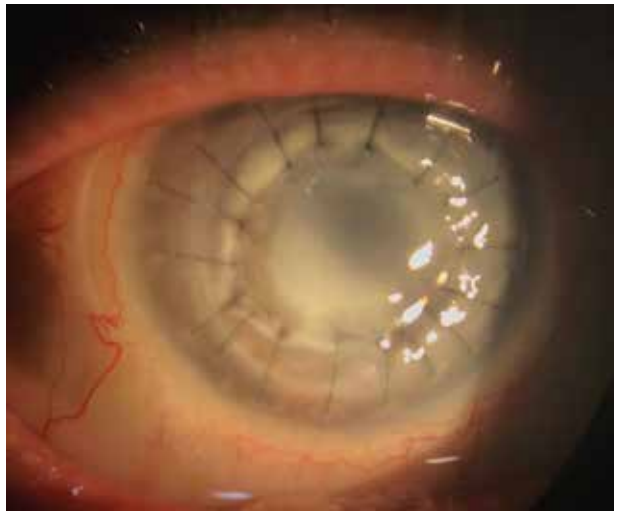


Figura 4. Colagenolisis periférica y pérdida de estructura (perforación) en el segundo transplante de córnea realizado.

terapia tópico-empírica con colirios de anfotericina 50mg/ml, voriconazol 1% y fluconazol cada dos horas, además de fluconazol 200 mg por vía oral cada doce horas. Los resultados del directo y cultivo fueron negativos y la PCR para hongos no se pudo realizar por motivos económicos.

A los 30 días del segundo injerto se volvió a ver un infiltrado estromal en la unión donante-receptor por lo que se decidió realizar inyecciones intraestromales e intracamerales de anfotericina 10 µg, dos dosis separadas por una semana. Pero a pesar de los tratamientos al mes y 5 días se observó una nueva perforación corneal en la unión donante-receptor a nivel inferior (fig. 4).

Se realizó un tercer injerto corneal en caliente de mayor diámetro (8.5 mm). Se tomaron muestras para análisis con PCR y anatomía patológica. El resultado de la PCR a las 24 horas fue positivo para hongos universales sin poder identificar el tipo de hongo. A los 9 días el resultado de la anatomía patológica informó quistes de *Acanthamoeba* (recordamos que la paciente no era usuaria de lentes de contacto) y al mismo tiempo el examen directo informó la presencia de quistes de *Acanthamoeba*. Se continuó con el mismo tratamiento local y oral pero se agregó polihexametileno biguanida (PHMB) al 0.02% y clorhexidina 0.02%, ambas de forma tópica y a cada hora.

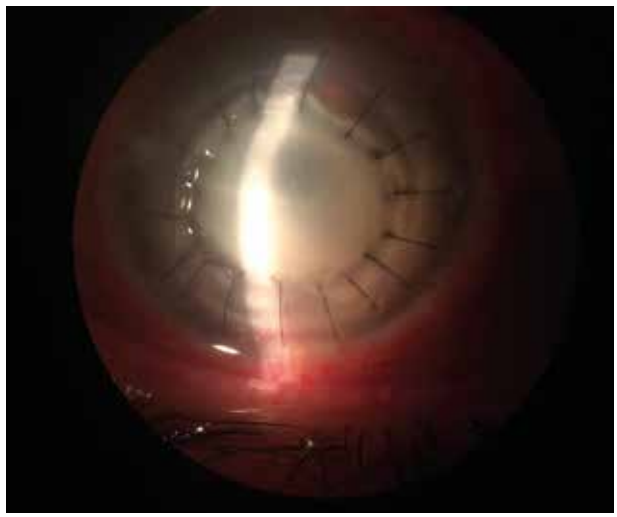


Figura 5. Recidiva de la infección en el tercer transplante corneal.

La evolución del tercer injerto corneal parecía ser favorable sin evidencia de recidiva del absceso corneal en la córnea receptora. Pero a pesar de haber estado manteniendo el tratamiento tópico, dos meses más tarde apareció un infiltrado corneal en la unión donante receptor y a nivel central (fig. 5). Ante tan mala evolución, 15 días después se realizó un cuarto injerto corneal "en caliente" de 8.5 mm.

La evolución del último injerto corneal fue favorable en el tiempo y sin signos de recidiva

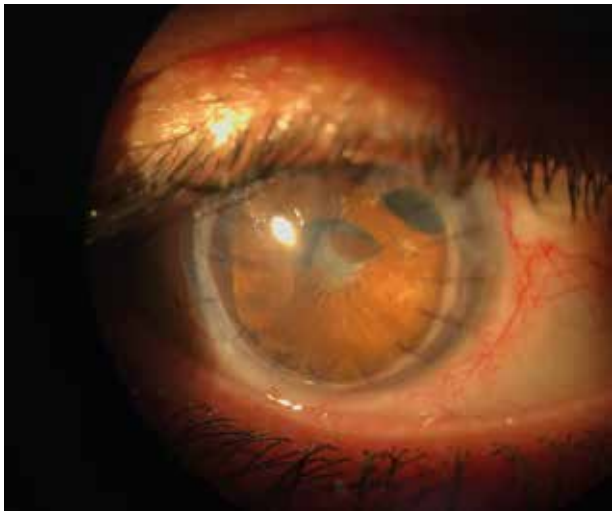


Figura 6. Aspecto de la catarata secundaria a todo el proceso inflamatorio previo a su cirugía.

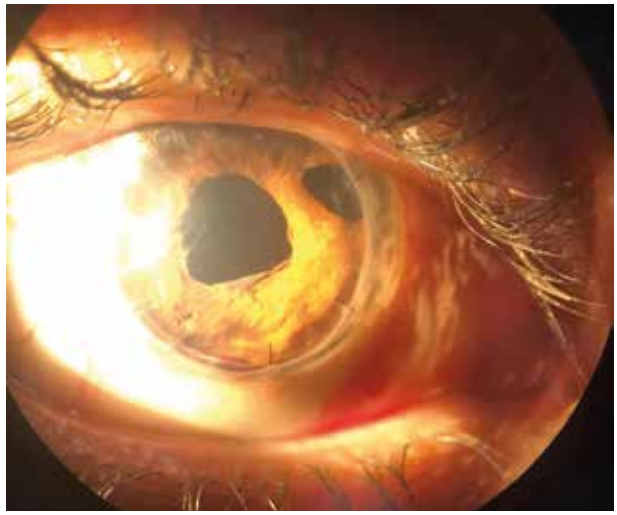


Figura 7. Aspecto en pseudofaquia, con tejido corneal transparente y sin signos de infección tras el cuarto transplante corneal.

de la infección. El examen del segmento anterior presentaba adherencia iridocorneal periférica sectorial, sinequias posteriores y catarata. Se continuó con PHMB 0.02%, clorhexidina 0.02% y voriconazol cada 6 horas y Prednefrin Forte cada 12 horas por 6 meses. A los 8 meses del último injerto corneal (y a 13 meses y 9 días del primero) se realizó cirugía de catarata con implante de LIO (figs. 6 y 7). Actualmente la visión es de cuenta dedos a un metro, su presión ocular promedio es de 18 mmHg con tratamiento antiglaucomatoso preventivo (timolol 0.5% cada 12 horas) y el fondo de ojos se mantiene sano, sin haberse alterado en todo el proceso.

Tras haber logrado resolver finalmente la patología infecciosa, se programa para un futuro cercano procedimiento refractivo para mejorar su resultado visual y el estricto control de la presión ocular, sin poder descartar la necesidad de una cirugía de glaucoma en el mediano plazo.

Discusión

La queratitis infecciosa puede llevar a una disfunción visual severa si no se realiza un correcto diagnóstico etiopatogénico y un tratamiento adecuado. En ciertas partes del mundo es parte de un serio problema de salud pública[1]. La identificación oportuna de los patógenos causantes del problema y la aplicación de la terapéutica anti-infecciosa apropiada son factores clave para un exitoso manejo de la queratitis infecciosa.

En relación con el caso clínico presentado, la paciente cursó claramente con una queratitis infecciosa polimicrobiana de difícil diagnóstico. Varios aspectos pueden discutirse respecto de la evolución tórpida observada. En un comienzo, una mala interpretación clínica de la queratitis, tal vez influenciada por la ausencia del factor de riesgo del uso de lentes de contacto (respecto de la etiología asociada a la ameba) que motivó una ineficaz selección inicial de los colirios anti-infecciosos. Respecto de la toma de muestra inicial, se podría pensar que se obtuvo escaso material de raspado corneal para análisis y también se podría tener dudas sobre el tamaño del primer injerto corneal en caliente, que podría haber sido más grande. Pero hay un punto muy importante que condicionó, a nuestro entender, la mala evolución del caso clínico y *fue la falta de identificación a tiempo de los gérmenes causales*.

La identificación de "el o los" germen/es causante/s de la queratitis infecciosa resulta un reto diagnóstico debido a varios factores: por un lado, no existen signos específicos que puedan asegu-

rar con total sensibilidad y especificidad el diagnóstico "clínico" de los agentes causales[7, 16]; por otro lado, la recolección de la muestra puede ser errónea o escasa, motivo por el cual en el 30-35% de los casos no se aíslan microorganismos en los directos y cultivos[17]. Si bien existen estudios moleculares como la PCR[18-19] y estudios por imágenes como la microscopía confocal[19], a veces resulta de difícil acceso y también pueden tener falsos positivos y negativos.

Finalmente, el estudio patológico del material extraído en las biopsias corneales no es simple de informar y se requiere un especialista en patología que esté acostumbrado a evaluar muestras oculares[16-17]. Por todo lo anterior, sumado al difícil acceso a los colirios "anti-infecciosos" fortificados de preparación magistral (por disponibilidad y el costo de algunos productos), más el incumplimiento del tratamiento por parte del paciente —ya que a veces no puede mantener la carga horaria de la posología establecida—, hace que a veces la evolución de las queratitis infecciosas sea complicada e incierta.

A pesar de que en más del 65% de los casos las queratitis infecciosas son de origen bacteriano y a su vez estas son causadas en un 80% por especies cocos Gram positivos[7-8], siempre es necesario estar alerta con respecto de la posibilidad de estar en presencia de otro agente causal o de una infección corneal polimicrobiana y no caer en el "hábito" de la presunción y el tratamiento puramente empírico; ya que, aunque se tiende a creer que las decisiones se toman luego de evaluar distintas alternativas, O'Hare y colaboradores demostraron en la Universidad de Duke de Estados Unidos que más del 40% de las acciones que realiza una persona promedio responde a hábitos antes que a decisiones conscientes[20].

Conclusión

A pesar de que el examen oftalmológico y los antecedentes del paciente son de mucha utilidad para aproximarse al agente causal, el reto clínico consiste en poder identificar el germen causal mediante exámenes microbiológicos, anatomía patológica, métodos moleculares (PCR) y microscopía confocal, ya que no existen signos clínicos específicos que confirmen la causa etiológica del germen causante. El plan terapéutico, luego de la toma de muestra corneal, se iniciará empíricamente basándose en los factores de riesgo, el aspecto del examen clínico y potenciales patógenos corneales hasta poder dilucidar el agente causal.

Se concluye que el examen oftalmológico y la cronología de los hechos son de suma importancia en las queratitis infecciosas pero la identificación del germen causante es el pilar esencial para el correcto tratamiento y evolución favorable de esta patología.

Referencias

1. Ung L, Bispo PJM, Shanbhag SS *et al*. The persistent dilemma of microbial keratitis: global burden, diagnosis, and antimicrobial resistance. *Surv Ophthalmol* 2019; 64: 255-271.

2. Na KS, Hwang KY, Lee HS *et al*. Wakayama symposium: interface between innate and adaptive immunity in dry eye disease. *BMC Ophthalmol* 2015; 15 (Suppl 1): 159.

3. Pérez del Palomar A, Montolío A, Cegoñino J *et al*. The innate immune cell profile of the cornea predicts the onset of ocular surface inflammatory disorders. *J Clin Med* 2019; 8: 2110.

4. Schallhorn JM, Schallhorn SC, Hettinger K, Hannan S. Infectious keratitis after laser vision correction: incidence and risk factors. *J Cataract Refract Surg* 2017; 43: 473-479.

5. Stapleton F, Naduvilath T, Keay L *et al*. Risk factors and causative organisms in microbial keratitis in daily disposable contact lens wear. *PLoS One* 2017; 12: e0181343.

6. Masters J, Kocak M, Waite A. Risk for microbial keratitis: comparative metaanalysis of contact lens wearers and post-laser in situ keratomileusis patients. *J Cataract Refract Surg* 2017; 43: 67-73.

7. Grandi G, Bianco G, Boattini M *et al*. Bacterial etiology and antimicrobial resistance trends in ocular infections: a 30-year study, Turin area, Italy. *Eur J Ophthalmol* 2019; (en prensa).

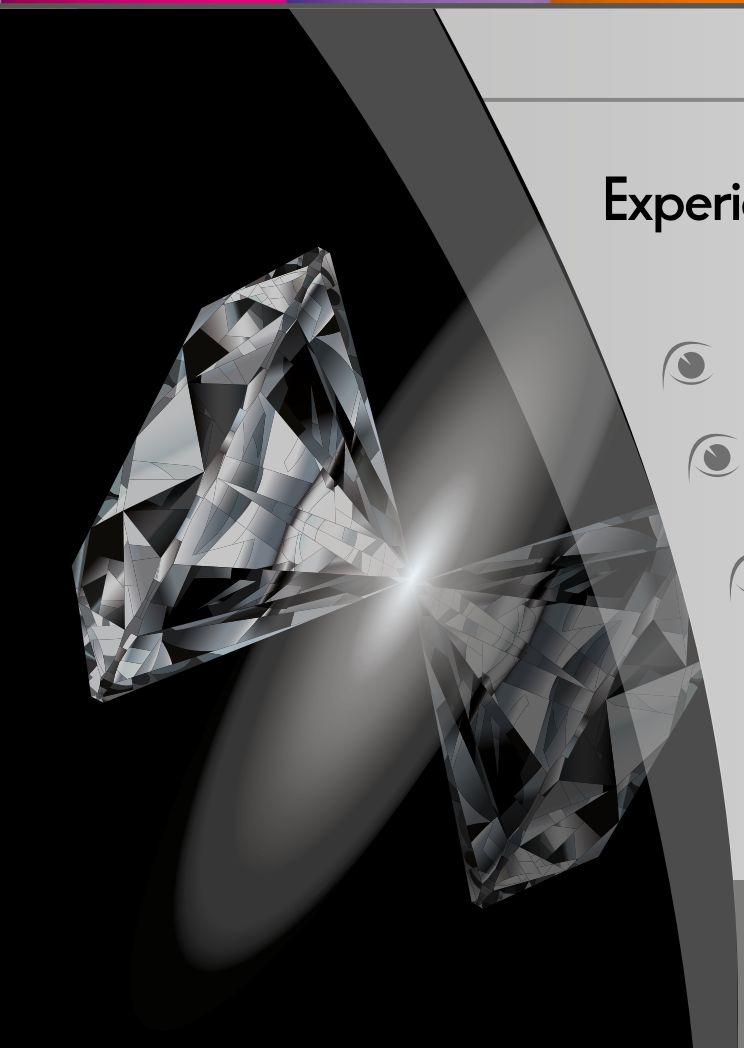
8. Acharya M, Farooqui JH, Gaba T *et al*. Delhi

infectious keratitis study: update on clinico-microbiological profile and outcomes of infectious keratitis. *J Curr Ophthalmol* 2020; 32: 249-255.
9. Ibrahim MM, Vanini R, Ibrahim FM *et al*. Epidemiology and medical prediction of microbial keratitis in southeast Brazil. *Arq Bras Oftalmol* 2011; 74: 7-12.
10. Mahmoudi S, Masoomi A, Ahmadikia K *et al*. Fungal keratitis: an overview of clinical and laboratory aspects. *Mycoses* 2018; 61: 916-930.
11. Manikandan P, Abdel-Hadi A, Singh YRB *et al*. Fungal keratitis: epidemiology, rapid detection, and antifungal susceptibilities of *Fusarium* and *Aspergillus* isolates from corneal scrapings. *Biomed Res Int* 2019; 2019: 6395840.
12. Rowe AM, St Leger AJ, Jeon S *et al*. Herpes keratitis. *Prog Retin Eye Res* 2013; 32: 88-101.
13. Lobo AM, Agelidis AM, Shukla D. Pathogenesis of herpes simplex keratitis: the host cell response and ocular surface sequelae to infection and inflammation. *Ocul Surf* 2019; 17: 40-49.
14. Maycock NJR, Jayaswal R. Update on Acanthamoeba keratitis: diagnosis, treatment, and outcomes. *Cornea* 2016; 35: 713-720.
15. Khurana S, Sharma M. Parasitic keratitis: an under-reported entity. *Trop Parasitol* 2020; 10: 12-17.
16. Moshirfar M, Hopping GC, Vaidyanathan U *et al*. Biological staining and culturing in infectious keratitis: controversy in clinical utility. *Med Hypothesis Discov Innov Ophthalmol* 2019; 8: 145-151.
17. Kaye SB, Rao PG, Smith G *et al*. Simplifying collection of corneal specimens in cases of suspected bacterial keratitis. *J Clin Microbiol* 2003; 41: 3192-3197.
18. Liu HY, Hopping GC, Vaidyanathan U *et al*. Polymerase chain reaction and its application in the diagnosis of infectious keratitis. *Med Hypothesis Discov Innov Ophthalmol* 2019; 8: 152-155.
19. Goh JWY, Harrison R, Hau S *et al*. Comparison of In vivo confocal microscopy, PCR and culture of corneal scrapes in the diagnosis of Acanthamoeba keratitis. *Cornea* 2018; 37: 480-485.
20. O'Hare J, Calakos N, Yin HH. Recent insights into corticostriatal circuit mechanisms underlying habits: invited review for current opinions in behavioral sciences. *Curr Opin Behav Sci* 2018; 20: 40-46.

Ojos que ven, corazón que siente.

Oftalmología
Ojos que ven, corazón que siente.

Laboratorio ELEA PHOENIX



ÓPTICA DE PRECISIÓN

Experiencia e innovación para brindar la máxima calidad visual

- Tallado digital con puntas de diamante
- Determinación de coeficiente de movimiento de ojos/cabeza
- Medida de posición del centro de rotación del ojo

Foucault

Nuestra recomendación es la visita periódica al médico oftalmólogo

Ayacucho 228 | (C1025AAF) | Ciudad de Buenos Aires
Teléfonos: 4950-0000 | 4953-2220 | 4953-4810
www.foucault.com.ar

NIDEK

CIRMÉDICA

tecnología japonesa de avanzada

YAG LÁSER + SLT
YC-200 S Plus

- Láser de funcionamiento fluído y mayor precisión
- Focalizar la patología: Óptica de alta resolución y definición
- Suministro preciso de energía: Alcanza umbral de plasma de 1.6 mJ facilitando tratamientos sólidos y precisos con menor energía
- Asistencia operativa: SLT Navi -progreso del tratamiento- y joystick motorizado de movimientos suaves e interruptor inteligente
- Con ángulo de 5.5º está diseñado para disminuir la densidad de la energía en la córnea protegiendo el tejido en tratamientos sucesivos

Gallo 1527 Piso 7 (C1425EFG)
Ciudad Autonoma de Buenos Aires
ventas@cirmedica.com
www.cirmedica.com
Tel (011) 4826-1100

LANZAMIENTO

Johnson&Johnson VISION

DISTRIBUIDOR OFICIAL

BioMat Instrumental

La LIO **TECNIS Eyhance™** tiene la misma geometría de base que la LIO monofocal **TECNIS™** de una pieza y visualmente no se distingue de aquellas sin anillos o zonas. En comparación con la LIO monofocal **TECNIS™** de una pieza, la LIO **TECNIS Eyhance™** proporciona una visión intermedia mejorada y de lejos similar, gracias a un diseño de superficie asférica de orden superior, lo que consigue un aumento continuo de la potencia desde la periferia hasta el centro de la lente, al mismo tiempo que reduce la aberración esférica casi a cero.

TECNIS Family of IOLs

TECNIS Eyhance™
Una LIO monofocal para hoy

- Rendimiento revolucionario que desafía a la monofocalidad para ofrecer una visión intermedia mejorada
- Los mejores resultados en condiciones de baja iluminación
- Ayude a que sus pacientes puedan realizar sus actividades diarias con confianza

Biomat Instrumental S.R.L. Concepción Arenal 3425 piso 2 of. 44 (C1427EKA) C.A.B.A. - Argentina
Tel. Rot. (54-11) 4555-1957 • info@biomat.com.ar • www.biomat.com.ar

NUEVA LÍNEA DE PERÍMETROS

Frey

Todos incluyen desviaciones estándar por edad y curva de Bibie

4686-0052 / 0175 - Saladillo 2579 - CABA
micromedicaepsilon@gmail.com
@micromedicaepsilon

Micromédica Epsilon

Tuttnauer

Autoclaves de mesa automáticos

Beneficios

- Ciclos rápidos que optimizan la disponibilidad del instrumental esterilizado, listo para ser usado.
- Sistema de control fácil de usar, con teclas de una sola acción, aumentando asi la productividad.
- Monitoreo mejorado para registrar constantemente los resultados de la esterilización.
- Autoclaves duraderos, fáciles de mantener, que prácticamente garantizan la ausencia de tiempos muertos.

Tres Arroyos 826 2ºC. CABA
+5411 4585 3170
contacto@casin.com.ar
www.casin.com.ar
/casininnovacion
/casinARG/
/company/casin-sa
casin innovacion

casin
Oftalmología + innovación

Curso de Simulación Virtual de Cirugía de Catarata

El curso que todo oftalmólogo necesita para adquirir o mejorar su habilidad quirúrgica.

Destinado a:

- Residentes
- Oftalmólogos principiantes
- Cirujanos que quieran perfeccionarse

Programa, aranceles y más detalles:
www.oftalmologos.org.ar/simulador

CAO
EDUCACIÓN

CAO CONSEJO ARGENTINO DE OFTALMOLOGÍA

Tte. Gral. Juan D. Perón 1479, PB
C1037AAO Buenos Aires, Argentina
Teléfono 54 (11) 4374-5400 líneas rotativas

Oftalmología Clínica y Experimental
www.oftalmologos.org.ar/oce/