

Target Intraocular Pressure in the Management of Glaucoma

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ABSTRACT

Achievement of target intraocular pressure is the goal of every efficient antiglaucoma therapy. Target intraocular pressure is the level of intraocular pressure which is associated with minimal likelihood of visual field or optic nerve lesion, or an existing lesion progression due to elevated intraocular pressure. Results of large clinical studies which have offered some new concepts on target intraocular pressure in the management of glaucoma are reviewed. An association between the curve of intraocular pressure decrease and glaucoma progression was demonstrated in these studies. Generally, a lower value of target intraocular pressure implies better protection from the loss of vision and visual field impairment in glaucoma patients. In advanced glaucoma, the greatest possible reduction from the initial intraocular pressure should be attempted. A 20% reduction from the initial intraocular pressure or decrease to <18 mmHg in advanced glaucoma has been recognized as a favorable strategy to reach target intraocular pressure. In normal tension glaucoma, a lower value of target intraocular pressure is associated with a slower disease progression. In patients with initial glaucoma, 25% reduction from the initial intraocular pressure will slow down the disease progression by 45%. The value of target intraocular pressure depends on the pretreatment level of intraocular pressure, optic nerve condition, glaucoma disease state, rate of glaucoma progression, patient's age, and other risk factors for the development of glaucoma.

Key words: target intraocular pressure, glaucoma, management

Introduction

Elevated intraocular pressure is the major risk factor for glaucoma, as it directly leads to optic nerve lesion and visual field impairment. Intraocular pressure decrease is the only modality of glaucoma treatment that definitely reduces the risk of glaucomatous visual field impairment¹. Achievement of the so-called target intraocular pressure is the goal of every efficient antiglaucoma therapy. After the turning point in the management of glaucoma with the introduction of local beta-blockers in the 1970s, considerable advances have been achieved in the last few years with the advent of new groups of local agents. These groups of agents include carbonic anhydrase inhibitors², alpha₂-adrenergic agonists³, prostaglandin agonists⁴ and prostamides⁵. Novelty in intraocular pressure decrease in cases refractory to conservative treatment include argon laser and Nd-YAG laser, and some new approaches in the opera-

tive treatment of glaucoma such as antimetabolites and nonpenetrating glaucoma surgery.

Target intraocular pressure can be defined as the level of intraocular pressure associated with minimal probability of pressure induced visual field or optic nerve lesion, or of the existing lesion progression. The current state-of-the-art in the management of glaucoma and achievement of target intraocular pressure has failed to answer some important questions such as: what is the value of target intraocular pressure in mm Hg; which patients are susceptible to rapid disease progression due to elevated intraocular pressure; does intraocular pressure reduction prevent the ocular hypertension progression to glaucoma; and is it necessary to decrease intraocular pressure in patients with normal tension glaucoma? Large clinical studies published over the last few years have offered some new concepts on

target intraocular pressure, and tried to answer the above questions.

Review of Relevant Clinical Studies

The clinical studies presented in this review were properly designed, multicenter, randomized, prospective, double blind trials conducted for several years, with masked professionals reading off the field of vision and optic nerve head findings. The studies included patients with ocular hypertension, early glaucoma, or advanced glaucoma.

Ocular Hypertension Treatment Study (OHTS)^{6,7}

The study included 1836 patients with ocular hypertension (intraocular pressure between 24 and 32 mm Hg, without visual field and optic nerve lesions) divided into two groups and followed-up for more than 6 years. A 20% initial intraocular pressure decrease was achieved in one group of patients, whereas the other group of patients were left untreated and served as a control group.

The 5-year probability of glaucoma development was 4.40% in the group of patients with 20% reduction from the initial intraocular pressure, and 9.50% in the control group without intraocular pressure reduction. In ocular hypertension, the progression of glaucoma is efficiently delayed by intraocular pressure reduction. The results of this study suggest that a greater intraocular pressure reduction, i.e. achievement of a target intraocular pressure lower by more than 20% of the initial value, leads to a lower rate of glaucoma progression, as indicated by clear correlation of the level of intraocular pressure and the risk of glaucoma⁸.

*Collaborative Initial Glaucoma Treatment Study (CIGTS)*⁹

The study included 607 patients with newly detected simple glaucoma from 14 hospital centers, followed-up for 5 years. In one group of patients, target intraocular pressure was achieved by conservative therapy followed by argon laser trabeculoplasty, or operative procedure of trabeculectomy in case of unsatisfactory result of conservative treatment. In the other group of patients, target intraocular pressure was achieved by surgical treatment, and in cases requiring better intraocular pressure control by laser or conservative therapy as ancillary methods. The value of target intraocular pressure was calculated for each individual patient by use of a formula including the mean of the last five intraocular pressure measurements and the grade of visual field impairment.

Operative treatment is more efficient than conservative therapy in intraocular pressure reduction (decreasing the initial intraocular pressure by 45% and 38%, respectively). Both the conservative and operative treatments are equally efficient in slowing down the disease progression as measured by the 5-year rate of visual

field impairment. The study pointed to the high importance of individualized determination of target intraocular pressure in the management of glaucoma.

Early Manifest Glaucoma Trial (EMT)^{10,11}

This 6-year study included 225 patients with newly diagnosed open angle glaucoma. Study patients were divided into two groups. In one group, 25% reduction of intraocular pressure was attained by use of betaxolol and argon laser trabeculoplasty, whereas the other group were left untreated. Glaucoma progression measured by visual field impairment was statistically significantly greater in the group of untreated patients than in those with intraocular pressure reduction.

The results indicated that intraocular pressure reduction by 1 mmHg decreased the risk of glaucoma induced visual field impairment by 10%, implying the need of setting a lower level of target intraocular pressure (25% reduction from the initial intraocular pressure decreased the risk of progression by 25%).

Advanced Glaucoma Intervention Study (AGIS)^{12,13}

The study included 591 patients with advanced open angle glaucoma with poor medicamentous control of intraocular pressure. The patients were divided into two groups and followed-up for 5 years. One group of patients underwent argon laser trabeculoplasty followed by trabeculectomy, and the other group received the same treatments in a reverse sequence. Target intraocular pressure was set at <18 mmHg.

During the 5-year follow-up, the patients with lower intraocular pressure (mean 12.3 mmHg) were free from visual field impairment, whereas those with higher values of intraocular pressure sustained visual field deterioration.

Collaborative Normal Tension Glaucoma Study (CNTGS)^{14–16}

Out of 230 patients with normal tension glaucoma (intraocular pressure <20 mmHg) aged 20–90 years, a 30% intraocular pressure decrease was achieved by conservative or operative treatment in 61 patients; 79 patients were left untreated. The aim of the study was to assess the effect of intraocular pressure decrease on the disease progression in patients with normal tension glaucoma or low tension glaucoma.

The group of patients with intraocular pressure reduction showed a 12% rate of visual field impairment at 5 years. The control group without treatment for intraocular pressure reduction showed a 35% rate of progression of glaucomatous visual field impairment.

In patients with normal tension glaucoma or low tension glaucoma, intraocular pressure decrease delayed the progression of glaucomatous lesions by 3 years.

Discussion and Conclusion

The results of these large clinical studies point to a strong causative relationship between reduction of initial intraocular pressure and glaucoma progression. While other risk factors for glaucoma development cannot be excluded, intraocular pressure has been demonstrated to be the very focus of therapeutic intervention, and achievement of target intraocular pressure is a precondition to delay the progression of glaucomatous lesions. The AGIS investigators report on a 20% decrease from initial intraocular pressure or intraocular pressure decrease to <18 mmHg in advanced glaucoma to be a useful strategy to achieve a desirable level of intraocular pressure^{12,13}. The study comparing initial glaucoma patients with and without treatment revealed the initial intraocular pressure decrease by 25% to be associated with a 45% reduction in the risk of glaucoma progression^{10,11}. A lower target intraocular pressure in patients with normal tension glaucoma or low tension glaucoma decreased the rate of glaucoma progression

three times in comparison with the untreated control group^{14–16}.

Determination of target intraocular pressure level depends on a number of factors, among them pretreatment level of intraocular pressure and risk of optic nerve lesion induced by elevated intraocular pressure, which depends on the mean value of intraocular pressure. Also, the grade of glaucoma should be determined because advanced glaucomatous lesions require lower target pressure^{12,13}. On determination of target intraocular pressure level, patient's age and life expectancy should also be taken in consideration.

Yet, along with the indisputable relevance of target intraocular pressure, the role of other risk factors should by no means be overlooked. Thus, in CNTGS, 12% of patients sustained progression of the disease despite achievement of appropriate target intraocular pressure, indicating that factors other than elevated intraocular pressure also play a role in the progression of glaucomatous lesions.

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CILJNI OČNI TLAK U LIJEČENJU GLAUKOMA

SAŽETAK

Postizanje ciljnog tlaka u liječenju glaukoma cilj je svake djelotvorne antiglaukomske terapije. Ciljni očni tlak je ona razina očnog tlaka pri kojoj postoji najmanja vjerojatnost za nastanak oštećenja vidnog polja ili vidnog živca uzrokovanih tlakom ili progresije već nastalih oštećenja. U radu se prikazani rezultati velikih kliničkih istraživanja koja su u zadnjih nekoliko godina donijela nove spoznaje o ciljnom očnom tlaku u liječenju glaukoma. U svim studijama pokazana je veza između krivulje redukcije očnog tlaka i progresije glaukoma. Niža vrijednost ciljnog očnog tlaka općenito znači bolju zaštitu od gubitka vida i vidnog polja u glaukomu. U uznapredovalim glaukomima potrebno je postići što veću redukciju početne vrijednosti očnog tlaka. Snižavanje vrijednosti početnog očnog tlaka za 20% ili ispod razine 18 mmHg u uznapredovalom glaukomu dobar je put za postizanje ciljnog očnog tlaka. U normotenzivnom glaukomu niža vrijednost ciljnog očnog tlaka znači sporiju progresiju bolesti. U bolesnika s početnim glaukomom snižavanje vrijednosti početnog očnog tlaka za 25% dovodi do 45% usporavanja progresije bolesti. Vrijednost ciljnog očnog tlaka ovisi o vrijednosti tlaka prije liječenja, stanju optičkog živca, stadiju glaukomske bolesti, stupnju progresije glaukoma, dobi bolesnika i ostalim rizičnim faktorima za nastanak glaukoma.