

VISUAL FIELD ASSESSMENT IN HYPERTENSION GLAUCOMA

Lešták J., Fůs M.

Eye Clinic JL, Faculty of Biomedical Engineering, Czech Technical University in Prague

Sworn declaration:

The authors hereby 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. The study has not been submitted to any other journal or printed elsewhere.

Received: 17 August 2020

Accepted: 11 November 2020

Available on-line: 11 March 2021



doc. MUDr. Ján Lešták, CSc, MSc,
MBA, LLA, DBA, FEBO, FAOG
Oční klinika JL Fakulty
biomedicínského inženýrství
ČVUT v Praze
V Hůrkách 1296/10
158 00 Praha 5 – Nové Butovice
lestak@seznam.cz

SUMMARY

Aims: The aim of the work is to verify the necessity of full-field perimetry test in incipient glaucoma.

Material and methods: The study included group of 16 incipient hypertension glaucoma (HTG group) patients without obvious changes in visual field and control group of 10 patients with normal ocular findings and value 1.0 of visual acuity. In both groups, full-field perimetry test was performed followed by a glaucoma perimetry test (rapid threshold strategy in both cases). Evaluated parameters were pattern defect (PD) and overall defect (OD) using Pearson's correlation coefficient.

Results: Strong correlation coefficient between PD ($r = 0.74$) and OD ($r = 0.63$) of both perimetry test were found in HTG group. Moderate correlation of PD ($r = 0.54$) and strong correlation of OD ($r = 0.64$) in control group.

Conclusion: Results of the study shows, that expected changes of peripheral visual field will be recorded first in HTG group, but opposite is true. Perimetry glaucoma test is for incipient glaucoma sufficient to document the course and the examination of glaucoma disease.

Key words: hypertension glaucoma, perimetry test, pattern defect, overall defect

Čes. a slov. Oftal., 77, 2021, No. 1, p. 22–26

INTRODUCTION

A perimetry test is most often indicated in ophthalmological practice in the case of glaucoma pathology. With regard to the fact that the finding on the optic nerve papilla may conceal also a further neurogenic, mainly compressive lesion, this examination remains irreplaceable in the first contact between the ophthalmologist and the patient.

The recommendations on the selection of the scope of the perimetry test up to now have not differentiated between hypertension (HTG) and normal tension (NTG) glaucoma. Approximately one third of primary open-angle glaucomas are constituted by NTG [1,2].

NTG is characterised by changes in the central part of the visual field, which are accompanied by a deeper decrease of sensitivity [3,4,5,6,7].

After an increase of intraocular pressure (IOP) in experimental conditions, activation of microglia and macroglia takes place in the retina [8]. In addition to this change, direct alteration of the retinal ganglion cells

also occurs. Before the process of apoptosis is triggered, the cell defends itself against cell death by reducing not only its surface, but also the dendritic tree. Magnocellular ganglion cells are more heavily damaged [9,10,11,12]. These processes take place not only on the level of the retina, but also of the corpus geniculatum laterale (CGL) [12,13,14,15].

This issue has also been focused on by Quigley et al., who in cadaverous glaucomatous eyes determined a greater loss of large retinal ganglion cells, while the perifoveal region remained intact [16,17]. Because the magnocellular ganglion cells are located in the periphery of the retina, changes should take place precisely in the periphery upon examination of the visual field. The central part of the visual field should remain intact, at least in the early stages. For this reason, it was the aim of our study to determine whether it is sufficient to examine the central part of the visual field (with glaucoma perimetry test) in the case of incipient hypertension glaucoma, or whether it is necessary to conduct a full-field perimetry test.

Cohort and method of examination

The cohort included seven women with an average age of 53.6 years (34-70 years) and nine men with an average age of 65.4 years (44-77 years). All had verified hypertension glaucoma in the incipient stage, without manifest changes in the visual fields, persisting for at least three years. The control group comprised seven women with an average age of 39.7 years (26-61 years) and three men with an average age of 40.7 years (29-

45 years) with a normal ocular finding and visual acuity equal to 1.0.

In all of the subjects, we examined the visual field by means of a fast threshold strategy and subsequently, after a ten minute interval, also by a glaucoma perimetry test on the instrument Medmont M700 (Medmont Pty Ltd., Victoria 3124, Australia). The glaucoma perimetry test examines in 104 points within the range of 0 to 22 degrees temporally and 0 to 50 degrees nasally.

Table 1. Summary data

| Glaucoma patients | | | | | Control group | | | | |
|-------------------|---------------------------|----------|-------------------------|----------|---------------|---------------------------|----------|-------------------------|----------|
| sex-birth | Full-field perimetry test | | Glaucoma perimetry test | | sex-birth | Full-field perimetry test | | Glaucoma perimetry test | |
| | PD | OD PO/LO | PD PO/LO | OD PO/LO | | PD | OD PO/LO | PD PO/LO | OD PO/LO |
| F-1950 | 1.71 | 5.56 | 0.91 | 3.84 | F-1959 | 3.10 | 3.10 | 3.60 | 2.18 |
| | 1.98 | 5.40 | 2.34 | 3.01 | | 2.75 | 3.05 | 2.49 | 2.23 |
| F-1956 | 7.10 | 0.43 | 3.15 | 3.83 | F-1963 | 1.96 | 2.22 | 1.99 | 1.68 |
| | 5.46 | 2.98 | 3.61 | 3.34 | | 3.15 | 3.36 | 2.30 | 2.08 |
| F-1956 | 5.80 | 1.88 | 6.48 | 0.82 | F-1964 | 3.24 | 2.51 | 3.10 | 3.20 |
| | 3.74 | 3.59 | 3.77 | 2.53 | | 2.10 | 3.19 | 2.20 | 2.95 |
| F-1960 | 1.71 | 3.31 | 2.63 | 2.07 | F-1970 | 2.03 | 4.13 | 2.10 | 3.29 |
| | 2.01 | 4.06 | 2.19 | 3.57 | | 2.46 | 4.67 | 2.20 | 3.80 |
| F-1971 | 3.05 | 0.14 | 1.66 | 1.56 | F-1973 | 2.76 | 3.54 | 1.26 | 2.06 |
| | 2.22 | 3.26 | 1.38 | 2.79 | | 2.36 | 3.89 | 1.35 | 2.19 |
| F-1986 | 1.97 | 1.98 | 2.16 | 0.70 | F-1982 | 2.35 | 1.52 | 2.72 | 0.81 |
| | 2.11 | 1.67 | 1.92 | 1.18 | | 2.69 | 2.65 | 2.35 | 0.70 |
| F-1986 | 2.26 | 2.80 | 1.23 | 1.62 | F-2004 | 2.40 | 3.31 | 1.28 | 1.80 |
| | 1.44 | 3.19 | 1.69 | 2.35 | | 2.75 | 2.59 | 1.34 | 1.83 |
| M-1943 | 2.60 | 4.68 | 1.89 | 3.61 | M-1975 | 3.34 | 0.85 | 3.11 | 1.54 |
| | 4.08 | 3.99 | 2.12 | 3.36 | | 3.22 | 0.97 | 3.79 | 1.38 |
| M-1946 | 6.68 | 0.74 | 3.92 | -0.53 | M-1991 | 2.35 | 0.85 | 3.11 | 1.54 |
| | 6.34 | 2.05 | 6.65 | 2.01 | | 3.22 | 0.97 | 3.79 | 1.38 |
| M-1946 | 3.21 | 4.37 | 2.92 | 3.77 | M-1992 | 2.76 | 1.62 | 1.80 | 2.54 |
| | 3.62 | 3.02 | 2.80 | 2.60 | | 2.64 | 2.01 | 2.01 | 0.84 |
| M-1952 | 4.15 | 2.42 | 2.05 | 4.23 | | | | | |
| | 4.13 | 5.03 | 2.51 | 4.33 | | | | | |
| M-1954 | 3.00 | 4.24 | 2.17 | 2.85 | | | | | |
| | 3.09 | 4.19 | 2.46 | 3.43 | | | | | |
| M-1955 | 2.07 | 4.42 | 1.79 | 3.84 | | | | | |
| | 2.07 | 5.04 | 2.34 | 3.01 | | | | | |
| M-1955 | 2.73 | 5.55 | 1.99 | 3.32 | | | | | |
| | 2.46 | 4.20 | 1.78 | 3.29 | | | | | |
| M-1964 | 2.20 | 3.21 | 1.80 | 1.97 | | | | | |
| | 1.85 | 2.28 | 2.10 | 1.52 | | | | | |
| M-1976 | 2.43 | 3.15 | 1.63 | 2.58 | | | | | |
| | 3.25 | 3.40 | 3.43 | 3.17 | | | | | |

Table 2. Pearson's coefficient r : 0.00-0.19 very weak, 0.20-0.39 weak, 0.40-0.59 moderate, 0.60-0.79 strong, 0.80-1.00 very strong

| PEARSON'S R | | | |
|-------------------|--------------|---------|---------|
| GROUP | VISUAL FIELD | Defect | |
| | | Pattern | Overall |
| Glaucoma patients | GI/Full | 0.740 | 0.630 |
| Control group | | 0.543 | 0.636 |

The full-field perimetry test is within the range of 0 to 50 degrees and contains 164 points. In each visual field we evaluated the pattern defect (PD) and overall defect (OD). Losses of fixation, false positive and false negative responses in all subjects were less than 10 %. The summary data is presented in table 1.

RESULTS

By comparing the measured PD values in the glaucoma test and the full-field test, in patients with HTG we determined a strong correlation ($r = 0.74$). A similarly strong correlation was recorded in the case of OD values ($r = 0.64$). In the healthy individuals there was a moderate correlation of PD in both tests ($r = 0.54$). OD recorded a strong correlation ($r = 0.636$). Table 2.

DISCUSSION

In the incipient stages of HTG, unstable (transitional) and isolated changes take place in the sensitivity of the examined points. Due to the variability demonstrated in this study, the OCULAR Hypertension Treatment Study (OHTS) amended its protocol of the visual field for confirmation of abnormality. Three consecutive abnormal visual fields are required, in which the defect is not arthaphakic, incorporates the same index, and abnormality is in the same location. In this study the subjects were examined using a 30-2 test [18].

As regards the selection of the test, in the glaucoma perimetry test Heijl and Patella recommend the use of central 30 degrees in a number of 54 examined points (Humphrey field analyser from the company Carl Zeiss Meditec SRN) [19]. The authors share this opinion also in the next fourth edition of Essential perimetry [20].

At the beginning of this discussion, we must present a number of facts concerning the physiology and morphology of the retinal ganglion cells and psycho-physiological examinations (perimeter). The number of photoreceptors (rods and cones) which are connected with a single ganglion cell form a receptive field. The retina of the eye contains several types of ganglion cells. The types most frequently presented in connection with glaucoma are parvocellular (P), magnocellular (M) and coniocellular (C).

P retinal ganglion cells are characterised by:

- large number (1 000 000),
- localisation more centrally,

- low axonal conduction velocity,
- relatively small receptive field (as a result these cells are also responsible for central visual acuity),
- react to slowly flashing light stimuli,
- react to objects with a high spatial frequency and low contrast sensitivity,
- react to coloured stimuli,
- do not react to moving stimuli [21],

M retinal ganglion cells are characterised by:

- small number (100 000),
- localisation more peripherally,
- high axonal conduction velocity,
- relatively large receptive field,
- react to quickly flashing light stimuli,
- react to objects with low spatial frequency and high contrast sensitivity,
- react to moving stimuli,
- do not react to coloured stimuli [21].

If blue colour appears in the receptive field, C retinal ganglion cells react [21].

Significant changes in the visual field have been linked with a loss of 25-35 % of retinal ganglion cells, in which primarily M cells were the first to die. However, it is necessary to emphasise that for the examination the authors used a 30-2 test (Humphrey field analyser) [22].

These cellular processes may take place independently of damage to the nerve fibres of the retinal ganglion cells.

It has also been demonstrated that changes in the visual fields are preceded by changes in the RNFL [23]. We also arrived at similar results in another study, in which we determined vessel density (VD) in the peripapillary region by means of optical coherence angiography (OCTA). We demonstrated that in the case of HTG, VD has a very small influence on changes in the visual fields. A similar situation applies also regarding the RNFL on changes in the visual field. However, VD has a moderately strong influence on changes in the RNFL [24]. In another study, with the aid of SD-OCT RTvue-100, we compared the thickness of the layer of the ganglion cells complex (GCC) and the RNFL with the bilateral altitudinal half of the visual field. In HTG we did not determine any statistically significant correlation [25]. It is necessary to note that examinations of the GCC, RNFL and VD provide information about the central part of the retina, and not its peripheral part. This was also a reason why we wanted to examine also the periphery of the visual field in the incipient stages for this diagnostic group.

Similar conclusions were reached also by Na et al. [26]. Here it is also important to state that in glaucomatous eyes with IOP above 20 mmHg, there was a pronounced decrease of macular and papillary vessel density (VD) ($p < 0.05$) [27].

Following adjustment of IOP, In et al. observed a marked improvement of VD in the peripapillary region of patients with HTG [28].

Changes in the retinal nerve fibre layer in eyes with hi-

gher IOP have been known for more than thirty years. In an experiment on monkeys, Quigley et al. and Sommer et al. demonstrated that fibres of M cells atrophied more quickly than others, even when fibres of other cells were not spared [16,29].

When we examine the functions of M ganglion cells, we determine that they react to contrast, structure and movement in the receptive field. From this it is possible to deduce also that they are more sensitive to a perimetry test, in which the stimuli used are movement [30], contrast in combination with movement [31-34] and quickly flashing light stimuli [34-36].

Unfortunately, these technologies are not ordinarily used for examination of the visual field.

As stated in the introduction, following an increase of IOP in experimental conditions, an alteration of the main magnocellular retinal ganglion cells occurs. We

verified this conclusion also in a healthy individual, in whom we demonstrated, by means of electrophysiological measurement, that following an increase of IOP to 40 mmHg a blockade of transmission of electrical changes of voltage takes place precisely on the level of the retinal ganglion cells. Ganglion cells reacted similarly in another patient with HTG, in whom we determined a decrease of amplitude N50-N95 in both eyes following the discontinuation of antiglaucomatous drugs [37].

CONCLUSION

The results of our study did not demonstrate the significance of a full-field perimetry test in cases of incipient glaucoma. However, this does not mean that we shall begin to treat HTG only after the first changes have appeared in the visual field. It is important to examine the RNFL and also VD, which anticipate perimetric changes.

LITERATURE

1. Bonomi L, Marchini G, Marraffa M. et al. Prevalence of glaucoma and intraocular pressure distribution in a defined population. The Egna-Neumarkt Study. *Ophthalmology*. 1998;105: 209–215.
2. Klein BE, Klein R, Sponsel WE. et al. Prevalence of glaucoma. The Beaver Dam Eye Study. *Ophthalmology*. 1992;99:1499–1504.
3. Araie M, Yamagami J, Suzuki Y. Visual field defects in normal-tension and high-tension glaucoma. *Ophthalmology*. 1993;100:1808–1814.
4. Levene RZ. Low tension glaucoma: a critical review and new material. *Surv Ophthalmol*. 1980;24:621–664.
5. Zeiter JH, Shin DH, Juzych MS, Jarvi TS, Spoor TC, Zwas F. Visual field defects in patients with normal-tension glaucoma and patients with high-tension glaucoma. *Am J Ophthalmol*. 1992;114:758–763.
6. Caprioli J, Spaeth GL. Comparison of visual field defects in the low-tension glaucomas with those in the high-tension glaucomas. *Amer J Ophthalmol*. 1984;97:730–737.
7. Lestak J, Nutterova E, Bartosova L, Rozsival P. The visual field in normal-tension glaucoma and hypertension glaucoma. *IJSR*. 2014;3: 49–51.
8. Rojas B, Gallego BI, Ramírez AI. et al. Microglia in mouse retina contralateral to experimental glaucoma exhibit multiple signs of activation in all retinal layers. *J Neuroinflammation*. 2014;11:133. doi:10.1186/1742-2094-11-133.
9. Glovinsky Y, Quigley HA, Dunkelberger GR. Retinal ganglion cell loss is size dependent in experimental glaucoma. *Invest Ophthalmol Vis Sci*. 1991;32:484–491.
10. Morgan JE, Uchida H, Caprioli J. Retinal ganglion cell death in experimental glaucoma. *Br J Ophthalmol*. 2000;84:303–310.
11. Naskar R, Wissing M, Thanos S. Detection of Early Neuron Degeneration and Accompanying Microglial Responses in the Retina of a Rat Model of Glaucoma. *Invest Ophthalmol Vis Sci*. 2002;43:2962–2968.
12. Shou T, Liu J, Wang W, Zhou Y, Zhao K. Differential dendritic shrinkage of alpha and beta retinal ganglion cells in cats with chronic glaucoma. *Invest Ophthalmol Vis Sci*. 2003;44: 3005–3010.
13. Smith EL, Chino YM, Harwerth RS, Ridder WH, Crawford MLJ, DeSantis L. Retinal inputs to the monkey's lateral geniculate nucleus in experimental glaucoma. *Clin Vision Sci*. 1993;8:113–139.
14. Chaturvedi N, Hedley-Whyte ET, Dreyer EB. Lateral geniculate nucleus in glaucoma. *Am J Ophthalmol*. 1993;116:182–188.
15. Vickers JC, Hof RP, Schumer RA, Wang RF, Podos SM, Morrison JH. Magnocellular and parvocellular visual pathways are both affected in a macaque model of glaucoma. *Aust N Z J Ophthalmol*. 1997;25:239–243.
16. Quigley HA, Sanchez RM, Dunkelberger GR, L'Hernault NL, Baginski TA. Chronic glaucoma selectively damages large optic nerve fibers. *Invest Ophthalmol Vis Sci*. 1987;28:913–920.
17. Quigley HA, Dunkelberger GR, Green WR. Retinal ganglion cell atrophy correlated with automated perimetry in human eyes with glaucoma. *Am J Ophthalmol*. 1989;107:453–464.
18. Keltner JL, Johnson CH, Quigg JM. et al. Confirmation of Visual Field Abnormalities in the Ocular Hypertension Treatment Study. *Arch Ophthalmol*. 2000;118:1187–1194.
19. Heijl A, Patella VM. The field analyser primer. Essential perimetry. Third edition. Carl Zeiss Meditec Inc. 2002. ISBN: 0-9721560-0-3., s. 26.
20. Heijl A, Patella VM, Bengtsson B. The field analyser primer. Essential perimetry. Fourth edition. Carl Zeiss Meditec Inc. 2012. ISBN: 0-9884795-0-8, s. 29.
21. Skalkicky SE. Ocular and visual physiology. Clinical application. Springer Science+Business Media Singapore Pte Ltd., Australia 2016, Chapter 8, p. 123.
22. Kerrigan-Baumrind LA, Quigley HA, Pease ME, Kerrigan DF, Mitchell RS. Number of ganglion cells in glaucoma eyes compared with threshold visual field tests in the same persons. *Invest Ophthalmol Vis Sci*. 2000;41:741–748.
23. Klamann MK, Grünert A, Maier AK, Gonnermann J, Jousen AM, Huber KK. Comparison of functional and morphological diagnostics in glaucoma patients and healthy subjects. *Ophthalmic Res*. 2013;49:192–198.
24. Zakova M, Lestak J, Fus M, Maresova K. OCT Angiography and Visual Field in Hypertensive and Normotensive Glaucoma. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub*. 2020;164 – in press.
25. Lešták J, Pitrová Š. „Ganglion cells komplex“ a vrstva nervových vláken u hypertenzních a normotenzních glaukomů. [Ganglion Cells Complex and Retinal Nerve Fiber Layer in Hypertensive and Normal-Tension Glaucoma]. *Cesk Slov Oftalmol*. 2016;72:199–203. Czech.
26. Na JH, Lee K, Lee JR, Baek S, Yoo SJ, Kook MS. Detection of macular ganglion cell loss in preperimetric glaucoma patients with localized retinal nerve fibre defects by spectral-domain optical coherence tomography. *Clin Exp Ophthalmol*. 2013;41: 870–880.
27. Ma ZW, Qiu WH, Zhou DN, Yang WH, Pan XF, Chen H. Changes in vessel density of the patients with narrow anterior chamber after an acute intraocular pressure elevation observed by OCT angiography. *BMC Ophthalmol*. 2019;19:132. doi: 10.1186/s12886-019-1146-6.
28. In JH, Lee SY, Cho SH, Hong YJ. Peripapillary Vessel Density Reversal after Trabeculectomy in Glaucoma. *J Ophthalmol*. 2018;26:8909714. doi: 10.1155/2018/8909714. eCollection 2018.
29. Sommer A, Katz J, Quigley HA, Miller NR, Robin AL, Richter RC, Witt KA. Clinically detectable nerve fiber atrophy precedes the onset of glaucomatous field loss. *Arch Ophthalmol*. 1991;109:77–83.

30. Bosworth CF, Sample PA, Weinreb RN. Motion perception thresholds in areas of glaucomatous visual field loss. *Vision Res.* 1997;37:355–364.
31. Johnson CA, Samuels SJ. Screening for glaucomatous visual field loss with frequency-doubling perimetry. *Invest Ophthalmol Vis Sci.* 1997;38:413–425.
32. Arend KO, Plange N. Diagnostic approaches for early detection of glaucoma progression. *Klin Monbl Augenheilkd.* 2006;223:194–216.
33. Ferreras A, Polo V, Larrosa JM. et al. Can frequency-doubling technology and short-wavelength automated perimetries detect visual field defects before standard automated perimetry in patients with preperimetric glaucoma? *J Glaucoma.* 2007;16:372–383.
34. Nomoto H, Matsumoto C, Takada S. et al. Detectability of glaucomatous changes using SAP, FDT, flicker perimetry, and OCT. *J Glaucoma.* 2009;18:165–171.
35. Horn FK, Jonas JB, Korth M, Jünemann A, Gründler A. The full-field flicker test in early diagnosis of chronic open-angle glaucoma. *Am J Ophthalmol.* 1997;123:313–319.
36. Horn FK, Tornow RP, Jünemann AG, Laemmer R, Kremers J. Perimetric measurements with flicker-defined form stimulation in comparison with conventional perimetry and retinal nerve fiber measurements. *Invest Ophthalmol Vis Sci.* 2014;55:2317–2323.
37. Lešták J, Fůs M. Neuroprotection in glaucoma-electrophysiology. *Exp Ther Med.* 2020;19:2401–2405.