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Hypotensive Effect of Selective Laser Trabeculoplasty in Patients with Medically Uncontrolled Primary Open-Angle Glaucoma

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SUMMARY

Introduction Glaucoma is a chronic, progressive disease of the optic nerve which if left untreated can lead to blindness at end stages. A decrease of intraocular pressure (IOP) has proven to slow down the progression of the disease. IOP decrease can be achieved by medical, laser and surgical treatment.

Objective The aim of this study was to evaluate the response of patients with medically uncontrolled primary open angle glaucoma to selective laser trabeculoplasty (SLT).

Methods The study involved baseline characteristics recorded for each of 35 patients (48 eyes) in whom, despite being under full medication we could not achieve a satisfactory IOP. Patients, who had pressure above 25 mmHg under the maximal medication therapy, were not included into the study and were referred for surgical treatment. IOP was measured on admission, 1 hour, 7 days, 1, 3, 6 and 12 months after SLT. We considered satisfactory surgical result if IOP was decreased more than 20% of the initial value. Also, we investigated the influence of baseline IOP on SLT outcome after 12 months. Patient inclusion criteria were inability to reach target IOP with maximal medical therapy. Exclusion criteria were congenital glaucoma, any type of angle closure glaucoma, advanced-stage glaucoma, eyes with previous laser or surgical glaucoma applications and patients with baseline IOP >25 while fully medicated. Patients who could not be followed for at least 12 months were also excluded.

Results The mean age of our patients was 73±12 years. The mean baseline IOP was 20.48 mmHg (SD=1.91), and the mean change in IOP from baseline of the treated eye after one year was 4.47 mmHg (SD=2.12). In eyes with a higher baseline IOP the reduction of pressure at the end of the study was significantly higher. Satisfactory effect of IOP reduction after one year was achieved in 64.58% of eyes. The IOP reduction did not show to be dependent as regarding age and gender.

Conclusion SLT effectively lowers IOP in patients with primary open-angle glaucoma, and the intervention is not followed by significant complications. Our results confirm that the IOP reduction is more significant if the initial value is higher. Our first reliable results of IOP reduction were confirmed one month after the procedure so that the procedure should not be repeated before one month has elapsed. The study is limited by a small number of eyes, which is insufficient to make a complete case analysis.

Keywords: laser; primary open-angle glaucoma; selective laser trabeculoplasty; treatment

INTRODUCTION

Glaucoma is a chronic, progressive disease of the optic nerve which if left untreated can lead to visual field decay and blindness at end stages [1]. Decrease of the intraocular pressure (IOP) has proven to slow the progression of the disease [2]. IOP decrease can be achieved by medical, surgical and laser treatment. Selective laser trabeculoplasty (SLT) was introduced by Latina and Park [3] in 1995 as an option for the treatment of open-angle glaucoma (OAG) and has been in commercial use since 2001. This procedure calls for Q-switched, frequency doubled laser with a wavelength of 532 nm to be directed at the trabecular meshwork (TM) with the pulse duration of 3 ns. Using a short duration and wavelength of 532 nm spares the TM from coagulation necrosis and affects mainly pigmented cells. Effective IOP reduction and minimal side effects have been proven during clinical trials of SLT [4].

The position of SLT on the treatment scale is still a cause of great controversy. This treatment consists of the application of laser spots in the TM, the structure responsible for the aqueous humor drainage, leading to an increase in the outflow facility through it and in consequence, decreasing IOP [5]. Advantages of such treatment are in the fact that it does not depend on chronic instillation of eye drops nor does it have as many complications as incisional surgery.

OBJECTIVE

The aim of this study was to analyze the effects of laser trabeculoplasty on Serbian patients with medically uncontrolled OAG, particularly the significance of IOP reduction compared to baseline IOP, correlation between baseline IOP value and percentage of IOP reduction 12 months after SLT procedure and influence of sex and age on the value of IOP reduction.

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METHODS

All patients included in this study gave informed consent and the study was approved by the institutional review board and ethics committee. Baseline characteristics of all patients were recorded, including age, gender, diagnosis, baseline IOP, and the number and the type of taken medications, as well as the degree of angle pigmentation which was evaluated at the time of the procedure. Thirty-five patients (48 eyes) were enrolled in this prospective study conducted from June 2011 to June 2012.

All studied patients had primary open-angle glaucoma (POAG) which was uncontrolled despite maximum medication therapy. All eyes were treated by SLT. Starting back at 4 weeks before SLT procedure IOP was measured at least 2 times in all patients so as to ascertain the baseline IOP as a mean value of these measurements. IOP was measured using the Goldmann applanation tonometer. On the day of SLT, IOP was measured and one drop of 0.5% apraclonidine was instilled in the studied eye one hour before treatment in order to prevent IOP spikes [6, 7]. As preoperative assessment we performed ophthalmic examination, Snellen visual acuity test, IOP measurement by Goldmann applanation tonometry, slit-lamp examination and gonioscopy, and funduscopy with evaluation of cup:disc ratio and pallor. Visual field testing was performed first in all patients as the initial diagnostic step.

Patient inclusion criteria were inability to reach target IOP with maximal medical therapy in patients with POAG who were older than 18 years. Exclusion criteria were congenital glaucoma, any type of angle closure glaucoma, advanced-stage glaucoma, eyes with previous laser or surgical glaucoma applications, eyes with previous anterior segment surgery within the past 6 months and patients with baseline IOP >25 while fully medicated. Patients who could not be followed for at least 12 months were also excluded.

The procedure was performed with the patient under topical anesthesia using benoxinate hydrochloride 0.4%. With the patient seated at the laser slit-lamp system, the Goldmann three-mirror goniolens or Latina lens was placed on the eye with methylcellulose 2%. The patients were treated with the Ellex, Tango® SLT laser (Ellex Medical Pty. Ltd, Adelaide, Australia) a frequency-doubled, Q-switched Nd:YAG laser emitting at 532 nm with pulse duration of 3 ns and a spot size of 400 μm. A low-power helium–neon laser served as an aiming beam to provide easy targeting of the treatment area. The laser is capable of delivering pulse energies ranging from 0.3 to 2.6 mJ. Treatment began at 0.8 mJ and was titrated according to the response. If cavitation bubbles appeared the laser energy was reduced by 0.1 mJ until no bubbles formed, and treatment was continued at this energy level. If no cavitation bubble was observed, the pulse energy was increased by 0.1 mJ until bubble formation and then decreased as described above. Sometimes higher energy was required for the treatment of the superior, less pigmented angle. Approximately 100 adjacent but nonoverlapping laser spots were placed over 360° of the TM.

Immediately after the laser treatment, diclofenac eye drops were administered once in the treated eye then three times daily for 3 days. The IOP of the treated eye was measured and recorded 1 hour after surgery. The same preoperative antiglaucoma medication regimen was continued. The patients were evaluated at 1 hour, 1 week, and at 1, 3, 6 and 12 months. At each visit, the visual acuity and IOP were measured, and the slit-lamp examination of the anterior segment was performed. All major and minor complications and complaints were recorded and treated appropriately.

The data was analyzed using SPSS statistical software (version 17) using ANOVA for repeated measures, T test for dependent samples and Tukey's multiple comparison test. A p value of less than 0.05 was considered to be statistically significant.

RESULTS

This paper presents the results of a prospective, nonrandomized, interventional cohort study undertaken at our institution to assess the response to SLT according to baseline medical treatment, age, gender and baseline intraocular pressure. The total of 35 patients (48 eyes) was included in the study. Baseline characteristics of included patients are presented in Table 1. The patients' average age was 73.27 (SD=6.13) and baseline IOP was 20.48 (SD=1.91).

On the first check-up 1 hour after SLT treatment IOP value dropped to 17.18 (SD=2.95), and after one week IOP dropped to 16.25 (SD=2.04). At one month checkup IOP dropped to 15.93 (SD=1.93). Reduction in IOP was maintained at a yearly checkup when average IOP value was 16.00 (SD=1.45). IOP was also checked at 3 and 6 months milestones and results are presented in Table 2. Results

Table 1. Baseline characteristics of patients

Characteristics		Male (%)	Female (%)	All
Number (%)	Patients	16 (45.71)	19 (54.29)	35
	Eyes	21 (43.75)	27 (56.25)	48
Age (years)	Mean	74	72.7	73.27
	SD	6.52	5.88	6.14
	Min	61	63	61
	Max	84	85	85
Baseline IOP (mmHg)	Mean	20.61	20.37	20.48
	SD	1.90	1.94	1.91
	Min	18	17	17
	Max	25	25	25

IOP – intraocular pressure; SD – standard deviation; Min – minimal value; Max – maximal value

Table 2. Intraocular pressure (IOP) values over time (mmHg)

	IOP values (mmHg)			
Period	Mean	SD	Min	Max
Base	20.48	1.91	17	25
1 hour	17.18	2.96	11	26
7 days	16.96	2.04	11	23
1 month	15.94	1.92	10	21
3 months	15.73	1.79	12	19
6 months	16.04	1.84	11	21
12 months	16.00	1.45	12	20

Table 3. Intraocular pressure (IOP) reduction over time

Period	IOP reduction	
	mmHg	%
1 h	3.29	16.07
7 days	3.52	17.19
1 month	4.54	22.17
3 months	4.75	23.19
6 months	4.44	21.67
12 months	4.47	21.87

Table 4. Reduction percentage by groups

Group – reduction	0–10%	10–20%	20–30%	>30%
Number of eyes	5	12	21	10
%	10.42	25.00	43.75	20.83

Table 5. Influence of baseline IOP on outcome of selective laser trabeculoplasty

Baseline IOP groups	Mean reduction (%)	N	SD
Group 1 (17–19 mmHg)	15.54	15	6.35
Group 2 (20–22 mmHg)	22.46	27	8.30
Group 3 (23–25 mmHg)	31.19	6	2.72
All groups	21.39	48	8.64

Table 6. Tukey's multiple comparison test to compare the difference between each pair of means

Baseline IOP groups	Group 1 (M=15.54)	Group 2 (M=22.46)	Group 3 (M=31.19)
Group 1 (17–19 mmHg)		0.0332*	0.0016*
Group 2 (20–22 mmHg)	0.0332*		0.1067
Group 3 (23–25 mmHg)	0.0016*	0.1067	

* statistically significant difference at $p<0.05$

M – mean reduction

presented in Table 3 show that the main IOP reduction happens up to one month after SLT treatment. Follow-up measurements at 3, 6 and 12 months checkups show small difference compared to values at one month checkup.

We used paired-samples T test to compare the means of baseline IOP and IOP after 12 months and difference is highly statistically significant ($p<0.001$).

Percentage of IOP reduction after 12 months related to the starting value show that in 33% of patients the reduction was between 10 and 20% of starting value, in 31% reduction was 20-30%, 22.9% reduction was greater than 30% while in 12.5% of patients the effect was insufficient meaning that the reduction was between 0 and 10% (Table 4).

We divided our patients into three groups based on the baseline IOP. In the first group we selected patients with the baseline IOP of 17-19 mmHg. The second group consisted of patients with the baseline IOP of 20-22 mmHg, and in the third group of patients with the IOP of 23-25 mmHg. Then we analyzed the influence of baseline IOP at outcome of SLT treatment. We found that the higher the baseline IOP the greater was the rate of reduction. Results showed the average IOP reduction of 21.39% from the baseline value (SD=8.64) with the highest percentage of reduction detected in the group of patients with the baseline IOP of 23-25 mmHg, with the reduction measured at 31.19% (SD=2.72), while in the group of patients with baseline IOP of 20-22 mmHg, measured at 22.4%, and in the group with baseline IOP of 17-19 mmHg the reduction was lowest and it was measured at 15.54% (Table 5). We used the Tukey's multiple comparison test to compare the difference between each pair of means with appropriate adjustment for the multiple testing and we found statistically significant differences of the IOP reduction in group 1 as compared with group 2 and group 3 (Table 6). When analyzing our data set we could not find any correlation between the age and effect of SLT. Also, no significant difference was found of the effect of SLT on IOP between male and female patients.

All patients enrolled in the study were on fully tolerated local medical therapy. The mean number of different eye drops was 2.83. None of the patients were on systemic glaucoma therapy with carbonic anhydrase inhibitor (CAI). After one year of follow-up the mean number of eye drops was reduced to 2.68.

In regard to the safety issues, we noticed a mild anterior chamber inflammation in 7 eyes (14.58%). At 7 days follow-up there were no signs of inflammation in any of the eyes. After surgery all patients were treated with diclofenac eye drops. In addition, 2 patients reported a mild ocular discomfort during treatment which vanished after lowering the SLT power. No patients complained of pain after treatment. IOP spikes greater than 5 mmHg were noticed in 3 eyes (6.25%), and were reduced after 7 days.

DISCUSSION

Selective laser trabeculoplasty proved to be a useful tool for the treatment of OAG and ocular hypertension [8]. It is still unclear, which is the precise mechanism of action that causes the decrease in IOP following laser trabeculoplasty. The cellular theory proposes that there is a migration of macrophages at the site of laser treatment and their phagocytic activity clears the debris from TM and improves outflow [9]. According to the mechanical theory thermal damage of TM, which results in collagen shrinkage and scarring from the laser, allows better drainage of aqueous humor [10]. The third possible mechanism of action for SLT-induced IOP lowering is that there is a release of extra amounts of enzyme known as matrix metalloproteinases (MMPs) to clean TM and improve aqueous humor flow through TM [11, 12, 13].

In our group of patients, a satisfactory reduction of IOP (>20%) by usage of SLT was found to be 64.58% which is a similar percentage reported by other authors [14, 15, 16]. Achieved IOP reduction by 10-20% of baseline value was found to be 25%, which can be assessed as useful, taking into account that all patients were fully medicated before the procedure. Our study showed that SLT had the same effect on IOP both in male and female patients, which is consistent with findings of other authors as well as that the age also did not show significant influence on SLT effects.

If analyzing the average IOP values measured over the periods of 1 hour, 7 days, 1 month, 3 months, 6 months and one year after SLT intervention and compare it to the baseline IOP value, (Table 3) we can see that the IOP value reduction stabilizes after 1 month period following the

SLT intervention. This suggests that 1 month is the minimum amount of time between SLT and the assessment of procedure success.

Most studies have reported low complication rates, which correlates well with our findings. Transistent IOP elevation of treated eyes has been reported in other studies, usually within 2 hours after surgery and resolved within 24 hours. Damji et al. [4] reported that 4.5% of treated eyes exhibited an IOP rise of 6 mmHg or greater within 1 hour after treatment. Lai et al. [17] reported IOP spike of 5 mmHg or higher in 10.3% of treated eyes. To our opinion, a careful selection power 0.1 mJ lower than cavitation bubbles formation power is very important for low complication rate, like IOP spikes and anterior chamber reaction, especially in heavily pigmented angles.

Reduction in the mean number of medications used in this group of patients rating from 2.83 to 2.68 is similar to other authors findings in patients with medically uncontrolled glaucoma [18], although we preferred for this group of patients' target IOP to be as low as possible, thus we did not aim at reducing the number of eye drops.

CONCLUSION

SLT effectively lowers IOP in patients with medically uncontrolled primary open-angle glaucoma, and the intervention was not accompanied by significant complications. Our results confirm the finding that a higher baseline IOP is the predictor of better IOP response after SLT [19]. We also found that first conclusive results were visible 1 month after the procedure. Our results also confirm that there were no significant side effects of selective laser trabeculoplasty [20].

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Хипотензивни ефекат селективне ласерске трабекулопластике код болесника с медикаментно нерегулисаним примарним глаукомом отвореног угла

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КРАТАК САДРЖАЈ

Увод Глауком је хронична, прогресивна болест очног живца која, уколико се не лечи, доводи до неповратног губитка вида. Доказано је да снижавање интраокуларног притиска (ИОП) успорава напредовање болести. Снижавање ИОП се постиже медикаментном, ласерском или хируршком терапијом.

Циљ рада Циљ рада је био да се утврди одговор болесника с медикаментно неконтролисаним примарним глаукомом отвореног угла на примену селективне ласерске трабекулопластике (СЛТ).

Методе рада У студију је укључено 35 болесника (48 очију) код којих и уз примену пуне медикаментне терапије нису постигнуте циљне вредности ИОП. Болесници који су под оваквом терапијом имали притисак већи од 25 *mm Hg* нису били укључени у истраживање, већ су упућени на хируршко лечење. ИОП је мерен на пријему, те један сат, седам дана, месец дана, три, шест и дванаест месеци после СЛТ. Као задовољавајући ефекат узимано је снижење ИОП од најмање 20% од почетне вредности. Такође је испитан утицај почетне вредности ИОП на његову вредност на крају периода клиничког праћења.

Резултати Испитаници су у просеку имали 73±12 година. Средња вредност почетног ИОП била је 20,48 *mm Hg* (*SD*=1,91), док је просечно смањење ИОП после примене СЛТ било 4,47 *mm Hg* (*SD*=2,12). Код очију с вишим почетним вредностима ИОП пад притиска на крају испитивања био је статистички значајно већи. Задовољавајући ефекат снижења ИОП после годину дана постигнут је код 64,58% очију. Снижење ИОП није зависило од пола и старости испитаника.

Закључак СЛТ ефикасно снижава ИОП код болесника с примарним глаукомом отвореног угла, а интервенција није праћена значајним компликацијама. Резултати истраживања потврђују да је снижење ИОП значајније уколико је почетна вредност већа. Први поуздани резултати снижења ИОП утврђени су месец дана од интервенције, тако да ју не би требало понављати пре истека првог месеца.

Кључне речи: ласер; примарни глауком отвореног угла; селективна ласерска трабекулопластика; лечење

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