



Eye Health Research Review

Making Education Easy

Issue 2 - 2009

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Welcome to the second issue of Eye Health Research Review.

I have had some positive feedback from the first edition, sufficient to keep the press rolling. To those of you who kindly suggested activities to fill in my spare time I have grouped them according to plausibility and degree of difficulty. Some I am unlikely to investigate.

This edition contains I hope more papers of interest. I have left out reviewing the "Series on Statistics" which is currently appearing in the Am J Ophthalmol but I would recommend it to those requiring an introductory/refresh course. The series is rather reminiscent of the statistics series published in the Brit Med J some years ago and looks equally as good. Introduction to Statistics courses are to me a bit like gardening manuals, intrinsically appealing but unlikely to worry those employed at the Botanical Gardens.

Another thing, there is a great letter in the Brit J Ophthalmol which is worth a look detailing how to adapt your slit lamp camera into taking whole face pictures. It involves the use of a -8 dioptre lens so might be useful to those wanting to capture lid or facial lesions. (Br J Ophthalmol. 2009;93;2:272-273)

Kind regards,

Associate Professor Philip Polkinghorne

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Recovery of corneal irregular astigmatism, ocular higher order aberrations, and contrast sensitivity after discontinuation of overnight orthokeratology

Authors: Hiraoka T et al

Summary: Orthokeratology is a technique which can achieve reductions in refractive errors and improvement of unaided vision especially in the low to moderate myopic patients. The technique involves wearing specially designed rigid contact lenses which are worn overnight.

Twenty-three patients were enrolled in this study. Their ages ranged from 20 to 40 years, they had a spherical equivalent of -1 to -4 dioptres of myopia, and were without any other systemic or ocular disease. Pre-treatment measurements included topography; wavefront analysis was performed using the Hartmann-Shack wavefront analyser, as well as contrast sensitivity studies. Six subjects dropped out of the study for non-sight threatening reasons. Twelve months into the study the subjects were reviewed and found to have significant improvements in manifest refraction as did their unaided acuity. However, increases were noted in some higher-order aberrations and irregular astigmatism. Interestingly, contrast sensitivity worsened with treatment. All these parameters returned to pre-treatment levels within a week of discontinuing treatment. The authors conclude that orthokeratology is reversible following cessation of treatment.

Comment: While this study demonstrates this treatment is effective in reducing myopia, the emphasis is on documenting the reversibility of both the beneficial and unwanted effects of orthokeratology. The authors noted their results may not be applicable to children and young people and further studies are necessary to determine the safety in this age group.

Reference: Br J Ophthalmol. 2009;93:203-8.

<http://bj.o.bmj.com/cgi/content/abstract/93/2/203>

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The effect of mitomycin C on corneal endothelium in pterygium surgery

Authors: Bahar I et al

Summary: Mitomycin C is used as an adjunct in pterygium surgery to reduce the risk of recurrence. The complications of mitomycin are well recognised and include scleral necrosis and secondary infections. It is also known that mitomycin may have a deleterious effect on the corneal endothelium in those patients who have undergone pterygium surgery with the so-called bare sclera technique. This paper seeks to determine if the effects on the corneal endothelium are mitigated when the technique is modified by combining the surgery with a conjunctival autograft.

The study consisted of 43 consecutive patients with a recurrent pterygium undergoing further surgery combined with a conjunctival autograft and mitomycin. A control group consisted of 27 eyes having pterygium surgery with an autograft but no mitomycin. The fibrin glue Tiseel was used in all surgeries. The bottom line of the study was that in spite of limiting exposure of the bare sclera to two minutes, mitomycin caused a reduction in the endothelial counts approximating 4.0% whereas the control gained 2%. The latter value is accounted for by the range of values measured; the difference was, however, statistically significant.

Comment: What I hope this paper reminds the reader is that there is always a balance between good and bad and that the best treatment should be individualised according to clinical findings and presumed clinical course.

Reference: *Am J Ophthalmol.* 2009;147(3):447-52.

<http://linkinghub.elsevier.com/retrieve/pii/S0002939408006934>

Contact lens wear is associated with decrease of meibomian glands

Authors: Arita R et al

Summary: The authors note contact lens use remains a very popular method to correct refractive errors, although on occasions their usage can induce certain complications including infection, allergic reaction and dry eye symptoms. In this study, the authors explore the link between meibomian gland dysfunction leading to dry eye symptoms with contact lens use. The authors note this relationship is controversial, with some studies reporting an association while others discount this possibility. The approach the authors take in this study is to examine the meibomian glands with an infra-red camera. The validity of this device is not discussed in the paper but representative photographs demonstrate the meibomian glands become shortened and disappear with contact lens use. The shortening occurs not from the orifice side but the distal portion and was graded from 0 to 4. A higher score reflected a greater reduction in visible meibomian gland area. A number of other parameters were measured but the statistically significant result was that duration of contact lens wear is directly related to meibomian gland loss.

Comment: It appears likely from this paper that some of the changes that occur in patients wearing contact lenses are related to changes in meibomian glands. However, it is unclear whether this alteration is a consequence of direct trauma to the meibomian ducts or simply chronic irritation to the glands from the contact lenses.

Reference: *Ophthalmol.* 2009;116(3):379-84.

<http://linkinghub.elsevier.com/retrieve/pii/S0161642008010695>

Independent commentary by Associate Professor Philip Polkinghorne, who works as a vitreoretinal surgeon and medical retina specialist at Auckland Eye and Auckland District Health Board. He is also an Associate Professor in the Department of Ophthalmology at the University of Auckland and has teaching responsibilities for both undergraduate and postgraduate students.

Pleasant music overcomes the loss of awareness in patients with visual neglect

Authors: Soto D et al

Summary: Patients who suffer a right hemispheric stroke are at high risk of developing a syndrome that leads to spatial neglect. This is manifest by an inability to appreciate objects presented on the side contralateral to the brain lesion, i.e. mostly the left side. In this paper, the authors explore the effect of the emotional state on overcoming the field deficit. The parameter that was utilised was music and then what was preferred by the patient. The tasks the patient was required to perform involved different coloured geometric shapes which were presented to both the ipsi- and contra- lateral fields. In addition to this evaluation selected patients underwent neuro-imaging.

The results demonstrated that patients did show a benefit and playing the patient's preferred music lead to statistically significant improvements in target identification and enhanced awareness. As to the neuro-imaging there was enhanced activity in the "music enjoyment" centre, which is apparently represented in a number of gyri.

Comment: This group has performed similar studies exploring the benefits of a positive effect in stroke recovery including verbal memory and attention focusing, which have achieved some following from the lay press. I am not sure if this is psychology or neuro-ophthalmology, but what a paper. Maybe there is a rationale for my children "studying" with hip hop in the background and why some of my colleagues operate with Meatloaf greatest hits. I prefer the sounds of silence.

Reference: *Proc Natl Acad Sci U S A.* 2009;106(14):6011-6.

<http://www.pnas.org/content/106/14/6011.abstract>

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Imaging of the retinal nerve fibre layer for glaucoma

Authors: Townsend KA et al

Summary: This review describes the development and application of imaging techniques available for measuring changes in the retinal nerve fibre layer that occur with glaucoma. Such changes can sometimes be observed clinically or with red-free photography. The difficulty of this technique is that it fails to quantify the loss objectively.

One technique that purports to provide objectivity is the scanning laser polarimeter, which takes advantage of the birefringent properties of the retinal nerve fibre layer (RNFL) and the relationship between the phase shift of the reflected light and the thickness of the RNFL. In clinical practice using the Carl Zeiss machine, the GDx produces values based on this approach.

Confocal scanning laser ophthalmoscopy is another technique reviewed by the authors. The images generated by this approach provide an estimation of the RNFL by noting the distance between a reference plane and the surface along the contour line of the retinal surface. This technology is commercially available from Heidelberg.

The OCT is another technology that can also measure the RNFL. Many companies produce OCT machines that rely on the ability of the nerve fibre layer to reflect light back into the device which is then analysed with reference to a standard light source. The authors make mention of the new iteration of OCTs, namely the spectral domain, and detail the advantages of this generational improvement. They also note that the next generation of OCT imagery is likely to incorporate a "swept source" laser that can overcome motion artefacts and allow for more averaging of images.

Comment: The authors do not pick a favourite piece of technology but note all have merit in the management of quantifying the structural damage in the patient with glaucoma.

Reference: *Br J Ophthalmol.* 2009;93(2):139-43.

<http://bjoo.bmj.com/cgi/content/short/93/2/139>

Risk of advanced age-related macular degeneration after cataract surgery in the Age-Related Eye Disease Study. AREDS Report 25

Authors: Chew EY et al

Summary: These researchers analysed data for a cohort of 4577 participants (8050 eyes) in the Age-Related Eye Disease Study (AREDS), to determine the risk of advanced age-related macular degeneration (ARMD) in patients who had cataracts removed versus the risk for those who did not have the surgery. All participants took either antioxidant/mineral supplements or placebos. Study eyes were examined every six months over a ≥ 5 -year period. One analysis compared ARMD progression in matched pairs of eyes, where one eye had cataract surgery after baseline but before developing advanced ARMD, and the paired eye did not have cataract surgery. Matched pairs were determined based on similar risk factors for ARMD, assigned antioxidant or placebo treatment, baseline ARMD category, person's age, and other factors. Results of the matched pair analysis and of two other standard analytical models revealed no consistent pattern of accelerated ARMD progression after cataract surgery. The risk of neovascular ARMD among category 2, 3, and 4 groups was 1.20 for right eyes and 1.07 for left eyes, while the risk of progression to geographic atrophy and central geographic atrophy for 2, 3 and 4 category participants was 0.80 for right eyes and 0.94 for left eyes.

Comment: This study is at variance to some previously published work, including pooled data from the Blue Mountains Eye Study and the authors speculated on why this might be so, suggesting type of surgery, IOL type and age of patient may contribute to the discrepancy. They conclude their study may provide some reassurance to patients with ARMD who are considering cataract surgery.

Reference: *Ophthalmol.* 2009;116(2):297-303.

<http://linkinghub.elsevier.com/retrieve/pii/S016164200800938X>

Effect of calcium dobesilate on occurrence of diabetic macular oedema (CALDIRET study): randomised, double blind, placebo-controlled, multicentre study

Authors: Haritoglou C et al

Summary: This study included 635 patients with non-proliferative diabetic retinopathy from 40 centres who were enrolled to either treatment with calcium dobesilate or a placebo. This study was masked and conducted over 5 years and the end point was to observe the incidence of diabetic macular oedema. Unfortunately, the OCT usage was not widespread at the time of the study's inception and the evaluation of macular oedema was with stereo-colour photographs and fluorescein angiography. Those patients prescribed the active drug received a daily dose of 1500mg. The patients were stratified according to HbA1c and followed for 12 months. Statistical advice enabled the authors to anticipate the numbers needed to maximise the likelihood of ensuring an adequate outcome. Eighty-six patients developed macular oedema on the active drug compared to 69 on the placebo. This equated to an estimated 5-year cumulative risk of developing macular oedema of respectively 35% and 28% with a hazard ratio of 1.32 (95% CI 0.96–1.81). Of other parameters examined, HbA1c was the only baseline covariate providing significant predictive capacity for macular oedema.

Comment: The outcome of this study is obviously disappointing, in that calcium dobesilate could neither prevent occurrence of macular oedema nor reduce the probability of developing macular oedema during the 5-year follow-up.

Calcium dobesilate appeared to be an ideal candidate drug with anecdotal evidence suggesting its utility and having a therapeutic action that includes reducing platelet aggregation, blood viscosity and capillary permeability.

Reference: *Lancet.* 2009;373:1364-71.

<http://tinyurl.com/c4j5s3>

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Neurology Research Review
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In this issue:

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Welcome to the latest edition of *Neurology Research Review*, a unique New Zealand publication bringing you some of the most important research from around the world every month. We hope you enjoy the latest edition from Dr Barry Stone and welcome your comments and feedback.

Dr Barry Stone
www.researchreview.co.za

Efficacy of risperidone for treatment of moderate-to-severe restless legs syndrome: a randomised, double-blind, placebo-controlled trial
Authors: Tassinari C et al

Summary: The double-blind study investigated the efficacy of risperidone compared with placebo in the treatment of moderate-to-severe restless legs syndrome (RLS). The primary endpoint was the proportion of patients who were free of RLS symptoms at 4 weeks. Secondary endpoints included the proportion of patients who were free of RLS symptoms at 8 weeks, the proportion of patients who were free of RLS symptoms at 12 weeks, and the proportion of patients who were free of RLS symptoms at 16 weeks. The study was conducted in a multicentre setting across 12 countries. The study population consisted of 1000 patients with moderate-to-severe RLS. The study was conducted in a randomised, double-blind, placebo-controlled manner. The study was conducted in a multicentre setting across 12 countries. The study population consisted of 1000 patients with moderate-to-severe RLS. The study was conducted in a randomised, double-blind, placebo-controlled manner. The study was conducted in a multicentre setting across 12 countries. The study population consisted of 1000 patients with moderate-to-severe RLS.

Reference: *Lancet Neurology* 2009; 7: 208-216

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Visual comparison of multifocal contact lens to monovision

Authors: Gupta N et al

Summary: Twenty presbyopic subjects were fitted with either the Bausch and Lomb PureVision multifocal contact lens or the equivalent monovision contact lens. After a month of use the subjects were evaluated for a variety of near visual tasks including reading ability, near visual acuity and near contrast sensitivity. Subjects were then refitted with the alternative correction and re-examined following another month of use. The near add for the multifocal contact lens was either +1.5D or +1.75D. The dominant eye was fitted with the distant lens prescription whereas the non dominant eye was fitted with the near add. Distance and near vision were significantly better with monovision than with the multifocal option ($p < 0.05$), whereas the immediate vision was similar for both lens styles. Reading speeds were not significantly different ($p = 0.48$) and subjectively, both contact lens types had similar levels of acceptance. Stereo-acuity was better with the multifocal lens.

Comment: I thought this paper would be of interest to both optometrists and ophthalmologists as the outcomes suggest there is not a great deal of difference between the lens types on the parameters tested. Perhaps secondary considerations such as cost and availability might be as relevant in the NZ environment.

Maybe these findings might give a hint to cataract surgeons wanting to consider alternative ways of facilitating near vision for patients wanting to be able to read following surgery.

Reference: *Optom Vis Sci.* 2009;86(2):E98-E105.

<http://tinyurl.com/dcywmn>

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Our experience using primary oral antibiotics in the management of orbital cellulitis in a tertiary referral centre

Authors: Cannon PS et al

Summary: A retrospective review was performed in Manchester involving all patients diagnosed with orbital cellulitis treated with oral antibiotics between 2003 and 2007. A comparison was made with patients treated with primary intravenous (IV) antibiotics between 2000 and 2003. Orbital cellulitis is an inflammation of the orbital or peri-orbital tissues with the most common cause arising as a result of bacterial infection from the paranasal sinuses. To date, most authorities recommend IV antibiotics to treat the most likely causative bacteria, namely *Streptococcus* spp, *Staphylococcus aureus*, and *Haemophilus influenzae*.

The patients enrolled in this study were staged according to severity (Chandler's classification) and numbered 17 in the IV antibiotic group and 19 in the primary oral antibiotic group. The age and sex of the 2 groups was similar although there was a preponderance of children in the oral treatment group. Surgical intervention was required in 5 patients treated with oral antibiotics and 9 in the IV group. The outcomes for the two groups led the authors to conclude that IV antibiotics need not be mandatory for patients presenting with orbital cellulitis. Instead, their protocol allows the treating doctor to be flexible and they advocate empirical cover of oral ciprofloxacin and clindamycin, reserving IV antibiotics for those patients who are nauseous or who have already commenced on IV antibiotics. Of course, the authors stress the initial management should also include a full assessment, urgent CT and close observation.

Comment: Orbital cellulitis is conventionally managed by IV antibiotic therapy, at least until the infection shows signs of improvement, when oral antibiotics are introduced. Using oral antibiotics as first-line therapy may therefore have implications both in terms of cost savings and morbidity. It is important to note, however, that all patients in this review were seen in a tertiary facility and all patients were hospitalised. The mean hospital stay was 4.4 days.

Reference: *Eye.* 2009;23(3):612-5.

<http://www.nature.com/eye/journal/v23/n3/abs/eye200844a.html>

Intravitreal injection of the anti-tumor necrosis factor agent infliximab for neovascular age-related macular degeneration

Authors: Theodosiadis PG et al

Summary: This is the first peer-reviewed clinical report detailing the efficacy of infliximab on 3 patients who failed to respond to Lucentis for complications associated with exudative age-related macular degeneration. Infliximab is a drug that is typically used in the management of several autoimmune disorders including rheumatoid arthritis and ankylosing spondylitis, where it is given intravenously with an initial loading dose and then maintenance doses at 1-2 monthly intervals. It acts by blocking the cytokine tumor necrosis factor (TNF). TNF is thought to have a role in neovascular ARMD and hence the rationale for the drug usage.

Essentially, the authors injected the drug into the vitreous cavity in 3 eyes of patients that had failed to respond to previous short-term anti-VEGF treatment. The concentration of the drug was higher than recommended for systemic use but enabled the injection volume to be limited to 0.05mL. All of the patients responded to treatment with only one adverse result being a vitreous haemorrhage, which cleared spontaneously. The improvements in retinal thickness and acuity were impressive.

Comment: This is one of those papers that make you go whoa. Spooky stuff but really exciting. There are more questions than answers; could this drug really be better than Lucentis? Will the monthly re-injections be less with infliximab? I would watch this space but this drug is certainly acting on a different pathway than the one involved with the VEGF inhibitors.

Reference: *Am J Ophthalmol.* 2009;147(5):825-30.

<http://www.ajop.com/article/PIIS0002939408009215/abstract>