Resident Perspectives: Obstructive sleep apnea screening in patients with retinal vein occlusion

Obstructive sleep apnea (OSA) is a common disorder involving repeated bouts of upper airway collapse during sleep, causing partial or complete obstruction of breathing, oxygen desaturation, hypercapnea and fragmented sleep. Among the general working-aged population, OSA occurs in 2% of women and 4% of men. Major risk factors include male sex, obesity, and cigarette smoking. OSA has been shown to cause excessive drowsiness and systemic hypertension. It is also associated with increased risk of myocardial infarction, congestive heart failure, and stroke. From the ophthalmology perspective, OSA is more common among patients with glaucoma, non-arteritic anterior ischemic optic neuropathy, central serious retinopathy, retinal vein occlusion, and floppy eyelid syndrome. OSA may directly increase the risk of these ocular conditions by altering retinal and optic nerve perfusion.

The most common treatment for OSA is nasal continuous positive airway pressure (CPAP), which has been shown to improve hypertension and quality of life of patients with OSA. There is conflicting evidence for whether CPAP reduces the risk of cardiovascular morbidity and mortality. We also do not know whether treatment of OSA improves outcomes of associated ophthalmic disorders, though this is a natural area for future investigation. Given the potential for improved quality of life, and possible improvements in severe systemic diseases, ophthalmologists have an obligation to their patients to be aware of which ocular diseases are associated with OSA, and to consider referring affected patients for diagnostic testing. The results of the present study would seem to suggest that in-office screening questionnaires, at least for RVO patients, add little in this regard. Home-based diagnostic tests are generally more accessible and may be considered for some patients but are considered less accurate than polysomnography.

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Article being referenced: https://www.canadianjournalofophthalmology.ca/article/S0008-4182(19)31294-3/fulltext

References

Safety first: preventing endophthalmitis post-intravitreal injections

Anti-vascular endothelial growth factor (anti-VEGF) therapy has revolutionized treatment of neovascular ocular diseases. It is the most commonly performed invasive procedure in Ophthalmology with a low incidence of serious complications such as endophthalmitis. Although the incidence of endophthalmitis ranges between 0.02% to 0.09%, the associated visual morbidity is devastating. This intraocular inflammation is characterized by progressive vitritis, pain, redness and decreased vision. Despite abundance of existing literature, there remains inconsistency in clinical practice for administration of intravitreal injections.

In this issue, Storey, Patel and Garg summarize the evidence-based clinical strategies to reduce the risk of post-injection endophthalmitis. The results of their review suggest that minimizing oral flora exposure, treatment of blepharitis, pre-filled syringes, and sterilization with povidone iodine after placement of speculum can significantly decrease the risk of endophthalmitis during intravitreal injections. Factors that did not influence the risk of infection include location of injection, use of gloves, subconjunctival lidocaine, type of anti-VEGF, and prophylactic topical antibiotics. The authors emphasized the use of povidone iodine as having the strongest evidence for reducing the rate of endophthalmitis. However, the dilution of povidone influences its ability to sterilize the ocular surface. A recent study simulated an intravitreal injection procedure and measured growth of oral flora using blood agar plates, which were subjected to different concentrations of povidone iodine from 1%-5% and no pre-application (control). Results showed that povidone concentrations less than 5% were not effective in reducing growth from bacterial droplets dispersed during speech. Therefore, recommendations suggest instillation of 5% or 10% povidone solution to the treatment area for at least 30 seconds prior to injection. Use of at least 5% povidone has also been shown to be more effective than wearing masks or no-speech protocol alone.

Storey et al. also highlighted one of the existing controversies on injection technique that remains with the use of eyelid speculum during injections. While a speculum helps to remove eyelids and associated pathogens from the injection site, some authors have argued that the manipulation of lids during speculum placement may release pathogens onto the ocular surface. A 5-year retrospective study of 78,000 intravitreal injections showed that manual eyelid retraction had similar rate of infection as use of the metal speculum. Furthermore, manual retraction may minimize patient discomfort and length of procedure. Consequently, the current review and existing literature conclude that the use of eyelid speculums is at the discretion of the clinician and does not increase or decrease the risk of endophthalmitis.

The Endophthalmitis Vitrectomy study (EVS) in 1997 established the treatment guidelines for acute endophthalmitis post-cataract surgery. However, to date, there is no such randomized clinical trial on treatment of endophthalmitis following intravitreal injections. The EVS study showed that intravitreal antibiotics with vancomycin and amikacin mark the initial steps in the management of endophthalmitis; although pars plana vitrectomy showed better results for patients with light perception vision or worse. Since there is still no consensus on whether to extend these recommendations to the treatment of endophthalmitis post-intravitreal injection, the risks of endophthalmitis must be mitigated by maintaining strict safety precautions, as suggested in this review. Further, there is no current standardized protocol for the administration of intravitreal injections. This review provides up-to-date evidence-based strategies to establish consistency among clinicians. Despite these precautions, in clinical practice, clinicians should maintain a low threshold to treat with intravitreal antibiotics if endophthalmitis is suspected.

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Article being referenced: [https://www.canadianjournaleofophthalmology.ca/article/S0008-4182(20)30042-9/fulltext](https://www.canadianjournaleofophthalmology.ca/article/S0008-4182(20)30042-9/fulltext)

References

OCT-A segmentation errors and motion artifacts in eyes with epiretinal membrane

Optical coherence tomography angiography (OCT-A) is a non-invasive method of imaging the microvasculature of the retina and choroid. By analyzing consecutive cross-sectional scans, changes between scans can be used to determine flow in the region of interest and at specific depths. OCT-A functionality allows further evaluation of various retinal diseases, such as epiretinal membranes (ERMs). For patients with ERMs, the depth of the tractional layer is a visual prognostic factor as it is strongly associated with intraretinal changes; OCT-A enables visualization and quantification of vascular changes and depth-dependent tangential distortion of retinal layers by ERMs. Automatic retinal layer segmentation is performed by OCT-A software, and as with all image recognition algorithms, its accuracy is dependent on image quality. In pathological states that disrupt normal retinal anatomy, segmentation errors are also more likely.

In this issue, Bontzos et al. examine image quality, segmentation errors, and motion artifacts in patients with ERM imaged with OCT-A. They imaged and compared 39 eyes with ERM and 40 healthy controls. The average quality index score for the ERM group was lower than that of the controls (7.46 ± 0.94 vs. 8.22 ± 0.76, respectively, \( p = 0.002 \)). The authors attributed this to poorer fixation among ERM patients due to visual diminution and metamorphopsia (though not quantitatively measured). The number of motion artifacts detected, including blink lines, displacement, stretch artifacts, and vessel doubling, was 1.21 ± 0.91 in the ERM group vs. 0.12 ± 0.40 in the control group. This represented a 14-fold increased risk among ERM patients. No segmentation errors occurred in the control group, but there was a high segmentation error rate (69.2%, 29/39) in the ERM group. Inner plexiform layer (IPL) segmentation errors were associated with retinal thickness and disease duration. Inner limiting membrane (ILM) segmentation errors were associated with disease duration only.

The findings by Bontzos et al. are clinically relevant because they suggest that extra care should be taken by the operator to obtain good quality images for patients with ERM. Perhaps manual segmentation should be considered in select cases, but this is time-consuming and subject to inter-grader variability. Furthermore, segmentation errors and motion artifacts are not an issue related solely to ERMs but are more widespread. Lauermann et al. report that these errors are present in other retinal diseases such as age-related macular degeneration, central serous chorioretinopathy, retinal vein occlusion, and retinitis pigmentosa. Given this, technologically-based solutions may be more appropriate and provide opportunities for future research. In fact, eye tracking algorithms incorporated into OCT-A imaging have already reduced motion artifacts, though further improvements are still warranted. Convolutional neural networks (CNNs) are particularly useful in image recognition and machine-learning solutions have successfully segmented pathological areas in OCT images. This can be extended to OCT-A images to create CNNs for different retinal pathologies. As OCT-A becomes increasingly used in research and clinically, it is important to optimize image quality to allow for reliable intra- and inter-patient comparisons and to accurately determine clinical implications of identified biomarkers.

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Article being referenced: https://www.canadianjournalofophthalmology.ca/article/S0008-4182(18)30958-X/fulltext

References

Resident Perspective: Comparison of acute histopathologic changes in cadaver eyes after MicroPulse and continuous wave transscleral cyclophotocoagulation

Transcleral cyclophotocoagulation (TSCPC) is a procedure that lowers intraocular pressure (IOP) by cycloablating the nonpigmented ciliary body epithelium. However, traditional continuous wave transscleral cyclophotocoagulation (CWCP) is unfortunately often associated with poor visual outcomes and is usually only reserved for patients with advanced glaucoma. Recently, MicroPulse cyclophotocoagulation (MPCPC), which delivers pulsed thermal energy, has been advocated for its less severe side effect profile. However, the exact mechanism of how TSCPC reduces IOP and which structures are injured and to what extent is not well understood.

In this issue, Maslin and colleagues explore the histopathological effects of MPCPC and CWCP on the ciliary body and adjacent structures in cadavers. The authors performed traditional CWCP, low burn CWCP, or MPCPC on 6 eyes obtained from 3 different human cadaver eyes. Traditional CWCP was applied at 2000 mW for 2 seconds in the first quadrant, low burn CWCP was applied at 1250 mW for 4 seconds in the second quadrant, MPCPC was applied using CYCLO G6 Glaucoma Laser with a 0.5 ms laser bursts followed by 1.1 ms rest period over 90 seconds in the third quadrant, and a fourth quadrant received no treatment serving as the internal control. The treated eyes were then dissected, set in paraffin with haemotoxylin and eosin staining and analyzed using light microscopy.

The histopathologic results of the study showed that traditional and low burn CWCP exhibited variable coagulative tissue damage to the ciliary body, in the ciliary loose connective tissue stroma, ciliary vascular network, smooth muscle, and basement membrane of the pigmented ciliary epithelium with variable involvement of the pars plicata, pars plana, and root of the iris. Comparing traditional to low burn CWCP, the authors noted much less damage to the ciliary body with low burn compared with traditional CWCP. When comparing CWCP to MPCPC, the authors found that the MPCPC treated tissue showed minimal damage to the ciliary body, localized to the basement membrane of the outer pigmented ciliary epithelium. No histopathologic effects were observed in the conjunctiva, sclera, trabecular meshwork, or Schlemm’s canal using CWCP and MPCPC.

The authors noted that the mechanisms for IOP lowering using MPCPC are difficult to elucidate, given the lack of changes in the nonpigmented ciliary epithelium. Possible mechanisms include mechanical restructuring of the trabecular outflow facility and a larger extracellular space from the anterior chamber to the suprachoroidal space may lead to increased uveoscleral outflow, leading to the lowering of IOP post MPCPC. Although the mechanism of IOP lowering is unclear, the study indicated that the acute changes after MPCPC is less damaging to tissue compared with CWCP, suggesting that it may be a safer and a more selective method compared with CWCP.

Clinical Practice Point: MPCPC results in less structural damage compared with low burn and traditional CWCP, suggesting a potentially safer and more selective method for lowering IOP.

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Article being referenced: https://www.canadianjournalofophthalmology.ca/article/S0008-4182(18)31281-X/fulltext

References

Corneal findings in patients with Loeys-Dietz syndrome type 4: a genotype-phenotype correlation study

Precision medicine is a rapidly developing approach to healthcare that evaluates the effects of genetic, environmental, and lifestyle parameters on an individual patient level. Currently, there are several examples of precision medicine applied to ophthalmology, including the first FDA approved gene therapy for inherited disease (for RPE65-associated Leber congenital amaurosis), BAP1 genotyping for prognostication in patients with uveal melanoma, and numerous genome-wide studies examining genetic elements associated with multifactorial diseases such as glaucoma and age-related macular degeneration. As a result of improved access to molecular genetic testing, phenotype-genotype correlations are being identified. Reports of these associations highlight possible disease mechanisms and provides an avenue of investigation for improving the diagnosis and prevention of disease in patients.

In this issue, Eghrari et al. report an association of corneal guttae and reduced corneal thickness in patients with Loeys-Dietz syndrome caused by mutation in $\text{TGFB2}$. Loeys-Dietz syndrome is an autosomal dominant connective tissue disorder caused by mutations in genes involved in TGF-$\beta$ signaling and shares similarities with Marfan syndrome and Ehlers-Danlos syndrome. All three typically involve some degree of pathology in the cardiac, skeletal, and cutaneous systems. Previously reported ophthalmic manifestations of Loeys-Dietz syndrome include hypertelorism, axial myopia, blue sclerae, and corneal thinning. Notably, ectopia lentis is not a prominent feature, unlike in patients with Marfan syndrome. While corneal thinning has previously been identified in a group of patients with Loeys-Dietz syndrome, this association had not been established on a gene-specific level until now.

Eghrari et al. comprehensively assessed the ocular features of three probands who each had a unique mutation in $\text{TGFB2}$ causing Loeys-Dietz syndrome. The first and second proband each demonstrated reduced central corneal thickness and the presence of corneal guttae at a young age. To reduce the likelihood of a confounding corneal endothelial dystrophy diagnosis, presence of CTG trinucleotide repeat expansion of $\text{TCF4}$, occurring in approximately 70% of cases of Fuchs endothelial dystrophy, was investigated and was negative. The third proband, including two other affected family members, all demonstrated reduced corneal thickness compared to two unaffected family members. The third proband and his family members did not, however, demonstrate corneal guttae.

While the association of corneal thickness and guttae with mutations in $\text{TGFB2}$ may be further strengthened by statistically comparing these parameters to those in patients without Loeys-Dietz syndrome, the authors still highlight an interesting finding that supports the role of TGF-$\beta$ signaling in the cornea. This study corroborates existing evidence for the involvement of the TGF-$\beta$ pathway in the development of corneal guttae and may prompt further investigation into potential therapeutic targets for endothelial dystrophies. Furthermore, from a clinical standpoint, reduced central corneal thickness is a risk factor for the development of open-angle glaucoma. With this knowledge, patients with $\text{TGFB2}$-related Loeys-Dietz syndrome may benefit from...
regular ophthalmology evaluation to assess for glaucomatous changes, in addition to monitoring for corneal endothelial changes.

In summary, Eghrari et al. have provided evidence for the presence of corneal thinning and guttae in patients with TGFB2 mutations. Although Loeys-Dietz syndrome is a rare disorder, this study eloquently highlights the importance of establishing genotype-phenotype correlations to guide more specific diagnostic and treatment considerations as part of an evolving precision medicine landscape.

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Article being referenced: https://www.canadianjournalofophthalmology.ca/article/S0008-4182(18)30958-X/fulltext

References


