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ORIGINAL RESEARCH

Influence of Laser Trabeculoplasty on Combined Phacoemulsification/Kahook Dual Blade Goniotomy

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Purpose: To investigate the influence of laser trabeculoplasty (LTP) on subsequent surgery with combined phacoemulsification/Kahook Dual Blade goniotomy (phaco-KDB) in patients with open-angle glaucoma or intraocular hypertension.

Patients and Methods: Patients undergoing phaco-KDB between 2019 and 2021 were divided into previously LTP treated and previously non-LTP treated, and LTP-treatment included argon laser trabeculoplasty (ALT) and selective laser trabeculoplasty (SLT). The primary goal was to investigate if previous LTP influenced later surgical outcome of phaco-KDB. The secondary goal was to investigate if the outcome of LTP could be predictive of the outcome of subsequent phaco-KDB. We also compared IOP- and medication reductions between LTP and non-LTP treated patients.

Results: A total of 111 LTP treated patients were compared to 139 non-LTP treated patients. In LTP treated patients, surgical success of phaco-KDB was 82.9%, compared to 88.5% in non-LTP treated patients (P=0.20). Reductions in IOP and medications were similar between groups. Furthermore, within the LTP group, patients with successful LTP-treatment had a subsequent surgical success of phaco-KDB in 80.7%, compared to 83.0% in patients with unsuccessful LTP-treatment (P=0.765).

Conclusion: Previous LTP treatment does not predict the outcome of phaco-KDB. Furthermore, no correlation was found between the LTP effect and a later surgical success of phaco-KDB.

Keywords: laser trabeculoplasty, Kahook Dual Blade, goniotomy, glaucoma, phacoemulsification

Introduction

Microinvasive glaucoma surgery (MIGS) has gained increasing popularity in the last decade, and many of these surgeries target Schlemm's canal (SC) and the trabecular meshwork (TM). One of these commonly used trabecular MIGS is goniotomy with Kahook Dual Blade (KDB). KDB is a surgical knife that increases the outflow through SC by removing the inner wall consisting of the trabecular meshwork (TM).

The TM is also the target for laser trabeculoplasty (LTP), which is often used early in glaucoma treatment, and can be divided into argon laser trabeculoplasty (ALT) and selective laser trabeculoplasty (SLT). SLT acts selectively on pigmented cells, while ALT acts on both pigmented and non-pigmented cells and also causes more coagulative damage to the treated area.[1] In both SLT and ALT, laser spots are applied to the TM, which induce mechanical and cellular changes that affect the TM permeability, thereby increasing the aqueous outflow and reducing the intraocular pressure (IOP).[2–5]

Since ALT is more tissue damaging and cannot be repeated more than once, SLT is nowadays the treatment of choice. The efficacy has been shown to be similar between those two treatments.[6–8]

A few previous studies have looked at the relationship between LTP and trabecular surgery with MIGS, but no clear correlation in outcomes has been found. However, the number of included patients has been few, with numbers ranging from 24 to 66.[9–12] Therefore, it is still not clear if LTP can affect the outcome of trabecular MIGS or if the outcome of LTP can be predictive for subsequent surgical success. In theory, LTP – and especially ALT – may induce TM changes

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that increase fibrosis and make future surgery with trabecular MIGS less likely to succeed. However, there is currently no evidence that supports this statement, and if LTP does not negatively impact future surgery in the TM area, it may serve as a clinical predictor of success after KDB and other trabecular bypass procedures.

LTP is a common first- or second-line treatment in glaucoma, and patients who are candidates for cataract surgery and MIGS will often have had one or more previous LTP treatments – ALT and/or SLT. It would therefore be valuable to know if a previous LTP treatment can impact future MIGS in the TM area.

The aim of this study is first to examine if previous LTP treatment can influence the outcome of surgery with phaco-KDB, and second, to examine if the outcome of LTP is predictive of the outcome of subsequent phaco-KDB.

Materials and Methods

The protocol for this study was approved by the Institutional Review Board of the Swedish Ethical Review Authority (DNR. 2121–02970) and adhered to the ethical tenets of the Declaration of Helsinki. As the study is retrospective in its nature and all information de-identified, informed consent was not required. Data were collected from medical records of patients with open-angle glaucoma or intraocular hypertension who had undergone a goniotomy with KDB in combination with phacoemulsification (phaco-KDB) at the Östersund Hospital in Östersund, Sweden between October 1, 2019, and December 31, 2021. Patients were excluded if having had previous glaucoma surgery or another eye disease that would likely affect the intraocular pressure (IOP). To minimize bias, we excluded the second operated eye if a patient had surgery on both eyes during the period. Glaucoma severity was classified according to the Hoddap–Parrish–Anderson criteria.[13] If visual field examinations had not been performed, the glaucoma was classified as of undetermined severity.

Electronic medical records of patients undergoing phaco-KDB during the specified time-period were investigated regarding previous laser treatment, including ALT and SLT. ALT and SLT were performed in a similar fashion with power titrated up until champagne bubbles were observed and around 50 continuous nonoverlapping treatments spots were applied to 180 degrees of the TM. If an eye had first one or more ALT treatments and then one or more SLT treatments, these eyes were included in the ALT treated group.

The phaco-KDB procedure was performed by an experienced surgeon and began with a standard phacoemulsification, followed by goniotomy with KDB as described previously.[14]

First, patients were divided into two groups: non-LTP treated and LTP treated, with the LTP-treated group including both ALT and SLT. The primary outcome was to examine if this previous LTP treatment could impact the outcome of subsequent surgery with phaco-KDB.

Second, the LTP-treated group was divided into successful and unsuccessful LTP treatments. The secondary outcome was to examine if there was an association between success of LTP and success of subsequent surgery with phaco-KDB.

Successful outcome after LTP and phaco-KDB was defined as an intraocular pressure (IOP)-reduction of ≥20% without added medications and/or reduction of at least one medication after three months (± two months) and one year (± six months) respectively. If an eye had another glaucoma surgery within the follow-up time, the LTP or phaco-KDB procedure was classified as a failure.

All data were de-identified and analyzed using SPSS Statistics version 28 (SPSS Inc, Chicago, IL, USA). Descriptive data are presented as mean and standard deviation. Independent-samples *t*-test (for normally distributed data) or Mann–Whitney *U*-test (for non-normally distributed data) was used to detect and compare differences between groups, and Chi-square test or Fisher's exact test to compare outcomes between binary data. $P<0.05$ was considered statistically significant, and tests were two-tailed.

Results

A total of 250 patients with open-angle glaucoma or intraocular hypertension, that received phaco-KDB between 2019 and 2021, were included. Patients were excluded due to a lack of IOP and/or medication data (n=12), death (n=9), another eye disease affecting the IOP (n=4), or another glaucoma operation or cyclodiode laser before the phaco-KDB operation (n=8). Out of the 250 included patients, 111 had one or more LTP treatments: 43 ALT and 68 SLT. In seven of

these LTP-treated patients, there was not enough data to determine if the LTP had been successful or not. The time from laser treatment to phaco-KDB was a mean of 4.7 years, with a range from 1 month to 29.4 years.

Baseline characteristics were similar between LTP and non-LTP treated patients regarding gender, glaucoma type, and pre-operative IOP levels, while age, glaucoma severity, and number of preoperative medications differed between groups (Table 1). All patients were white.

The success after phaco-KDB was similar between LTP treated and non-LTP treated patients, and this was regardless of whether SLT or ALT had been performed (Figure 1). The IOP-reduction in LTP-treated patients one year after phaco-KDB was 6.3 ± 6.2 mmHg (from 21.5 ± 6.5 to 15.0 ± 4.4 mmHg), compared to 6.9 ± 6.5 mmHg (from 20.8 ± 6.0 to 13.9 ± 3.4 mmHg) in non-LTP treated patients (P=0.615). The medication reduction in LTP-treated patients was 0.8 ± 1.1 (from 2.6 ± 1.1 to 1.8 ± 1.3), compared to 0.9 ± 1.1 (from 2.0 ± 1.0 to 1.1 ± 1.1) in non-LTP treated patients (P=0.220).

In patients receiving LTP, 54.8% had a successful first-time laser treatment with an IOP-reduction of 8.8 ± 4.7 mmHg, from 24.6 ± 6.0 to 15.8 ± 3.3 mmHg, and a medication reduction of 0.1 ± 0.4, from 2.1 ± 1.1 to 2.0 ± 1.0. In patients with unsuccessful LTP treatment, the IOP reduction was 2.3 ± 3.7 mmHg, from 22.2 ± 5.1 to 20.0 ± 4.4 mmHg, and the number of medications increased with 0.36 ± 0.5, from 1.7 ± 1.0 to 2.0 ±0.9.

In patients with successful LTP, subsequent surgical success with phaco-KDB was 80.7%, compared to 83% in patients with unsuccessful LTP (P=0.765). Similar results were seen, regardless of whether ALT or SLT had been performed (Figure 2).

Table 1 Baseline Demographic and Glaucoma Status

	LTP Treated	Non-LTP Treated	*P*-value
Patients	n=111	n=139	
Age, mean ± SD	74.3 ± 6.9	76.2 ± 6.1	0.026*
Gender, % (n)			
Female	49.5 (55)	49.6 (69)	0.989
Male	50.5 (56)	50.4 (70)	
Glaucoma type % (n)			
Primary open-angle	33.3 (37)	32.4 (45)	
Pseudoexfoliative	59.5 (66)	55.4 (77)	0.520
NTG	0.9 (1)	5.0 (7)	
OHT	5.4 (6)	7.2 (10)	
Pigmentary	0.9 (1)	0	
Glaucoma severity, % (n)			
OHT to mild glaucoma	26.1 (29)	46.0 (64)	
Moderate	27.0 (30)	21.6 (30)	
Severe	45 (50)	27.3 (38)	0.006*
Undetermined	1.8 (2)	5.0 (7)	
Type of LTP, % (n)			
ALT	38.7 (43)		
SLT	61.3 (68)		
IOP (mmHg)	21.5 ± 6.5	20.8 ± 6.0	0.431
Medications	2.6 ± 1.1	2.0 ± 1.0	<0.001**

Note: *p<0.05, ** p<0.001.

Abbreviations: ALT, argon laser trabeculoplasty; LTP, laser trabeculoplasty; NTG, normal tension glaucoma; OHT, ocular hypertension; SD, standard deviation; SLT, selective laser trabeculoplasty.

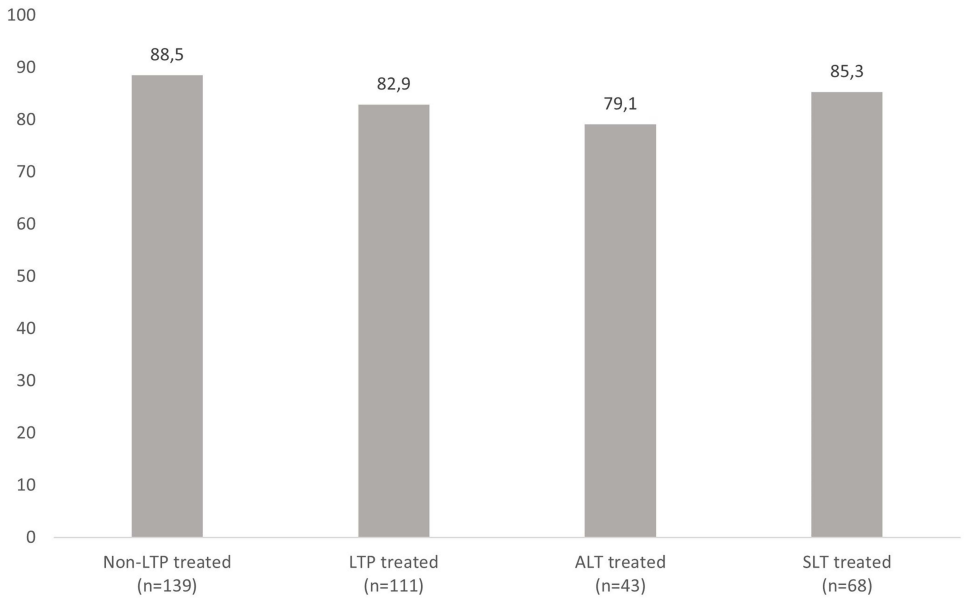

Figure 1 Success rates (%) of phaco-KDB depending on previous laser treatment. No significant differences in phaco-KDB success were found in the different laser groups.

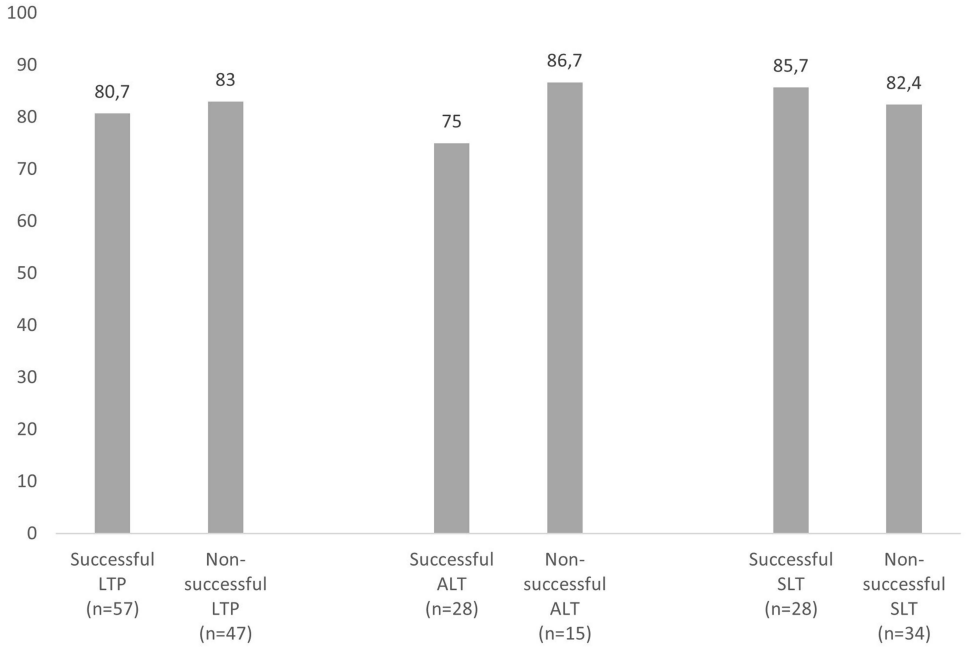

Figure 2 Success rates (%) of phaco-KDB depending on success after laser treatment. No significant differences in phaco-KDB success were found in the different laser groups.

Discussion

Our results showed that previous LTP treatment did not affect subsequent surgery with phaco-KDB. This is in line with previous studies on patients having iStent, KDB, or trabectome surgery after LTP.[9,10,12] In these studies, the authors did not find any relationship between SLT and subsequent surgery with iStent, KDB, or trabectome. On note, iStent was performed as stand-alone, while KDB and trabectome were performed in combination with phacoemulsification. These results together with ours indicate that LTP is probably not a factor to consider when deciding upon trabecular MIGS.

Furthermore, we did not see any correlation between the success of prior LTP and the surgical success of subsequent phaco-KDB. The response to LTP-treatment is therefore not a good predictor for determining the best candidates for later surgery with phaco-KDB. On the other hand, our findings also suggest that even if a patient has had a poor response to LTP, a phaco-KDB procedure will still have a good chance of success. In fact, the results of phaco-KDB were overall promising, with 86% of patients reaching success, defined as ≥20% IOP-reduction and/or reduction of ≥1 medication after one year. These results are better than those reported by King et al in a previous study on 24 patients with previous SLT treatment.[11] As in our study, they found no relationship between LTP success and subsequent phaco-KDB success, but their overall success rate six months after phaco-KDB was only 60%, which is in line with what Phillips et al found in a similar study.[12] This low success rate may be due to more advanced glaucoma cases and lower baseline IOP-levels compared to in our study. The heterogeneity of glaucoma patients can make comparisons between studies difficult since glaucoma severity, number of medications and IOP-levels will likely affect the results.

This heterogeneity between glaucoma patients may also affect comparisons within studies. In our study, we included consecutive patients during a specified time-period, and since no matching was made, we did see differences in baseline characteristics. Most importantly, patients in the LTP treated group had more advanced glaucoma compared to the non-LTP treated group. Interestingly, even though LTP-treated patients in our study had more severe glaucoma, more medications and were on average a few years younger compared to the non-LTP treated patients, their results were not inferior. This fact may strengthen the finding that LTP-treatment does not affect subsequent MIGS in the TM area.

Since we found preoperative differences, we did not compare absolute IOP- and medication levels, but instead looked at reductions in IOP and medications. We found reductions in both IOP and medications after phaco-KDB to be similar between LTP and non-LTP treated patients. In contrast to our findings, a previous study looking at ALT and subsequent trabectome surgery found an increase in glaucoma medications in patients with previous ALT before surgery.[15] However, they found overall success rates to be similar between laser treated and non-laser treated patients, as in our study.

Although LTP and KDB have different mechanisms of action, they both enhance conventional outflow via the TM. Therefore, it would be useful to determine if the response to LTP would be predictive for the response to phaco-KDB and other trabecular surgeries. Such a determination would allow for better patient selection, providing guidance regarding which patients that are suitable for trabecular MIGS and which should instead have subconjunctival bleb-forming surgery.

Our data showed that eyes that were unresponsive to LTP still showed a good response to phaco-KDB. The reason for that is unclear, but it could be hypothesized that LTP may not be as effective in eyes with stiff and rigid TM, whereas KDB can still be effective by mechanically removing a part of the TM. While both LTP and KDB impact outflow through the TM, their mechanisms diverge. LTP, particularly SLT, enhances TM permeability by recruiting macrophages and upregulating cytokines,[16,17] whereas KDB mechanically excises TM tissue.

The major weakness of the present study is its retrospective design. All patients were also white, limiting the applicability to other ethnicities. Although the operations were performed by the same surgeon, the LTP-treatments were performed by different ophthalmologists. Also, the time from laser-treatment to surgery was variable.

The strength of this study is the inclusion of all glaucoma severities, making the results transferable also to patients with advanced glaucoma. Additionally, compared to previous similar studies, we included a higher number of subjects, thus making the results more robust. A further strength is that all operations were performed by the same surgeon.

So far, all published studies comparing LTP and subsequent trabecular MIGS have come to roughly the same conclusions. Future studies that may strengthen these results include real-world results from prospective databases and large registries. Further investigations should also include other predictive factors for the outcome of trabecular procedures. The possibility of identifying reliable clinical biomarkers for trabecular procedures, including KDB, is intriguing and would allow for a better selection of patients in the future.

Conclusion

Our results show that LTP does not seem to impact future surgery with phaco-KDB, and this is regardless of whether ALT or SLT has been performed. Furthermore, the outcome of LTP does not seem to predict the outcome of subsequent phaco-KDB. These two findings together suggest that previous LTP is not an important factor to consider when deciding

upon adding a trabecular MIGS procedure in combination with phacoemulsification in patients with glaucoma or intraocular hypertension.

Ethics

The protocol of this study was approved by the Institutional Review Board of the Swedish Ethical Review Authority (DNR. 2121−02970).

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Disclosure

Anna Barkander has received consulting for iStar Medical, Medilens, and Santen. Gauti Jóhannesson has received speaking honoraria and/or consulting for Thea, Santen, AbbVie, Alcon, and Oculis, and Mario Economou has received lecture fees from Glaukos Corp. and New World Medical Inc. The authors report no other conflicts of interest in this work.

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