

CANADIAN ASSOCIATION OF PEDIATRIC OPHTHALMOLOGISTS

SATURDAY 14 JUNE

Paper #A-00059

An investigation of the genetic causes of congenital stationary night blindness: correlating genetic mutational changes, clinical and electrophysiological findings

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Purpose: Congenital stationary night blindness (CSNB) is a condition due to a defect in retinal neurotransmission, which shows phenotypic and genetic heterogeneity. The electrophysiology of the autosomal recessive and X-linked forms have a Schubert-Bornschein pattern which has 2 subsets; complete CSNB (cCSNB) and incomplete CSNB (iCSNB). With the identification of the genes for X-linked iCSNB and cCSNB, we sought to evaluate the genetic cause for CSNB in a set of patients and correlate it to their clinical and electrophysiological findings.

Methods: Based on electroretinogram findings of a Schubert-Bornschein pattern, we diagnosed 34 patients with iCSNB and 12 patients with cCSNB between June 1997 and December 2002 in the British Columbia Children's Hospital. Each patient consenting to partake in the study was asked if they had a family history of CSNB, had a Mennonite ancestry and if they experienced nyctalopia. Visual acuity, refractive error and presence or absence of nystagmus was recorded. The patients' DNA samples were analyzed for mutations in the *CACNA1F*, *NYX* and *CABP4* genes.

Results: 46 patients were eligible for the study of which 29 patients from 23 families were enrolled. Of the 9 cCSNB patients, unique *NYX* mutations were found in 5 of the 8 families. Of these mutations, 3 were novel (2 nonsense, 1 missense) mutations. Among the 20 iCSNB patients, the *CACNA1F* (c.3166dupC) founder mutation was present in 8 families of Mennonite ancestry. 6 other patients had different *CACNA1F* mutations of which 5 were novel (2 splice site, 2 missense, 1 nonsense) mutations. The one patient with iCSNB who had no mutation in *CACNA1F* also had normal *NYX* and *CBP4* genes. All 9 patients with cCSNB had nyctalopia and were myopic (range -3.0D to -12.50D), with visual acuities from 20/30 to 20/100, 5 of these patients had nystagmus. All 3 cCSNB patients with a normal *NYX* gene had nystagmus and nyctalopia. Their visual acuity ranged from 20/30 to 20/50 and myopia from -3.0D to -6.5D. Of the 20 patients with iCSNB, nyctalopia was absent in 11, mild in 5 and troublesome in 4. The iCSNB patients refractive errors ranged from +4.5D to -12.5D and visual acuities from 20/30 to 20/200. The phenotypes of the patients with the Mennonite founder mutation varied; out of 12, 3 had nystagmus and 6 had mild nyctalopia. Visual acuity ranged from 20/30 to 20/80 and refraction from +0.25D to -12.5D. However the severity of phenotype among siblings (4 pairs) was observed to be similar. The patient with normal *CACNA1F*, *NYX* and *CABP4* genes has nyctalopia, no nystagmus, visual acuity of 20/50 OU and is emmetropic.

Conclusions: Mutations in either the *CACNA1F* or *NYX* genes were found in 25/29 patients supporting the notion that X-linked CSNB is the commonest form. There is considerable phenotypic variability within our group; this also existed among our patients with the *CACNA1F* founder mutation though this variability was reduced among sibling pairs.

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Paper #A-00060

Relationship between feeding schedules and gastric distress during retinopathy of prematurity screening eye examinations

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Purpose: To determine if there is a relationship between the timing of feeding prior to ROP screening eye examinations and gastric side effects and distress associated with this exam.

Methods: The design was a prospective, randomized, single-blinded, study involving 57 infants from the neonatal intensive care unit (NICU) requiring an ROP screening eye exam, and receiving normal or full enteral feeds, between December 2006-2007. Infants were randomly assigned to 1 of 2 study arms: feeding 1 hour prior to the ROP exam (arm 1, n=25) or feeding schedule adjusted to ensure no feeding 2 hours prior to the ROP exam (arm 2, n=32). Physiological data (systolic and diastolic blood pressure [SBP, DBP] and mean arterial pressure [MAP], pulse, respiratory rate, oxygen saturation) was collected at the following time points: before mydriatic drops, 5 minutes prior to exam, start, during, after exam, and 10, 30 and 60 minutes after the exam. Crying time during the exam, presence or absence of vomiting and gastric aspirates, and gastric aspirates volume 24 hours after the ROP exam were recorded. Data was analyzed using both univariate and multivariate, repeated measures ANOVA, by SPSS.

Results: The two feeding arms were similar with no significant differences in sex, race, APGAR, birth weight, gestational age at birth and during exam, exam number, and soother or oxygen use during the exam. There was significantly less crying time (79.5 ± 12 vs 88.3 ± 8 [s], $p=0.002$) and lower crying percentage (23.8 ± 3 vs 28 ± 3 , $p=0.013$) in arm 1 vs arm 2. There was significantly less gastric aspirates in arm 1 vs arm 2 (0.3 ± 0.1 vs 0.4 ± 0.09 , $p=0.001$), although the gastric volume (cc) was more in arm 1 vs arm 2 (3.5 ± 1.35 vs 2.3 ± 0.96 , $p=0.029$). No significant differences in vomiting between the feeding arms were found. There was a significant effect of the exam on all the physiologic indices ($p<0.01$), with both blood pressure and pulse significantly increased during the exam. The diastolic blood pressure was significantly lower during the exam in arm 1 vs arm 2 ($p=0.018$). Overall, there were no significant differences in the MAP, SBP, pulse, respiratory rate or oxygen saturation between the two feeding arms.

Conclusions: Our study supports prior studies indicating the ROP exam is stressful; it is the first study to our knowledge to specifically examine the effect of feeding schedules on gastric distress and stress in neonates undergoing this exam. Our results suggest that feeding infants in the NICU 1 hour compared to 2 or more hours prior to the ROP exam may lessen the stress the infant undergoes as measured by crying time and percentage during the exam. There is no increased vomiting with this feeding schedule. The incidence of gastric aspirates is less in infants fed 1 hour prior to the exam, although the volume may be higher when present. Further studies to investigate methods to reduce stress in infants undergoing ROP screening eye exams are required.

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Paper #A-00061

Rapid measurement of corneal diameter in children in clinic using digital photography

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Purpose: Corneal diameter is an important part of the ophthalmic examination of children, and yet can be one of the most challenging to do in a clinic setting. We describe a convenient non-invasive and non-threatening technique to obtain this measurement accurately.

Methods: 40 eyes of 20 children undergoing general anaesthesia were examined pre-operatively. A ruler was held vertically by a parent on one side of the face in the plane of the cornea. A digital photograph was taken of the ruler and eye. This image was then viewed immediately on the camera and magnified to life-size. This was achieved by using the zoom function in the camera until the ruler in the image exactly matched a real ruler placed on the LCD screen. The real ruler was then rotated to measure the white-to-white corneal diameter. This measurement was compared to that obtained from the same children under anaesthesia with the "gold standard" corneal measurement using callipers and a ruler.

Results: Measurement of the horizontal diameter of the pediatric cornea is achieved conveniently in a non-threatening manner. The accuracy of the results obtained is comparable to that of traditional measurement using callipers and a ruler under general anaesthesia.

Conclusions: Digital photographic measurement can be invaluable in the initial assessment and follow-up of children with suspected glaucoma, cataract or other conditions in which there is an increased or reduced corneal diameter for age. It may avoid an unnecessary examination under anaesthesia. This technique is convenient, atraumatic and accurate.

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Paper #A-00062

Ahmed glaucoma valve implant with mitomycin C in pediatric glaucoma: a retrospective review

T. J. Pollock, N. Puvanachandra, C.J. Lyons

Purpose: In children, the management of glaucoma unresponsive to medical management presents unique challenges. We reviewed the surgical outcomes of a consecutive case series of Ahmed glaucoma valve implantation (GVI) augmented with mitomycin C (MMC) with the aim of assessing the longevity of the ocular hypotensive effect and of documenting the incidence of complications.

Methods: Retrospective review of the records of a consecutive series of patients who underwent Ahmed GVI over a 10 year period ending in 2006. The surgical database of a single surgeon was used to identify cases. Kaplan Meier life-table analysis was performed to assess the duration of surgical effect. Study end-points were assessed with respect to glaucoma etiology, age at diagnosis, surgical technique and dose of MMC.

Results: 85 Ahmed GVI procedures were identified in 68 eyes of 55 patients. At last follow-up, intraocular pressure (IOP) was controlled in 88% of eyes. For each procedure, the probability of unqualified success (IOP controlled without any medications) at 1 year was 33%. Qualified success (IOP controlled using medication) accounted for an additional 43% of procedures at 1 year. 60% of all procedures were followed by complications of any kind, a large proportion of these were minor or self-limiting. Only 3% of all procedures were complicated by severe visual loss. The rate of bleb leak and endophthalmitis were equivalent to previously reported Results: for MMC augmented trabeculectomy and or trabeculotomy in children.

Conclusions: Mitomycin C augmentation of Ahmed GVI represents a useful technique in the management of resistant pediatric glaucoma. In a large group with diverse etiology and long follow-up, we report efficacy at least equivalent to other filtration procedures reported in the literature. The low but potentially serious side-effect profile is acceptable in the context of a relentless, potentially blinding condition.

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Paper #A-00063

Endoscopic goniotomy: early clinical experience in congenital glaucoma

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Purpose: To review the technique and early outcomes of endoscopic goniotomy (EG) in children with opaque corneas and primary congenital glaucoma (PCG) or developmental glaucoma with ocular or systemic anomalies (DGA).

Methods: The technique for EG involved injecting Miostat into the anterior chamber followed by Healon 5. The 20g endoscope (Endoptiks) was introduced through a 3.2 mm clear corneal incision, and angle structures were incised with a 25g needle for approximately 300 degrees via 2 sites (temporal and superonasal) using adjacent ports for the endoscope and needle while observing the angle details on a monitor. At the end of surgery, the viscoelastic was washed out and the corneal wounds were sutured. In bilateral glaucomas, both eyes were typically operated at the same sitting using separate surgical setups. We reviewed consecutive cases from 2003 (when the technique was initiated) to 2007. The primary outcome was IOP change from baseline (IOP at first presentation). Secondary outcomes included horizontal and vertical corneal diameter, axial length, vertical cup/disc ratio, adverse events, and the need for additional medical or surgical intervention.

Results: A total of 14 eyes of 8 consecutive patients (6 males, 2 females) were included: 4 patients with PCG, 2 with aniridia and 1 each with Rubinstein-Taybi syndrome and neurofibromatosis. The mean age at surgery was 3.88 ± 3.68 months (range=0.5-11). The average follow-up was 11.75 ± 6.23 months. During this period, corneal diameter, axial length and cup disc ratio remained stable in all eyes; however IOP changes were variable. Overall, IOP reduction from baseline was 14.79 ± 17.22 mm (PCG 26.33, DGA 6.13) with or without extra medication but no further surgical intervention. 2 patients with DGA needed additional surgery after 8-9 months. Cataract and zonular dialysis were noted in 2 patients with aniridia. Other complications were hyphema (8 eyes: 2 PCG, 6 DGA), subretinal hemorrhage (1 PCG), micropannus (1 DGA) and peripheral anterior synechiae (4 DGA).

Conclusions: EG is a technically feasible and safe procedure in a variety of pediatric glaucomas presenting with opaque corneas. Similar to conventional goniotomy, our early results demonstrate that IOP control post EG is better in eyes with PCG than DGA. A larger sample size and comparison to other angle surgery techniques is needed to further study and understand the value of this procedure.

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SATURDAY 14 JUNE

Paper #A-00064

Idiopathic orbital inflammatory syndrome associated with central retinal artery and vein occlusion

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Purpose: Describe vascular complication of idiopathic orbital inflammatory syndrome (IOIS) resulting in unilateral loss of vision.

Methods: Case report describing clinical presentation, radiological findings, treatment and histopathology.

Results: A 3-year-old female was referred from the emergency department at another hospital to our unit with 24 hours history of left superior eyelid swelling and eye pain accompanied by complete ipsilateral visual loss. Fundus examination showed severe optic disc edema, dilated veins, almost confluent retinal hemorrhages extending to midperiphery obscuring retinal details. Intravenous fluorescein angiography (IVFA) revealed optic disc hyperfluorescence with absence of retinal vascular filling in early and late phases. Fundus and IVFA findings were consistent with central retinal vein and artery occlusion. MRI study showed diffuse swelling of the optic nerve, extraocular muscles and retro-orbital fat with marked contrast enhancement around the optic nerve. The orbital inflammation resolved with intravenous steroids without any improvement of visual function. Investigations confirmed absence of systemic association. Absence of visual recovery despite high dose intravenous steroids motivated a surgical exploration to rule out optic nerve compression. An anterior orbitotomy via desinsertion of the medial rectus was performed. Intraoperative assessment revealed normal optic nerve caliber and diffuse "woody" induration of periorbital tissues. Incisional multiple biopsies were taken from affected tissues. Histopathology report indicated presence of mature adipose tissue and vessels in all samples interpreted as normal orbital fat histology. Absence of inflammatory reaction was likely due to treatment with systemic steroids. The patient underwent panretinal photocoagulation. However, persistent ocular ischemia resulted in neovascular glaucoma. Further retinal photocoagulation was associated with regression of new vessels. The final outcome was poor with no light perception, cataract and phthisis bulbi. Clinical, radiological and intraoperative findings were all consistent with idiopathic orbital pseudotumor.

Conclusions: IOIS is a condition that may rarely be associated with severe visual loss despite treatment. To our knowledge this is the first case of IOIS accompanied by combined central retinal artery and vein occlusion and total loss of vision in the affected eye, a devastating possible complication that can develop in the course of acute IOIS secondary to severe diffuse orbital inflammatory reaction. Inflammation pattern was consistent with the perioptic neuritis form of IOIS which in addition to the severity of inflammation likely resulted in the vascular complications described.

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Paper #A-00065

Visual performance, perceptual, academic and motor outcomes of school-aged children born pre-term with and without retinopathy of prematurity

Katya Feder, William Hodge, Annick Fournier, Michael O'Connor, Ella Ross, Asha Nair, Jocelyn Faubert

Purpose: Visual performance is often compromised in pre-term children but long term motor, academic and visual perceptual outcomes of pre-term children with and without retinopathy of prematurity has not been investigated.

Methods: Pre-term subjects with ROP (n=15), without ROP (n=11) and controls (n=16) (MA: 10.1 years) were evaluated during 2 visits as part of a larger study (n=50 per group). Visual, motor, perceptual, and academic performances were assessed using standardized instruments.

Results: Visual performance/ophthalmic evaluation (visual field, contrast sensitivity, depth perception, color vision, perceptual processing, refraction) found no significant differences between the three groups with the exception of dark contrast sensitivity and Gardner visual discrimination subtest (p=0.05). Clinically, varying tortuosity in pre-terms compared to controls was reported.

Conclusions: No significant differences in visual/perceptual outcome (pre-terms with/without ROP) seen at this time. A larger sample may be more conclusive of ophthalmic sequelae in this high risk population.

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Paper #A-00066

The National Retinoblastoma Strategy: development of best-practice guidelines

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Purpose: The rarity of retinoblastoma results in inequalities in the diagnosis, treatment and management of retinoblastoma patients and their families across Canada. This project aims to improve the access to and quality of clinical care for all Canadian children affected by retinoblastoma, through the development, dissemination, and implementation of Canadian Best Practice Guidelines (BPGs). These BPGs will be relevant to all those who impact on the wellbeing of these children, including primary health care personnel, ophthalmologists, oncologists, geneticists, parents, Ministries of Health, charities and others.

Methods: A collaborative, multidisciplinary team involving experts and families from across Canada is currently developing the BPGs. Through a series of meetings and Internet communications between clinical experts, patients and parents, a preliminary framework for the BPGs was developed, based on identified issues. Relevant experts on the following topics have drafted the BPGs and corresponding recommendations: referral/screening/diagnosis, genetic testing, treatment, follow-up, psychosocial care, and future research directions. Each recommendation is preliminarily referenced and graded for evidence and strength. A guideline expert is editing the BPGs into one document and appraising the overall BPGs using the Agree Collaboration Tool. The International Advisory Board and the stakeholders will finally review the BPGs at a national consensus meeting, and submit them for publication. The BPGs will be updated every 5 years to incorporate new knowledge.

Results: While dissemination of the BPGs for retinoblastoma presents some challenges in light of the rare nature of the disease and the potential involvement of multiple caregivers, a number of dissemination strategies will be employed and their effectiveness will be evaluated: modules on retinoblastoma for training of health personnel and public education, computer websites and regional workshops. Questionnaires will score the effectiveness of dissemination strategies and implementation of BPGs on outcomes. Health records, structured interviews and participation in a National Retinoblastoma Tumor Board will be used to measure adherence to and audit the impact of the BPGs.

Conclusions: BPGs encourage high quality and consistent healthcare and stimulate further research in areas where knowledge and scientific evidence is of low quality. For a disease as rare as retinoblastoma, BPGs must deal with awareness, referral paths, access to care, and family issues, in addition to the traditional medical care description. The uniform approach for Canada will facilitate data collection and research to achieve future improvements in management and treatment.