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Aim: The aim of the study was to determine whether hypertensive glaucoma (HTG) with different types of treatment leads to significant damage in any of the evaluated parameters.
Sample and methodology: The sample, consisting of 36 HTG patients (72 eyes), was divided into three subgroups:
In the first group, patients were treated with combination therapy (latanoprost + timolol, latanoprost + dorzolamide + timolol, dorzolamide + timolol). The group consisted of seven women and five men, with an average age of 64 years (49-81).
In the second group, patients were treated with beta-blockers (carteolol, betaxolol, timolol). The group consisted of five women and five men, with an average age of 62 years (27-77).
In the third group, patients were treated with prostaglandins (latanoprost, bimatoprost). The group consisted of eleven women and three men, with an average age of 61 years (61-78).
Criteria for inclusion in the study were visual acuity of 1.0 with a possible correction of less than ±3 dioptres, approximately the same changes in the visual fields of all patients, an intraocular pressure (IOP) of less than 18 mmHg, and no other ocular or neurological disease.
The retinal nerve fibre layer (RNFL) on the optic nerve target and vessel density (VD) was measured using an Avanti RTVue XR from Optovue. We determined the values of VD in whole image (WI) and VD of peripapillary (PP). In both cases, we then measured all vessels (VDa) and small vessels (VDs). The visual field was examined by means of a fast threshold glaucoma program with a Medmont M 700 instrument. In addition to the sum of sensitivities in apostilbs (asb) in the range of 0-22 degrees, the overall visual field defect (OD) was also evaluated. The statistical analysis was carried out using a multivariate regression model with adjustment for age and gender. The measured values of the third group were taken as baseline.
Results: In the statistical analysis, we have found differences in visual field in the combination treatment group ($p = 0.0006$) and differences were recorded for RNFL in the beta-blocker group ($p = 0.04$).
Keywords: vessel density, RNFL, visual field, hypertensive glaucoma, various kinds of glaucoma treatment

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INTRODUCTION

In our previous study, where we looked at vessel density (VD) and visual field in HTG, we demonstrated a moderate relationship between these parameters ($r = 0,64$) [6]. We were interested in how the VD and retinal nerve fiber layer (RNFL) would look in approximately equally advanced glaucoma patients who take various types of antiglaucomatous medicines. This was also the aim of our study, where we tried to find out whether some drugs have a greater protective effect on the evaluated parameters.

In hypertensive glaucoma (HTG), the ganglion cells of the retina and subsequently the entire visual pathway are damaged, with high intraocular pressure (IOP) playing a cardinal role [1-4]. In an experimental study in mouse models, Soto et al. found that retinal ganglion cell degeneration in glaucoma has two separate stages. The former involves atrophy of ganglion cells and the latter damage to their axons. The retrolaminar degeneration of axons takes place before the degeneration of their intraretinal.

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Group and methodology of examinations

The group, which consisted of 36 patients with HTG (72 eyes), was divided into three groups:

In the first group, patients were treated with a combination therapy (latanoprost+timolol, latanoprost+dorzolamide+timolol, dorzolamide+timolol). The group consisted of seven women and five men, with an average age of 64 years (49–81).

In the second group, patients were treated with beta blockers (carteolol, betaxolol, timolol). The group consisted of five women and five men, with an average age of 62 years (27–77).

In the third group, patients were treated with prostaglandins (latanoprost, bimatoprost). The group consisted of 11 women and three men, with a mean age of 61 years (61–78).

Inclusion criteria for the study were a visual acuity of 1.0 with a possible correction of less than ±3 dioptres, approximately equal changes in visual fields in all patients, intraocular pressure (IOP) of less than 18 mmHg, and no other ocular or neurological disease.

RNFL on the optic disc and VD were measured using the Avanti RTVue XR from Optovue. We investigated whole-image (WI) and peripapillary (PP) VD values. In both cases, we then measured all vessels (VDa) and small vessels (VDs).

The visual field was examined with a rapid threshold glaucoma program using the Medmont M700. We evaluated the overall defect (OD) of the visual field.

Because gender and age were very unevenly distributed between the groups, statistical analysis was performed using a multivariate regression model with adjustment for age and gender. The measured values of group number three (no treatment) were taken as a control.

RESULTS

The mean values of the measured parameters of the untreated group were considered as reference values. Table 1 presents the difference of the mean values of the other groups (Δ diameter) by treatment type from the mean value of the reference group, including the standard deviation (SD) and statistical significance of the difference (p-val) of the following parameters: overall defect (VF OD), peripapillary vessel density of all vessels (PPVDa) and small vessels (PPVDs), vessel density of the whole image of all vessels (WI VDa) and small vessels (WI VDs), and nerve fibre layer thickness (RNFL). The results are included in Table 1.

The results showed that there are statistically significant changes in RNFL in compensated IOP, and in patients treated with beta-blockers ($p = 0.04$). The OD values of the visual field showed statistically significant differences in the group of patients on combination therapy ($p = 0.006$).

DISCUSSION

Slowing disease progression and preserving quality of life are the main goals of HTG treatment.

Reduced quality of life may occur earlier than initially thought, confirming the importance of early diagnosis and treatment [7].

Reduction of IOP is the only proven method of glaucoma treatment [8]. There is no doubt about the hypotensive effect of available antiglaucomatous medicines today [9].

We confirmed the protective effect of beta-blockers and prostaglandins in HTG patients in a study where

Table 1. Average results of the measured values

	PG		FK			BB		
	mean	SD	Δ mean	SD	p-val	Δ mean	SD	p-val
VF OD	1,74	0,53	-0,73	0,25	**0,006**	0,42	0,34	0,22
PPVDa [%]	64,81	2,38	-0,008	0,29	0,907	-2,05	1,13	0,11
PPVDs [%]	58,84	2,37	-2,20	1,14	0,06	-2,2	1,29	0,09
WI VDa [%]	62,14	2,12	-1,30	1,02	0,2	-1,70	1,16	0,14
WI VDs [%]	55,69	2,07	-1,22	1,00	0,23	-1,75	1,13	0,13
RNFL [um]	121,32	7,75	-6,81	3,74	0,07	-8,85	4,23	**0,04**

VF OD – visual field overall defect; PPVDa – peripapillary vessel density of all vessels; PPVDs – peripapillary vessel density of small vessels; WI VDa – vessel density of the whole image of all vessels; WI VDs – vessel density of the whole image of small vessels; RNFL – retinal nerve fiber layer thickness, PG – prostaglandins, FK– combination therapy, BB– beta-blocker

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we found no statistically significant effect on visual field changes over five years of follow-up. There was a pattern defect (PD) (p = 0.35) and OD (p = 0.09) for prostaglandins. The PD (p.=.0.37) and OD (p.=.0.23) of beta-blockers were similar [10].

We now focus on the issue of the parameters evaluated.

The visual field examination for HTG is the oldest of the above methods. With the introduction of static automated perimetry, the examination area was narrowed to 30 degrees from the point of fixation [11,12]. Obviously, in the early stages of HTG, where the first changes occur in the retinal ganglion cells, we cannot even theoretically detect a decrease in sensitivity in the central visual field [13].

The ratio of one ganglion cell associated with one cone in the fovea would require so many Henle fibres that these would be directed away from the foveal centre [14].

This means that when one or two ganglion cells are lost, both central visual acuity and sensitivity in the central visual field are preserved. These are the reasons that are currently pushing visual field testing to the next places in the order of diagnosis. However, few ophthalmologists realise that the only measured examination that is able to determine the condition of the entire visual analyser is the visual field examination. With the alteration of retinal ganglion cells, the ganglion cells of the subcortical and cortical visual centres are damaged. However, these centres are not able to examine RNFL and VD.

As mentioned in the introduction, retrolaminar degeneration of axons takes place before the degeneration of their intraretinal part [5]. We are not yet able to selectively diagnose this part of the optic nerve. In relation to retinal cell morphology and visual field examination, Harwerth et al. also found that RNFL measurement is more sensitive in the early stages of glaucoma and visual field examination is more sensitive in the intermediate and advanced stages of HTG [15].

The relationship between RNFL loss and IOP was also addressed in an experiment by Tu et al. who found greater RNFL loss at higher IOP. RNFL in the superior and inferior quadrants of the optic nerve target showed a greater decrease than the nasal and temporal quadrants [16]. This corresponds to the damage of retinal ganglion cells, which axons enter the vertical quadrants. That changes in the RNFL are outpacing changes in the field of view has been known for quite some time. This was confirmed by monitoring RNFL in the altitudinal halves of the retina with secondary altitudinal changes in the central field of view (0–22 degrees), where we were able to show no statistical dependence [17]. Obviously, in the range of the visual field examined by the glaucoma program or the 0–30 degree program, incipient glaucomatous changes will not be shown. Therefore, it is still important to investigate RNFL and VD as well. OCT angiography is a relatively new, non-invasive and reproducible method. Initial results of studies have shown high diagnostic potential in glaucoma [18].

The relationship of VD in different stages of HTG has been addressed by other authors. All have found that VD decreases with advancement of glaucoma disease [19–24]. The IOP value also plays a significant role in the VD value. By reducing IOP in young individuals with high IOP, Holló observed an increase in VD [25]. Conversely, after its increase above 20 mmHg, the density of blood vessels in the macula and peripapillary decreased significantly [26].

A positive surprise of the present work was the finding that none of the evaluated therapies had an ischemic effect on VD. Another surprise is why there was no statistically significant change in RNFL in patients treated with prostaglandins compared to the other groups. Because the OD of the visual field is more specific for HTG, we expected greater changes in both VD and RNFL for prostaglandins [10,27].

We will have to wait for an answer.

CONCLUSION

Our results showed that only RNFL changes in HTG are statistically significant in compensated IOP and OD in patients treated with beta-blockers and OD in patients on combination therapy. Other values did not show statistically significant differences.

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