Eye Health Research Review™

Making Education Easy

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In this issue:

Abbreviations used in this issue:

AMD = age-related macular degeneration; **CNV** = choroidal neovascularisation; **DME** = diabetic macular oedema; **DSAEK** = Descemet stripping automated endothelial keratoplasty; **IOP** = intraocular pressure; **OCT** = ocular coherence tomography; **VEGF** = vascular endothelial growth factor.

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Welcome to the 25th issue of Eye Health Research Review.

It seems that the list of risk factors for AMD continues to grow. Based on the results of a study from our colleagues at The Westmead Institute, thyroid dysfunction has now been added to the list.

There has been much talk about iStents and their role in glaucoma management. In this issue we review two small case series which both show that combined phacoemulsification and iStent insertion can lower IOP and reduce medication burden.

We hope you enjoy our selection for this issue and welcome your comments and feedback.

If you have colleagues or friends within Australia who would like to receive our publication, send us their contact email and we will include them for the next issue.

Kind Regards,

Lance Liu

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A randomized multicenter clinical trial of ultrathin descemet stripping automated endothelial keratoplasty (DSAEK) versus DSAEK

Authors: Dickman MM, et al.

Summary: DSAEK and ultra-thin DSAEK were compared in a randomised controlled trial in 66 eyes from 66 patients with irreversible corneal endothelial dysfunction due to Fuchs' dystrophy. Patients were randomised to undergo DAESK (n=32) or ultra-thin DSAEK (n=34). Best spectacle-corrected visual acuity was significantly better after ultra-thin DSAEK than after DSAEK at 3, 6 and 12 months (12 months: 0.13 logMAR vs 0.20 logMAR; p=0.03). There were no significant differences between ultra-thin DSAEK and DSAEK for refraction, endothelial cell density and complications such as donor loss and graft dislocation.

Comment: Which is better: thin or thinner corneal endothelial transplants? This small randomised controlled trial shows that, at 12 months, ultra-thin DSAEK resulted in similar reactive outcomes, endothelial loss and complications compared to standard DSAEK in patients with Fuchs' endothelial dystrophy. Corneal transplant surgery has come a long way from full thickness grafts.

Reference: Ophthalmology. 2016;123(11):2276-2284.
Abstract

Thyroid dysfunction and ten-year incidence of age-related macular degeneration

Authors: Gopinath B, et al.

Summary: Overt hyperthyroidism was found to be independently associated with an increased risk of incident AMD in a study of 906 adults aged ≥50 years. After adjusting for age, sex, smoking, fish consumption and variants in AMD susceptibility genes, the odds ratio for developing AMD was 3.51 in participants with overt hyperthyroidism compared to those with normal thyroid function (95% CI 1.16–10.65). Participants who had ever taken thyroxine medication (n=77) also had an increased risk of any AMD compared with those who had never taken thyroxine (odds ratio 1.91; 95% CI 1.18–3.09).

Comment: It seems that the list of risk factors for AMD continues to grow. This study shows that patients with overt hyperthyroidism or on thyroxine medication have an increased risk of incident AMD. Whether this finding is an associative or causal effect remains to be determined.

Reference: Invest Ophthalmol Vis Sci. 2016;57(13):5273-5277.
Abstract

Clinical correlation to differences in ranibizumab and aflibercept vascular endothelial growth factor suppression times

Authors: Fauser S, Muether PS.

Summary: The correlation between intraocular VEGF-A suppression times and CNV activity was investigated in seven eyes with treatment-naïve neovascular AMD. All eyes showed persistent CNV activity throughout treatment with intravitreal ranibizumab given as needed for 28 months followed by intravitreal aflibercept given as needed for 15 months. VEGF-A concentrations were assayed from 160 aqueous humour specimens collected before each intravitreal injection. CNV activity was determined by spectral-domain OCT. Mean duration of VEGF-A suppression was longer with aflibercept than ranibizumab (67 days vs 34 days; p<0.001). CNV re-activity occurred about halfway through the duration of VEGF-A suppression.

Comment: How long do anti-VEGF agents work to suppress intraocular VEGF-A? This interesting study looked at periodic VEGF-A concentrations in aqueous humour before injections of ranibizumab then aflibercept were given in the same patients with persistent CNV. It showed that the mean duration of suppression of VEGF-A concentrations was longer for afilbercept than ranibizumab and this was also reflected in the CNV activity measured with OCT. However, clinical re-activity occurred about 50% earlier than the respective VEGF-A suppression times for both anti-VEGFs. It suggests that there are other pathophysiologic mechanisms at play in patients with persistent CNV.

Reference: Br J Ophthalmol. 2016;100:1494-1498.
Abstract

Intravitreal aflibercept for diabetic macular edema: 148-week results from the VISTA and VIVID studies

Authors: Heier JS, et al.

Summary: This long-term follow-up of the phase 3 VISTA and VIVID studies showed that visual improvements achieved with intravitreal aflibercept at 1- and 2-years are maintained to 3 years in patients with DME. A total of 872 eyes with central-involved DME were randomised to laser control or intravitreal aflibercept 2 mg given every 4 or 8 weeks after 5 monthly doses. Rescue laser or aflibercept could be given from week 24 if rescue treatment criteria were met and all laser control patients were treated with intravitreal aflibercept given as needed from week 100. Change from baseline in best-corrected visual acuity at week 148 was significantly better in patients treated with either regimen of aflibercept compared with laser (10.3–11.7 letters vs 1.4–1.6 letters; p<0.0001). Vision gains from baseline ≥15 letters were achieved at week 148 in significantly more patients treated with aflibercept than with laser control (35.8–42.9% vs 13.6–18.9%; p<0.0001). Improvement of ≥2 steps on the Diabetic Retinopathy Severity Scale score was also achieved by significantly more patients treated with aflibercept than with laser control (29.9–47.8% vs 17.4–20.1%; p<0.0001). The most frequent serious ocular adverse event was cataract which occurred in 2.1–3.1% of patients in the aflibercept groups and in 0.3% of patients in the laser control group.

Comment: The management of DME is changing. In the past, the gold standard was laser treatment but this has been surpassed with intravitreal injections. This long-term follow-up of the VISTA and VIVID studies shows that treatment with intravitreal aflibercept 4 weekly or 8 weekly was much better in terms of mean visual acuity gain (10.4 or 10.5 letters) as well as the Diabetic Retinopathy Severity Scale score compared to laser treatment. The most common complication was cataract formation. The findings from this analysis are consistent with many other studies in the literature.

Reference: Ophthalmology. 2016;123(11):2376-2385.
Abstract

Independent commentary by Dr Lance Liu, who graduated from the University of Melbourne in 1992 before completing his ophthalmology training at the Royal Victorian Eye and Ear Hospital (Melbourne, Australia). He then undertook fellowship training in Glaucoma at Moorfields Eye Hospital (London, UK), the National University of Singapore (Singapore) and the Wills Eye Hospital (Philadelphia, USA). Currently, he works in private practice in Preston and Glenroy (Melbourne, Australia) as well as a Glaucoma Consultant at the Royal Victorian Eye and Ear Hospital (Melbourne, Australia). Recently, he was made an Honorary Fellow of the University of Melbourne (CERA). He has an interest in clinical research that includes angle closure and pigment dispersion glaucoma, gonioscopy, anterior segment imaging, cataract surgery and glaucoma practice patterns.

Visual recovery after retinal detachment with macula-off: is surgery within the first 72 h better than after?

Authors: Frings A, et al.

Summary: The influence of lag time between onset of central visual acuity loss and surgical intervention for macula-off retinal detachment was investigated in a retrospective case series of 89 eyes from 89 patients. There was no clinically relevant difference in final visual acuity after 10 days, but eyes with symptom duration ≤3 days before surgical intervention had the best final visual acuity. Eyes that underwent vitrectomy had better outcomes than those that underwent scleral buckling surgery. The authors concluded that surgery for macula-off retinal detachment cannot be delayed without compromising the patient's visual prognosis.

Comment: How urgent should one intervene in a patient with a macula-off retinal detachment? This large retrospective case series of 1727 patients shows that the final visual acuity was better if operated on (vitrectomy better than scleral buckle) within the first 3 days, compared to those 10–30 days, from the time of central acuity loss. However, this study did not take into account other causes of visual impairment such as cataract. So, the longer the duration of vision loss, the worse the final visual acuity following successful retinal surgery.

Reference: Br J Ophthalmol. 2016;100:1466-1469.
Abstract

Long-term outcome after topical ciclosporin in severe dry eye disease with a 10-year follow-up

Authors: Straub M, et al.

Summary: Clinical improvements following treatment with topical ciclosporin were maintained through 10 years of follow-up in a retrospective review of 26 patients with severe dye eye syndrome related to keratoconjunctivitis sicca. All patients were initially treated with topical ciclosporin A for 6 months. During the 10-year follow-up, the median duration of topical ciclosporin treatment was 23 months after prolonged induction treatment lasting 20 months. There was no significant difference in the ocular surface disease index at baseline and at the 10-year follow-up. Significant improvements in clinical signs achieved during the initial treatment period were sustained and still evident at the 10-year follow-up. Only 6.5% of patients required reintroduction of topical ciclosporin after prolonged induction treatment.

Comment: "True" dry eye or keratoconjunctivitis sicca is uncommon. Treatment options include artificial tear replacement or anti-inflammatory agents. This small but long-term retrospective study shows that there was significant clinical improvement that was sustained after 10 years after an initial treatment period of topical ciclosporin; 6.5% required a repeat course of ciclosporin. It is important to exclude the common causes of ocular surface disease (e.g. blepharitis) before diagnosing "true" dry eye.

Reference: Br J Ophthalmol. 2016;100:1547-1550.
Abstract

Outcomes after combined phacoemulsification and trabecular microbypass stent implantation in controlled open-angle glaucoma

Authors: Seibold LK, et al.

Summary: Combined phacoemulsification and iStent implantation was effective in reducing IOP and medication use in a retrospective case series of 64 eyes from 45 patients with open-angle glaucoma and a low preoperative IOP. Mean IOP decreased from 14.7 mmHg to 13.2 mmHg 1 year after surgery (p<0.01), which translated to an estimated IOP reduction of 12.2% (p=0.002). Mean medication use decreased from 1.81 prior to surgery to 1.41 at 1 year (p=0.0001) with 41% of patients becoming medication free 1 year after surgery. Corrected distance visual acuity improved from 0.4 logMAR at baseline to 0.17 logMAR at 1 year (p<0.0001). Treatment success, defined as a ≥20% reduction in IOP or discontinuation of ≥1 medication, was achieved in 76.1% of patients. The authors commented that the physician and patient should consider the clinical benefit of modest IOP lowering and a reduction in medication use during the surgical consent process.

Comment: The "talk" from the ophthalmic community is consistent with the findings of this small retrospective case series looking at combined phacoemulsification and iStent and its effect on IOP in open-angle glaucoma patients. At 1 year, the IOP was lower and the mean number of medications used was less with 41% of patients being medication free. However, long-term studies are needed to assess the duration of efficacy of this device.

Reference: J Cataract Refract Surg. 2016;42(9):1332-1338.
Abstract

Manchester iStent study: 3-year results and cost analysis

Authors: Tan SZ, Au L.

Summary: The safety and efficacy of combined phacoemulsification and single iStent insertion was investigated in a prospective uncontrolled case series of 41 patients with open-angle glaucoma. For 36 patients who completed 3 years of follow-up, mean IOP prior to the procedure was 21.2 mmHg on 2.1 medications. Mean IOP decreased to 15.9 mmHg on 0.5 glaucoma drops at 1 year, 16.1 mmHg on 1.0 drops at 2 years, and 17.1 mmHg on 1.3 drops at 3 years (all $p<0.001$). The overall cost of the combined phacoemulsification iStent procedure varied depending on whether brand name or generic eye drops were used.

Comment: There has been much talk about iStents and their role in glaucoma management. This small prospective case series shows that iStents (in combination with cataract surgery) can lower IOP and reduce the number of topical glaucoma medications after 3 years. However, there was a gradual increase in the number of glaucoma drops needed to lower the IOP. At 3 years, invasive surgery was still more expensive but it did not take into consideration the improvement of the patient's vision or quality of life.

Reference: Eye (Lond). 2016;30(10):1365-1370.
Abstract

Treatment outcomes and prognostic factors of selective laser trabeculoplasty for open-angle glaucoma receiving maximal-tolerable medical therapy

Authors: Miki A, et al.

Summary: The efficacy of selective laser trabeculoplasty (SLT) was retrospectively investigated in 75 eyes of 59 patients with open-angle glaucoma. Mean IOP was 23.3 mmHg with 3.4 IOP lowering medications prior to the procedure. One year after surgery, IOP was the same or lower than baseline in 45.3% of patients, with IOP reductions of ≥20% in 14.2% of patients. The proportion of patients meeting each of these two criteria for successful treatment was greatest in patients with primary open-angle glaucoma (n=39; 61.1% and 21.7%) compared to patients with exfoliation glaucoma (n=23; 29.3% and 14.5%) or secondary open-angle glaucoma (n=13; 15.4% and 7.7%). The authors concluded that types of glaucoma and preoperative IOP were significant prognostic factors for treatment success.

Comment: SLT can be used as primary or as adjunctive treatment in lowering IOP in glaucoma. This retrospective review of a cohort of glaucoma patients receiving maximal tolerated medical therapy showed that, at 1 year, 45.3% of all patients had IOP lower than their baseline and 14.2% of all patients had ≥20% IOP lowering after SLT. The success rate was lower in those with pseudoexfoliation and secondary open-angle glaucoma. SLT does play a role in glaucoma management but one needs to consider the success rate, IOP lowering efficacy and duration of effectiveness for each individual glaucoma patient.

Reference: J Glaucoma. 2016;25(10):785-789.
Abstract

Effectiveness of early lens extraction for the treatment of primary angle-closure glaucoma (EAGLE)

Authors: Azuara-Blanco A, et al.

Summary: The effectiveness of clear-lens extraction and laser peripheral iridotomy was compared in a randomised controlled trial of 419 patients with primary angle-closure or primary angle-closure glaucoma. All patients were aged ≥50 years with no cataracts and had newly diagnosed primary angle-closure with IOP ≥30 mmHg (n=155) or primary angle-closure glaucoma (n=263). They were randomised to undergo clear-lens extraction (n=208) or receive standard care with laser peripheral iridotomy and topical medical treatment (n=211). Patient-reported health status scores and mean IOP were significantly higher after clear-lens extraction than after standard care. Clear-lens extraction was also more cost-effective with an incremental cost-effectiveness ratio of £14,282 compared with standard care. No patients had serious adverse events, but irreversible vision loss occurred in one patient who underwent clear-lens extraction and in three patients who received standard care.

Comment: Further to my previous comments regarding this study presented in the last issue, I forgot to mention that further treatment to control IOP was needed in 21% of those undergoing clear lens extraction compared to 61% of those having laser iridotomy. This observation could be explained by angle closure causing a combination of damage to the trabecular meshwork and persistent angle closure due to non-pupil block mechanisms. Now the question arises, when should you remove the lens in these patients?

Reference: Lancet. 2016;388(10052):1389-1397.
Abstract

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