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Original Research Article

Effect of brimonidine on central corneal thickness in normal tension glaucoma patients

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ABSTRACT

Background: Brimonidine is a potent ocular hypotensive agent widely used in glaucoma treatment. A reduction in central corneal thickness can lead to an underestimation of intraocular pressure by Goldmann applanation tonometry and vice versa. The aim of this study is to determine whether brimonidine has an effect on central corneal thickness.
Methods: 30 eyes of patients who attended the Ophthalmology OPD between the time period October 2017 and June 2018 who were newly diagnosed with normal tension glaucoma with no history of any systemic illness or not on any medication were included. Each patient underwent a complete ophthalmic evaluation including fundus examination, visual field assessment, intraocular pressure, central corneal thickness measurement by pachymetry before as well as 1 month and 6 months after starting treatment with 0.2% topical brimonidine twice daily.
Results: Administration of brimonidine 0.2% resulted in an increase in central corneal thickness from 525±21 µm before starting brimonidine to 528±21 µm ($p<0.05$) after 1 month and 535±20 µm ($p<0.001$) after 6 months. It also resulted in a reduction in intraocular pressure from an initial value of 16±2 mmHg before starting brimonidine to 14±2 mmHg ($p<0.05$) and 13±2 mmHg ($p<0.05$), 1month and 6 months after starting treatment, respectively.
Conclusions: The data presented in this study show that topical administration of 0.2% brimonidine twice daily results in a significant increase in central corneal thickness in patients with normal tension glaucoma.

Keywords: Brimonidine, Central corneal thickness, Normal tension glaucoma

INTRODUCTION

Normal tension glaucoma (NTG) is a form of open angle glaucoma characterized by glaucomatous optic neuropathy in patients with intraocular pressure (IOP) measurements consistently equal to or less than 21 mmHg with visual field loss as damage progresses, consistent in pattern with the nerve appearance.[1] With the introduction of widespread central corneal thickness (CCT) assessment, NTG in some patients has been explained by very low CCT, and overall CCT in patients with NTG is lower than in primary open angle glaucoma. The measured IOP of NTG patients is likely to be underestimated because of their thinner corneas.[2]

Brimonidine is a selective alpha-2 adrenergic receptor agonist that shows upto 1780-fold selectivity for alpha 2 over alpha-1 adrenergic receptors.[3] After topical instillation, brimonidine reduces IOP within 1 hour, and the peak effect occurs at 2-3 hours after dosing.[4] Brimonidine has dual mechanism of IOP lowering: it both reduces aqueous humor production and stimulates

aqueous humor outflow through the uveoscleral pathway.[5] After topical application, brimonidine is rapidly absorbed by the cornea and conjunctiva and spreads quickly in the entire eye.[6] In corneal epithelial and endothelial cells , many alpha2-adrenoceptors have been detected. Their stimulation by brimonidine leads to decrease in intracellular cAMP concentration and thus a limited protein kinase A (PKA) activity resulted. The blockage of corneal beta adrenoceptors, also with a reduction in the intracellular cAMP concentration and a decrease in the PKA activity, resulted in a measurable increase in central corneal thickness.[7]

While the interaction of brimonidine with posterior segment alpha2-adrenoceptors had been the goal of numerous research projects, there are only few studies available on the impact of brimonidine on the receptors of the cornea although it is known that it is quickly taken up by the cornea following topical administration, hence the need for this study.[8]

METHODS

A hospital based prospective study was done on 30 eyes of patients who attended the Ophthalmology OPD between the time period October 2017 and June 2018 who were newly diagnosed with normal tension glaucoma.

Inclusion criteria

All patients, newly diagnosed with NTG, with age more than 18 years, consent to participate in the study.

Exclusion criteria

- Patients with prior history of glaucoma therapy,
- Previous ocular surgery,
- Very old non-compliant patients,
- Patients with severe systemic illness,
- Patients on any medication.

Patients' details and relevant past medical history were noted. Each patient underwent a complete ophthalmic evaluation including fundus examination, visual field assessment by Humphrey Field Analyzer, intraocular pressure by Goldmann applanation tonometry, central corneal thickness measurement by pachymetry (PACSCAN plus) before as well as 1 month and 6 months after starting treatment with 0.2% topical brimonidine twice daily.

Statistics

The Excel and Statistical Package for Social Sciences (SPSS) (16.0) software packages were used for data entry and analysis. Descriptive statistical analysis using frequency, percentage, mean and standard deviation and inferential statistics including paired t was done.

RESULTS

A total of 30 eyes of 18 patients newly diagnosed with NTG were studied. Of the 18 patients, 10 were males and 8 were females (Figure 1).

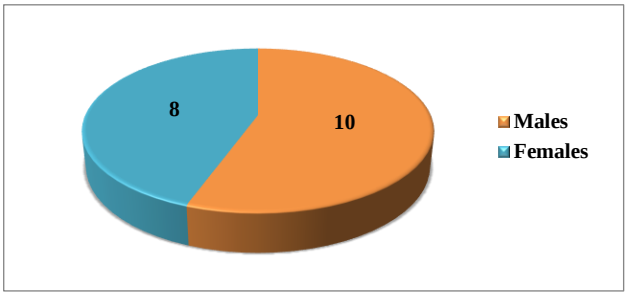

Figure 1: Gender distribution.

Intraocular pressure (IOP) and central corneal thickness (CCT) were measured before starting treatment with 0.2% brimonidine eye drops. The same were measured 1 month and 6 months after commencement of treatment.

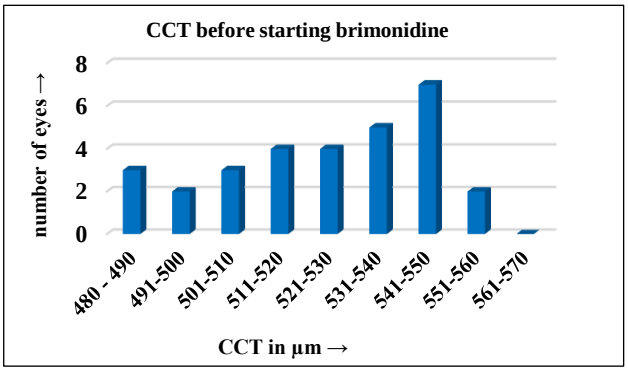

Figure 2: Central corneal thickness (CCT) of 30 eyes before starting brimonidine.

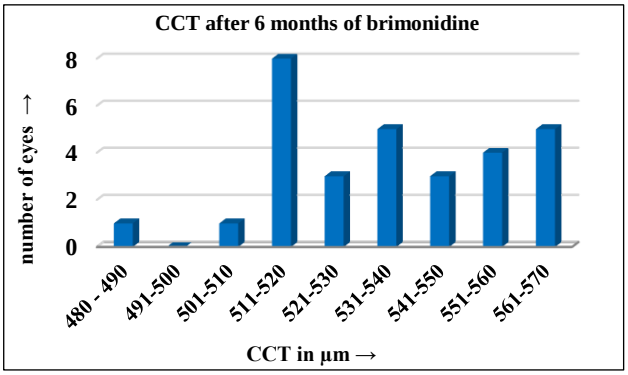

Figure 3: Central corneal thickness (CCT) of 30 eyes 6 months after starting brimonidine.

Figure 2 shows the values of CCT of 30 eyes measured during their first visit in OPD before starting 0.2% topical brimonidine. There was a wide range of CCT, ranging from 480 µm to 558 µm, with majority belonging to an average thickness of 520-540 µm. After 6 months of

treatment with brimonidine 0.2%, there is an increase in CCT of 30 eyes and the range changed to 491µm to 570µm (Figure 3).

Administration of brimonidine 0.2% resulted in a statistically significant increase in central corneal thickness from 525±21 µm before starting brimonidine to 528±21 µm ($p<0.05$) after 1 month and 535±20 µm ($p<0.001$) after 6 months of treatment (Figure 4).

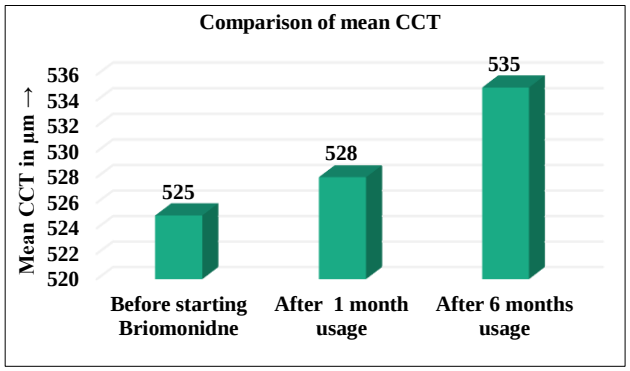

Figure 4: Comparison of mean central corneal thickness before and after starting brimonidine.

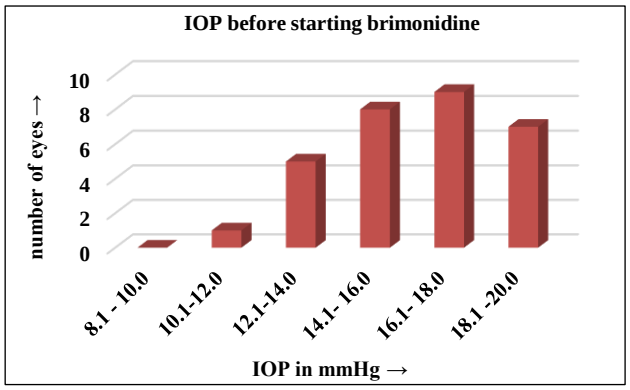

Figure 5: Intraocular pressure (IOP) in 30 eyes before starting brimonidine.

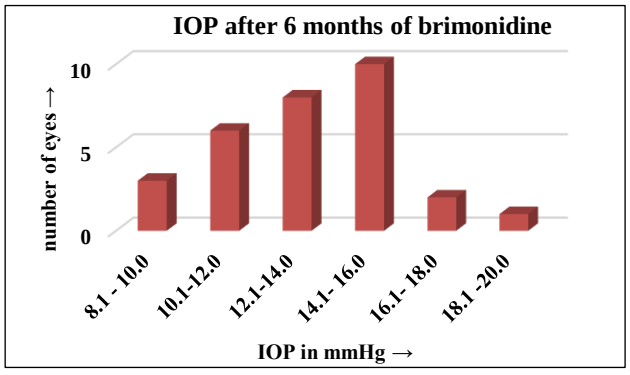

Figure 6: Intraocular pressure in 30 eyes 6 months after starting brimonidine.

Figure 5 shows the IOP values of 30 eyes measured during their first visit in OPD before starting 0.2% topical brimonidine and it included a range between 11.5 to 19.6 mm Hg. After 6 months of treatment with brimonidine, there is a decrease in IOP of 30 eyes and the range changed to 8.4 to 18.6 mmHg (Figure 6).

Thus, it resulted in a statistically significant reduction in intraocular pressure from an initial value of 16±2 mmHg before starting 0.2% brimonidine to 14±2mmHg ($p<0.05$) and 13±2 mmHg ($p<0.05$), 1month and 6 months after starting treatment, respectively (Figure 7).

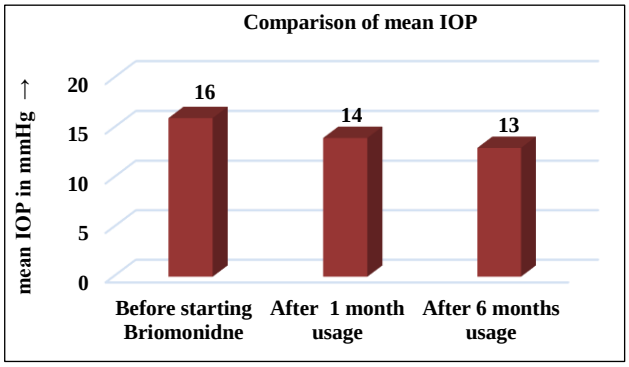

Figure 7: Comparison of mean intraocular pressure before and after starting brimonidine.

DISCUSSION

Brimonidine is an effective and safe medication that is widely used in glaucoma treatment. It is quickly taken up by the cornea following topical administration as cornea has alpha-2 adrenoceptors and also affects the corneal thickness. Intraocular pressure is overestimated in thicker corneas and underestimated in thinner ones. A thin central cornea (e. g. 490µm) may explain loss of visual field in an eye despite normal applanation measurements of IOP, because the measurements do not reflect a higher true IOP. Conversely, a thick central cornea (e.g. 610µm) may explain high measured IOP associated with a longstanding normal visual field and optic disc due to a lower true IOP.

Based on a study by M Grub et al, on effect of brimonidine on central corneal thickness, regular application of brimonidine 0.1% eye drops twice a day resulted in a reduction of intraocular pressure from an initial value of 17±2 mmHg to 13±4 mmHg after four days ($P=0.001$) as well as an increase in central corneal thickness from 559±8 µm from the time of the baseline examination to 581±11 µm ($P<0.001$).[9] Our study shows an increase in central corneal thickness from a value of 525±21 µm before starting topical brimonidine 0.2% to 535±20 µm ($p<0.001$) after 6 months of treatment.

Fan S et al, following treatment with topical brimonidine 0.2%, found that eyes with thinner corneas had lower IOPs than eyes with thicker corneas.[10] After topical instillation, brimonidine reduces IOP within 1hour and the peak effect occurs 2-3 hours after dosing.

Brimonidine induced reduction in IOP is associated with a decrease in aqueous flow, and after chronic treatment, with an increase in uveoscleral outflow. Gandolfi et al., in their study, showed that 0.2% brimonidine eye drops can induce a significant IOP reduction in eyes with normal tension glaucoma (from 17.1±0.7 mmHg to 13.9±2.2 mmHg, P<0.001).[11] In our study also, there is a significant reduction in IOP from 16±2 mmHg to 13±2 mmHg (P<0.05) after 6 months of treatment, in eyes with NTG.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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