"GANGLION CELLS COMPLEX" AND THE RETINAL NERVE FIBRE LAYER IN HYPERTENSIVE AND NORMOTENSIVE GLAUCOMAS.

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The authors of the study declare that no conflict of interest exists in the compilation, theme and subsequent publication of this professional communication, and that it is not supported by any pharmaceuticals company.

Do redakce doručeno dne 22. 11. 2016
Do tisku přijato dne 2. 12. 2016

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SUMMARY

Aim: To determine, if in the group of hypertensive (HTG) and normal-tension glaucomas exists correlation among ganglion cell complex (GCC) and retinal nerve fiber layer (RNFL) in the same altitudinal half of the retina and sum of sensitivities of the visual field's opposite half (hemifield test) of the same eye.

Materials and methods: In the HTG group, there were 25 patients; thereof 12 women of the average age 53.23 years (range, 34 – 69 years) and 13 men of the average age 60.38 years (37 – 74 years). In the second group with NTG were 17 women of the average age 55.35 years (25 – 75 years) and 8 men of the average age 55.5 years (32 – 69 years). The including criteria in the study were: visual acuity 1.0 with possible correction smaller than ± 3 dioptres, approximately the same extent of changes in visual fields in all patients (with beginning stage of the disease), no other ophthalmologic or neurological disease. In patients with NTG, the diagnosis was confirmed by means of electrophysiological examination. The thicknesses of the GCC, as well as the RNFL were measured by means of SD-OCT RTvue – 100. The visual fields were examined by fast threshold glaucoma program with the Medmont M 700 perimeter. Th e summation of sensitivities in apostilbes (asb) was counted in the extent 0 – 22 degree in the upper as well as in the lower half of the visual field. Afterwards, the results of the sensitivities summations were compared to the opposite altitudinal half of the retina of the same eye (GCC and RNFL). To compare the dependence among selected parameters, the Pearson's correlative coefficient r was used.

Results: To compare the dependence among selected parameters, the Pearson's correlative coefficient was used. Comparing GCC and the sensitivity in the hemifield test we determined medium-strength correlation in NGT-patients only. Similar correlation we noticed also between RNFL and visual field, except of RNFL in the upper half of the retina and lower hemifield test (r=0.3, p=0.1). In HTG, we did not determine any statistically significant correlation.

Conclusion: Comparing GCC, RNFL, and visual fields, we determined medium-strength correlation in NTG only, which shows the evidence of difference of both diagnostic groups.

Key words: GCC, RNFL, visual field, hypertensive glaucoma (HTG), normal-tension glaucoma (NTG)

Čes. a slov. Oftal., 72, 2016, No. 6, p. 199–203

INTRODUCTION

Glaucomas are still defined as a chronic progressive neuropathy with excavation and atrophy of the disc of the optic nerve and subsequent changes in the visual field. This formulation does not fully represent the current knowledge and requires correction. In a more modern conception, it is possible to define glaucoma as a pathology in which progressive loss of retinal ganglion cells and their axons is manifested in changes in the visual field with atrophy and excavation of the disc of the optic nerve. However, even this definition, emphasising damage to the retinal ganglion cells before their axons is not complete, because it does not at the same time point to the damage to the ganglion cells of the subcortical and cortical centres in the brain. The current definitions do not differentiate between hypertensive and normotensive glaucomas.

In comparison with hypertensive glaucoma (HTG), normotensive glaucoma (NTG) differs in a number of aspects: in addition to the level of intraocular pressure there are changes in the visual field which in the case of NTG cause more damage to the central part and have deeper defects of sensitivity (1, 11, 13), the nerve fibres are more damaged in the central part of the retina in NTG and the damage is of a focal character (20), excavation is generally broader and deeper (4), furthermore in patients with NTG vasospasms occur (5), as well as nocturnal systemic hypotension, reduction of ocular pulse amplitude and fluctuations of ocular perfusion pressure (16, 17, 19), narrow retinal veins and even deteriorated haemorheological properties of blood (6, 7) and others.

In the case of HTG, diffuse damage to the ganglion cells takes place throughout the entire retina, with subsequent necrosis of their axons. The amount of time it takes from the occurrence these changes until the alteration of the subcortical and cortical visual centres in the brain is not exactly known. In NTG, by contrast with HTG, the electric response of the ganglion cells is relatively good. However, alteration takes place in the visual pathway (10). On the basis of this knowledge it is possible to assume that in the case of HTG there shall be a diffuse diminution of the "ganglion cell complex" (GCC), and that changes in the retinal nerve fibre layer (RNFL) will be only secondary in the initial stages of the disorder. With regard to the fact

that the visual field is a reflection of the entire visual pathways, the results of GCC and RNFL need not necessarily correlate.

In NTG, the GCC should be less damaged mainly in the initial stages of the pathology, in contrast with changes in the RNFL, which should precede changes in the GCC. In our last study on this theme, in both cohorts we demonstrated a medium-strong correlation between GCC and RNFL in the same halves of the retinas. We did not record any differences in thickness of GCC and RNFL in both altitudinal halves. Through a comparison of GCC, RNFL and change sin the visual fields – pattern defect (PD) and overall defect (OD) – we determined a medium -strong correlation only in patients with NTG beteween PD and GCC superior (r=-0.41, p=0.003), and PD and RNFL superior (r=-0.4, p=0.005), as well as between PD and RNFL inferior (r=-0.3, p=0.03). In HTG we did not determine any statistically significant correlation (12).

On the basis of these hypotheses we set the target of our study, which is to determine whether a correlation exists within the group of HTG and NTG between GCC and RNFL in the same altitudinal half of the retina with opposite sum of sensitivities of half of the visual field of the same eye.

COHORT AND METHODOLOGY

The HTG group comprised 25 patients, of which 12 were women with an average age of 53.25 years (range 34-69 years) and 13 men with an average age of 60.38 years (range 37-74 years). The second NTG group comprised 17 women with an average age of 55.35 years (range 25-75 years) and 8 men with an average age of 55.5 years (range 32-69 years).

Criteria for inclusion in study: visual acuity 1.0 with applicable correction less than ±3 dioptres (21), approximately the same changes in the visual fields in all patients,

Table 1 Summary table of measured values for HTG

HTG												
Sex / age	GCC RE SHS	GCC RE IHS	GCC LE SHS	GCC LE IHS	RNFL RE SHS	RNFl RE IHS	RNFL LE SHS	RNFL LE IHS	SHF RE	IHF RE	SHF LE	IHF LE
f/65	73,8	71,7	74,7	77,6	77,7	83,8	83,7	74,4	1110	1039	1072	1026
f/35	92,7	92,7	97,5	93,1	109,2	107,6	114,2	109	1083	1055	1004	1057
f/66	88,3	89,6	90,6	93,2	95,8	107,6	103,6	108,6	1001	1020	934	947
f/48	88,9	90,2	88,1	89,3	108,9	93,5	106,2	101,3	1113	1100	1038	1012
f/34	84,5	88,5	89,1	88,7	110,8	109,1	114,5	103,6	1023	1020	864	963
f/67	96,1	97,6	100,7	98,9	99,9	99,6	102,9	101,4	1058	1045	947	937
f/59	92,3	95,1	89,6	94,3	103,2	107,6	101,9	107,2	1073	1022	973	1029
f/57	98,3	98,6	96,3	103,3	97,4	104	101,5	105,3	1107	1064	1062	1052
f/69	93,9	90,4	89,4	88,6	110,9	93,7	98,2	93,2	1095	973	1072	1060
f/55	85,1	86,2	85,1	86,5	101,1	101,5	100	107	1099	1083	1107	1076
f/65	91,4	90,6	106,3	96,9	104,9	119,9	105,2	110	1082	1032	1012	1014
f/67	87,8	86,2	87,8	84,8	125	117,7	114,8	107,6	973	999	1023	1012
m/74	90,1	97,3	89,1	90,1	91,9	88,6	99,4	94,6	1036	1068	1077	1047
m/55	69,2	65,2	61,5	60,7	87,2	79	83	77,5	1069	1049	1019	946
m/37	95,9	102,6	103,1	99,5	96,3	99,7	101,7	105,7	1077	1078	1055	1063
m/69	83,1	81,4	84,6	82,7	101	88,3	90,5	85,9	974	854	1042	979
m/59	92,1	91,7	85,1	85,7	105,1	100,4	104,5	93,4	1079	1070	1022	975
m/62	75,3	79,1	74,3	76,9	81,3	79,1	81,3	79,6	939	965	733	755
m/53	90,4	93,6	92,9	91,5	93,4	113,3	103,6	102,6	1149	1099	1026	1060
m/65	85,2	91,6	85,2	87,5	95,6	106,7	95,3	102,9	1094	1085	1068	1070
m/57	86,9	84,4	85,6	85,7	102,1	104,3	96	100,7	1144	1100	1108	1126
m/72	70,8	77,6	71,6	77,2	134,9	99,8	84	90,3	982	935	1020	998
m/65	99,5	105,9	93,6	100,6	93,5	115,8	102,7	115,8	1124	1059	1100	1042
m/68	87,3	87,5	86,8	86,6	92,5	95,9	89,3	84,5	1021	1024	1001	981
m/49	87,5	91,2	87,7	91,3	87,9	89,7	87,6	89,1	1084	1073	1018	1081

(f/67 = female/age 67, m/74 = male/age 74, HTG = hypertension glaucoma, GCC = ganglion cell complex, RNFL = retinal nerve fiber layer, RE = right eye LE = left eye,

Table 2 Summary table of measured values for NTG

NTG												
Sex / age	GCC RE SHS	GCC RE IHS	GCC LE SHS	GCC LE IHS	RNFL RE SHS	RNFl RE IHS	RNFL LE SHS	RNFL LE IHS	SHF RE	IHF RE	SHF LE	IHF LE
f/33	79,6	72,5	80,9	80,9	92	92,3	93	95,4	1098	1081	1193	1104
f/72	83,2	81,3	78,5	80,2	94,4	94,7	92,9	92,5	1122	1064	960	1024
f/47	79,8	80,3	79,6	80,6	78,3	88,2	86,2	80,2	960	965	1035	1033
f/65	88	88,2	88,4	88,3	90,9	91,4	99,3	92,5	1103	1093	1107	1044
f/46	89,3	91,2	93,8	89,9	103,2	104,8	99,3	99,6	1073	1119	1062	1046
f/59	86,4	90,8	84,6	81,5	91,1	106,7	94,7	103,8	988	1076	982	1021
f/75	89,5	92,2	85,6	85,6	107,4	111,9	118,8	99,4	1009	1040	957	1033
f/61	77,6	78,7	77,7	81,2	93,5	93,3	98,5	85,2	998	1042	919	1020
f/30	99	100,4	96,7	101,9	105,3	107,9	91,9	107,7	1077	1056	1073	1142
f/74	91,6	93,1	103,3	140,3	88,8	113	101	92,8	1060	1016	978	1020
f/62	102	97,2	103,1	98,6	105,6	106,2	104,8	106,7	1087	1122	1089	1131
f/71	69,7	75,6	67,6	56,6	76,5	84,8	84,4	77,3	986	1024	543	948
f/53	77,4	62,3	92,2	91,5	96	73,4	97,5	96,3	546	1076	1099	1044
f/49	82,5	84,5	88,3	87,7	92,7	102,6	99,1	101	986	953	1010	1020
f/51	90,2	93,6	85,5	88,9	102,6	126,7	119,9	120,3	1162	1156	1161	1130
f/25	87,4	82,2	86,1	84,1	101,1	88,4	98,9	98,6	1010	1020	1005	1011
f/68	98,7	99,2	95,9	93,8	110,2	108,5	108,3	120,7	1042	1050	1029	1037
m/47	96,5	100,3	104,8	98,9	99,3	101,7	103,9	104,9	1028	1100	1089	1081
m/65	84,8	83,1	79,7	75,8	88	89	88	83	1058	1055	978	1042
m/69	67,3	63,8	60	65,9	79,6	73,4	73,7	74	848	943	692	787
m/67	93,2	97	86	92,4	129,6	112,5	101,8	111,7	891	997	950	1006
m/51	94,3	96,4	86,6	87,6	88,5	91,6	90,3	98,2	1081	1051	1049	1053
m/59	78,1	79,1	70,6	72	77,8	82	81,5	97,3	1019	1027	1037	1025
m/32	101,8	102,7	105,1	101,3	115,9	130,4	110	111	1093	1084	1074	1076
m/54	102,5	104,2	97,2	99,1	108,4	99,1	102,9	98,1	1067	1060	1076	1086

(f/33 = female/age 33, m/47 = male/age 47, NTG = normal tension glaucoma, GCC = ganglion cell complex, RNFL = retinal nerve fiber layer, RE = right eye,

in which this concerned incipient glaucoma pathology, no other ocular or neurological pathology.

In the patients with NTG the diagnosis was confirmed by an electrophysiological examination. The thickness of the GCC layer was measured with the aid of SD-OCT RTvue -100. The same applied to the RNFL. The visual field was examined by a rapid threshold glaucoma program using the instrument Medmont M 700. The sum of sensitivities in apostilbs (asb) was evaluated on a scale of 0-22 degrees, in both the superior and inferior half of the visual field. The sensitivity results in the visual field were then compared with the opposite altitudinal half of the retina of the same eye (GCC and RNFL). The Pearson correlation coefficient r was used for a comparison of the dependency between the selected parameters.

RESULTS

The measured and calculated values for HTG and NTG are presented in summary in tables 1 and 2.

The correlation between GCC and the corresponding opposite half of the visual field is presented in summary in table 3.

The correlation between RNFL and the corresponding opposite half of the visual field is presented in summary in table 4.

Upon statistical processing of the values of GCC, RNFL and the sum of sensitivities in the opposite half of the visual field of the same eye we determined a statistically significant correlation only in the case of NTG.

DISCUSSION

The layer of retinal ganglion cells is composed of three layers: the inner plexiform layer or inner nuclear layer (INL), which is formed by dendrites of ganglion cells, the ganglion cell layer (GCL), formed by the bodies of the ganglion cells themselves, and the retinal nerve fibre layer (RNFL), formed by axons of the ganglion cells. These

three layers are referred to as the "ganglion cell complex" (GCC), and are ideal for monitoring progress of glaucoma pathology (8, 14, 15). The macular region contains 50% of all the ganglion cells of the retina, and therefore becomes an appropriate location for the detection of early changes in glaucoma, as well as for monitoring the progression of this disorder.

There is a relatively large amount of academic communications on the theme of GCC and RNFL in hypertensive glaucomas, but less on the theme of HTG and NTG. In NTG, where retinal ganglion cells are relatively undamaged, we determined a medium-strong correlation in our study between GCC and the visual field. Similarly also between RNFL and the visual field, with the exception of RNFL of the superior half of the retina of the right eye and the inferior half of the visual field of the same eye (p=0.1). In HTG we did not record a similar correlation. Our expressed hypothesis is supported also by the results of the study by Kim et al. (9), who state that loss of GCC in the NTG group was more localised in comparison with the diffuse loss in the group of primary open angle glaucomas (POAG). The authors also note that perimacular GCC parameters could be a good alternative or substitute for measurement of peripapillary RNFL for diagnosis and scientific studies on patients with NTG.

All our patients had a glaucoma pathology in the initial stages. As a result we expected a statistically significant correlation only in the case of NTG. The results of our study confirmed this. An alternative opinion is expressed by Distante et al. (3), who compared GCC, RNFL and changes in visual fields, and determined a medium correlation in various stages of HTG. Similarly Rao et al. (18) state that upon a diagnosis of glacuomatous optic neuropathy, in comparison with static automatic perimetry, the majority of parameters of RNFL and GCC had better sensitivity and a negative probability of participation.

Examinations of GCC and RNFL are technically used for structural imaging, but say nothing about the functional condition of ganglion cells and their axons. Before a ganglion cell necrotises, it collapses, which then proceeds to its death only once the fundamental cause of this condition exceeds the given time limit. As a result it is possible to provide a decrease of PERG (pattern electroretinogram) before structural changes occur. This fact was demonstrated also by Bowd et al. (2), who state that PERG amplitude has a significant (but weak) connection with the thickness of GCC and RNFL, and of the macula itself.

CONCLUSION

Examination of GCC and RNFL in the same altitudinal half of the retina and a comparison thereof with the opposite sum of sensitivities of half of the visual field of the same eye demonstrated a medium-strong correlation only in patients with NTG. This conclusion also points to two different pathologies, which thus require also different therapeutic approaches.

Tab. 3 Correlation between GCC and corresponding opposite half of visual field

GCC	Visual field	r	p value
superior hemisphere RE	inferior hemifield RE	0,5	p = 0,01
inferior hemisphere RE	superior hemifield RE	0,6	p = 0,002
superior hemisphere LE	inferior hemifield LE	0,6	p = 0,001
inferior hemisphere LE	superior hemifield LE	0,5	p= 0,01

(GCC = ganglion cell complex, RE = right eye, LE = left eye,

Tab. 4 Correlation between RNFL and corresponding opposite half of visual field

RNFL	Visual field	r	p value
superior hemisphere RE	inferior hemifield RE	0,3	p = 0,1*
inferior hemisphere RE	superior hemifield RE	0,5	p = 0,008
superior hemisphere LE	inferior hemifield LE	0,6	p = 0,008
inferior hemisphere LE	superior hemifield LE	0,6	p = 0,002

(RNFL = retinal nerve fiber layer, RE = right eye, LE = left eye, r = Pearson correlation coefficient) *statistically not significant

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