Resident Perspective: Micropulse trans-scleral laser therapy outcomes for uncontrolled glaucoma

Cyclophotocoagulation (CPC) uses laser cycloablation to treat glaucoma. CPC is typically used in refractory end-stage glaucoma to decrease aqueous secretion and intraocular pressure (IOP). In traditional transscleral cyclophotocoagulation (TSCPC), a continuous 810nm diode laser is applied to ablate the ciliary body epithelium and stroma as energy is absorbed by the melanin. The effect is unpredictable and nonselective, leading to serious complications including chronic hypotony, uveitis, and sympathetic ophthalmia. Therefore, TSCPC is often limited to patients with advanced glaucoma and poor prognoses.1

Micropulse transscleral laser therapy (mTLT) was recently developed to selectively target the ciliary processes, with less collateral damage. The delivery of energy in short on cycles, with off cycles in between, allows energy to build up to the target threshold in pigmented tissues and thermal dissipation in adjacent tissue.2,3 Prior studies have shown mTLT and TSCPC to have comparable efficacy, however these are limited in sample size or duration.4,5,6

In this issue, Marchand and colleagues evaluate the long-term efficacy of mTLT in this prospective interventional study of 52 patients (52 eyes) with uncontrolled glaucoma over 18 months.3 All 52 patients underwent treatment with mTLT with treatment duration adjusted based on iris pigmentation and glaucoma severity.

The primary outcome was the absolute success of mTLT at 18 months. Absolute success was defined by three criteria post-intervention: 1) an IOP between 6 and 21 mmHg; 2) at least a 25% reduction in IOP compared to baseline; and 3) an equal or fewer number of IOP medications. Partial success was defined by criteria 1 and 2 but allowed for an increased number of IOP medications. Failure was defined as the inability to meet the criteria, need for incisional glaucoma surgery, or significant progression of glaucoma. A less than 25% reduction in IOP from baseline after 1 month on 2 consecutive visits separated by a 1-week interval was the basis for a repeat treatment. Requiring repeat mTLT treatments did not constitute a failure.

Treatment absolute success was 59.6% and mean IOP was reduced by 35.6% at 18 months. mTLT treatment did not significantly reduce the number of topical glaucoma medications, however showed a 9% reduction in eyes requiring oral medication. 8 patients (15%) experienced vision loss of ≥ 2 lines following mTLT. Of those patients, 2 patients (4%) experienced persistent vision loss at 18 months. The retreatment rate was 19.2% and not associated with additional complications. 25% of patients required further incisional glaucoma surgery despite treatment with mTLT. The rate of hypotony at 18 months was 0%. Eye pain by verbal analogue scale was scored as mild to no pain in 89% of patients.

Interestingly, there was greater IOP reduction in patients treated with a longer duration but no difference in rate of complications. The concept of titrating treatment duration to glaucoma severity requires further research but holds significant potential.3

There are, however, a few limitations to this study. Firstly, the sample size is limited, though its prospective design and long-term follow up add significant value to current literature. Secondly, with no comparative group it is difficult to compare the efficacy and safety of mTLT and TSCPC.

In summary, Marchand and colleagues suggest mTLT is a safe and effective option for moderate IOP reduction. Additional studies are required to address the limitations of this study in comparing long-term efficacy and safety of mTLT and TSCPC in uncontrolled glaucoma.

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Article being referenced: https://www.canadianjournalofophthalmology.ca/article/S0008-4182(21)00031-4/fulltext

References


Resident Perspective: Visual outcomes following cataract surgery in AMD

Cataract and age-related macular degeneration (AMD) are two of the leading causes of blindness and visual impairment worldwide, and are often comorbid. Cataract surgery is effective at improving visual acuity (VA) and quality of life. However, in patients with AMD, the visual benefit becomes difficult to predict due to preexisting maculopathy. In this issue, Chen and colleagues compare postoperative VA for patients with intermediate non-exudative AMD (iAMD), fovea-involving geographic atrophy (GA), and neovascular AMD (nAMD) with healthy VA-matched controls.

Through a retrospective chart review, 216 iAMD, 35 GA, and 184 nAMD eyes were identified. The control groups included 130 iAMD control eyes (iAMDC), 31 GA control eyes (GAC), and 129 nAMD control eyes (nAMDC). While age was similar between iAMD and iAMDC, and GA and GAC groups, nAMD patients were on average, older than nAMDC patients (79.6 ± 8.4 years vs. 75.5 ± 6.3 years, p < 0.001). Baseline VAs were similar within comparative groups. All control groups showed significant improvement in postoperative month (POM) 1 and 12 VAs, which were greater than those of their respective AMD groups (p < 0.01). At POM1 and POM12, significant VA gains were seen in iAMD (+7.0 ± 14.9 and +10.1 ± 14.5 letters, p < 0.001) and nAMD (+8.9 ± 17.3 and +9.7 ± 18.9 letters, p < 0.001) groups, however not in the GA group. There is already a guarded visual prognosis for patients with fovea-involving GA so cataract surgery may not improve VA. Though, this does not necessarily mean there is no utility for cataract surgery in this patient subset — improvements in functional vision, accounting for factors such as glare and contrast sensitivity, should be considered as well and have been previously reported.

Chen and colleagues also determined preoperative predictors of postoperative VA for AMD patients. Preoperative VA was a strong predictor of visual outcomes, with the greatest benefit for patients with lower preoperative VA. However, in patients with good preoperative VA ≥20/40, the final VA was similar to that of control patients. For iAMD eyes, longer AMD duration was associated with worse final VA. In GA, central subfield thickness (CST) was associated with better visual outcomes. In nAMD, ellipsoid zone (EZ) disruption on optical coherence tomography (OCT) predicted worse visual outcomes. Potential explanations for these predictors relate to their effects on the health of the retina and subsequently, on visual potential. A longer AMD duration may be associated with more chronic retinal degeneration, lower CST values are indicative of greater retinal damage, and EZ disruption indicates a disruption of outer retinal integrity. Interestingly, preoperative macular edema, choroidal neovascularization, and anti-VEGF injection frequency were not predictive of postoperative VA. This suggests that patients with more advanced AMD should not be precluded from cataract surgery.

There is also ongoing debate regarding the association between cataract surgery and AMD progression. Studies including the large-scale epidemiological Beaver Dam Eye Study supported cataract surgery as a risk factor for AMD, however other studies have not shown this association. The current study did not report an increased risk for progression to advanced AMD post cataract surgery. They reported a low rate of conversion from iAMD to nAMD by 12 months (3.7%) and no change in injection frequency for nAMD patients.

In summary, Chen and colleagues demonstrate that AMD patients may safely undergo cataract surgery, which
improved postoperative VA for iAMD and nAMD patients, though had less visual improvement compared to VA-matched healthy controls. By identifying predictors of visual benefit in AMD patients undergoing cataract surgery, more accurate prognostication models can be developed.

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Article being referenced: https://www.canadianjournalofophthalmology.ca/article/S0008-4182(21)00034-X/fulltext

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Resident Perspectives 56-6

Resident Perspective: Intravitreal anti-VEGF vs. panretinal laser photocoagulation for proliferative diabetic retinopathy

Panretinal photocoagulation (PRP) has been a mainstay for the treatment of proliferative diabetic retinopathy (PDR). Unfortunately, PRP can cause impaired contrast sensitivity, scotopic vision and visual field impairment. Furthermore, a small proportion of patients can develop severe complications from PRP, including tractional retinal detachment, diabetic vitreous hemorrhage, and neovascular glaucoma. Therefore, alternative treatments with less collateral visual impairment are actively being investigated. Given previous diabetic macular edema studies that have shown the effectiveness of anti-vascular endothelial growth factor (anti-VEGF) in reducing severity of diabetic retinopathy, anti-VEGF has been of interest as an alternative treatment for PDR. While several studies have compared combined PRP + anti-VEGF versus PRP alone, only limited number of studies have investigated anti-VEGF monotherapy versus PRP for PDR. In this issue, Yates and colleagues present a systematic review and meta-analysis of the current literature comparing anti-VEGF monotherapy to PRP in managing PDR.

Yates and colleagues performed a systematic review and analysis of literature found in Ovid MEDLINE, Ovid MEDLINE In-Process, CENTRAL (Cochrane Eyes and Vision Group Trials Register) and ClinicalTrials.gov. Their inclusion criteria were all randomized controlled trials investigating anti-VEGF monotherapy (either aflibercept 2 mg, ranibizumab 0.5 mg, or bevacizumab 1.25 mg) versus complete PRP monotherapy (as defined by the Diabetic Retinopathy Study) in patients ≥18 years of age with PDR from either type I or type II diabetes. Primary outcome was mean change in best-corrected visual acuity (BCVA). Secondary outcomes were the proportion of patients developing severe (<6/60) or moderate (6/24-6/60) vision loss, rates of vitreectomy or vitreous hemorrhage, center-involving macular edema (C1-DME), and reduced visual field indices.

Five studies of varying quality met the inclusion criteria (n = 632). Regarding the primary outcome (mean change in BCVA), the anti-VEGF intervention arm had a mean difference of 0.08 logMAR or 4 Early Treatment Diabetic Retinopathy Study (ETDRS) letters gained (p = 0.02) when compared with PRP at 12 months. Regarding the secondary outcomes, first, anti-VEGF led to lower likelihood of
moderate vision loss when compared to PRP: risk difference (RD) 0.12. Second, there was no difference between anti-VEGF and PRP for severe vision loss (RD 0.03). Third, Anti-VEGF resulted in lower rates of vitrectomy (RD 0.10) and vitreous hemorrhage (RD 0.10) than PRP. Fourth, anti-VEGF resulted in a lower incidence of CI-DME than PRP at 12 months (RD 0.09). Last, for visual field loss, while the results could not be pooled owing to differences in testing modalities between the studies, each individual study showed: aflibercept lead to superior Esterman visual field, and ranibizumab lead to better Humphrey visual field when compared to PRP.

This meta-analysis demonstrates that anti-VEGF monotherapy may be superior to PRP in terms of the outcome measures: mean change in BCVA, visual field loss, as well as the proportions of patients with moderate vision loss, vitrectomy and vitreous hemorrhage. While these results may be in favor of anti-VEGF over PRP, Yates and his colleagues stress that it is important to keep in mind that the maintenance of treatment effect by anti-VEGF requires ongoing assessment and intervention, as the angiogenic drive continues if intravitreal anti-VEGF injections are ceased. Patients with PDR are at a high risk for blindness, which may affect up to 25% of those lost to follow-up over a 4-year period. On the other hand, the effects of PDR are presumed to be permanent. Hence, the use of anti-VEGF monotherapy without concurrent PRP should be carefully considered with the patient’s likelihood of adherence to therapy and follow up. Something else to be mindful of is the modest treatment effect of anti-VEGF over PRP; although the difference is considered statistically significant, the benefit of anti-VEGF over PRP is only 4 ETDRS letter-gain at 12 months. Furthermore, examination of the treatment effect (in terms of BCVA) over the duration of the studies demonstrates that the benefit of anti-VEGF over PRP occurs in the early stage of PDR but is not sustained in the long term.

The key take-home point from this study is that while anti-VEGF may provide some benefits over PRP in PDR, clinicians should take a judicious approach to treatment selection as: 1) anti-VEGF monotherapy has higher risk of adverse visual outcome than PRP when patients are lost to follow up, and 2) the benefit of anti-VEGF over PRP may decrease in the long-term. While many retinal specialists use combination therapy of anti-VEGF and PRP, there is limited literature examining the efficacy of combination therapy. Yates and colleagues have contributed valuable information about some of the factors that need to be taken into consideration for choice of treatment.

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Article being referenced: https://www.canadianjournalofophthalmology.ca/article/S0008-4182(21)00033-8/fulltext

Reference


Resident Perspective: Cost-related nonadherence with glaucoma medications in Ontario

In glaucoma management, patient nonadherence to topical therapies is a common problem, and is shown to lead to faster disease progression and in the long term, to reduced quality of life. Cost-related nonadherence (CRNA) are the subset of nonadherence behaviours resulting from the financial burden of taking medication. They may include delaying or failing to fill a prescription or skipping doses.

In this issue, Buys and colleagues examine rates of CRNA with glaucoma medications among a sample of patients attending subspecialty glaucoma clinics at a single tertiary-level hospital in Toronto, Ontario. CRNA was reported by 15.5% of patients aged 25-64 years old. In contrast, among patients aged 65+, who are covered by a provincial prescription drug plan, CRNA was reported by only 2.0%. Because the study sampled a relatively socially advantaged population, rates of CRNA with glaucoma medications among other segments of the Canadian population may be higher.

For all medications, CRNA is an important issue in Canada. A recent systematic review estimated the prevalence in the general population to be 5-10%. Among other factors, lack of prescription drug insurance and higher out-of-pocket spending are associated with greater likelihood of CRNA. Pharmaceutical coverage and pricing varies widely between
provinces, in part because there is a lack of co-ordination in pharmaceutical policy between provincial governments and the federal government.\(^5\)

In a study comparing eleven high-income countries, the prevalence of CRNA in Canada was 2-3x higher than in countries with universal prescription drug coverage and lower direct patient costs (i.e., France, Germany, Netherlands, New Zealand, Sweden, Switzerland, and the United Kingdom).\(^6\) Only in the United States, where most insurance is private and many people are not adequately insured, was the rate higher.

It is argued that a national pharmaceutical strategy would enable Canada to meet its commitments to universally accessible health care. Indeed, this has been an important item in recent federal election party platforms. A national strategy could involve universal, public coverage of necessary medications, national purchasing contracts, and coordinated monitoring of the safety and quality of prescribing.\(^5\)

Findings from the present study may help to engage ophthalmologists in advocating for the necessary political action.

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**References**


