

doi> http://dx.doi.org/10.17545/e-oftalmo.cbo/2015.22

## Personal impressions on the ARVO 2015 meeting<sup>1</sup> Impressões pessoais sobre a reunião da ARVO 2015

### Impresiones personales de la reunión de ARVO 2015

Short title: ARVO 2015

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#### INTRODUCTION

ARVO stands for The Association for Research in Vision and Ophthalmology. Founded in 1928 by 73 ophthalmologists in Washington, DC in the United States, it is the world's largest society dedicated to ophthalmic research. Its annual meeting is essential for hundreds of scientists from both basic and clinical-surgical areas of ophthalmology.

In 2015, the meeting took place in Denver, Colorado, United States, from May 3 to 7. Approximately 11,000 participants from over 75 countries attended the meeting; among them were 200 Brazilians. The theme was "*Powerful Connections: Vision Research and Online Networking.*"

Because I have dedicated myself to the areas of retina and vitreous for many years, I tried to focus my attendance and, as a result, these observations on the correlated scientific activities.

#### IMAGING

Numerous studies using modern techniques of optical coherence tomography (OCT) angiography and swept-source OCT (now associated with high-resolution images in ultra-wide field) to study peripheral lesions were presented. OCT has been used to study the choroid for some years now; similarly, new computed tomography (CT) scanners allow for a more detailed evaluation of the vitreous, especially on the retinal interface.

Adaptive optics combined with OCT or scanning laser ophthalmoscopy (SLO), a feature that allows for improvement in the optical systems by reducing the distortion caused by wave fronts, provides a more detailed structural assessment and will likely be incorporated into the vitreoretinal introductory arsenal in the near future.

# NEONATAL OPHTHALMIC EVALUATION AND RETINOPATHY OF PREMATURITY (ROP)

Many children present visual impairment of unknown cause. Though other reasons are possible, this may be due to retinal hemorrhages during the perinatal period.

A study by Ludwig et al.<sup>1</sup> (Stanford University, San Francisco) demonstrated the benefits of imaging using Ret Cam III Digital Imaging in newborn children; when compared to transillumination, the angiography was found to produce greater reliability in the detection of alterations to the ocular posterior segment.

Fonte de financiamento: declaram não haver. Parecer CEP: não se aplica. Conflito de interesses: declaram não haver. Recebido em: 18/05/2015 Aprovado em: 20/05/2015

Como citar: Nóbrega MJ. Impressões pessoais sobre a reunião da ARVO 2015. e-Oftalmo.CBO: Rev. Dig. Oftalmol., São Paulo, 2015; 1(2). http://dx.doi.org/10.17545/e-oftalmo.cbo/2015.22

In a comparative study on the screening and treatment of ROP conducted at the Bascom Palmer Eye Institute (Miami, Florida, United States), Kaakour et al.<sup>2</sup> demonstrated that from 2002 to 2012, the annual number of children assessed increased, but the frequency of ROP treatment decreased. In total, 10,924 children were examined and 231 were treated with laser (2.1%); the average time between the date of birth and treatment was three months.

Regarding the use of intravitreal anti-vascular endothelial growth factor (VEGF) for ROP treatment, two studies conducted at the Hospital for Sick Children (Toronto, Canada) observed ocular results after an injection of bevacizumab (0.625 mg) that were similar to the results found when retinal photocoagulation was used. Development of myopia was higher in children who were treated with laser, and the systemic adverse effects of pharmacological therapy in the medium and long term cannot be predicted yet<sup>3.4</sup>.

Additionally, a study by Yonekawa et al.<sup>5</sup> (Associated Retinal Consultants, Birmingham, Michigan, United Stated) provided evidence for progression to severe retinal detachment with retinal fibrosis in preterm infants treated with intravitreal bevacizumab. The observed aspect was similar to proliferative diabetic retinopathy and tractional retinal detachment preoperatively treated with anti-VEGF for over seven days.

#### AGE-RELATED MACULAR DEGENERATION (AMD)

This is one of the most frequently studied areas of ophthalmology due to increased population longevity, high prevalence in individuals over 60 years of age, and new diagnostic and therapeutic resources.

Researchers presented the results of a study of 17 British centers conducted by Johnston et al.<sup>6</sup> (Cheltenham General Hospital) on the use of intravitreal VEGF treatment of exudative AMD in the real world. In the six years of follow-up, six injections were needed in the first year, a number that decreased over time, until three injections were reached in the fifth year. It was observed that most of the subjects treated had preserved functional visual acuity for driving vehicles or reading. In the British healthcare system, there is a preference for the "treat and extend" approach in cases of neovascular AMD.

Lim et al.<sup>Z</sup> (University of Illinois) presented the phase I results of the Verisome<sup>®</sup> drug delivery system IBI 20089 combined with triamcinolone, which allows for a controlled release of the intraocular corticosteroid for one year. A study in 10 eyes that evaluated the association of intravitreal IBI 20089 and intravitreal ranibizumab demonstrated a need for fewer anti-VEGF injections to control macular disease in a two-year follow-up. Nonetheless, this drug combination did not prevent the progression to geographic atrophy.

Freeman et al.<sup>6</sup> (University of California, San Diego, United States) demonstrated that the administration of 0.1 ml of intravitreal aflibercept (40 mg/ml) can control the neovascular process in cases resistant to previous treatments. The criteria for the change were frequent relapses or continued macular thickening.

#### **DIABETIC MACULAR EDEMA (DME)**

Diabetic retinopathy is the most common cause of blindness in the working population. Macular edema is the most important cause of visual impairment in diabetics.

According to Agathe et al.<sup>9</sup> (University Hospital of Poitiers, France), the use of macular grid photocoagulation after three intraocular injections of ranibizumab can reduce the need for future intravitreal applications for DME control, in a one-year follow-up.

Chen et al.<sup>10</sup> (University of Illinois, United States) observed a lower incidence of DME after two sessions of panretinal photocoagulation with pattern scan laser (Pascal) in patients previously treated with intravitreal bevacizumab.

Tarik et al.<sup>11</sup> (Eye Hospital Oxford, United Kingdom) studied the use of intravitreal ranibizumab for the treatment of DME. They observed that after three monthly injections of anti-VEGF, individuals with persistent DME and central macular thickness > 400 microns had reduced chance of success with new applications of the drug.

Valdeanu-Collins et al.<sup>12</sup> (Hartlepool, United Kingdom) reported good results when using a biodegradable fluocinolone implant (lluvien®), with controlled release of 0.2 micrograms per day in patients with DME over a six-month follow-up period. The substance can last three years in the vitreous, but higher risk of ocular hypertension and cataracts occur.

Conversely, Tsai et al.<sup>13</sup> (University of California, San Diego) used intravitreal triamcinolone at a dose of 20 mg (decanted for one hour) for the treatment of DME, venous occlusion, uveitis, and in the postoperative period. When comparing a group of eyes that underwent previous vitrectomy with those that did not, the authors observed that triamcinolone was effective in both groups; however, it was more

effective in the group that had not undergone vitrectomy. In some cases, the intraocular presence of corticosteroid was observed up to 12 months after injection.

#### **RETINAL VEIN OCCLUSION**

This is the second most common vascular cause of visual impairment, particularly in individuals with hypertension and primary openangle glaucoma.

Feltigen et al.<sup>14</sup> (University of Goettingen, Germany) presented the results of the comparative and multicenter COMRADE-C study conducted in Germany and in the United Kingdom. It considered the treatment of macular edema in central venous occlusion. In the sixmonth follow-up period, the authors observed that intravitreal injections of ranibizumab (three initial monthly applications and then "pro re nata") presented better anatomic and visual results than the intravitreal application of a dexamethasone 0.7 mg implant (single application).

Similarly, Eter<sup>15</sup> (University of Muenster, Germany) presented the results of the COMRADE-B study, the design of which was similar to that of COMRADE-C, but applied to macular edema in branch retinal vein occlusion. That study also showed better results with anti-VEGF therapy than with intravitreal corticosteroids in the six-month follow-up.

#### VITREORETINAL INTERFACE DISEASES

The advances in treatment using ocriplasmin intravitreal injection of and in surgical treatment are noteworthy, leading to an active search for participants to be included in further investigations.

In October 2012, ocriplasmin was approved by the Food and Drug Administration (FDA) for intravitreal treatment of vitreomacular traction syndrome. In Brazil, the National Health Surveillance Agency (ANVISA) approved its use in 2015. A multicenter, stage IV study by Duker et al.<sup>16</sup> (New England Eye Center, Boston, United States – ORBIT Study) of subjects treated with intravitreal ocriplasmin revealed 61% vitreomacular traction resolution and 31% macular hole closure at the six-month follow-up.

Moreover, Dyer et al.<sup>12</sup> (Retina Associates, Overland Park, Kansas, United States) observed that, in the one-year follow-up, the results of ocriplasmin in vitreomacular traction were unfavorable in patients with diabetic retinopathy, epimacular membrane, adherence > 500 microns, and age > 65 years.

Day et al.<sup>18</sup> (Austin Retina Associates, Texas, United States) demonstrated that vitreomacular traction was released in five of nine patients treated with injections of 0.3 ml pure sulfur hexafluoride (SF6; 55% positive). The result is similar to the use of perfluoropropane (C3F8), but SF6 has a more rapid elimination from the vitreous cavity.

Surgery may be indicated for vitreomacular traction, particularly if there is visual impairment and metamorphopsia. Tzu et al.<sup>19</sup> [Bascom Palmer Eye Institute (BPEI), Miami, Florida, United States], after a follow-up time of 98–2,337 days, observed that surgery was indicated in 10 of 230 eyes with vitreomacular traction (4.1%). Progression to macular hole was the main surgical indication.

#### **INTRAVITREAL INJECTIONS**

Albeit rare, endophthalmitis is the most serious complication of intravitreal injections. Numerous retrospective studies have described its incidence and the results with treatment.

Flynn et al.<sup>20</sup> (BPEI, Miami, Florida, United States) reported 20 cases of endophthalmitis in 121,285 intravitreal injections (0.016%) from 2005 to 2014. There was a positive culture in 45% of cases; *Streptococcus* spp. and *Staphylococcus epidermidis* were the most frequently cultured bacteria. In 2014, BPEI registered 7,895 aflibercept injections, 5,781 bevacizumab injections, and 2,767 ranibizumab injections. There is a tendency not to use topical antibiotics before and after the injections; the use of mask by the physician is optional.

Bonaffini et al.<sup>21</sup> (Bradenton, Florida, United States) reported a decreasing endophthalmitis incidence in intravitreal injections. In 2003, the risk was 0.01% per application and in 2012, it was 0.001%. The risk of a patient acquiring the infection during intravitreal therapy was 0.72% in 2003 and 0.024% in 2012.

In the United Kingdom, intravitreal injections have been increasingly applied by nurses in order to speed up treatment. A study by Raguro et al.<sup>22</sup> (Camberley) demonstrated that, in 3,461 injections performed by physicians and 1,000 injections performed by nurses,

71% of individuals had no preference, 11% preferred physicians, and 17% preferred nurses; most considered the application "excellent", and there were no complaints regarding the procedures.

Kirk et al.<sup>23</sup> (Cheltenham General Hospital) observed 0.05% incidence of endophthalmitis in intravitreal injections performed by physicians (6 injections out of 12,176) and 0.10% incidence in those performed by nurses (6 injections out of 5,692). In other words, the risk was double in procedures performed by nurses; however according to the authors, this value was not statistically significant.

#### CONCLUSIONS

ARVO's Annual Meeting promotes recent research in ophthalmology and visual sciences. Contact with professionals from various fields allows for scientific improvement and encourages authors to submit studies to the specialized community. The retina and vitreous areas are highly in-demand by professionals worldwide due to the advances in recent years, particularly in diagnostic imaging and pharmacological treatment. More innovations should take place in the coming years, with more favorable prospects in various diseases of the ocular posterior segment, for the benefit of all age groups.

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