Subthreshold Micropulse Laser for Macular Oedema Secondary to Branch Retinal Vein Occlusion

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Background

Macular oedema is one of the commonest complications following branch retinal vein occlusion (BRVO) and it is usually treated with anti-VEGF therapy, whilst intravitreal dexamethasone implant and macular grid laser photocoagulation (LP) may also be introduced. The anti-VEGF therapy has been shown to be an effective treatment for macular oedema secondary to BRVO as demonstrated by 'The Ranibizumab for the Treatment of Macular Oedema following Branch Retinal Vein Occlusion: Evaluation of Efficacy and Safety' (BRAVO) study.

However, there are several disadvantages of this anti-VEGF therapy including short vitreous half-life, high economic burden, as well as the associated risks and complications of each intravitreal injections including retinal detachment and endophthalmitis. Due to these limitations, the adjunct LASER treatment is proposed to address this issue and hence reduce the number of anti-VEGF injections necessary.

LP has been proposed to target the nonperfusion areas as it is believed that there will be continuous VEGF production from this area responsible for the recurrence of macular oedema following the anti-VEGF (Goel *et al*. 2019). However, the 'branch retinal vein occlusion' study (BVOS) which shows the benefit of traditional LP has several drawbacks which include laser scar enlargement, retinal scarring, subretinal fibrosis, reduce macular sensitivity, and choroidal neovascularisation which may eventually compromise visual function (Chhablani *et al*. 2017).

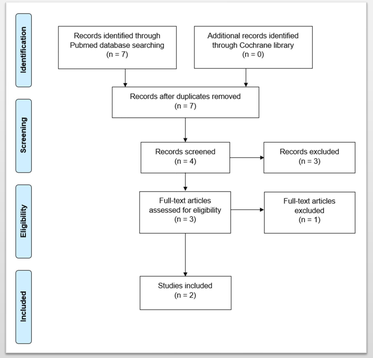
Therefore, a less invasive option, the subthreshold micropulse laser (SML) is designed as an alternative to the conventional LASER. The SML is introduced to precisely target the RPE once the oedema settled by Ranibizumab intravitreal injection. This will then allow a more precise and efficient RPE coagulation (Terashima *et al*. 2019). The yellow (577nm) SML also has a lower degree of scattering due to its longer wavelength (Lock and Fong, 2010). This means less energy and duration of laser necessary to achieve the intended benefit. Because it applies a different principle compared to continuous laser, SML is believed to be safer and less invasive as it requires less total amount of energy delivering shorter impulses with on (active time) and off (inactive time to enable cooling) mode (Lock and Fong, 2010). This SML should therefore offer a safer approach and greater efficacy by increasing precision and accuracy of intended area to treat while causing less unwanted collateral damage.

Objective

The aim of this review is to evaluate the safety and efficacy profile of yellow (577nm) SML in addition to intravitreal ranibizumab (IVR) injection in macular oedema secondary to BRVO.

Methods

A literature search has been conducted via Pubmed database and Cochrane library using the keyword macular oedema, branch retinal vein occlusion, BRVO, subthreshold micropulse laser, and ranibizumab. Articles available in English, full text and published within the last 5 years has been selected. From the 4 full-text articles assessed, 2 studies have been included following screening and eligibility assessment. Another 2 studies have been excluded due to unsuitable evaluation criteria and different types of anti-VEGF included.

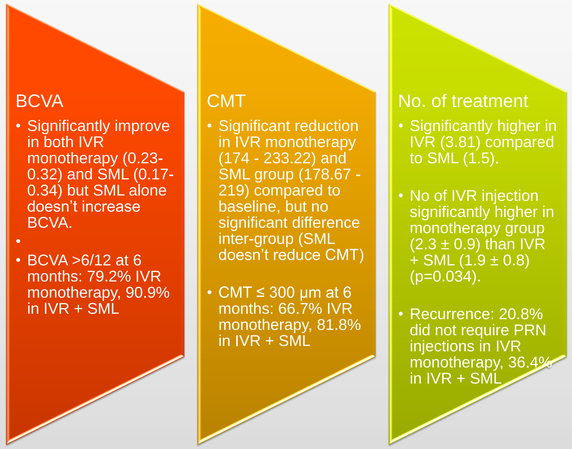


The two studies included are:

Authors	Study design	Follow-up	Sample	Outcome
Buyru Özkurt et al. (2018)	Retrospective.	12 months.	51 eyes. 27 in IVR group 24 in SML group	BCVA CMT No of treatment required
Terashima et al. (2019)	Retrospective, consecutive, case-control.	6 months.	46 eyes. 24 in IVR group 22 in IVR + SML (1/12)	BCVA CRT No of IVR injections

Discussions

Results



Limitations

- ❖ Variation in SML power setting
- ❖ Difference in retreatment criteria
- ❖ Ranibizumab protocol
- ❖ Retrospective study design
- ❖ Small sample & short follow-up
- ❖ Complications

Future research

Multi-centre, prospective, randomised, clinical trial study to assess the efficacy, and safety of SML in subjects with macular oedema secondary to BRVO:

- ✓ Study of SML power setting (laser power, duty cycle, duration, treatment interval) to identify optimum treatment protocol
- ✓ Direct comparison with conventional LP (with Ranibizumab)

Conclusion

With limited evidence available, the application of SML in macular oedema secondary to BRVO has been proven to reduce the number of IVR injections required but is not superior enough to replace the anti-VEGF therapy (Ranibizumab) as it does not significantly improve the visual or anatomical outcome.
SML may however be a potential alternative in selected cases as it may reduce financial burden but offering comparable visual outcome.

Further large-scale research studies is required to directly compare SML with conventional LP in addition to anti-VEGF (Ranibizumab) to enable safer and effective clinical practice.

References

- Buyru Özkurt, Y. *et al*. (2018). 'Comparison of ranibizumab and subthreshold micropulse laser in treatment of macular edema secondary to branch retinal vein occlusion', *European Journal of Ophthalmology,* 28(6), pp. 690-696.
- Campochiaro, P. A. *et al*. (2019). 'Ranibizumab for macular edema following branch retinal vein occlusion: six-month primary end point results of a phase III study', *Ophthalmology,* 117, pp. 1102-1112.
- Chhablani J. *et al*. (2018). 'Restorative retinal laser therapy: Present state and future directions', *Survey of Ophthalmology,* 63, pp. 307-328.
- CASP, CASP Checklist. Available at: https://casp-uk.net/casp-tools-checklists/.
- Gaweçki, M. (2019). 'Micropulse Laser Treatment of Retinal Diseases', *Journal of Clinical Medicine*, 8(2), 242.
- Goel, S. *et al*. (2019). 'Comparison of ranibizumab alone versus ranibizumab with targeted retinal laser for branch retinal vein occlusion with macular edema', *Indian Journal of Ophthalmology*, 67(7), pp. 1105-1108.
- Greenhalgh, T., 2014. *How to Read a Paper: The Basics of Evidence-based Medicine.* 5 ed. Chichester: John Wiley & Sons.
- Inagaki, K. *et al*. (2014). 'Clinical Study Subthreshold Micropulse Photocoagulation for Persistent Macular Edema Secondary to Branch Retinal Vein Occlusion including Best-Corrected Visual Acuity Greater Than 20/40', *Journal of Ophthalmology*, 2014.
- Kanski, JJ. *et al*. (2011). *Clinical Ophthalmology: A Systematic Approach*. 7 ed. London: Elsevier Saunders.
- Kumar, P. *et al*. (2019). 'Comparison of the safety and efficacy of intravitreal ranibizumab with or without laser photocoagulation versus dexamethasone intravitreal implant with or without laser photocoagulation for macular edema secondary to branch retinal vein occlusion', *Folia Medica,* 61(2), pp. 240-248.
- Krohne, T. U. *et al*. (2012). 'Intraocular pharmacokinetics of ranibizumab following a single intravitreal injections in humans', *American Journal of Ophthalmology*, 154(4), pp. 686-686.
- Lock, J. H. & Fong, K. C. (2010). 'Retinal Laser Photocoagulation', *Med J Malaysia*, 65(1), pp. 88-95.
- Moher , D. *et al*. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Medicine.
- Parodi, M. B. *et al*. (2006). 'Subthreshold grid laser treatment of macular edema secondary to branch retinal vein occlusion with micropulse infrared (810 nanometer) diode laser', *Ophthalmology*, 113(12), pp. 2237-2242.
- Pielen, A. *et al*. (2015). 'Ranibizumab for branch retinal vein occlusion associated macular edema study (RABAMES): Six-month results of prospective randomized clinical trial', *Acta Ophthalmol*, 93(1), pp. 29-37.
- Tadayoni R. *et al*. (2016). 'Individualized stabilization criteria-driven ranibizumab versus laser in branch retinal vein occlusion: Six-month results of BRIGHTER', *Ophthalmology,* 123(6), pp. 1332-1344.
- Terashima, H. *et al*. (2019). 'Combination Therapy Of Intravitreal Ranibizumab And Subthreshold Micropulse Photocoagulation For Macular Edema Secondary To Branch Retinal Vein Occlusion: 6-month Result', Retina, 39(7), pp. 1377-1384.
- The Branch Retinal Vein Occlusion Study Group. (1984). 'Argon laser photocoagulation for macular edema in branch retinal vein occlusion', *American Journal of Ophthalmology*, 98(3), pp. 271-282.

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