

Ganglion cell complex depending on the intraocular pressure

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Abstract

Objective: The aim of the study was to determine whether high intraocular pressure (IOP) affects the GCC thickness.

Patients and methods of examination: Patients were divided into two groups. The first control group included eight women (from 25 to 65 years) and two men (25 and 59 years). The second group consisted of six women (from 30 to 75 years) and four men (from 30 to 58 years). This was a group of patients who were diagnosed with high intraocular pressure (IOP), either as a first detection of glaucoma or after cataract surgery, or as a manifestation of poorly controlled glaucoma. All patients had their IOP monitored both before and after its compensation.

Further, the average thickness of the ganglion cell complex (GCC) (using the SD-OCT RTvue-100) and the visual field (using the fast threshold program of Medmont M 700 device) were measured before and one month after IOP compensation. The first group was also measured after the additional interval of one month.

Results: The correlation between the value of intraocular pressure and GCC before and after the compensation was evaluated. The resulting correlation coefficient was $r = -0.0297$, $p = 0.9010$ in the control group and $r = -0.03$, $p = 0.9328$ in the second group with high intraocular pressure. Dependence in both groups was negligible and statistically insignificant.

Conclusion: Although, at first glance, the GCC values appear to be increased after the correction of IOP, statistically significant changes in the thickness of the GCC were not recorded.

Keywords: GCC, IOP, visual field, hypertension glaucoma

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Introduction

Glaucoma is currently defined as a disease with progressive loss of retinal ganglion cells and their axons, which leads to changes in the visual field with atrophy and excavation of the optic nerve. [13] This definition, which emphasises the damage of retinal ganglion cells before the damage of their axons, is not complete because it does not take into account the damage of ganglion cells in the subcortical and cortical centres of the brain.[5]

Retinal ganglion cells encompass three layers in the retina: the inner plexiform layer (IPL) made up of the ganglion cell dendrites, the ganglion cell layer (GCL) made up of the ganglion cell bodies and the retinal nerve fibre layer (RNFL) made up of the ganglion cell axons. All three layers, collectively known as the ganglion cell complex (GCC), become thinner as the ganglion cells die from glaucoma, making it an ideal site for the imaging and early detection of glaucoma progression. [3, 6, 7]

The macular region contains over 50 % of all retinal ganglion cells and is an ideal region to detect early cell loss and changes over time because of the high density of cells.

The aim of the study was to determine whether high intraocular pressure (IOP) affects the macular thickness of GCC.

Material and methods

The study was conducted between January 2015 and December 2015 and the subjects were divided into two groups. The first control group included eight women (from 25 to 65 years) and two men (25 and 59 years). The second group consisted of six women (from 30 to 75 years) and four men (from 30 to 58 years). This was a group of patients who were diagnosed with high intraocular pressure (IOP), either as a first detection of glaucoma or after cataract surgery, or as a manifestation of poorly controlled glaucoma. All patients had their IOP monitored both before and after its compensation. The other eye served as a control. IOP was monitored in all patients before and after the compensation with the Ocular Response Analyzer II (Reichert Technologies). Further, the average thickness of the ganglion cell complex (GCC) (using the SD-OCT RTvue-100, Optovue Inc, CA USA) and the visual field (using the fast threshold program of Medmont M 700 device, Medmont International Pty Ltd Australia) were measured before and one month after IOP compensation. The first group was also measured after the additional interval of one month. The average GCC values were used because, in hypertensive glaucoma, the number of ganglion cells does not decrease locally but diffusely across the retina.

Results

The measured values are summarized in the tables. The first table shows data for the control group. The second shows data for patients with high intraocular pressure.

Gender	Age	Refraction RE/LE	VA RE/LE	Before			After		
				IOP	GCC RE	GCC LE	IOP	GCC RE	GCC LE
female	65	-3.0	1.0	18/20	95.5	99.3	20/20	99.45	101.3
female	58	+0.5	1.0	18/18	90.7	87.29	17/18	90.74	89.12
female	51	- 0.5	1.0	17/16	91.66	93.59	17/17	92.69	92.54
female	50	-0.5	1.0	14/15	97.7	97.33	15/15	96.75	99.85
female	47	+1.0	1.0	11/12	103.74	101.92	11/11	103.34	103.41
female	45	-0.5	1.0	17/17	87.41	87.29	17/17	87.49	88.94
female	30	0	1.0	16/17	102.18	96.93	17/17	101.93	96.44
female	25	-0.5	1.0	17/17	99.83	98.39	16/15	98.56	99.9
male	59	0	1.0	15/15	98.9	97.6	17/15	98.5	97.6
male	25	-1.5	1.0	18/18	89.38	89.06	18/19	89.6	89.7

Table 1. Control group. Refraction of both eyes was the same. The same is true for the visual acuity.

Gender	Age	Refraction VA RE/LE	VA RE/LE	Before			After			VF PD RE/LE	VF OD RE/LE
				IOP	GCC RE	GCC LE	IOP	GCC RE	GCC LE		
female	75	0	1.0	14/35	76.47	62.22	13/13	79.5	64.5	0	0
female	62	+4	1.0	23/36	95.51	93.81	17/22	93.63	96.46		
female	48	-1.5	1.0	11/44.5	71.11	70.22	11.5/15.2	69.05	73.04	3.87/2.82	3.24/2.21
female	52	0	1.0	10.5/32.3	96.94	87.92	9.5/9.5	94.31	94.71	0	0
female	35	-0.5	1.0	10.2/46.3	98.58	98.8	7/7.5	98.6	98.9	1.56/1.79	0.97/0.95
female	30	0	1.0	30.8/25.4	86.32	85.1	17.3/20.7	85.08	84.47	3.27/2.38	1.58/0.88
male	58	-1/-6	1.0/0.1	41/8	68.57	69.76	19.2/12.3	70.08	68.5	15.2/18.9	1.3/4.31
male	43	-6/-5	1.0	30/19	59.55	71.23	20/20	63.98	80.93	15.7/2.1	0.59/0.84
male	70	+6/+3	0.4/1.0	11.2/46.5	85.86	66.98	12.5/17.5	89.86	68.8	6.0/11.53	3.07/0.71
male	30	-1.0	1.0	30/27	86.19	86.08	15.1/16.1	85	85.05	1.99/2.61	2.35/2.47

Table 2. Patients who had high IOP on one eye. Refraction (unless presented as two number divided by a slash) was the same for both eyes. The same is true for the visual acuity.

Discussion

In 1987, we previously had doubts about damage affecting only the axons of retinal ganglion cells in HTG when we simultaneously measured the Pattern Electroretinogram (PERG) and the Pattern Visual Evoked Potential (PVEP). We examined the healthy eyes of a 20-year-old man with an Intraocular Pressure (IOP) of 15 mmHg.

Subsequently, we increased the IOP to 40 mmHg and repeated the examination. To our surprise, neurotransmission at the level of ganglion cells became blocked, while the PVEP changed only slightly. Based on our findings, we concluded that initial changes will be at the level of the ganglion cells and not their axons and that not only the retinal ganglion cell layer but the entire visual pathway will be included in the process of elevated IOP. [5]

Similar results at the retinal level were also obtained by Crowston *et al.*, who described a model of acute intraocular pressure (IOP) elevation in the mouse eye that induced reversible loss of inner retinal function associated with oxidative stress, glial cell activation and minimal loss of retinal ganglion cell (RGC) number. Young healthy mouse eyes recovered inner retinal function within 7 days, but more persistent functional loss was seen in older mice. They believe that systematic investigation into the characteristics and determinants of RGC recovery following an IOP challenge will shed light on the processes that govern RGC vulnerability in the early stages of glaucoma. [1]

The morphological basis of these findings, in terms of changes of ganglion cells and their axons, can be obtained from the works of Hyashi *et al.*, Weber *et al.*, Pavlidis *et al.*, Shou *et al.*, Kim *et al.* and others. [2,4,8,10]

Hayashi *et al.* hypothesised that a reduction of dendrite projections and the dendrite tree itself is not sufficient to induce apoptosis of retinal ganglion cells. Dendrite projections are extremely variable elements, providing a structural mechanism for synaptic plasticity. [2]

According to Weber *et al.*, changes observed within the ganglion cells are mutually linked and dendritic changes are steps to ensure cell survival. The authors assume that the first change necessary for the survival of retinal ganglion cells is to avoid excessive use of the most distal dendrites, to conserve energy and maintain homeostasis at the level of the cell body. [11]

Shou *et al.* found in retinal ganglion cells that cell density, cell body size, dendrite radius, the length of the protrusions and the number of dendrite bifurcations decrease significantly in glaucoma eyes compared to controls. Dendrite structural changes and corresponding physiological deficiency of retinal ganglion cells appeared before cell death. [9]

Similar conclusions were reached by Kim *et al.*, who, after cauterisation of episcleral veins and prior retrograde labelling of retinal ganglion cells by Fluoro-Gold (Fluorochrome, Denver, USA), investigated the number of cells that died of apoptosis using the TUNEL method. [3]

Soto *et al.*, in their work on DBA/2 mice models, found that degeneration of retinal ganglion cells in glaucoma comprises two separate stages. The first stage involves atrophy of ganglion cells and the second stage involves the damage of their axons. Retrolaminar degeneration of axons occurs before the degeneration of intraretinal parts of cells. [10]

Similar conclusions in human glaucoma were reached by Roddick *et al.*, who demonstrated a reduction in the number of dendritic bifurcations in both major classes of retinal ganglion cells — parvocellular and magnocellular. [8]

A histological study of the final stages of glaucoma in humans was also presented by Pavlidis *et al.* In the advanced stages of the disease, there was almost no retinal ganglion cell layer, which degenerated and could not even be visualised by staining. The remaining ganglion cells were considered glaucoma resistant. These cells showed drastic morphological alterations, abnormal axonal beading, cell bodies were smaller and their dendrite branches were also shorter. [7]

The above overview was provided intentionally, because it points to the shrinkage of ganglion cells, reduction of their dendritic tree and dendrite length before cell death. This is important information because, after the increase of intraocular pressure, the thickness of the retinal ganglion cell layer is reduced, while the layer of cell axons should remain intact at least temporarily.

Our work was therefore aimed in this direction. The assumption was that acute increase of IOP will decrease the thickness GCC, which may increase again after the treatment of IOP. The question remains whether such a small change is detectable by current OCT techniques. Statistical results of our work did not confirm this assumption.

There is a sufficient number of works evaluating GCC in patients with hypertensive glaucoma. None of them, however, evaluated the GCC thickness in patients with high IOP before and after its treatment. We cannot therefore compare our results with those in the literature.

Conclusion

Although, at first glance, the GCC value appears to be elevated IOP after treatment, statistically significant changes in the thickness of the GCC were not recorded.

The study protocol was approved by the local Ethics Committee and the study was performed in accordance with Good Clinical Practice and the Declaration of Helsinki.

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Conflict of interest statement

The authors state that there are no conflicts of interest regarding the publication of this article.

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