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Original Scientific Paper

THE EFFECT OF PRIMARY ARGON LASER TRABECULOPLASTY ON INTRAOCULAR PRESSURE REDUCTION AND QUALITY OF LIFE IN PATIENTS WITH PSEUDOEXFOLIATION GLAUCOMA

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SUMMARY – The aim of the study was to assess the impact of primary argon laser trabeculoplasty (ALT) on intraocular pressure (IOP) lowering and quality of life improvement in patients with pseudoexfoliative glaucoma. Sixty patients with newly diagnosed pseudoexfoliative glaucoma who underwent primary ALT (group 2) or medication therapy (group 1) were followed-up. The effect of ALT on IOP reduction, dry eye development and number of antiglaucoma drugs used was examined. Patients were examined at the beginning of the study and then after 6, 12, and 18 months. A statistically significant difference between IOP values was observed throughout the 18-month follow-up, with the highest significance recorded 6 months after ALT (p=0.009). Twelve months after the start of the study, the TBUT value was 6.0±0.8 s in group 1 and 8.4±0.7 s in group 2. In group 2, the value of Schirmer test was constantly above 10 millimeters. The number of antiglaucoma medications used in group 1 was statistically significantly higher as compared to group 2 throughout the 18-month study period. ALT was found to be better choice for temporary regulation of IOP in patients with pseudoexfoliative glaucoma.

Key words: *Argon laser trabeculoplasty; Intraocular pressure; Antiglaucoma drugs*

Introduction

Pseudoexfoliation syndrome (PXS) was initially mentioned at the beginning of the 20th century. It was described as a progressive, age-related ocular disorder resulting in accumulation of fibrillar material within the extracellular matrix of the eye[1]. The origin of this material still remains unknown. Pseudoexfoliation (PEX) can lead to the intraocular pressure (IOP) rise by blocking the trabecular meshwork, and it can cause intraocular inflammation. Untreated high IOP induces a characteristic optic nerve damage and visual field defects. This condition is known as pseudoexfoliation glaucoma (XFG)[2]. It represents secondary open-angle glaucoma, usually seen in older people. In the eye, pseudoexfoliations affect conjunctiva, cornea, anterior chamber, ciliary zonule, iris, and lens. Pseudoexfoliations also affect visceral organs, as well as blood vessels. This indicates that PXS could be only ocular manifestation of a massive systemic disorder[3]. The most common ocular signs of PEX are deposits at the iris pupillary margin (Fig. 1) and anterior lens capsule (Fig. 2).

Other signs include corneal deposits, anterior chamber inflammation, poor mydriasis, zonulolysis, cataract development, and high IOP fluctuation[2,3]. XFG can be treated by using antiglaucoma medications, argon laser trabeculoplasty (ALT) or glaucoma

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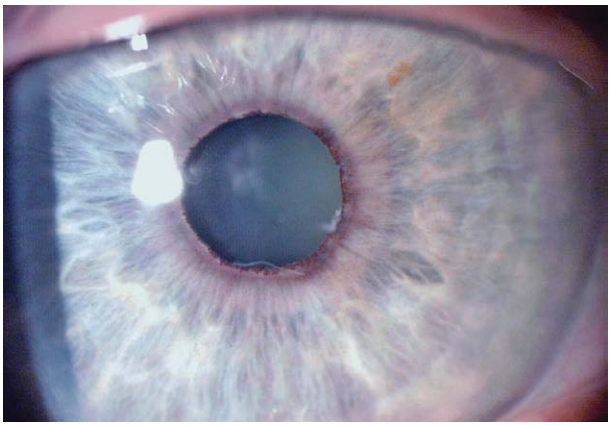

Fig. 1. Pseudoexfoliation deposits at the iris pupillary margin.

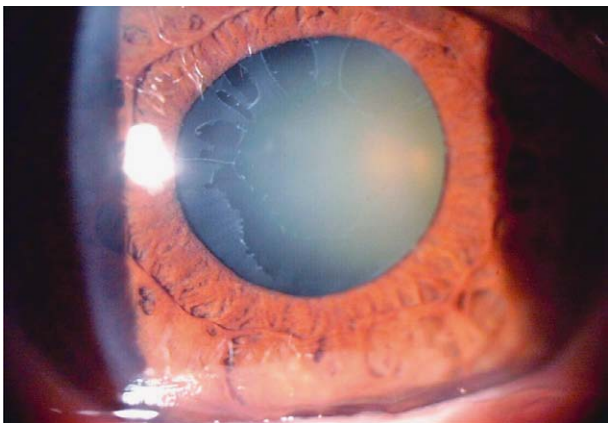

Fig. 2. Pseudoexfoliation deposits on the surface of the anterior lens capsule.

surgery, i.e. trabeculectomy[4]. Antiglaucoma medications are commonly the first choice in glaucoma treatment. These agents decrease aqueous humor production or increase its resorption. They include beta-blockers, alpha adrenergic agonists, carbonic anhydrase inhibitors, and prostaglandin analogs[5]. This kind of therapy has limitations such as side effects, allergies, poor compliance, and dry eye development. If adequate IOP values cannot be reached by using antiglaucoma drugs, other treatment possibilities are required. Electromagnetic energy generated by argon laser gets converted into thermal energy. This causes thermal burn of the trabecular meshwork, which consecutively improves aqueous humor resorption[6,7]. In some cases, argon laser trabeculotomy can be used primarily.

The aim of this study was to investigate the effect of the primarily used ALT for IOP reduction and life quality improvement in patients with XFG.

Patients and Methods

The study included 60 newly diagnosed XFG patients divided into two groups. All patients were treated at the Department of Ophthalmology, Kragujevac Clinical Center, Kragujevac, Serbia. The study was carried out between June 1, 2018 and January 1, 2020. The most important inclusion criterion was no glaucoma disease before the beginning of the study. Patients who had another type of glaucoma were excluded from the study. Patients with a history of intraocular surgery or inflammation, laser treatment, dry eye, eyelid abnormality and contact lens users were also excluded. All patients underwent thorough ophthalmologic examination including best-corrected visual acuity, biomicroscopic and funduscopic examination, intraocular pressure measurements by using Goldmann applanation tonometer, and standard automated perimetry. Gonioscopy was performed to detect open iridocorneal angle. Dry eye examination included Schirmer and tear breakup time test (TBUT). Then the participants were randomized into two groups. Group 1 included 32 patients treated for XFG by using antiglaucoma eye drops, whereas group 2 consisted of 28 patients scheduled for primary ALT. With approval from the institutional Ethics Committee and according to the tenets of the Declaration of Helsinki, all patients gave their written consent at the beginning of the study.

All patients were examined at the beginning of the study, and then at 6, 12 and 18 months. During the 18-month follow-up, we analyzed IOP values, dry eye parameters, and number of antiglaucoma drugs used. Antiglaucoma drugs include beta-blockers, alpha adrenergic agonists, carbonic anhydrase inhibitors, and prostaglandin analogs. They were administered as eye drops, primarily as monotherapy, usually 0.25% timolol maleate as the most widely used topical beta-blocker. If the desired IOP value was not achieved, then another eye drops were added. These agents have many side effects and contain benzalkonium chloride as well.

Argon laser trabeculoplasty was performed in 28 patients (group 2) at the beginning of the study. These patients received 1 drop of 0.5% tetracaine and 1 drop of 0.5% apraclonidine approximately 30 minutes before laser treatment. Gonioscopic lens was applied to reveal the structures of the iridocorneal angle. The initial laser settings for ALT treatment were laser power of 700 mW, spot size of 50 μm in diameter, and duration of 0.1 second. The power was adjusted up or down

depending on the pigmentation degree of trabecular meshwork. The treatment involved about 180 degrees of the angle, initially inferiorly, and then superiorly, if the second treatment was needed. When the laser procedure was completed, 0.2% brimonidine was applied, and prednisone acetate 1% 4 times *per* day for the next 3 days. These agents were prescribed to prevent intraocular inflammation and consecutive IOP rise caused by particular disruption of the blood-ocular barrier during laser treatment. If necessary according to IOP value, patients from the ALT group also received antiglaucoma drugs during the study.

The tear breakup time test is used as an indicator of the lipid layer of the tear film. The test was performed by using the cobalt blue light of the slit lamp biomicroscope. Before the examination, both eyes were stained by using fluorescein strips. We measured the time until the appearance of the first dry spots on the corneal surface. Values above 10 seconds were considered as physiologic. Tear secretion test was measured by using Schirmer's strips. They were applied at the lateral side of the inferior fornix, without previous topical anesthetic application. The wet part of the paper was observed. Values shorter than 5 mm indicated dry eye syndrome.

IBM SPSS Statistics, Version 22.0 (IBM Corp., Armonk, NY, USA) was used in all calculations in the study. For comparison of the variables, Student's t-test was used. The level of statistical significance was set at $p<0.05$.

Results

The patient mean age was 66.24±5.5 years in group 1 and 57.15±4.8 years group 2, yielding no statistically significant between-group difference (p=0.46). In both groups, the female to male ratio was approximately equal. One patient developed peripheral anterior synechiae after the ALT procedure, which compromised aqueous humor outflow, so he was excluded from the study.

At the beginning of the study, the mean IOP values were increased in both groups (group 1, 24.2±0.6 mm Hg and group 2, 25.01±0.2 mm Hg), without statistically significant difference (Fig. 3). At six-month follow-up, the mean IOP was 18.5±0.7 mm Hg in group 1 and 14.0±0.5 mm Hg in group 2, yielding a statistically significant difference (p=0.009). This trend continued on the next two measurements at 12 months (group 1, 16.8±0.4 mm Hg and group 2, 14.8±0.6 mm Hg; p=0.042) and 18 months (group 1, 17.3±1.2 mm Hg and group 2, 15.7±0.8 mm Hg; p=0.045).

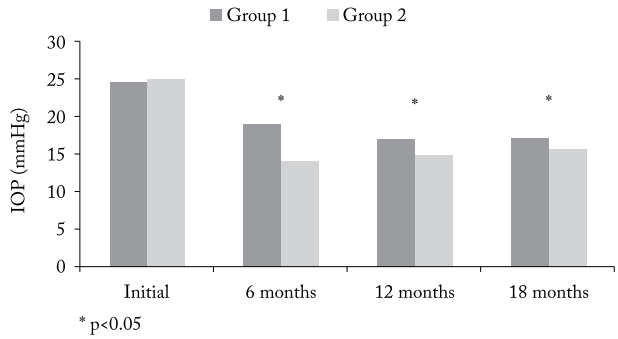

Fig. 3. Intraocular pressure (IOP) values during 18-month follow-up.

In both patient groups, dry eye tests were physiologic before the diagnosis of glaucoma. Schirmer test was 17.0±1.2 mm in group 1 and 16.5 ± 0.7 mm in group 2, without any statistically significant difference (Fig. 4). During the next 18 months, the mean Schirmer test value was constantly lower than 10 millimeters in group 1, and we considered it as dry eye (6 months, 7.1±0.9 mm; 12 months, 8.0±0.4 mm; and 18 months, 6.5±0.6 mm). Comparison of these results with those recorded in the ALT group (6 months, 13.5±0.8 mm; 12 months, 12.1±0.7 mm; and 18 months, 14.6±0.3 mm) showed a prominent statistically significant difference on all three measurements (p<0.001).

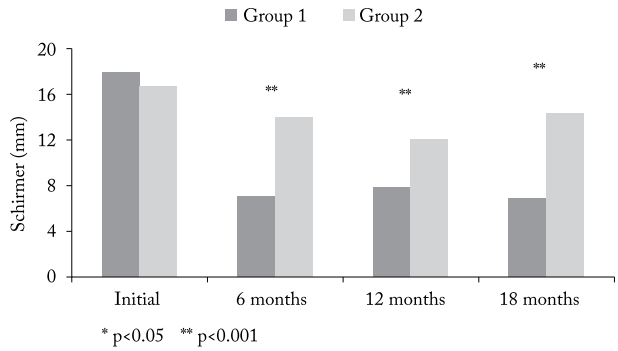

Fig. 4. Schirmer test values during 18-month follow-up.

The most obvious difference between the groups was found in TBUT results (Fig. 5). Except for the first measurement (group 1, 15.0±1.1 s and group 2, 16.1±0.5 s; p=0.067), all other results were lower than

the limit value both in group 1 (6 months, 5.3±1.4 s; 12 months, 6.0±0.8 s; and 18 months, 5.5±1.3 s) and group 2 (6 months, 9.4±1.7 s; 12 months, 8.4±0.7 s; and 18 months, 7.9±0.6 s), yet yielding statistically significant between-group differences (6 months, p= 0.019; 12 months, p=0.032; and 18 months, p=0.038).

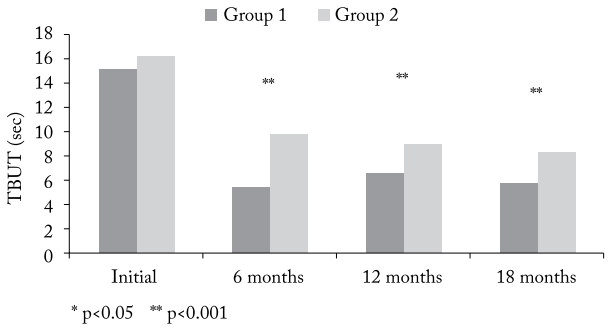

Fig. 5. Tear breakup time test (TBUT) values during 18-month follow-up.

Group 1 patients used 1.5±0.5 antiglaucoma drugs at the beginning, then 2.2±0.4, 2.3±0.6 and 2.6±0.5 drugs during the follow-up period (Fig. 6). On the other hand, after primary ALT, group 2 patients were without any antiglaucoma drops in the first 6 months. Then, they used 0.6±0.4, 0.7±0.4 and 0.7±0.5 drugs until the end of the study. Statistically significant differences were recorded throughout the study period (p<0.001).

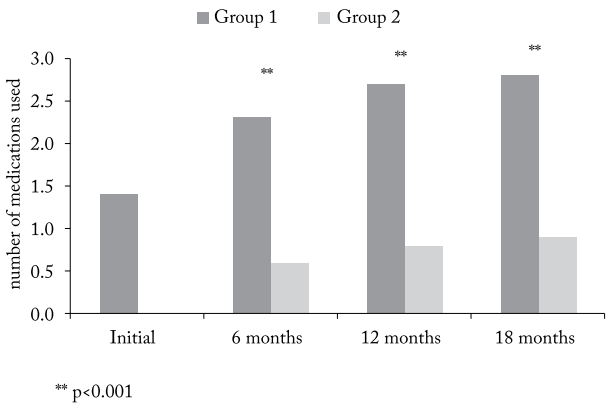

Fig. 6. Number of antiglaucoma drugs used during 18-month follow-up.

Discussion

Pseudoexfoliation glaucoma is a difficult type of glaucoma due to its rapid progression, commonly late diagnosis, high baseline IOP, and daily fluctuation. Some studies marked XFG as the most frequent secondary open-angle glaucoma worldwide[8-10]. Due to these facts, XFG usually requires more aggressive clinical approach than other types of open-angle glaucoma. If the treatment is based on antiglaucoma drugs, most often more than two drugs are necessary[11,12]. These findings are in correlation with our results. Only one year after the diagnosis of XFG, patients without primary ALT used 2.5 different antiglaucoma drugs. The usage of multiple medications is always associated with many difficulties, especially in local ophthalmologic therapy. Inappropriate usage of eye drops, wash out effect, drug allergies, and poor compliance are the most frequent problems in glaucoma treatment[12].

Beta blockers can cause corneal epithelial erosion. By decreasing the production of the aqueous component, they lead to tear film instability. They are contraindicated in patients with cardiac or bronchial diseases as well, due to their systemic anti adrenergic effect[13]. Alpha adrenergic agonists and carbonic anhydrase inhibitors show local allergic manifestations. These drugs, applied as eye drops, act by decreasing aqueous humor production[14,15]. Prostaglandin analogs improve uveoscleral outflow as an alternative way of the aqueous humor resorption. Containing prostaglandins, they amplify intraocular inflammation, so they should be avoided in XFG treatment[16]. All of these agents contain benzalkonium chloride, a substance that provides prolonged shelf life of the opened vial of eye drops. It is proven that benzalkonium chloride disturbs epithelial cells of the conjunctiva and cornea, thus additionally deteriorating tear film stability[15].

Cellular examinations of the conjunctival and periorbital tissues verified the accumulation of pseudoexfoliation material[17]. The presence of pseudoexfoliation material in conjunctival tissue influences goblet cell function. They are responsible for the production of mucin layer of the tear film. By disturbing them, pseudoexfoliation causes tear film instability. That is also reported in some earlier studies[18,19]. In our investigation, pseudoexfoliation seemed to be responsible for the development of dry eye syndrome in both groups. TBUT values were lower than 10 seconds on all measurements after the initial one. Despite that, obvious statistically significant between-group differences were noticed in dry eye test results. A strong effect on these results was attributed to the usage of antiglaucoma drugs containing benzalkonium chloride.

In our study, ALT was demonstrated to be a more efficient method in IOP lowering. IOP was statistically significantly lower throughout the follow-up period. ALT procedure proved to be a safe and efficient treatment option for patients with XFG. It is known that ALT has a specifically strong effect in XFG[1,3,4]. This is explained by extensive pigmentation of the trabecular meshwork in these patients. Only one of our patients developed peripheral anterior synechiae and had to undergo glaucoma surgery. Another two patients from this group had transient IOP elevation, which was efficiently treated within the next 3 days. Although the exact mechanism of action of ALT is still unknown, there are two theories trying to explain how ALT acts in reducing IOP[7]. According to the mechanical theory, transmitted thermal energy causes tissue contraction and stretching of the trabecular meshwork. Dilatation of the Schlemm's canal follows, which improves the aqueous humor outflow[8,20]. The biologic theory indicates that energy generated by argon laser stimulates cellular activity. This leads to the amplified number and function of macrophages in the trabecular meshwork, which causes remodeling of the extracellular matrix and increased aqueous humor outflow[8].

Analysis of our study results revealed that by far superior results were recorded in the life quality parameters. Many problems associated with polypragmasy were avoided in the ALT group. The main restriction in primary ALT could be its transient effect. It is known that after approximately five years, laser-made spots fade away, which causes IOP rise and the procedure has to be repeated[7,8,20]. Some investigators advocate that primary ALP be part of glaucoma treatment in some specific conditions[20,21], including patients suffering from dementia, rheumatic and mental disorders, or noncompliant patients. Patients who have severe dry eye disease or confirmed eye drops allergy, could also be candidates for primary ALT.

This research showed that ALT proved to be a better method in temporary IOP regulation. By reducing the number of antiglaucoma drugs, ALT reduces the problems of polypragmasy such as side effects of eye drops, wash out effect, and increased concentration of preservatives. Knowing that pseudoexfoliation material disturbs goblet cells and worsens tear film condition, ALT showed a strong effect in preserving tear film stability. On the other hand, ALT has a transient effect of IOP lowering. Since we analyzed all these facts, we suggest that ALT be considered as a primary treatment of XFG, particularly in patients who have problems concerning daily application of eye drops.

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Sažetak

UČINAK PRIMARNE ARGON LASERSKE TRABEKULOPLASTIKE NA SNIŽENJE INTRAOKULARNOG TLAKA I KVALITETU ŽIVOTA U BOLESNIKA S PSEUDOEKSFOLIJACIJSKIM GLAUKOMOM

D. Todorović, T. Šarenac Vulović, S. Srećković, S. Jovanović i *N. Petrović*

Cilj studije bio je utvrditi utjecaj primarne argon laserske trabekuloplastike (ALT) na snižavanje intraokularnog tlaka (IOP) i poboljšanje kvalitete života bolesnika s pseudoeksfolijacijskim glaukomom. Praćeno je šezdeset bolesnika s novodijagnosticiranim pseudoeksfolijacijskim glaukomom koji su bili podvrgnuti primarnom ALT-u ili antiglaukomskim lijekovima. Ispitan je utjecaj ALT-a na sniženje IOP-a, razvoj suhog oka i broj korištenih antiglaukomskih lijekova. Bolesnici su pregledani na početku ispitivanja, a zatim nakon 6, 12 i 18 mjeseci. Statistički značajna razlika između vrijednosti IOP-a uočena je tijekom svih 18 mjeseci praćenja, a najveća značajnost 6 mjeseci nakon ALT-a (p=0,009). Dvanaest mjeseci nakon početka ispitivanja vrijednost TBUT bila je 6,0±0,8 s u 1. skupini i 8,4±0,7 s u 2. skupini. Vrijednost Schirmerova testa u 2. skupini bila je stalno iznad 10 milimetara. Broj antiglaukomskih lijekova korištenih u 1. skupini bio je statistički značajno veći u usporedbi s 2. skupinom tijekom svih 18 mjeseci. ALT je bio bolji izbor u privremenoj regulaciji IOP-a u bolesnika s pseudoeksfolijacijskim glaukomom.

Ključne riječi: *Argon laserska trabekuloplastika; Intraokularni tlak; Antiglaukomski lijekovi*