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

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

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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 endophthalmitis¹⁻². However, there is no consensus about recommendations regarding the optimal protocol about security measures for patients³⁻⁴.

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 ophthal-mology 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

practiciti	y anne.
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)

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

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 pre-filled 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

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)

Table 2. Post intravitreal injection complications report.

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 levo-floxacin (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 them⁵.

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 lacking⁶. 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 patient⁷.

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 UK⁸. 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 responded⁹.

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 injection¹⁰. 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 others¹⁰.

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 injections¹¹. 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 prophylaxis¹². 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 others⁴. 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 IVI⁵. In contrast, in cases where povidone-iodine is not used the risk of post IVI endophthalmitis appears to be higher¹⁴. 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-iodine¹⁵.

Topical antibiotics have not proven to decrease the rate of endophthalmitis and increase the chances of antibiotic resistance and overall cost of the procedure¹⁶⁻¹⁷. Moreover, there is some evidence that they could increase endophthalmitis 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 survey²¹. 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 less²². 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 services²³.

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 significance²⁴. 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 patient²⁵. 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 endophthalmitis²⁶. Experts recommend to minimize talking during IVI, and to wear face masks⁵. 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 injections¹¹. 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.

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