Protective effect on visual functions of long-term use of trimetazidine in treatment of primary open angle glaucoma and degenerative myopia

Michał S. Nowak, Katarzyna Wybór, Roman Goś, Alicja Zeman-Miecznik, Arleta Waszczykowska, Mirosław Pastuszka, Anna Kłysik, Agnieszka Gajdowska

Department of Ophthalmology and Visual Rehabilitation, University Hospital No. 2, Medical University of Lodz, Poland

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Corresponding author:
Michał S. Nowak, MD
Department of Ophthalmology and Visual Rehabilitation
University Hospital No. 2
Medical University of Lodz
113 Żeromskiego str.
90-549 Lodz, Poland
Phone: +48 42 639 36 34
Fax: +48 42 639 36 36
E-mail: michaelnovak@interia.pl

Abstract

Introduction: The purpose of the study was to evaluate selected visual parameters in the group of patients undergoing long-term treatment with trimetazidine as an adjuvant therapy for primary open angle glaucoma and degenerative myopia.
Material and methods: Thirty patients, including 20 patients with advanced primary open angle glaucoma (40 eyes) and 10 patients with severe degenerative myopia (20 eyes), were treated with trimetazidine 20 mg twice a day. We excluded from the study patients with: systemic hypertension and/or diabetes, cataract, history of chronic and recurrent severe inflammatory eye disease and smokers. Patients with primary open angle glaucoma were taking various ocular hypotensive drops topically. Ophthalmic examination has been performed before administration of trimetazidine and then every month. Visual acuity, contrast sensitivity test (Pelli-Robson test), glare test, color vision (Farnsworth-Munsell test) and visual field were recorded. Follow-up period was 6 months. For statistical analysis paired Student's t- test ($p<0.05$) was used.
Results: The contrast sensitivity and visual acuity improved in all patients and the results were statistically significant. Glare tests, colour vision and visual fields did not reveal any statistically significant changes.
Conclusions: The results of the study demonstrate that long term use of trimetazidine improved contrast sensitivity and visual acuity. The drug was well tolerated and might be considered as the adjunctive therapy in patients with primary open angle glaucoma and degenerative myopia.

Key words: primary open angle glaucoma, degenerative myopia, trimetazidine, ischemia.

Introduction

Tissue ischemia as one of the important factors in the development of several eye diseases according to the current opinions. Ischemia causes tissue hypoxia, affects cellular metabolism, impairs functioning of the cells. This results in intracellular acidosis, accumulation of Ca^{2+} ions and aggressive free radicals. All the above contributes to irreversible tissue injury including the neurosensory retina and the optic nerve. The commonly accepted idea regarding management of ischemic effects is that a normal blood flow has to be increased or restored [1].

Trimetazidine is a cytoprotective drug in ischaemia. Its mechanism of action is associated with:

- enhancement of metabolic processes in the cell,
- induction of highly energetic compounds – ATP, and phosphocreatine,
- decrease in acidosis and production of free radicals,
- counteraction of Na^+ and Ca^{2+} accumulation and mitochondrial damage,
- preservation of cellular membrane integrity,
- inhibition of lipid oxidation processes, neutrophil accumulation and platelet aggregation.

Trimetazidine is 90% absorbed from the digestive tract: its maximal blood concentration is reached 2-3 hours since the administration, and is excreted via kidney. The drug demonstrates a cytoprotective activity for the cells of, among others, myocardium, liver, retina and choroid.

Trimetazidine has been used in adjuvant therapy of cardiac ischemia, vertigo of vascular character or in association with Meniere's disease, in hearing impairment and in microvascular abnormalities of the choroid and the retina [1-4].

The aim of the study was to evaluate the effect of long-term use of trimetazidine on the selected visual parameters as the adjuvant therapy in the treatment of patients with primary open angle glaucoma and degenerative myopia.

Material and methods

The study comprised 30 patients, 20 with primary open angle glaucoma (40 eyes) and 10 with degenerative myopia (20 eyes), treated at the outpatients' clinic.

The criteria for exclusion from the investigations were as follows: systemic diseases such as hypertension and/or diabetes, smoking or other addictive substances, history of uveitis, advanced cataract. Patients were divided into 4 groups according to the age and the type of eye disease (Table I). They were treated with trimetazidine – metazidine (Polfa Pabianice, Poland) at the dose of 20 mg twice a day. Patients with primary open angle glaucoma also received various hypotensive drops topically to the conjunctival sac. Such parameters as visual acuity, contrast sensitivity test (Pelli-Robson test), glare test, color vision (Farnsworth-Munsell test) and visual field were assessed.

The follow-up period was performed every month for half a year since the time of metazidine administration. For statistical analysis paired Student's t-test was used with the significance level at $p<0.05$.

Results

Contrast sensitivity (Pelli-Robson test) improved already after the first month of trimetazidine therapy in all patients with glaucoma and in the group of patients aged 20-40 years with degenerative myopia. This improvement was sustained until the end of the follow-up, and the differences were statistically significant ($p<0.05$) (Figures 1-3).

In the group of patients above 40 years of age with degenerative myopia the improvement in contrast sensitivity was also observed, but the differences were not statistically significant ($p>0.05$).

The comparison of treatment results revealed that visual acuity was improved in the patients with primary open angle glaucoma already after the first month of trimetazidine administration, sustained until the end of the observation period and the differences were statistically significant ($p<0.05$) (Figures 4-5).

In patients with degenerative myopia the improvement in visual acuity was also observed, however the differences were not statistically significant ($p>0.05$).

During the follow-up, the remaining tests of glare, color vision, and visual field did not demonstrate any statistically significant changes.

Discussion

Primary open angle glaucoma is a chronic progressive optic neuropathy difficult for early diagnosis, prevention and treatment. It leads to atrophy of the retinal ganglion cells and nerve fibre layer resulting in characteristic widening of optic nerve cup with the loss of neuroretina, and typical visual field defects. Vascular impairment at the level of the optic nerve head inhibits axoplasmic flow and leads

Table I. Thirty patients divided into 4 groups

Age	Group I – glaucoma		Group II – degenerative myopia	
	Group I A (age 30-60)	Group I B (age >60)	Group II A (age 20-40)	Group II B (age >40)
Number of people	10	10	5	5
Age range (minimum-maximum)	41-59	61-83	21-30	44-64
Mean age	50.2	72.5	26.5	52.6
Median age	49.0	70.0	27.5	52.0
Standard deviation	12.5	13.8	10.8	16.2

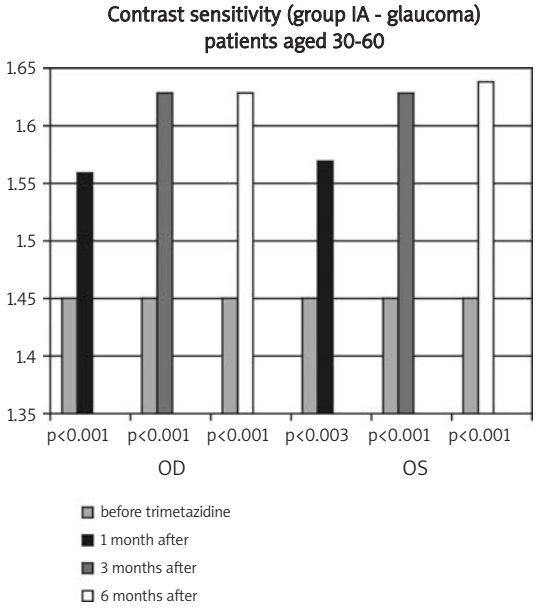

Figure 1. Contrast sensitivity in group of glaucoma patients aged 30-60

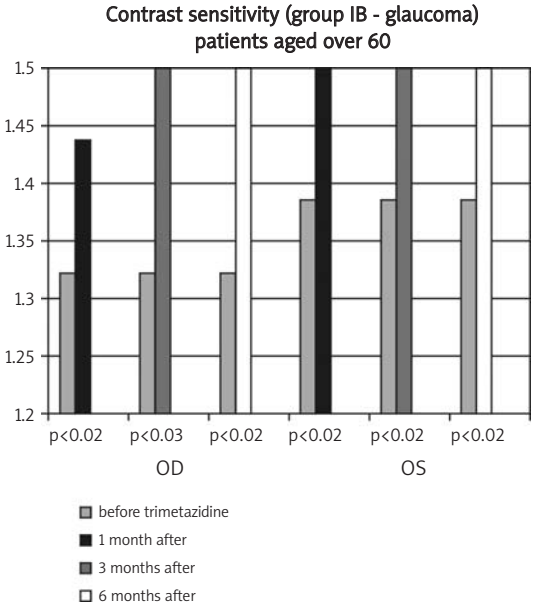

Figure 2. Contrast sensitivity in group of glaucoma patients aged over 60

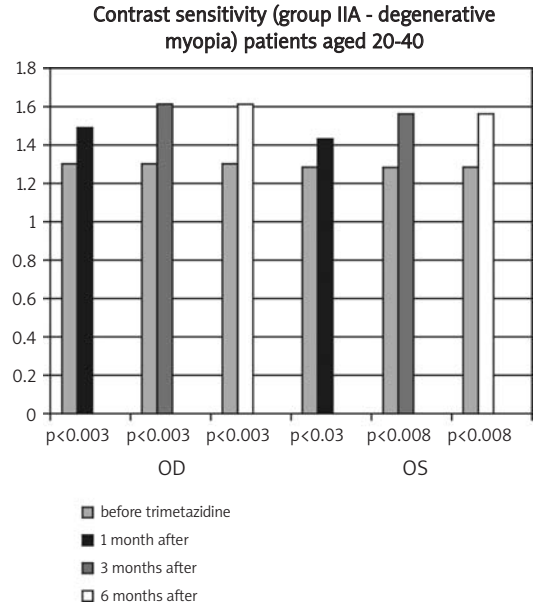

Figure 3. Contrast sensitivity in group of degenerative myopia patients aged 20-40

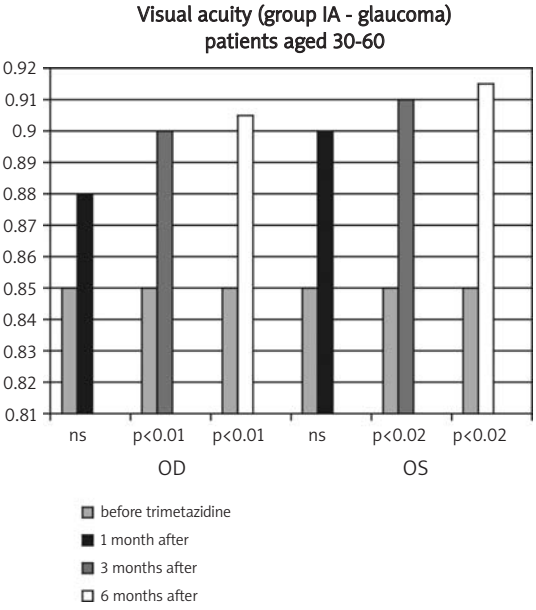

Figure 4. Visual acuity in group of glaucoma patients aged 30-60

to retinal ganglion cell apoptosis [5-7]. Is is postulated to be an important factor in the development of glaucoma, besides elevated intraocular pressure. Clinical studies have provided evidence that appropriate blood flow in the posterior segment of the eye appears to be an absolute prerequisite for maintaining the function of the optic nerve.

It was stated that in the group of patients with the initial glaucomatous changes of blood flow velocity in the ciliary circulation there were no statistically significant differences between pharmacologically and surgically treated patients [5, 8]. Administration of drugs enhancing optical nerve perfusion plays an important role in glaucoma treatment, especially in low tension glaucoma, where intraocular pressure does not seem to be a factor. Drugs that not only decrease the intraocular pressure but also improve optic nerve perfusion include antiglaucoma drops instilled into the conjunctival sac such as: betaxolol, dorzolamide and brimonidine. Perfusion of the optic nerve can be enhanced by systemic drugs e.g. vinpocetine,

pentoxifylline, nicergoline. Recently, the attention has been paid to the use of neuroprotective drugs administered systemically in the treatment of primary open angle glaucoma [5, 9, 10].

In our previous studies we observed a statistically significant improvement in contrast sensitivity and visual acuity in patients with primary open angle glaucoma already after the first month of trimetazidine therapy [11].

Further observations confirmed that the achieved level of improvement was maintained for the 6-month follow-up and that the drug was well tolerated by all patients without any noticeable adverse events.

Degenerative myopia causes a considerable decrease in visual acuity, impairment of color vision, and visual field defects. Progressive increase of the axial length of the eyeball plays a crucial role in the etiopathogenesis of the disease causing complications in the function and structure of the retina. Degenerative changes are associated with: thinning of the retina, choroid, optic nerve; vasocontriction within the retina, choroid and ciliary body; loss of the pigmented retinal epithelium; rapture of the Bruch's membrane, as well as enlargement and malformation of the lamina cribrosa with the signs of glaucomatous neuropathy. In the pharmacological treatment of degenerative myopia are recommended the following vessel-sealing drugs improving perfusion: difrarel, sadamine, trental, rutinoscorbine, calcium, biostimulative medicaments and vitamins [12, 13].

In the group of patients with high degenerative myopia at the age of 20-40 years, the improvement in contrast sensitivity was observed already after the first month of trimetazidine treatment [11], which persisted until the end of the follow-up period, and the differences were statistically significant.

Improvement in visual acuity was also diagnosed in the group of patients with high degenerative myopia, however the differences were not significant.

All patients tolerated trimetazidine well and no adverse effects were noticed during the follow-up period.

Trimetazidine due to its cytoprotective is beneficial for neurosensory cells of the retina and the optic nerve in ischemic conditions.

The studies conducted on animals have provided evidence that this drug administered prophylactically prevents injury of the retinal cells in ischemia induced by the intraocular pressure increase and the blood flow disorders [4, 14, 15].

Our study on volunteers with primary open angle glaucoma and high degenerative myopia has revealed that the long-term use of trimetazidine favorably affects the selected visual functions and does not cause any obvious adverse events. Trimetazidine is an effective adjunctive therapy in patients with vascular disorders of the eye.

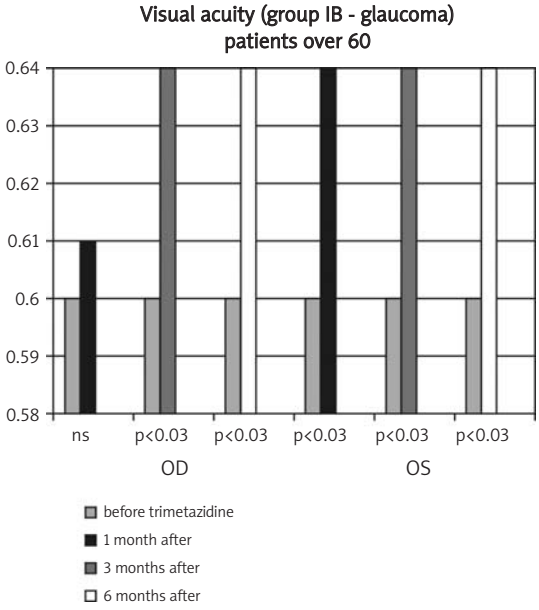

Figure 5. Visual acuity in group of glaucoma patients aged over 60

Conclusions

On the basis of the 6 months observations the following conclusions can be drawn:

1. Trimetazidine improved contrast sensitivity and visual acuity in patients with primary open angle glaucoma and high degenerative myopia.
2. Trimetazidine can be used as an adjunctive treatment in patients with primary open angle glaucoma and high degenerative myopia.
3. The drug was well tolerated by patients during the long-term administration.

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