MODERN DIAGNOSTICS AND TREATMENT OF

GLAUCOMA

Ph.D. THESES

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INTRODUCTION

Glaucoma is one of the most frequent causes of irreversible blindness. Estimations from the early 1990th showed that the number of people suffering from primary glaucoma would be 66.8 million at the millennium, one tenth of these people would get bilateral blindness due to glaucoma, and a further 6 million people would suffer from secondary glaucoma.

Progression of glaucoma is slow, severe loss of the visual functions develops during many years. According to the recent knowledge vascular dysregulation of the optic nerve head and the peripapillary retina is an especially important process of the development and progression of glaucoma. Pathologically increased diurnal fluctuation of the intraocular pressure (IOP), which is frequently observed after laser treatments of the anterior eye segment, is another risk factor for the progressive loss of the retinal ganglion cells and their axons.

Glaucoma cannot be cured but it can be effectively managed, if diagnosed early and treated in an appropriate way in order to prevent the functionally significant impairment of vision. In addition to the conventional diagnostic techniques (applanation tonometry, diurnal IOP curve, evaluation of compliance, photodocumentation and graphical documentation) detailed evaluation of the visual functions (automated threshold perimetry), diurnal home tonometry, optic nerve head morphometry (scanning laser tomography), or measurement and monitoring of the retinal nerve fibre layer thickness (scanning laser polarimetry) are important in the modern glaucoma diagnosis and long-term care.
I. AIMS

1. To investigate the alterations of the retinal capillary perfusion due to standard cold provocation in vasospastic subjects with and without capsular glaucoma.
2. To investigate the influence of the topical IOP lowering drugs on the diameter of the human retinal arteries.
3. To evaluate the measuring accuracy of the portable Ocuton A tonometer, and to compare it to the accuracy of the Goldmann tonometer. To compare the self-tonometric measurements with the Ocuton S instrument and the measurements with the Ocuton A and Goldmann tonometers, i.e. instruments used by the trained technician or by the ophthalmologist. To compare 24 hours diurnal IOP curves obtained with the Ocuton S self-tonometer and the Goldmann tonometer.
4. To evaluate the practical usefulness of the Heidelberg Retina Tomograph II (HRT II), and to investigate its value in glaucoma screening.
5. To compare the IOP lowering efficacy and tolerance of two similar, non-selective beta-receptor blocking eye drops.
6. To evaluate retrospectively the IOP lowering efficacy and the tolerance and adverse events of latanoprost eye drops.
II. METHODS

The Ethics Committee of the Semmelweis University approved the clinical and experimental protocols.

In our first study on ocular perfusion changes of capillary perfusion of the retina and optic nerve head due to standard cold provocation were investigated using scanning laser Doppler flowmetry on 10 healthy vasospastic subjects and 5 vasospastic patients suffering from capsular glaucoma. The measurements were performed with the Heidelberg Retina Flowmeter (software version 1.02).

In our second study on ocular perfusion the change of the diameter of the retinal arterioles was investigated after the instillation of different IOP lowering eye drops (betaxolol 0,5%, brinzolamid 1%, brimonidin 0,2%, latanoprost 0,005% or timolol 0,5%). Using the Retinal Vessel Analyser 6 healthy volunteers and 16 primary open-angle glaucoma patients controlled with topical monotherapy (non-selective beta-blocker, selective beta-blocker or prostaglandin F2α analogue) were evaluated.

In the studies on Ocuton tonometers Ocuton A tonometry by trained ophthalmologists and Ocuton S self-tonometry were performed on medically treated primary open-angle glaucoma patients with controlled IOP, who were able to perform self-tonometry. IOP readings with the Ocuton tonometers were compared to the readings obtained with Goldmann tonometry on 30 eyes of 15 patients. Diurnal IOP curves with the Ocuton S tonometer and the Goldmann tonometer were investigated on 14 eyes of 7 patients. Central corneal thickness of the same eyes was diurnally measured using the Humphrey 855 ultrasound pachymeter.

Scanning laser tomography with the Heidelberg Retina Tomograph II (HRT II) was performed on 110 eyes of 56 subjects. Twenty-seven of them suffered from glaucoma, 12 subjects were clinically considered borderline, and 17 were healthy volunteers with clear refractive media. Reproducibility of the measurement was investigated on 44 eyes of 22 subject. Reliable visual field reports (Octopus 101, program G2, TOP, or Dynamic strategy) were available on 54 eyes of 33 subjects in the study population, scanning laser polarimetric reports (GDx Software version 1.0.16.) were present for 26 eyes of 13 of our subjects.

In our study on the beta-receptor blocking eye drops timolol-maleate and levobunolol maleate were compared in a 4 week, open-labelled, prospective, comparative investigation on 31 primary open-angle glaucoma eyes of 17 patients. The IOP was controlled with either of
the two monotherapies for at least three months before the study period. Visual acuity, intraocular pressure (IOP) tear secretion (Schirmer I test), tear film stability (break up time), and ocular tolerance were evaluated.

**To study the effects of the prostaglandin-analogue latanoprost eye drop** data on 179 eyes of 100 randomly selected glaucoma patients were analysed retrospectively. Latanoprost was administered either in monotherapy or in combined medication. One hundred and forty-seven of the 179 eyes suffered from primary open-angle glaucoma. The follow-up time varied between 3 months and 28 months. IOP was measured with either Goldmann applanation tonometry or with Tono-Pen XL tonometry before latanoprost was introduced in the treatment, and at month 3, 12, and 18 after that. Reliable visual field tests (Octopus 500, program G1 or Octopus 101, program G2) were obtained on 12 eyes with a follow-up of at least 18 moths. The visual field indices of these fields were studied.
III. SUMMARY OF THE NEW RESULTS

1. A similar response to the standard cold provocation was seen on the vasospastic patients suffering from capsular glaucoma and on the vasospastic healthy subjects as measured with the Heidelberg Retina Flowmeter. Cold provocation of the skin induced a similar acute reduction of the retinal and optic nerve head capillary perfusion. The reduction of the perfusion diminished, and tended to return to the baseline value when the skin was stimulated with warm water. These results suggest that the potential role of vasospasm in the development of capsular glaucoma requires further investigations, since the reactions in capsular glaucoma were similar to those seen in the non-glaucomatous vasospastic eyes.

2. The diameter of the retinal arteries studied with the Retinal Vessel Analyser in healthy young volunteers, as well as in glaucoma patients controlled with IOP lowering monotherapy (betaxolol, brimonidin, brinzolamid, latanoprost or timolol), showed no alteration between the baseline value and the value measured at two hours after the instillation.

3. Measuring accuracy of the portable Ocuton A tonometer was sufficient to the clinical purposes as compared to the Goldmann applanation tonometry. However, the readings with the Ocuton A tonometer were on average 2 mm Hg higher than the readings obtained with the Goldmann tonometer. No difference was seen between the results of Ocuton S self-tonometry and Ocuton A tonometry. Ocuton S self-tonometry was found suitable for IOP monitoring for patients with sufficient skill for using the instrument. No difference was found in the mean IOP obtained during 24 hours diurnal IOP curves with the Ocuton S self-tonometer and the Goldmann tonometer. However, the curves themselves were different: compared to the gold standard Goldmann tonometry Ocuton S self-tonometry underestimated the IOP during the night and at daybreak. This suggests that diurnal IOP curves as measured with the Ocuton S tonometer must be evaluated with a great care. IOP readings with the Goldmann tonometer and with the Ocuton S tonometer were differently influenced by the diurnal fluctuation of the central corneal thickness.
4. The Heidelberg Retina Tomograph II (HRT II) was found simple and fast to use in clinical practice. The instrument with its present software version, however, still cannot be considered suitable for mass glaucoma screening due to its low sensitivity. But to complete other diagnostic investigations and to support the correct diagnosis, the HRT II seems to be useful in clinical practice.

5. No significant difference was seen in the IOP lowering efficacy and tolerance between the two non-selective beta-receptor blocker eye drops containing timolol-maleate or levobunolol-hidrochloride in our short-term investigation. The two drops were found equally effective.

6. In our retrospective study on 100 randomly selected glaucoma patients treated with topical latanoprost, an additional 23 % IOP decrease was measured on average after latanoprost was introduced in the therapy. The IOP decrease remained stable during the whole follow-up period, and the visual functions were fully preserved. Latanoprost was well tolerated.
IV. PUBLICATIONS IN THE TOPIC OF THE Ph.D. RESEARCH

Articles in foreign languages:


Articles published in Hungarian scientific journals:


Published abstracts:


V. PRESENTATIONS IN THE TOPIC OF THE Ph.D. RESEARCH

Presentations on international scientific meetings and congresses:

1. Holló G, Süveges I, Kóthy P: Increase of aqueous humour endothelin-1 concentration due to argon laser trabeculoplasty is associated with an early elevation and a later decrease of intraocular pressure in the rabbit. Congress of the European Association for Vision and Research (EVER). 6-9 October 1999, Palma de Mallorca


Presentations in Hungarian scientific meetings:


8. Kóthy P: Diagnosis of glaucoma with the Heidelberg Retina Tomograph II instrument and the GDx Nerve Fiber Analyser: evaluation and practical comparison (in Hungarian).