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# REGULATION OF THE UVEOSCLERAL OUTFLOW IN THEPATIENTS WITH PRIMARY OPEN-ANGLE GLAUCOMA

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***Abstract. Background.*** *The aim of our study was to investigate the role of visual load levels in the IOP elevation in the patients taking prostaglandin analogues and to try to optimize the conditions for their effects on the uveoscleral outflow.*

***Material and Methods.*** *33 patients (40 eyes) with first diagnosed primary open-angle glaucoma and resistance to latanoprost 0,005 % intraocular pressure were included in this study. These patients were pre-examined with the definition of visual and reading acuity, refraction, true, tolerant and target IOP with perimetry and ophthalmoscopy. Subjects were divided into 2 groups of comparable age, sex, refraction. In each group the thickness of the ciliary body by ultrasound biomicroscopy was investigated, level of near visual load and tolerated correction for near were defined.*

***Results****. It was found, that in both groups 85% of the eyes with POAG had moderately high (3-6 hours per day) and high (more than 6 hours a day) near visual load. Maximal ciliary body thickness in both groups was significantly higher than the results received by other authors: 0.881±0.039 mm in group 1 and 0.889±0.049 mm in group 2. Also a direct dependence of the ciliary body thickness and the true value of intraocular pressure(r=0.52) was observed. The hypercorrection of presbyopia was made in group 1 gradually, in steps of 0.25diopters.The value of additional correctionaveraged0.5 ± 0.13diopters. The magnitude of additional correction was inversely related toage (r=0.79).To assess the effectiveness of presbyopia overcorrection in reducing IOP one year later tonometry, the checking of visual acuity, perimetry (MD/year method), ophthalmoscopy, the thickness of the ciliary body were estimated.In the group 1the reduction of intraocular pressure (17.3 ± 0.84 mm Hg) was statistically significant (p <0.01), its value was close to the average tolerant IOP (17.0 ± 0.67 mm Hg), but was higher than the target (14.3 ± 0.67 mm*

*Hg). Also in this group statistically significant ($p < 0.01$) decrease in the thickness of the ciliary body was observed, more marked in patients with high near visual load ($r = 0.47$). Progression of glaucoma according to perimetry was significantly less ($p < 0.01$) in the group with a hypercorrection of presbyopia as compared with group with ordinary correction.*

***Conclusions.****Overcorrection of presbyopia, as a way to regulate IOP may be in addition to antihypertensive therapy for patients with high near visual load and POAG.*

***Key words:*** *primary open-angle glaucoma, resistant intraocular pressure, near visual load levels, presbyopia correction, maximal ciliary body thickness.*

Glaucoma is the second leading cause of blindness and the first cause of irreversible blindness worldwide [1].Glaucoma is sensitive to intraocular pressure (IOP)optic neuropathy that produces characteristic structural changes to the optic nerve head, often with correlating the visual field defects [2]. It is a chronic disease, in which the control of intraocular pressure (IOP) is the only evidence-based method of treatment [3-5]. Medical therapy is usually the first line of treatment for POAG, with treatment directed to reaching and maintaining a preestablished "target pressure range" that is expected to stop an optic nerve damage and visual field loss [3,6-8]. The first line medicines are prostamide analogues and beta-adrenergic antagonists. In general, beta-adrenergic antagonists and carbonic anhydrase inhibitors decrease the production of aqueous humour. Prostaglandin and prostamide analogues, which primarily increase uveoscleral outflow, while cholinergics increase trabecular outflow. Finally, alpha$_2$-adrenergic agents both decrease aqueous production and increase uveoscleral outflow [2]. When one particular drug does not help the patient to reach the target pressure level, physicians can change it to a different class medicine or add an another drug from a different class. However, combination with drugs which reduce the production of intraocular fluid and the level of eye hemodynamics can lead to poor nutrition of the anterior eye segment. It can cause premature aging of the anterior eye segment structures with cataract development and so on. Besides cholinergic drugs usage is inappropriate after 40-45 years old due to age-related decrease of sclera elasticity [9].Furthermore monotherapy with prostaglandin analogues needs to create the optimal conditions for their impact. According to I.N. Koshits et al[10]such conditions occur at a sufficient width of ciliary muscle intralaminar spaces in the state of intermediate (not maximal) contraction. When the tension of ciliary muscle is maximal or its fiber hypertrophy occurs, uveoscleral outflow decreases significantly. The relaxation of the ciliary muscle leads to not maximal state of outflow [10,11]. The aim of our study was to investigate the role of visual load levels in the IOP elevation in the patients taking prostaglandin analogues and to try to optimize the conditions for their effects on the uveoscleral outflow.

***Material and Methods.*** Patient selection was performed in the outpatient department of the Kharkiv Regional Clinical Hospital among the patients with first diagnosed primary open-angle glaucoma, for whom latanoprost 0.005% was prescribed as antihypertensive therapy. These patients were pre-examined with the definition of visual and reading acuity, refraction, true, tolerant and target IOP with perimetry and ophthalmoscopy. For visual acuity estimation decimal notation was used, the table with optotypes was shown to patients at the distance of 5 m. Refraction was determined by autorefractometry and spherical equivalent of refraction was calculated. True IOP was measured using Goldmann applanation tonometry, tolerant intraocular pressure was calculated by following formula:

$P_0tl = 12.2 + 0.07xDBP – 0.024xAge$ [12], where $P_0tl$ is tolerant intraocular pressure, DBP – diastolic blood pressure, Age – age of patients in years.

Target intraocular pressure was calculated with the help of the next formula:

$P_0targe = 9.5 + 0.07xDBP – 0.024xAge$ [12], where $P_0targe$ is target intraocular pressure, DBP – diastolic blood pressure, Age – age of patients in years.

Visual field examinations were performed with the Humphrey Field Analyzer (program 24-2). MD was used for analysis. Visual field progression of each patient with POAG was analyzed using the method of MD progression per year [13, 14]. A regression analysis of all available MD values during follow-up was performed. The

MD progression per year was calculated. The precondition to analyze the visual field tests was to fulfill the criteria of reliability, that is, false positive fault ≤ 20% and false negative fault ≤ 30%.

In direct binocular ophthalmoscopy was performed with a slit lamp and aspheric ophthalmoscopic lens AOL90D.IOPcontrol was performed after 12, 24hours, on the thirdday,1, 2, 3 and 4 weeks later after the examination and latanoprost prescribtion. 33 participants were selected as the result of further study. These thirty three subjects (forty eyes) aged 43 to 68 years old (average, 54.9±7.17; seventeen men, sixteen women) gave informed consent to take part in the study. In twenty six patients only one eye was examined and in seven patients – two eyes. Inclusion– exclusion criteria were a primary open angle glaucoma (without any other ophthalmic abnormality such as diabetic retinopathy, corneal problems or macular problems), best corrected visual acuity 0,6 and more, IOP was higher than individual tolerance at the background of latanoprost 0,005% usage for 4weeks. The research was performed with the principles of the Helsinki Declaration and was approved by the ethical committees.

Subjects were divided into 2 groups of comparable age, sex, refraction. Groups characteristics are presented in Table 1. In each group the thickness of the ciliary body by ultrasound biomicroscopy was investigated, level of near visual load defined and tolerated correction for near were defined. Maximal thickness of the ciliary body was determined using Sonomed VuMax UBM, in the room lighting, all the patients were instructed to consider the finger.

Amount of near visual load (reading, computer work, etc.) hours during the day in the patients was determined by questioning. In accordance with the results of the questionnaire, patients were devided into four subgroups: 1. insignificant near visual load - near visual load irregular, less than 1 hour per day, 2. low near visual load - up to 3 hours a day 3. moderately high near visual load - from 3 to 6 hours per day, 4. high near visual load - more than 6 hours a day.

Measurement of reading acuity was performed with the help of MNREAD acuity charts. The chart was evenly illuminated and the luminance of the white background of the charts was80 cd/m2.The MNREAD sentences were shown to patients at the testing distance of 40 cm (16 inches).

An estimate of reading acuity was given by the smallest print size at which the patient can read the entire sentence without making significant errors. After the patient had read as much of the chart as possible, the number of sentences that the patient read or attempted to read was counted. Then the number of words that the patient read incorrectly was counted. For calculating of reading acuity (in logMAR) was using the following formula: Acuity = 1.4 – (sentences×0.1) + (errors×0.01). Reading acuities in logMAR was expressed as a Snellen fraction with the help of application tables.

***Results***. As a result, the true intraocular pressure was in average19.8 ± 0.83mmHg, which is 16.5% more than the average tolerated pressure and 38.5% more than the target IOP.

It was found, that in the first group three patients (3 eyes) had low near visual load, six patients (7 eyes) – moderately high near visual load, seven patients (10 eyes) – high near visual load. In the second group two patients (3 eyes) had low near visual load, four patients (5 eyes) – moderately high near visual load, eleven patients (12 eyes) – high near visual load. Thus in both groups 85% of the eyes with POAG had moderately high and high near visual load. Uncorrected visual acuity was 0.16±0.08 in the first group, and 0.15±0.07 in the second one. Best corrected visual acuity was 0.68±0.07 in the first group and 0.67±0.06 in the second one. Maximal tolerated near correction was 4.13±2.25 D in group 1 and 4.45±1.88 D in group 2.Maximal ciliary body thickness in both groups was significantly higher than the results received by other authors. Thus Lossing L. A. et al. [15] measured maximal ciliary body thickness by anterior segment OCT and received the results: considering the remote object - 0.795 ± 0.065 mm, considering close objects (0.25 m) - 0.869 ± 0.083 mm. The study was conducted in young people aged 25-28 years. In another study [16]in patients with glaucoma, we measured the maximal thickness of the ciliary body using ultrasound biomicroscopy in similar to our conditions. Subjects were aged 56.8±3.9 years old, and the rate was 0.707±0.03 mm. Earlier we also studied the maximal thickness of the ciliary body of 128 eyes of patients with primary open-angle glaucoma at the age of 53.14±3.78 years old [17]. Data obtained using ultrasound biomicroscopy for the maximal thickness of the ciliary body were 0.687 ± 0.072 mm.

Thus our results in the first (0.881±0.039 mm) and the second (0.889±0.049 mm) groups were significantly higher than the average in patients with POAG and with the corresponding age in other studies. These results, however, were comparable with measurements of the ciliary body thickness in young healthy people with tense of accommodation. It was also a direct dependence of the ciliary body thickness and the true value of intraocular pressure with a correlation rate r=0.52.

According to the hypothesis of increased intraocular pressure due to accommodative system tone, which is consistent with our data, to reduce intraocular pressure the tone of accommodation should be reduced. For this purpose, we prescribed hypercorrection of presbyopia for the first group of patients with POAG. The correction was made gradually, in steps of 0.25diopters with intervals of 1-2 weeks. If in a week or earlier after increasing near vision correction patients complained of headache, blurring, image distortion, etc., the value of the correction was reduced to 0.25 diopters. As a result, the value of additional correctionaveraged0.5 ± 0.13diopters (from 0.25 to 1.0diopterswith a median of 0.5 diopters). The magnitude of additional correction was inversely related to age, with correlation r = 0.79. In the second group optical correction as administered with considering of refraction, age and individual tolerability only.

Patients in both groups were followed up with periodic examinations: tonometry was performed monthly and once in three months a visual acuity was checked, perimetry and ophthalmoscopy were made. These examinations were conducted to avoid missing a significant progression of POAG in the observed groups. Significant progression of glaucoma was considered in which the MD according to perimetrywas-0,5 dB for 3 months, i. e.-2 dB per year. If there was a significant decrease in visual function or increase of intraocular pressure, patients were offered various ways of combined antihypertensive therapy, laser or surgical procedures. To assess the effectiveness of presbyopia overcorrection in reducing IOP one year later tonometry, the checking of visualacuity, perimetry, ophthalmoscopy, the thickness of the ciliary body were estimated. As a result, five patients were excluded from the study: four of them were in the group without hypercorrection and one in the group with overcorrection of presbyopia. Data before and after one year are presented in the table 2.

In the group with hypercorrection the reduction of intraocular pressure (17.3 ± 0.84 mm Hg) was statistically significant (p <0.01), its value was close to the average tolerant IOP (17.0 ± 0.67 mm Hg), but was higher than the target (14.3 ± 0.67 mm Hg). In seven eyes the target pressure was achieved, in five eyes IOP was at the level of tolerance, and in eight eyes it was higher than tolerance. And all eyes reached the target pressure belonged to patients with a high near visual load. In normal correction of presbyopia group no significant IOP changes were observed.

1 year later in the group with hypercorrection a statistically significant (p <0.01) decrease in the thickness of the ciliary body also was observed, more marked in patients with high near visual load (r = 0.47). Progression of glaucoma according to perimetry was significantly less (p <0.01) in the group with a hypercorrection of presbyopia as compared with group with ordinary correction. Negative progress of perimetry data was observed in 8 patients whose IOP had higher tolerance.

***Conclusions.*** Overcorrection of presbyopia, as a way to regulate IOP may be in addition to antihypertensive therapy for glaucoma. The advantages of this method is its gentle physiological effects on the system of development and outflow of aqueous humor. However, using this method, lowering IOP is limited by several factors. First, a requirement for compliance to treatment, because of the use of overcorrection in the early stages may be accompanied by some discomfort. To avoid rejection of correction of such patients there should be carried out discussions with the explanation of all the advantages of this method of regulation of intraocular pressure. Second, based on our research, it was found that the greatest impact of presbyopia overcorrection had on ophthalmotonus of glaucoma patients with high visual load (more than 6 hours / day). Patients with moderately high visual load are less affected by overstated optical correction of persbyopia. This may be associated with more prolonged exposure to the overcorrection of the ciliary muscle tone in patients with high near visual load. However, the role of increased visual load in rigidity of IOP to the effects of prostaglandins seems high because 85% of such subjects had near visual load more than 3 hours a day.

***Conflict of Interests.*** The authors declare that there is no conflict of interests regarding the publication of this paper.

**References.**

1. Ge J, Zhao JL, Cui H (2005) Ophthalmology. People's Medical Publishing House: 246–273.

2. Adatia FA, Damji KF Chronic open-angle glaucoma. Review for primary care physicians.Can Fam Physician. 2005 Sep; 51:1229-37.

3. HeijlA, Leske MC, Bengtsson B, Hyman L, Bengtsson B, Hussein M; Early Manifest Glaucoma Trial Group. Reduction of intraocular pressure and glaucoma progression: Results from the early manifest glaucoma trial. Arch Ophthalmol. 2002;120(10): 1268-79.

4. Van Buskirk EM, Cioffi GA. Glaucomatous optic neuropathy. Am J Ophthalmol. 1992; 113(4):447-52.

5. Quigley HA. Number of people with glaucoma worldwide. Br J Ophthalmol. 1996; 80(5):389-93.

6. Lichter PR, Musch DC, Gillespie BW, Guire KE, Janz NK, Wren PA. Interim clinical outcomes in the Collaborative Initial Glaucoma Treatment Study comparing initial treatment randomized to medications or surgery. Ophthalmology. 2001;108:1943–1953.

7. Gordon MO, Beiser JA, Brandt JD, Heuer DK, Higginbotham EJ, Johnson CA, etal. The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary open-angle glaucoma. Arch Ophthalmol. 2002; 120:714–720.

8. Jampel HD. Target pressure in glaucoma therapy [review]. J Glaucoma. 1997;6(2):133–138.

9. Iomdina EN, Ignat'eva NIu, Danilov NA, Arutiunian LL, Kiseleva OA, Nazarenko LA. Biochemical, structural and biomechanical features of human scleral matrix in primary open-angle glaucoma. Vestn Oftalmol. 2011 Nov-Dec;127(6):10-4.

10. KoshitsIN, SvetlovaOV, ZaseevaMV, ShukhaevSV, MakarovFN, KotliarKE, Smolnikov BA. Physiological principles of hypotensive therapy of openangle glaucoma during presbyopia period. Part I. Initial theoretical presuppositions, hypotheses and facts.Glaukoma.2006; 3:35-70.

11. Koshits IN, Svetlova OV, Zaseeva MV, Shukhaev SV, Makarov FN, Kotliar KE, Smolnikov BA.Physiological principles ofhypotensive therapy of openangle glaucoma during presbyopia period. Part II. Perspective algorithms of practical sparing effects. Glaukoma.2006; 4:51-70.

12. BalalinSV, Fokin VP. On tolerated and target–oriented intraocular pressure in primary open–angle glaucoma.Rus. Med. Jurn. 2008; 9:117–119.

13.ChauhanBC, Garway-HeathDF, Goñi FJ et al. Practical recommendations for measuring rates of visual field change in glaucoma. British Journal of Ophthalmology.2008; 92(4):569–573.

14. European Glaucoma Society, Terminology and Guidelines for Glaucoma.2008; 82–88, Editrice DOGMA, Savona, Italy.

15. Lossing LA, Sinnott LT, Kao CY, Richdale K, Bailey MD. Measuring changes in ciliary muscle thickness with accommodation in young adults. Optom Vis Sci. 2012 May;89(5):719-26.

16. Egorova EV, Bessarabov AN, Uzunyan DG, Sarukhanyan AA. Anatomy-topographic featuresof the eyes in various types of refraction and their changes in glaucoma according to the results of ultrasonic biomicroscopy. Glaukoma. 2006. 2:17-23.

17.Bezdetko P, Abdoola, AMD, Shchadnykh M. Anterior segment morphometric parameters of presbyopic eyes with and without POAG and varying refraction. Kharkiv Surgical School.2012; 4:84-87.

***Резюме. Метою*** нашого дослідження було вивчення впливу різних рівнів зорового навантаження на рівень внутришньоочного тиску (ВОТ) у хворих на первинну відкритокутову глаукому (ПВКГ), які використовували аналоги простагландинів та оптимізувати їх вплив на відтік водянистої вологи ока.

***Матеріал та методи***. У дослідження було включено 33 хворих (40 очей) з вперше діагностованою первинною відкритокутовою глаукомою та стійким до латанопросту 0,005 % ВОТ. Ці хворі були попередньо досліджені з визначенням гостроти зору вдалеч та зблизька, рефракції, істинного, толерантного та цільового ВОТ, з виконанням периметрії та офтальмоскопії. Хворих було розподілено на 2 групи, подібні за віком, статтю, рефракцією. В кожній групі було визначено товщину циліарного тіла за допомогою ультразвукової біомікроскопії, а також рівень зорового навантаження зблизька та величину стерпної корекції для близька.

***Результати***. Було встановлено, що в обох групах 85% очей хворих з ПВКГ мали помірно високе (3-6 годин на день) та високе (більш ніж 6 годин на день) зорове навантаження зблизька. Максимальна товщина циліарного тіла в обох групах була значно вищою, ніж дані, що було отримано іншими авторами: 0.881±0.039 мм у 1 групі і 0.889±0.049 мм у 2-й групі. Також не спостерігалось прямої залежності товщини циліарного тіла та ВОТ (r=0.52). Гіперкорекція далекозорості в першій групі проводилася поступово з кроком 0,25 дптр. Значення додаткової корекції в середньому складало 0,5 ± 0.13 дптр. Величина додаткової корекції була зворотно пов'язана з віком (r=0.79). Для оцінки ефективності гіперкорекції пресбіопії через рік проводилися тонометрія, візометрія, периметрія (MD/год метод), офтальмоскопія, товщина циліарного тіла. В 1 групі спостерігалося зниження ВОТ (17.3 ± 0,84 мм рт. ст.) було статистично значущим (p <0.01), його значення було близьким до середнього показника толерантного ВОТ (17.0 ± 0,67 мм рт.ст.), але було вищим, ніж тиск мети (14.3 ± 0,67 мм рт. ст..). Також в цій групі спостерігалось статистично значуще (p <0,01) зменшення товщини циліарного тіла, що було більш виразне у пацієнтів з високим зоровим навантаженням зблизька (r = 0.47). Прогресування глаукоми за даними периметрії було значно меншим (p <0,01) в групі з гіпркорекцією пресбіопії порівняно з групою зі звичайною корекцією.

***Висновки***. Гіперкорекція пресбіопії, як спосіб регулювання ВОТ може бути доповненням до антигіпертензивної терапії для пацієнтів з високим зоровим навантаженням з близька та ПВКГ.

***Ключові слова:*** первинна відкритокутова глаукома, резистентний внтришньоочний тиск, рівні зорового навантаження зблизька, корекція пресбіопії, максимальна товщина циліарного тіла.

**Резюме.** Целью нашего исследования было изучение влияния различных уровней зрительной нагрузки на уровень внутриглазного давления у больных первичной открытоугольной глаукомой, которые использовали аналоги простагландинов и оптимизировать их влияние на отток водянистой влаги глаза.

В результате работы, установлено, что гиперкоррекция пресбиопии, как способ регулирования открытоугольной глаукомы может быть дополнением к антигипертензивной терапии для пациентов с высокими зрительными нагрузками.

**Ключевые слова:** первичная открытоугольная глаукома, резистентное внутриглазное давление, уровни зрительной нагрузки вблизи, коррекция пресбиопии, максимальная толщина цилиарного тела.

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