CANADIAN GLAUCOMA SOCIETY

FRIDAY 13 JUNE

Paper #A-00039
Efficacy and cost-effectiveness of glaucoma drugs for first line use

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Purpose: As part of a Health Canada mandate to the Canadian Agency for Drugs in Technology and Health and the University of Ottawa Department of Ophthalmology, a systematic review was undertaken to study the efficacy and cost-effectiveness of first line agents in glaucoma therapy.

Methods: A systematic review was undertaken using six databases to assess efficacy and cost-effectiveness. The economic analysis was performed from the perspective of a public third-party payer (Ontario Ministry of Health) and conducted in the framework of a decision analytic model. For both efficacy and cost-effectiveness, the included treatment comparators were: latanoprost, travoprost, timolol, brimonidine and dorzolamide.

Results: The most efficacious and cost-effective drugs were from the prostaglandin and beta-blocker category. Using three month data, the prostaglandins decreased IOP more than beta-blockers (WMD: -1.26 mmHg, 95% CI: -1.63 to -0.89 mmHg), but beta blockers were more cost effective: ICER for beta-blockers over prostaglandins: $34.48 per mmHg reduction.

Conclusions: Although prostaglandins are the most efficacious first line treatment for glaucoma, beta-blockers are more cost-effective.

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Paper #A-00040
What is the long term follow-up of appositional angle closure following laser peripheral iridotomy in Caucasian with normal pressure at diagnosis?

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Purpose: To evaluate the long-term outcome of Caucasian patients treated with laser peripheral iridotomy for angle closure with normal pressure at diagnosis.

Methods: It is a retrospective study, chart review from January 1981 to June 2007. All patients were diagnosed, by the same observer, using a Goldmann gonioscope in dim light with a small slit. Inclusion criteria were: appositional angle closure, intraocular pressure ≤21 mmHg, Caucasian race, follow-up ≥2 years, YAG or Argon iridotomy and phakic patients. Exclusion criteria were: use of anti-glaucomatous drops or a history of intra-ocular surgery at diagnosis, history of acute angle closure and presence of pseudoexfoliation. Observations were censored after any intraocular surgery. Outcome measures were intraocular pressure >21 mmHg and the start of hypotensive drop treatment. Secondary outcomes were laser trabeculoplasty, trabeculectomy or cataract surgery.

Results: 280 patients and 510 eyes satisfied the inclusion criteria. The mean follow-up time was 8.54±5.61 years. Females comprised 83.3% of patients. At diagnosis, the mean age was 60.51±11.59 years old and the mean IOP was 17.23±3.15 mmHg. Argon iridotomy was performed on 33.9% of patients, while YAG laser was used in 66.1%. Life table analysis did not reveal any statistical difference between the two types of iridotomies. After 10 years, 38.8% of eyes manifested a rise of pressure and 18.1% needed treatment. Laser trabeculoplasty, trabeculectomy and cataract surgery was performed in 3.14%, 2.16% and 26.67% of eyes respectively. Males and those with apposition after iridotomy had worst outcomes.

Conclusions: A significant proportion of patients treated with laser peripheral iridotomy for angle closure are at risk of developing high intraocular pressure in the future. Appositional glaucoma is not as benign as previously thought and a regular follow-up of these patients is needed to prevent glaucomatous vision loss. The incidence of cataract surgery was high.

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Paper #A-00041
Predictors of an adverse intraocular pressure rise one month following selective laser trabeculoplasty: results from a randomized controlled trial

Hussein Hollands, Delan Jinapriya, Donald S. Smallman, Sherif R. El-Defrawy, John Cheung, James P. Farmer, Mark D'Souza, Robert J. Campbell

Purpose: To determine predictors of an adverse increase in intraocular pressure (IOP) one month after selective laser trabeculoplasty (SLT). Specifically, clinical factors, factors related to the laser intervention and post laser anti-inflammatory therapies were investigated.

Methods: This report analyzes data from an ongoing randomized clinical trial investigating the effect of post-laser anti-inflammatory therapy on the IOP lowering effect of SLT. In this trial, patients undergoing 180 degrees SLT were randomized to either: prednisolone acetate 1.0% (PA), ketorolac tromethamine 0.5% (KT) or artificial tear placebo (PL) four times daily for five days post laser. Ophthalmologists or senior ophthalmology residents measured all IOPs and employed a strict measurement protocol adapted from the Ocular Hypertension Treatment Study. Two separate baseline IOP measures were taken prospectively for each patient. Angle pigmentation was assessed with direct reference to a standard. Total power used during SLT and the presence of cavitation bubbles were recorded for each patient.

Results: One eye from each of eighty-seven patients was enrolled and assessed at one-month post-SLT. Sixty-five patients (75%) had primary open angle glaucoma (POAG) whereas 22 (25%) had pseudoexfoliation glaucoma (PEXG). At enrollment overall mean IOP was 19.0 mmHg (SD=4.5) and patients were taking a mean of 1.6 IOP lowering agents. There were no statistical differences in baseline variables among treatment groups. At one-month post laser, mean IOP decreased 13.8% (SD=0.19), and 42.5% of patients attained a 20% lowering of IOP. However, seven patients (8%) developed an IOP rise of ≥20% at one-month post SLT. Univariate analysis demonstrated that subjects with PEXG were more likely than those with POAG to demonstrate a rise in IOP at one-month post laser (18.2% vs 4.6% developed an IOP rise ≥20%, respectively, p=0.065). Multivariate logistic regression with backwards selection (cut-off p=0.15) demonstrated that patients with PEXG were 12.9 times more likely than those with POAG to experience a 20% rise in IOP at one month (adjusted odds ratio 12.9, p=0.036). Type of postoperative anti-inflammatory therapy was not predictive of IOP rise (p=0.415, Analysis of Variance).

Conclusions: Patients with PEXG were significantly more likely to exhibit an adverse IOP rise at the one-month post SLT time point. As such, care must be taken when considering SLT as a treatment modality for patients with PEXG.

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Paper #A-00042
Evidence of a new uveolymphatic outflow pathway in human and sheep: implications for aqueous humor drainage and glaucoma

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Purpose: To determine whether a lymphatic circulation exists within the human and sheep ciliary body, and if present, its relationship to aqueous humor outflow.

Methods: Twelve normal human eyes with no history of ocular disease, atherosclerosis or stroke were obtained from the Eye Bank of Canada. Human eye sections were triple-immunostained with D2-40, CD34 and SMA antibodies for lymphatic vessels, blood vessels and smooth muscle actin respectively. Under general anesthesia, 50 µL fluorescent nanospheres (Invitrogen) were injected intracamerally in 3 sheep, with sacrifice 2 (n=2) and 4 (n=1) hours after the injection. Eyes were cryoprotected, serially sectioned and immunostained for a lymphatic endothelial marker (LYVE-1, Diagnostic Laboratories). Confocal laser microscopy was used to image ciliary body and capture images for 3-D construction.

Results: In normal human eyes, numerous fine D2-40 positive lymphatic channels were observed in circular, radial and longitudinal portions of the ciliary muscle, stroma, and ciliary processes. D2-40 positive lymphatic channels surrounded many blood vessels in the ciliary body. In the normal sheep, channels containing fluorescent nanospheres in the ciliary body were outlined by LVYE-1 immunoreactive lymphatic endothelial cells.

Conclusions: An uveolymphatic pathway is described for the first time in the human and sheep ciliary body. The flow of aqueous humor into these channels indicates a novel mechanism by which aqueous humor flows out of the eye, and if altered in glaucoma, is a possible novel therapeutic target.
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Paper #A-00043
Clinical trials comparing topical prostaglandins: potential industry bias

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Purpose: To evaluate potential bias between industry funded and non-industry funded publications comparing the efficacy of prostaglandin analogues. Several previous studies have found a significant association between funding source and pro-industry conclusions.

Methods: Systematic review of the literature. MEDLINE was searched until November 2007 using the keywords latanoprost, travoprost and bimatoprost. Inclusion criteria included English articles comparing prostaglandin analogues. Three independent observers reviewed each article. A standardized data collection sheet was used and any discrepancies were resolved by consensus. All studies were scored for methodological quality, statistical significance of study specified main outcome measure, correspondence of results of study specified main outcome to abstract conclusion and source of funding. The chi-square test and the Fisher's exact test were used to compare industry funded to non-industry funded studies.

Results: A total of 180 articles were identified by the original search. After reviewing the abstracts 39 studies published from 2001-2007 met the inclusion criteria. 27 were industry funded and 12 were not industry funded. Significant p-values for study specified main outcome measure were claimed in 8 of 27 industry funded versus 2 of 12 non-industry funded studies, p=0.69. Matching of the results of the main outcome measure claimed by the authors to the published abstract conclusions was found in 8 of 27 industry funded studies versus 10 of 12 non-industry funded studies, p=0.002. This suggests that on average industry-funded results were 92% less likely matching their abstract conclusions (odds ratio=0.08, 95% confidence interval 0.02-0.47) when compared with non-industry-funded studies. 24 of the 27 (88.9%) industry funded studies had positive sponsoring industry conclusions.

Conclusions: The published conclusions in industry funded studies were less likely to agree with the results of the main outcome measured and were usually pro the sponsoring company.

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Paper #A-00044
Prostaglandin efficacy and safety study undertaken by race

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Purpose: Latanoprost, travoprost and bimatoprost are prostaglandin or prostamide type anti-glaucoma medications, all of which are effective and safe for lowering elevated intraocular pressure (IOP). Most efficacy studies with these drugs have been performed with mainly Caucasian patients; however, some reports have suggested that there is a difference in response between Caucasian and African races. Because of the possibility that drugs may act differently in people of different ethnic background, we decided to study the racial effectiveness and safety of these drugs.

Methods: This was a prospective randomized single-masked multicentre study. The protocol was approved by the Research Ethics Board of each participating hospital. Patients with open angle glaucoma (primary, pseudoexfoliative or pigmentary) with an IOP >21 mmHg without therapy were randomized to receive one of three prostaglandin/prostamide drugs. Assignment of drug was balanced by racial group and study site, and the investigator was masked to the drug used. Patients were requested to self-identify their racial group as Caucasian, African, East Indian, Asian, or Hispanic; to minimize the possibility of heterogeneity, all four grandparents had to be known to originate from the same group. However, for purposes of analysis, the patients were divided into two groups - Caucasian or other. Patients were followed at two, six, twelve and twenty-four months; IOP and local side effects were assessed at each visit. Results were analyzed using Chi-square and t-tests.

Results: Eighty-three patients were recruited from 9 sites. The mean age of the patients was 61.5 ± 10.5 years. There were no differences in mean age or the distribution of gender between the patients whether examined by the two racial groups or the three drug groups. There was a highly statistically significant decrease in IOP from baseline to 12 and 24 months ($F = 439.3$, $p < 0.0001$; $F = 305.94$, $p < 0.0001$, respectively). There were no differences in treatment effect between the three drugs or between the two ethnic groups, ($p > 0.05$ for all comparisons). There were no significant differences in efficacy between race and drug.

Conclusions: At 24 months latanoprost, travoprost and bimatoprost all effectively lowered IOP. There were no differences in effect between the drugs, and no differences in response between Caucasian and the other racial groups.

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Paper #A-00045
Assessment of anterior chamber changes after laser peripheral iridotomy using anterior segment optical coherence tomography

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Purpose: To compare the anatomical changes that occur in the anterior chamber after laser peripheral iridotomy (LPI) using anterior segment optical coherence tomography (AS-OCT).

Methods: Using AS-OCT, we imaged 74 patients with closed or occludable angles as determined clinically, before and after LPI. We obtained low resolution scans of the horizontal and vertical meridians, as well as high resolution scans of all four quadrants. Data measures included anterior chamber depth (ACD), lens rise to anterior chamber ratio (LR:AC), iris convexity (IC), angle opening distance at 500 microns (AOD500), trabecular iris angle (TIA), and iris thickness at 1000 microns (IT1000).

Results: Preoperatively, the mean IC was 307um, which decreased to 150um after LPI ($p < 0.0001$). Mean AOD500 and TIA increased from 84um and 9.1° preoperatively to 139um and 15.0° postoperatively, respectively ($p < 0.0001$, $p < 0.0001$). We found that the patients could be divided into two groups, those whose angles improved significantly and those whose did not, defined as a change in TIA of less than or equal to 4°. There were 37 patients who improved and 37 who did not. Preoperatively, there was not a significant difference between the groups in ACD ($p = 0.96$), AOD500 ($p = 0.59$), TIA ($p = 0.31$), or IT1000 ($p = 0.49$). There was a significant difference in IC ($p < 0.05$) and LR:AC ($p < 0.0001$). In the group whose angles did not change significantly, the only significant change postoperatively was in IC (290um to 167um, $p < 0.0001$). In the group who had a significant change in TIA, there was also a significant change in ACD (2.21mm to 2.25mm, $p < 0.05$), IC (324um to 132um, $p < 0.0001$), AOD500 (79um to 189um, $p < 0.0001$), and TIA (7.8° to 19.3°, $p < 0.0001$). Between the two groups postoperatively, there was a significant difference in IC ($p < 0.05$), AOD500 ($p < 0.0001$), and TIA ($p < 0.001$).

Conclusions: AS-OCT was helpful in determining objective measurements before and after LPI. In the group of patients where TIA increased significantly, so did AOD500 and there was a significant decrease in IC. In patients that did not have a significant increase in TIA, there was also a lack of significant change in AOD500. They did show a significant change in IC. This may demonstrate that their narrow angles are likely due to a combination of pupillary block and plateau iris syndrome.

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Paper #A-00046
Transconjunctival suturing of the scleral flap for hypotony maculopathy after trabeculectomy

Laurence Letartre, Jean-Louis Anctil, Beatrice Des Marchais, Annie Goyette, Caroline Lajoie

Purpose: To assess the efficacy of transconjunctival suturing of the scleral flap in improving intraocular pressure (IOP) and visual acuity after hypotony maculopathy.

Methods: Retrospective review of a series of patients who underwent transconjunctival scleral flap suturing for hypotony maculopathy following trabeculectomy using mitomycin C. Hypotony maculopathy was defined as an IOP of less than 6 mm Hg combined with loss of two or more lines of central vision or tortuosity of the retinal vessels and chorioretinal folds in the posterior pole. The scleral flap was sutured through the conjunctiva using a spatulated needle with a 10-0 nylon suture.

Results: Twenty nine (29) eyes of twenty seven (27) patients were included in the study. The average age was sixty five (65) years ± 4.79 (range 39-82) and 66% were male. Before trabeculectomy, the mean IOP was 20 mm Hg ± 2.89 (range 10-42 mmHg), and the average visual acuity was 20/40. The mean IOP before transconjunctival suturing of the scleral flap was 2 mm Hg ± 0.52 (range 0-4 mmHg), and the average visual acuity was 20/100. The average duration of hypotony prior to transconjunctival suturing of the flap was 42 days ± 19,94 (range 1 to 259 days).The final mean IOP after transconjunctival suturing of the scleral flap was 10 ± 1,32 (range 5-21) and the average visual acuity was 20/40. Compared with visual acuity prior to transconjunctival suturing of the scleral flap, the average gain in visual acuity was 4.8 lines (range 1-9), with 72% returning to the vision level they had before trabeculectomy.

Conclusions: Transconjunctival suturing of the scleral flap for hypotony maculopathy after trabeculectomy is effective in raising IOP and improving visual acuity.

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Paper #A-00047
Anti-inflammatory treatments following selective laser trabeculoplasty: a randomized placebo controlled clinical trial

Delan Jinapriya, Don S. Smallman, Mark D'Souza, Hussein Hollands, Sherif R. El-Defrawy, James P. Farmer, John Cheung, Robert J. Campbell

Purpose: The role of anti-inflammatory treatment post selective laser trabeculoplasty (SLT) is unclear. This study was designed to determine whether the intraocular pressure (IOP) lowering effect of SLT is affected by the type of anti-inflammatory medication used post SLT.

Methods: A randomized observer-masked placebo controlled trial of 99 patients randomized to receive one of prednisolone acetate 1% (PA), ketorolac tromethamine 0.5% (KT) or artificial tear placebo (PL) four times a day for 5 days following 180 degrees of SLT. Patients with primary open angle glaucoma (POAG) (n=75) and pseudoexfoliation glaucoma (PXG) (n=24) were included. Pre-SLT IOP was measured on 2 separate occasions prior to SLT, and the average taken as the pre-treatment IOP. IOPs post SLT were measured at 1 hour and 1 month. All IOPs were measured according to a strict protocol adapted from the Ocular Hypertension Treatment Study.

Results: Overall mean baseline IOP was 19.0 mmHg (SD=4.5) and patients in the study were taking an average of 1.6 IOP lowering agents at enrollment. There were no statistically significant differences in baseline variables among the treatment arms. The mean IOP decreases at 1-month post SLT were 16.6%, 11.2%, and 13.8% in the PA, KT and PL groups respectively (p=0.56). The proportions of patients attaining a 20% or greater decrease in IOP at 1-month post SLT were 50%, 40%, and 36% in the PA, KT and PL groups respectively (p=0.57). Multivariate logistic regression analyses with backward selection demonstrated that those patients with higher baseline IOP had a greater probability of achieving a 20% IOP decrease at 1-month post laser (p=0.02).

Conclusions: Anti-inflammatory therapy in the doses studied in this trial did not significantly modify the IOP lowering effect of SLT.