Abstracts

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Intravitreal Triamcinolone Acetonide for Diffuse Diabetic Macular Edema: Phase 2 Trial Comparing 4 mg vs 2 mg

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Macular edema remains a major cause of visual impairment in diabetic patients. Intravitreal triamcinolone acetonide (TA) has been proposed as an alternative treatment for eyes with diabetic macular edema (DME) refractory *to* laser photocoagulation, and there is growing evidence that it effectively reduces macular thickness and improves visual acuity (VA) in DME.

In previous studies of the effects of triamcinolone on DME, various doses of TA were used. The most frequent is 4 mg, chosen empirically, because it constitutes 0.1 ml of the commercially available 40-mg TA formula. So far, the effects of different doses of intravitreal TA on macular edema have only been compared in one study, the authors of which found a correlation between dose and maximal increase in VA, but no difference in the increase of intraocular pressure (IOP) between doses. The main objective of this study was to compare the efficacy of the two doses by using central macular thickness (CMT), measured by optical coherence tomography (OCT), as the main criterion. The secondary objectives were to compare the side effects of the doses and the duration of their respective effects.

This study included thirty-two patients with diabetic macular edema unresponsive to laser photocoagulation. Patients were randomly assigned to receive 4 or 2 mg intravitreal TA in one eye (16 patients in each group). The main outcome was central macular thickness (CMT) measured by optical coherence tomography (OCT) at four, 12, and 24 weeks. Secondary outcomes were gain in Early Treatment Diabetic Retinopathy Study (ETDRS) scores, intraocular pressure (IOP), cataract progression, and duration of effect.

Before injection, mean (± SD) CMT was 564.5 ± 119 μm and 522.9 ± 148.5 μm in the 4- and 2-mg groups, respectively. At four, 12, and 24 weeks after injection, it was 275.0 ± 79.8, 271.4 ± 128.7, and 448.7 ± 146.4 μm respectively, in the 4-mg group, and 267.3 ± 82.4, 289.8 ± 111.4, and 394-7 ± 178.9 μm, respectively, in the 2-mg group. At no time was the difference in CMT between both groups statistically significant (P> 0.3). The between-group differences in the gain in the ETDRS score and in TOP were not statistically significant either. Diabetic macular edema recurred after a median period of 20 weeks vs 16 weeks in the 4- and 2-mg groups, respectively (P = 0.11).

Authors concluded that in the short term, intravitreal injection of 4 or 2 mg TA does not have different effects on CMT, visual acuity, or IOP.

The Treatment of Congenital Dacryocystocele

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Congenital dacryocystocele usually presents as a blue, cystic enlarged lacrimal sac at birth. The lacrimal drainage system is obstructed both proximally at the level of the common canaliculus, and distally at the level of the valve of Hasner. The proximal obstruction is functional. Fluid is thus trapped within the lacrimal drainage system. Dacryocystitis and preseptal cellulitis may develop within days or weeks. The treatment of dacryocystocele is controversial. Some physicians have advocated conservative treatment with antibiotics and massage, whereas others have recommended early surgical intervention if there is not a rapid response to conservative therapy or recommended prompt surgical therapy. This study evaluates the findings and results of treatment of patients with dacryocystocele and makes recommend-dations derived from this experience.

Twenty-seven consecutive patients with 29 congenital dacryocystoceles who presented from 1987 through 2006 are included in this study. Dacryocystitis and preseptal cellulitis requiring intravenous antibiotic therapy were present in 11 lacrimal systems (37.9%), and dacryocystitis without cellulitis was present in an additional 10 lacrimal systems (34.5%). One or more probing were performed in 26 patients

(89.7%). Resolution with conservative therapy occurred in three lacrimal systems. The initial probing was successful in seven of seven lacrimal systems (100%) that did not have infection, but was successful in only 10 of 19 lacrimal systems (53%) that had dacryocystitis with or without cellulitis. The mean age of probing in the surgical patients who did not develop infection was 5.9 days, whereas the mean age at first probing in surgical patients who developed infection was 17.3 days.

Authors concluded with remarks that patients with congenital dacryocystocele should have probing on an urgent basis and as early in life as possible, unless the lacrimal sac decompresses into the nose at the time of the initial examination. This approach will reduce the incidence of dacryocystitis and cellulitis, and improve the success rate of surgery.

A Control-Matched Comparison of Laser Epithelial Keratomileusis and Laser In Situ Keratomileusis for Low to Moderate

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Photorefractive keratectomy (PRK) was the most commonly performed surgical procedure until the introduction of laser in situ keratomileusis (LASIK) in the mid nineties. While PRK is safe and effective, the risk of corneal haze, especially in high myopia, is significant. Postoperative pain and slow visual rehabilitation are other limiting factors in PRK. LASIK has minimal postoperative pain, a faster visual recovery, less regression, and no haze even in high myopia. However, it is not a complication free procedure: flap-related complications (free cap, incomplete flap, irregular flap, button-holes, and lost flaps), interface related complications (epithelial ingrowths, deep lamellar keratitis, and interface debris), flap-related conical biomechanical instability, and iatrogenic keratectasia have been reported.

Laser epithelial keratomileusis (LASEK) may combine the advantages of PRK and LASIK while avoiding the disadvantages of both. It avoids all of the flap-related complications and reduces the risk of keratectasia associated with LASIK. In addition, it has relatively faster recovery periods with slightly less pain and haze than PRK. LASEK may be considered in patients with low to moderate myopia and myopic astigmatism, thin corneas with no signs of keratoconus, extreme keratometric values (such as steep or flat corneas), deep set eyes and small palpebral fissure, recurrent erosion syndrome, dry eye, glaucoma suspect, a wide scotopic pupil, scleral buckle, and for patients who are more predisposed to trauma, such as military personnel and athletes.

The purpose of this study was to compare the visual and refractive outcomes of laser epithelial keratomileusis (LASEK) and laser in situ keratomileusis (LASIK) for the treatment of low to moderate myopia.

The charts of 2257 eyes that underwent LASEK or LASIK treatment were reviewed. Patients who were 21 years of age or older having between -0.75 and -6.00 diopters (D) of myopia with up to -2.25 D of astigmatism were included. One hundred twenty-two LASEK-treated eyes were matched with 122 LASIK-treated eyes having preoperative spheres, cylinders, and spherical equivalent (SE) within ±0.50 D. Both groups had similar preoperative best spectacle-corrected visual acuity (BSCVA), laser platform, and follow-up durations. Outcome measures were visual and refractive results.

Preoperatively, the mean SE was -3.50 ± 1.40 D for LASEK and -3.50 ± 1.42 D for LASIK (P = .59). Postoperatively, the mean logarithm of minimum angle of resolution (logMAR) uncorrected visual acuity (UCVA) was 0.01 ± 0.08 (20/21) for LASEK and 0.06 ± 0.12 (20/23) for LASIK; the mean SE was -0.15 ± 0.40 D for LASEK and -0.37 ± 0.45 D for LASIK; and the mean logMAR of BSCVA was -0.03 ± 0.06 (20/19) for LASEK and -0.02 ± 0.05 (20/19) for LASIK. No eye lost 2 or more lines of BSCVA in both groups.

Slight differences in the visual and refractive results between LASEK and LASIK were observed, despite the use of the same nomogram. Both procedures were safe, effective, and predictable. Nomogram adjustment may be necessary for LASIK surgeons adopting surface ablation.

Retrobulbar haemodynamics in non-arteritic anterior ischaemic optic neuropathy

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The aetiology of non-arteritic anterior ischaemic optic neuropathy (NAION) is believed to be multifactorial, resulting in acute hypoperfusion of the short posterior

ciliary arteries (PCAs). The pathogenic mechanisms encompass various risk factors together with an acute incident of hypoperfusion for example, nocturnal arterial hypotension.

Several studies investigated circulatory abnormalities in patients with NAION. Patients with NAION showed decreased velocities of blood cells in the capillaries of the optic nerve head measured by laser Doppler velocimetry.

The retrobulbar haemodynamics of patients with NAION have been studied previously by means of colour Doppler imaging (CDI). CDI is an ultrasound technique with a simultaneous B-mode image using colour to represent intravascular movement on the basis of Doppler frequency shifts. Blood-flow velocities of the ophthalmic artery, the central retinal artery (CRA) and the short posterior ciliary arteries (PCAs) can be measured using CDI. A previously published study evaluated the peak-systolic velocities (PSVs) and Gosling's pulsatility indices of retrobulbar vessels in NAION before and after optic nerve sheath decompression. Preoperatively, eyes with NAION showed considerably lower PSVs in the CRA and the PCAs than the remarkable increase in blood flow velocities in the ophthalmic artery and CRA, and a marked decrease in vascular resistance in the PCAs.

The purpose of this study was to compare retrobulbar haemodynamics in patients with acute non-arteritic anterior ischaemic optic neuropathy (NAION) and age-matched controls by colour Doppler imaging (CDI).

25 patients with acute NAION and 35 age-matched controls participated in this study. By means of CDI, the blood flow velocities of the ophthalmic artery, central retinal artery (CRA), and nasal and temporal short posterior ciliary arteries (PCAs) were measured. Peak-systolic velocity (PSV) and end-diastolic velocity (EDV) and Pourcelot's resistive index were determined.

In the ophthalmic artery, no marked differences between patients with NAION and controls were detected. PSV and EDV of the CRA ($p<0.001$, $p = 0.002$) and PSV of the nasal PCA ($p<0.05$) were significantly decreased in patients with NAION compared with healthy controls. No marked differences between patients and controls were detectable for temporal PCAs.

Authors concluded that blood flow velocities of the nasal PCA and the CRA are considerably reduced in patients with acute NAION compared with controls. Patients with NAION in part showed markedly different retrobulbar haemodynamics.

Influence of tobacco use on cataract development

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Cataract is the lending cause of blindness and moderate visual impairment worldwide. It has been estimated that developing countries such as India have a large cataract burden, accounting for 44% of blindness. Numerous risk factors have been identified for early cataract development: environmental factors such as sunlight or ultraviolet exposure, systemic diseases such as diabetes mellitus, indices of nutrition such as low body mass index, and lifestyle factors such as smoking. Although effective treatment options are available to restore vision, identifying risk factors helps establish preventive measures as primary intervention. Tobacco use is a major public health problem worldwide and is the leading preventable cause of disease, disability and premature death. It has been reported to be responsible for a considerable amount of morbidity and mortality among middle-aged adults. It is estimated that one third of all women and two thirds of men in India use tobacco in some form, such as smoking tobacco in the form of cigarettes, bidis and cheroots, and smokeless tobacco in the form of snuff or chewing tobacco. In South Asia, the use of smokeless tobacco is common. The various forms are chewed, sucked, or applied to teeth or gums. The use of unprocessed tobacco, the cheapest form, varies in different parts of India. In Tamil Nadu, smokeless tobacco is sold as packets of strands and is used alone or along with betel leaf, areca nut and lime. Tobacco is also inhaled nasally in powdered form as dry snuff. Smoking is reported to be a risk factor for eye diseases such as cataract, age-related macular degeneration and glaucoma. No epidemiological studies have been carried out so far on the effect of smokeless tobacco on the eye. This paper reports the relationship between both use of both forms of tobacco (smoking and smokeless) and cataract in a population-based sample from rural south India.

3924 subjects from the Chennai Glaucoma Study conducted in rural south India underwent a comprehensive eye examination, including Lens Opacities Classification System II grading. Information

on tobacco use, type of tobacco (smoking and smokeless), duration and quantity of use was collected.

1705 (male:female (M:F) 1106:599) people used tobacco and were significantly older (mean (standard deviation (SD)) age 55.80 (10.64) years) than non-users (52.23 (10.51); p<0.001). 731 (M:F 730:1) people smoked, 900 (M:F 302:598) used smokeless tobacco, and 74 (M:F, 74:0) used tobacco in both forms. The unadjusted and adjusted (age and sex) odds ratio (OR) for a positive history of tobacco use and cataract was 1.72 (95% confidence interval (Cl) 1.51 to 1.96) and 1.39 (95% Cl 1.1 5 to 1.68), respectively. The unadjusted OR for smokers and smokeless tobacco users was 1.04 (95% Cl 0.88 to 1.23) and 2.74 (95% Cl 2.31 to 3.26), respectively. The adjusted OR was 1.19 (95% Cl 0.89 to 1.59) and 1.54 (95% Cl 1.22 to 1.95), respectively. No significant association was noted between smoking and any particular type of cataract. Smokeless tobacco use was found to be significantly associated with nuclear cataract even after adjusting for age and sex (OR 1.67, p = 0.067, 95% Cl 1.16 to 2.39).

Authors concluded with remarks that tobacco use was significantly associated with cataract. Smoking was not found to be significantly associated with cataract formation; however, smokeless tobacco use was more strongly associated with cataract.

Structural and functional assessment of the macular region in patients with glaucoma

Kanadani FN, Hood DC, Grippo TM, Wangsupadilok B, Harizman N, Greenstein VC, Liebmann JM, Ritch R Br J Ophlhalmol 2006; 90: 1393-7.

Despite recent technological advances, the diagnosis of glaucoma is still appearance of the optic disc. Some have suggested that in seeking early diagnosis of glaucomatous damage, it might be advantageous to assess the tissue loss in the perifoveal or macular region. Support for this comes from primate models of glaucoma, where considerable loss of retinal ganglion cells (RGC) occurs in the perifoveal region.

The macular region is rich in RGC bodies and undergoes thinning in glaucoma. Whereas RGCs cannot yet be counted directly in vivo in humans, retinal thickness can be measured with many different techniques. Loss of retinal thickness can be used as a surrogate measure for the loss of RGC bodies and nerve fibre loss, as these layers contribute up to 40% of the entire retinal thickness in normal eyes.

Macular retinal thickness, as measured by optical coherence tomography (OCT), can detect glaucomatous damage and corresponds with peripapillary nerve fibre layer (NFL) thickness, a measure of RGC axons as well as glial cells. Thus, the question arises as to how this structural measure (macular thickness) of glaucomatous damage compares with functional measures of macular function. This study compare OCT measures with two functional measures: the visual fields obtained with standard automated perimetry and the topographical information provided by the multifocal visual evoked potential (mfVEP). With the mfVEP technique, many (typically 60) responses, each associated with a local region of the visual field (or retina), are recorded simultaneously. Compared with other electrophysiological tests of visual function, the mfVEP has the advantage of producing a topographical measure of glaucomatous damage. Thus, mfVEP results can be compared with visual fields obtained with standard automated perimetry, as well as with structural measures.

The purpose of this study was to investigate the correlation of a structural measure of the macular area (optical coherence tomography (OCT)) with two functional measures (10-2 Humphrey visual field (HVF) and multifocal visual evoked potential (mfVEP)) of macular function.

55 eyes with open-angle glaucoma were enrolled. The 10-2 HVF was defined as abnormal if clusters of ≥3 points with p<5%, one of which had p<l%, were present. The mfVEP was abnormal if probability plots had ≥2 adjacent points with p< 1 %, or ≥3 adjacent points with p<5% and at least one of these points with p< 1 %. Two criteria were used for the macular OCT: (I) ≥2 sectors with p<5% or 1 sector with p<l% and (II) 1 sector with p<5%.

54 of the 55 eyes showed an abnormal 10-2 HVF and 50 had central mfVEP defects. The two OCT criteria resulted in sensitivities of 85% and 91%. When both functional tests showed a defect (in 49 eyes), the OCT was abnormal in 45. For the OCT the outer and inner inferior regions were the most likely to be abnormal, and both functional techniques were most abnormal in the superior hemifield.

Authors concluded with the remarks that good agreement exists between macular thickness and functional defects in patients with glaucoma. Study of

the macular region may provide a quantitative measure for disease staging and monitoring.

Peripapillary fundus perimetry in eyes with glaucoma

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Glaucoma is an optic neuropathy characterized by a specific and progressive injury to the optic nerve head (ONH) and retinal nerve fibre layer (RNFL), resulting in progressive loss of vision. Early detection and prevention of RNFL glaucomatous damage is mandatory, because injury to the RNFL is largely irreversible. The diagnosis of glaucoma is based on the appearance of the ONH and standard achromatic automated perimetry, but damage to the RNFL has been shown to precede visual field loss. It has been shown that 30-50% of retinal ganglion cells may be lost before an abnormality appears on standard automated perimetry. Therefore, morphological and functional evaluation of RNFL is essential in detecting and monitoring glaucoma. ONH and RNFL morphometry is carried out using different approaches, mainly optical coherence tomography. Many different functional tests (short-wavelength automated perimetry, frequency-doubling technology perimetry) have also been proposed with controversial results. Fundus perimetry, or microperimetry, is a functional test that quantifies differential light threshold (DLT) at selected areas, chosen by the examiner, under real-time fundus control. Fundus perimetry data are independent of eye movements, and exactly related to the stimulated areas. The aim of this study was to evaluate whether peripapillary fundus perimetry is modified in eyes with glaucoma and ocular hypertension (OHT), and to compare the functional data and morphological information obtained by peripapillary optical coherence tomography (OCT).

35 glaucomatous, 29 OHT and 24 control eyes were included. Peripapillary DLT at 1° from the optic nerve head was quantified with fundus perimetry; peripapillary RNFL thickness was measured over the same area by optical coherence tomography.

Mean (SD) peripapillary DLT was 19.2 (1.7), 17.6 (4.2) and 10.1 (6.9) dB in control, OHT and glaucomatous eyes, respectively ($p<0.001$). Mean (SD) RNFL thickness was 98.4 (35.3), 83.9 (35.1) and 55.8 (28.2) μm, respectively ($p<0.001$). Mean peripapillary DLT showed higher sensitivity and specificity in differentiating the three groups compared with RNFL thickness.

Authors concluded that progressive, significant reduction of peripapillary DLT was documented in OHT and glaucomatous eyes compared with controls ($p<0.001$). DLT reduction parallels RNFL reduction.

Detection of glaucoma using operator-dependent versus operator-independent classification in the Heidelberg retinal tomograph-Ill

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Primary open-angle glaucoma is a leading cause of blindness worldwide. Glaucomatous changes to the optic nerve head and retinal nerve fiber layer (RXFL) loss often precede achromatic visual field defects, which may become manifest only after a large percentage of retinal ganglion cells have been damaged. As such, early disease detection may be important in disease management strategies. Confocal scanning laser ophthalmoscopy has become an important tool for detecting structural damage of the optic nerve head and RNFL, and may assist in early glaucoma detection. There seem to be important racial differences between people of African and European ancestry regarding optic disc configuration and neuroretinal rim area. Given these variations, questions exist as to whether the current Heidelberg Retinal Tomograph (HRT)-II database of people of European ancestry can be applied to other racial groups.

Heidelberg retinal tomography (Heidelberg Engineering, GmBH, Dossenheim, Germany) uses confocal scanning laser technology to calculate topographic measurements of the optic nerve and parapapillary RNFL. One method of the HRT-II software analysis, Moorfields regression analysis (MRA), uses an algorithm to compare measured optic nerve parameters with those from a normative database. Although there is good reproducibility of HRT measurements, a major limitation of this device is the need for an operator to draw a contour line at the border of the optic disc. This can result in variability in measurements between different observers. The HRT-II uses a normative database consisting of 349 normal

eyes of white people, whereas HRT-III uses an enlarged race-specific database, consisting of eyes of 733 white and 215 black people.

The purpose of this study was to compare the abilities of a new Glaucoma Probability Scoring (GPS) system and Moorfields regression analysis (MRA) to differentiate between glaucomatous and normal eyes using Heidelberg retinal tomograph (HRT)-III software and race-specific databases.

In this prospective study, one eye (refractive error < 5 D) each of consecutive normal patients and those with glaucoma was enrolled. All patients underwent a full eye examination, standard achromatic perimetry (Swedish Interactive Threshold Algorithm-standard automated perimetry (SITA-SAP), program 24-2) and confocal scanning laser ophthalmoscopy (HRT-II) within 1 month. Normal patients had two normal visual fields in both eyes (pattern standard deviation (PSD) >5% and Glaucoma Hemifield Test within 97% normal limits) and a normal clinical examination. Glaucoma was defined on the basis of SITA-SAP visual field loss (PSD<5% or Glaucoma Hemifield Test outside normal limits) on two consecutive visual fields. HRT-II examinations were exported to the HRT-III software (V.3.0), which uses an enlarged race-specific database, consisting of 733 eyes of white people and 215 eyes of black people. Race-adjusted MRA for the most abnormal sector (operator-dependent contour line placement) was compared with the global race-adjusted GPS (operator independent). MRA sectors outside the 99.9% confidence interval limits (outside normal limits) and GPS 3≥0.64 were considered abnormal.

136 normal patients (72 black and 64 white patients) and 84 patients with glaucoma (52 black and 32 white patients) were enrolled (mean age 50.4 (SD 14.4) years). The average visual field mean deviation was -0.4 (SD 1.1) db for the normal group and -7.3 (SD 6.7) db for the glaucoma group ($p<0.001$). Mean GPS values were 0.21 (SD 0.23) and 0.73 (SD 0.27) for normal and glaucomatous eyes, respectively ($p<0.001$). Sensitivity and specificity values were 77.1% and 90.3% for GPS, and 71.4% and 91.9% for MRA, respectively.

In this cohort, GPS software sensitivity and specificity values are similar to those of MRA, which requires placement of an operator-dependent contour line. The development of software to detect glaucoma without a contour line is critical to improving the potential use of HRT as a tool for glaucoma detection and screening.