A review of selective laser trabeculoplasty in the Hong Kong Chinese population

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A B S T R A C T

Introduction: Selective laser trabeculoplasty was first introduced to Hong Kong in 2004 for intra-ocular pressure lowering in the treatment of primary glaucoma. Since then, it has gained popularity as an alternative to anti-glaucoma medications and as a bridging therapy prior to more invasive glaucoma surgeries because of the high safety profile of the laser.

Methods: An Ovid search was performed using "selective laser trabeculoplasty" as the key word, which identified 190 unique articles; 24 reviews and/or meta-analyses were excluded. All remaining abstracts of original articles were in English. This review particularly focuses on the local population by summarising the findings from peer-reviewed publications that involved a Hong Kong Chinese population.

Results and Conclusion: This review addresses some of the clinically relevant questions relating to selective laser trabeculoplasty including laser application, optimal energy, efficacies and success rates among different glaucoma subtypes, predictors of success, adverse effects, and intra-ocular pressure fluctuation after selective laser trabeculoplasty.

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Introduction

Glaucoma is a disease characterised by progressive optic nerve thinning. Intra-ocular pressure (IOP) remains an important modifiable risk factor even in normal- or low-tension glaucomas. Anti-glaucoma eye drops remain the mainstay of IOP-lowering therapy but their side-effects include conjunctival injection, allergy, hypertrichiasis, iris pigmentation, cystoid macular oedema, bradycardia, and bronchospasm. Laser trabeculoplasty describes the use of laser on the trabecular meshwork to promote aqueous output that in turn lowers the IOP. Laser trabeculoplasty is often performed when medications alone are inadequate for disease control, to avoid the side-effects of medication, or as a bridging therapy prior to more invasive glaucoma filtration surgery. Selective laser trabeculoplasty (SLT) was approved by the US Food and Drug Administration in 2001 for the treatment of open-angle glaucoma (OAG). Following the first clinical trial for the Hong Kong population in 2004 by Lai et al,[1] the procedure has since gained popularity in our locality. Based on our understanding of the former argon laser trabeculoplasty technology, we are aware that variations in race and trabecular meshwork pigmentation can potentially influence laser success.[2-4] This review aimed to summarise the published data on use of SLT in the Hong Kong Chinese population.

Methods

An Ovid search was made on 4 June 2015 using "selective laser trabeculoplasty" as the key word, which identified 190 unique articles; 24 reviews and/or meta-analyses were excluded. All remaining abstracts of original articles were in English. There were 15 abstracts in which an ophthalmology institution from Hong Kong Special Administrative Region (HKSAR) was identified as an affiliated institution. These 15 articles were reviewed to ensure that the study population contained participants from HKSAR prior to their inclusion in this review.

Selective laser trabeculoplasty

Laser application

Selective laser trabeculoplasty is a low-energy, Q-switched, frequency-doubled Nd:YAG laser with a wavelength of 532 nm. Lasers are delivered at a fixed duration of 3 nanoseconds and spot size of 400 μm. The initial energy is 0.8 mJ, titrated up until bubble formation is just visible and titrated down if pain is experienced. The pigmented area is usually treated with confluent, non-overlapping laser spots in a 360° fashion in a single session.[1,5,6] In cases of angle closure, SLT is applied to at least 90° to 180° of the visible trabecular meshwork, avoiding areas of peripheral anterior synechiae.[7,8]

An alpha-adrenergic agonist may be applied

回顧香港華籍人口中的選擇性激光小梁成形術

李煒業、黎少明

引言：香港自2004年首次引入選擇性激光小梁成形術治療原發性青光眼，以降低患者的眼內壓。這激光技術安全性高，故此提供了抗青光眼藥物以外的另一個治療方法，以及在進行更侵入性的青光眼手術前作為橋接療法。

方法：從Ovid數據庫系統內使用關鍵詞「選擇性激光小梁成形術」（selective laser trabeculoplasty）作檢索，找到190篇文章；另剔除了24篇評論和綜合分析。其餘所有原著論文的摘要均使用英語。本文也集中搜集經同行評審並涉及香港華籍人口參與的研究，並總結這些研究結果。

結果和結論：本文回顧有關選擇性激光小梁成形術的臨床相關問題，包括激光應用、最佳能量使用、在不同青光眼亞型中的療效和成功率、手術成功的預測因素、不利影響，以及成形術後眼內壓的變化。

prior to or immediately after the procedure to prevent IOP spikes that can occur in up to 10% of subjects within the first 1 to 2 hours of treatment.[1] Post-laser eye drops may vary from no eye drops, topical non-steroidal eye drops, or a weak topical steroid for a short duration. Excess inflammatory suppression should be avoided as SLT works via an inflammatory cascade of cytokine up-regulation, phagocytic activity, and trabecular matrix metalloproteinase expression that reduce outflow resistance at the trabecular meshwork.[9-11] The majority of anterior chamber reactions following SLT are mild and spontaneous, and resolve within the first week of laser.[12]

Optimal energy

Conventionally, 80 to 100 laser spots are delivered. Lee et al[13] postulated that it is the total energy density (number of spots multiplied by the mean energy) delivered that is important, rather than just the number of laser spots. In a group of 49 Chinese OAG subjects who received 360° SLT treatment, bandwidth selection by generalised cross-validation methods was used to determine the optimal interval and point of total SLT energy that provided the greatest IOP reduction. The 95% confidence band by bootstrap analysis revealed that at energy intervals between 214.6 and 234.9 mJ, the IOP was most likely to decrease by 25%, with the optimal total energy at 226.1 mJ.

Efficacy in different glaucoma subtypes

Primary open-angle glaucoma and ocular hypertension

Lai et al[1] conducted the first randomised controlled trial of SLT in a Hong Kong Chinese population with primary open-angle glaucoma (POAG) and ocular hypertension (OHT), comparing the effect of the laser versus topical anti-glaucoma medications alone over 5 years using the untreated eye as a control. Additional medical therapy was permitted for eyes that had inadequate IOP control despite SLT. In the study, 29 patients (17 POAG and 12 OHT) completed follow-up for 5 years and all were of Chinese ethnicity with a dark brown iris. The SLT eye had a mean IOP reduction of 32% (26.8 mm Hg to 18.3 mm Hg) at 5 years although this level of IOP reduction was statistically similar to the control eye. The SLT-treated eye, however, required fewer medications to maintain an IOP of ≤21 mm Hg (P<0.001); only 27.6% of eyes that received SLT required medications at 5 years. The failure rate, which was defined as an IOP of >21 mm Hg with maximal topical medications, was similar in both treatment arms (17.2% in the SLT-treated eye vs 27.6% in the eye that received medication alone; P=0.53).[1]

Similarly, in a randomised controlled trial studying the change in quality of life between subjects prescribed adjuvant SLT versus medication for the treatment of POAG, Lee et al[5] reported that at 6 months, the SLT group (n=22) had a 7.6% lower IOP (P=0.03) and required 40.0% less medication (P=0.02) compared with the medical group (n=19). When compared with its own baseline at 6 months, the SLT group had a 15.1% lower IOP (P<0.0001) on top of a 34.8% reduction in medication requirement (P<0.0001) while the medical therapy group demonstrated no change in IOP or medication requirement (P>0.8). Despite these significant reductions in IOP and medications in the SLT group, however, there was no statistical difference between the translated Chinese version of the Glaucoma Quality of Life–15 score or the simplified Comparison of Ophthalmic Medications for Tolerability survey score between both treatment arms (P>0.2). The absence of a detectable change in the short-term quality of life could be related to the design of the existing glaucoma-specific quality-of-life surveys that mainly focus on detecting changes in vision, dark adaptation, and outdoor mobility, and may be suboptimal in assessing the side-effects and inconvenience of medication use.

Selective laser trabeculoplasty seems to be an effective alternative to medication with sustainable IOP reductions for up to 5 years together with a lower medication requirement.

Primary angle-closure glaucoma

Primary angle-closure glaucoma (PACG) is characterised by ≥270° of angle closure where the trabecular meshwork is on Shaffer grades 0 to 1. Ho et al[7] reported the SLT outcome in 60 PACG patients with an IOP of >21 mm Hg in the presence

of a patent laser iridotomy with >90° of visible pigmented trabecular meshwork. In the study, SLT was delivered to 90° of open angle and at 6 months, 82% of subjects had >3 mm Hg reduction, 72% had >4 mm Hg reduction, 54% had ≥20% IOP reduction, and 24% had ≥30% IOP reduction. The mean IOP decreased from 24.6 mm Hg to 18.7 mm Hg after SLT, signifying a 24% IOP reduction at 6 months.[7,8]

In a recent three-centre randomised clinical trial involving Singapore, Jakarta, and Hong Kong,[8] 100 subjects with PACG or primary angle closure (angle closure without glaucomatous optic neuropathy) with 180° of visible trabecular meshwork were randomised to receive SLT versus travoprost 0.004% for IOP control. At 6 months, both treatment arms had a similar degree of IOP reduction (16.9% in the SLT group vs 18.5% in the medical therapy group; P=0.52). The absolute success (IOP ≤21 mm Hg without medications) was 60.0% in the SLT group and 84.0% in the medical therapy group (P=0.008). Selective laser trabeculoplasty is effective in primary angle closure or PACG where at least 90° of the pigmented trabecular meshwork is accessible.

Normal-tension glaucoma

Normal-tension glaucoma (NTG) is a subtype of POAG with the presence of glaucomatous optic neuropathy but IOP never exceeds 21 mm Hg. There is a high prevalence in Korea and Japan, accounting for 77% and 92% of their POAG cases respectively, although there is no published prevalence for Hong Kong.[14,15] The Collaborative Normal-Tension Glaucoma Study Group has demonstrated that a 30% IOP reduction may slow disease progression of NTG despite a non–pressure dependent, hypoperfusion element in the disease pathophysiology.[16]

Lee et al[6,17] prospectively treated 46 patients with NTG who were currently prescribed topical anti-glaucoma medications. They received a 1-month washout of medication and a single session of SLT before medications were gradually resumed in a step-wise manner. Selective laser trabeculoplasty reduced IOP by 20% and 15% at 6 months and 1 year, respectively. Medications were also reduced by 27% at both 6 months and 1 year after laser.[6,17] At 2 years, 34 subjects completed follow-up. The mean (± standard deviation) age was 65.1 ± 12.1 years with a post-washout IOP of 16.2 ± 2.3 mm Hg. The mean SLT shots delivered was 191.0 ± 27.3 with a mean energy of 1.0 ± 0.08 mJ. The mean IOP reduction at 24 months was 22% (P<0.0001) from the post-washout (without medication) level and 11.5% from the pre-study (with medication) level (P<0.0001), in addition to a medication reduction of 40% (P<0.0001).

There was a gradual decline in the absolute success rate (IOP reduction >20% without medication) following SLT, from 61% at 6 months, to 22% at 12 months, and to 11% at 24 months. It is well known that the effect of SLT decreases with time but the process may be repeated as needed.[6] Although the effect of SLT on NTG is not as prominent as in those with POAG or PACG, it remains a worthwhile procedure in NTG where drug compliance may be an issue. Patients are often asymptomatic in the early stages and are told they have 'normal' pressures during follow-up, compromising their understanding of the disease. Nonetheless, it must be noted that SLT only addresses the pressure-dependent component of the disease and not the hypoperfusion element of NTG that can be equally important in disease progression.

Success rates

The response or success rate to SLT is most commonly defined in the literature as an IOP reduction of ≥20%.[18,19] This success rate varied among the different glaucoma subgroups in our local population however—47% in POAG,[5] 54% to 60% in PACG,[7,8] and 60% in NTG.[6] Likewise, the mean IOP reduction also varies among different glaucoma subgroups—32% reduction at 60 months in POAG,[1] 24% reduction at 6 months in PACG,[7] and 22% reduction at 24 months for NTG.[20]

Predictors of success

Not all treated eyes respond to SLT, thus understanding the factors that may influence a successful outcome is useful for both the clinician and patient. Lee et al[21-23] analysed 25 potential covariates as detailed below, using univariate and multiple logistic regression analyses in Chinese subjects with OAG, NTG, and POAG independently. Success was defined as an IOP reduction of ≥20% while anti-glaucoma medications remained unchanged. The category of covariates included: type of glaucoma, age, gender, phakic status, presenting and pre-SLT IOP, IOP at various time intervals after SLT, number and type of anti-glaucoma medications, number of SLT spots, SLT energy, glaucoma severity via retinal nerve fibre layer thickness on optical coherence tomography and visual field index on Humphrey Visual Field, visual acuity, and pre-SLT corneal parameters.[21-23]

Among the 111 OAG eyes (60 NTG and 51 POAG) that were analysed, having a higher pre-laser IOP was a significant predictor of success on both univariate / multivariate analyses (coefficient=0.20 / 0.46, odds ratio [OR]=1.23 / 1.58, P=0.0017 / 0.0011). Use of three anti-glaucoma medications was more likely to result in a non-successful procedure on univariate / multivariate analyses (coefficient = –1.08 / –3.74, OR=0.3 / 0.024, P=0.037 / 0.0081).[22]

For the POAG subgroup, success was more likely in those with: an older age (coefficient=0.1,

OR=1.1, P=0.0003), a higher pre-laser IOP (coefficient=0.3, OR=1.3, P=0.0005), four types of anti-glaucoma medications (coefficient=2.1, OR=8.4, P=0.005), a larger dioptre of spherical equivalent (coefficient=2.1, OR=8.4, P=0.005), and the use of a carbonic anhydrase inhibitor eye drop (coefficient=1.7, OR=6.0, P=0.003).[21]

In those with NTG, success was most commonly seen in those with a higher pre-laser IOP (coefficient=1.1, OR=3.1, P=0.05) and in those who achieved a lower IOP at 1 week after SLT (coefficient= −0.8, OR=0.5, P=0.04).[23]

Thus, it seems that regardless of the type of glaucoma, having a higher pre-laser IOP is one of the more consistent predictors of success. Nevertheless, it is important to keep in mind that the mean IOP reduction from SLT is around 22% to 32% as detailed in the earlier sections, and SLT alone may not adequately manage those with extremely high pressures.

Adverse effects

Intra-ocular spikes and uveitis

Lai et al[1] have reported that in our population, the incidence of IOP spikes of >5 mm Hg after SLT can occur in up to 10.3% of patients within the first 1 to 2 hours of SLT. Ho et al[7] reported that 2.0% of their PACG population had IOP spikes of >5 mm Hg after SLT. The majority of anterior uveitis settle within 3 to 5 days of treatment.[12]

Corneal changes

Lee et al[12] investigated 111 eyes with OAG that had SLT treatment. The endothelial cell count (specular microscopy), central corneal thickness (CCT; videokeratography), and spherical equivalent (kerato-refractometer) were measured before and at 1 month after SLT. The mean endothelial cell count apparently decreased by 4.5% (from 2465.0 ± 334.0 cells/mm^2 to 2355.0 ± 387.0 cells/mm^2; P=0.0004) during the first week but increased back to baseline level by 1 month. This was due to the attachment of inflammatory cells on the endothelium or a microscopic cellular oedema separating the endothelial cells from the Descemet's, impairing the accurate counting of endothelial cells.[12] In PACG that received SLT to at least 180° of visible trabecular meshwork, it was reported that at 6 months, the endothelial cell count loss was 4.8% (P=0.001).[8] The differences between the permanence of endothelial cell damage between the two studies may be related to the closer proximity of the cornea to the trabecular meshwork in PACG subjects. Patients with PACG should be made aware of this potential damage to the endothelium from laser heat dissipation.

There was a transient 1.1% decrease in CCT at 1 week after SLT (from 549.4 ± 37.6 to 543.9 ± 40.2 μm; P=0.02) likely from temporary thermal contractions of the stromal collagen fibres. There was no change in the spherical equivalent but the mean vision after SLT was interestingly reported to improve from 0.3 logMAR to 0.2 logMAR (P<0.0003), possibly related to subjective variation in visual testing and not directly related to the laser itself.[12]

Intra-ocular spikes, uveitis, and corneal changes are only some of the potential side-effects of SLT that have been reported in studies involving the Hong Kong Chinese population. Although a full review of the side-effects of SLT is beyond the scope and focus of this review, a comprehensive summary of side-effects with incidences can be found in a recent meta-analysis by Wong et al.[24]

Influence of selective laser trabeculoplasty on fluctuation of intra-ocular pressure

At present, there is no effective means to measure the continuous 24-hour IOP profile in the gold-standard measurement of mm Hg but IOP fluctuation has been demonstrated as a potential risk factor in glaucoma progression.[25,26] The SENSIMED Triggerfish (Sensimed AG, Lausanne, Switzerland) is a wireless silicon contact lens sensor (CLS) that can measure the biodimensional changes at the corneoscleral junction, collecting more than 300 data points every 5 minutes. The IOP is measured in output units of millivolts equivalent, thus, the plotted data can only represent the degree of fluctuation from the individual's baseline pressure.[27]

Lee et al[27] utilised the CLS to measure IOP-related pattern changes in a group of Chinese NTG subjects treated with SLT. The CLS was worn for 24 hours before and for 1 month after the laser procedure while keeping the same number of anti-glaucoma medications. A cosine function was fitted to the mean CLS pattern and global variability was analysed in subjects that had success and non-success to laser, where success was defined as IOP reduction of ≥20%. Local variability from the mean curve was also measured at the diurnal, nocturnal, and 24-hour periods.[27] In 44% of subjects who had successful SLT, the global amplitude was reduced by 24.6% but in the non-successful group, subjects experienced a 19.2% increase in their global amplitude, which was primarily driven by a 34.1% greater diurnal local variability.[27]

Whether or not SLT affects IOP fluctuation remains controversial in the literature for other populations with different authors reporting differences in IOP fluctuation and at different periods of the day.[28,29] The majority of subjects in Lee et al's study[29] were prescribed an evening dose of prostaglandin analogues and it has been previously reported that the peak effect of the drug occurs between 8 and 12 hours.[30] It seems that in our population, patients who respond to SLT may

also benefit from a dampening of their 24-hour IOP-related pattern amplitude although larger-scale studies with 24-hour IOP monitoring in mm Hg would be required to draw more solid conclusions about SLT and IOP fluctuation.

Conclusion

Based on literature related to the Hong Kong Chinese population, SLT is an effective modality for lowering IOP in patients with POAG, OHT, PACG, and NTG. The response or success rate to laser and the amount of IOP reduction varies depending on the type of glaucoma. A higher pre-laser IOP was associated with greater success and delivering a greater total energy seemed to improve the level of IOP reduction. Adverse effects including IOP spikes and uveitis were usually transient although permanent endothelial cell loss may be seen after SLT in patients with anatomically narrow angles. Further research is warranted to assess the repeatability of SLT, long-term sustainability, influence on IOP fluctuation, and role as primary treatment for glaucoma.

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