The Effect of Oral Selective Alpha 1 Blocker on the Intraocular Pressure in Rabbits

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Purpose:
In patients taking doxazosin and 83% in patients taking tamsulosin [9]. The aforementioned studies agree that alpha 1 adrenergic antagonist [10]. Furthermore, Herd et al found an IFIS incidence of 37% taking tamsulosin compared with 19% in patients taking naltropen. Oshika et al found the incidence of IFIS to be 43% in patients with nonselective alpha antagonists. In a prospective study of 1968 cataract surgeries, IFIS syndrome occurring in patients taking nonselective alpha 1 blockers were measured immediately before and 2 hours after therapy. Ten observations for each rabbit were recorded. The mean values of IOP for the right eye before and after therapy were 13.6±3.8 and 11.1±4.6mmHg respectively (P<0.002). The mean values of IOP of the left eye before and after therapy were 13.1±4.2 and 10.1±4.4 mmHg respectively (P<0.005). The mean values of IOP for right and left eye in control group were 15.5±3.8 and 15.4±3.1 respectively. The control group showed no significant variation in the IOP neither in the right nor in the left eye, P<0.7, P<0.13, respectively.

Conclusion:
Oral alpha 1 adrenergic antagonists result in a significant reduction in IOP in rabbit’s eye. The data may implicate potential therapeutic potential for alpha 1 blockers for treatment of patients with high IOP. Further in vitro and vivostudies are required in a large cohort to confirm our results.

ABSTRACT

Material and Methods:
Selective alpha 1 blocker (tamsulosin) blocks contraction of the iris dilator smooth muscle, and that deficient muscle tone leads to poor pupil dilation, iris floppy, floppiness and propensity to prolapse, such as intraoperative floppy iris syndrome (IFIS) [3]. Later, many studies have confirmed the association between IFIS and the use of systemic alpha 1 antagonists and tamsulosin, in particular [4,9]. This syndrome is associated with higher rate of cataract surgical complications [1]. Although, tamsulosin is the most highly drug associated with IFIS, there are many reports of IFIS syndrome occurring in patients taking nonselective alpha 1 antagonists. In a prospective study of 1968 cataract surgeries, Oshika et al found the incidence of IFIS to be 43% in patients taking tamsulosin compared with 19% in patients taking naltropen [10]. Furthermore, Herd et al found an IFIS incidence of 37% in patients taking doxazosin and 83% in patients taking tamsulosin [9]. The aforementioned studies argue that alpha 1 adrenergic receptors have complex effects on ocular hydrodynamics, especially in regulating IOP and papillary diameters.

To our knowledge, today there is no study to investigate the therapeutic efficacy of oral selective alpha 1 blockers on the IOP. Herein we demonstrated the potential therapeutic benefits of oral selective alpha 1 blocker (doxazosin) on IOP in rabbits.

Material and Methods

The cohort of the experimental group consisted of healthy Palamino rabbits (n=8) weighing 3-3.5kg. Rabbits (n=4) from the same family were used as a control group. Oral selective alpha 1 blocker (doxazosin; Pfizer, USA) was given at an oral dose of 0.08 mg /kg. One tablet of doxazosin (2mg) was dissolved in 10cc of isotonic solution, and each rabbit was given the appropriate dose via an injector in the mouth. The control group received a vehicle control (10cc of isotonic solution) orally. The IOP of the left and the right eyes was measured using Schiotez Tonometer (Germany). The IOP was measured immediately before giving therapy at 12 o’clock AM and 2 hours after therapy, for each rabbit (Table 1). Local anesthetic eye drops, oxybuprocain hydrochloride 0.4% (Localin) was used before measuring IOP. The IOP of the rabbits in the control group was also measured twice a day at the same time similar to that of the study group without giving therapy. The IOP was measured over period of 3 months—thus total of 160 measurements were taken for each eye. All observations were done at intervals separated by one week to wash out the previous drug. The overall number of the IOP measurements, which was accomplished for the right and the left eyes for all rabbits were 320 measurements.

Statistical analysis: All data are expressed as mean ± standard deviation (SD). An independent sample t-test was used to compare IOP values between eyes before and after therapy administration. SPSS for windows 10.0 statistical packet was used in statistical analysis. Significance difference between control and experimental group was assessed at P<0.05.

Results

There were significant reductions in the IOP of both eyes after the doxazosin therapy. The IOP’s of the right eye before and after therapy were 13.6±3.8 and 11.1±4.6 mmHg, respectively (P<0.002) (Figure 1). The IOP of the left eye before and after therapy were 13.1±4.2 and 10.1±4.4 mmHg, respectively (P<0.005) (Figure 1). While the average percentage in the reduction in IOP of the right eye and left eye were 34.49% and 39.29%, respectively, there...
was no significant difference between both eyes (P=0.31). The mean values of the overall IOP of the right and left eyes before and after therapy were 13.6±3.9 and 11.9±5.1 mmHg (P=0.009), respectively (Figure 2). Out of 80 observations of the IOP for the right eye, 54 (67%) of them had reduction in the IOP, 12 (15%) showed no change, and 16 (20%) showed increment in IOP and. The control group showed no significant variation in the IOP neither in the right nor in the left eyes. The mean values of the IOP measurements in the control group for the right eyes were 15.5±3.8 and 16.4±1.2 mmHg, respectively (P=0.7), and those for the left eyes were 15.37±3.1 and 15.9±1.4 mmHg, respectively (P=0.13).

**Discussion**

The pharmacological effects of selective alpha 1 blockers on the prostate are well studied, however, the regulatory effects on the iris dilator muscle [11]. The pharmacological effects of selective alpha 1 blockers on the iris muscle [2-7]. Indeed, activation or inhibition of these mechanism(s) involved in drug-mediated reduction of IOP. However, no significant change was observed in the IOP of the right eye, 58 (73%) had showed reduction in the IOP; 6 (7.5%) showed no change, and 16 (20%) showed increament in IOP and. The control group showed no significant variation in the IOP neither in the right nor in the left eyes. The mean values of the IOP measurements in the control group for the right eyes were 15.5±3.8 and 16.4±1.2 mmHg, respectively (P=0.7), and those for the left eyes were 15.37±3.1 and 15.9±1.4 mmHg, respectively (P=0.13).

The mean reduction in the IOP in the right and left eyes were 34.49% and 39.29% respectively. Herd et al reported similar percentage of IFIS syndrome (37%) in patients taking doxazosin [9]. This finding may suggest that the patients with IFIS syndrome are susceptible to reduction in the IOP. Pupil constriction, which is one of the characteristics of IFIS syndrome, may allow opening of the angle –thus aqueous flow increases and IOP decreases. However, further studies are needed to prove this claim. Out of 80 observations for the IOP of the left eye 58 of them showed reduction in the IOP. The reduction IOP was more than 15% in all those patients. Thus, it is difficult to attribute this reduction in IOP by diurnal fluctuation of IOP, which is usually occurs in the morning (highest) and the early afternoon (lowest) with average of 4.4 mmHg in glaucoma patients [10]. Some other studies showed that during diurnal IOP measurements in an upright position there were no statistically significant differences in IOP changes [10]. Nonetheless, in a supine position the IOP was significantly higher than in a sitting position and increased more in the glaucoma patients than in healthy controls [10]. In the right eye out of 80 measurements, 54(67.5%) measurements showed reduction in IOP. Only 6 of them (7%) had reduction in IOP less than 15%. This also confirm that the reduction in the IOP is not consequent to diurnal change in the IOP but rather to the therapy, which was given to the rabbits. Similarly the control group showed no such reduction of IOP, which were measured at the same times of the study groups. This findings further support that the reduction in IOP is not attributed to diurnal fluctuation or machine error.

The majority of the studies regarding the ocular effect of adrenergic receptors failed to identify the underlying mechanisms and effect of alpha 1 antagonists on the IOP. This can be consider as one of the limitation for such kinds of studies as in our study too. The optimal dose of the drug can be considered another limitation for such studies. It is well known that the effect of alpha 1 antagonists is dose dependent, thus variations in doses of the drug may result in a different effects. Therefore, we recommend further studies with different doses to find out the exact effect of the drug. The third limitation is the long term effect of the drug, which may change with prolonged treatment. Thus, it is difficult to predict the exact effect of long term user of alpha 1 blocker on the IOP in patients with BPH. Despite all of these limitations, our study provides novel therapeutic potential for alpha 1 blockers. This is not unexpected advantage of alpha 1 blockers, which are already proved to have many valuable benefits besides its main usage as antihypertensive drug and in symptomatic treatment for patients with BPH. Alpha 1 antagonists have been reported to have beneficial effects in cholesterol and lipid profiles [10]. Spontaneous passage of lower and upper ureter stones as well as in improving the outcomes after extra-corporeal shock waves lithotripsy [2012].

**Conclusion**

Selective oral alpha 1 blocker results in acute reduction in the post-immediate therapeutic IOP in a rabbit model. While alpha adrenergic receptors have complex effect on the ocular hydrodynamics, an increase aqueous out flow, reduce production of aqueous and presence of additional receptors were speculated in mediating IOP reduction by alpha 1 blockers. However, further studies
should be carried out to corroborate our findings. Importantly, the fundamental mechanisms that govern the drug-induced reduction in the IOP certainly warrant further investigation.

We have no conflict of interest to declare.

**Table 1:** The values of IOP for right and left eyes before and after therapy in the study and control groups.

<table>
<thead>
<tr>
<th></th>
<th>Before therapy</th>
<th>After therapy</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP of right eye mmHg</td>
<td>13.62±3.82</td>
<td>11.08±4.59</td>
<td>0.002</td>
</tr>
<tr>
<td>IOP of Left eye mmHg</td>
<td>13.08±4.15</td>
<td>10.13±4.40</td>
<td>0.005</td>
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<tr>
<td>IOP of right eye (control group)*</td>
<td>15.11±3.7</td>
<td>16.36±1.18</td>
<td>0.7</td>
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<tr>
<td>IOP of left eye (control group)*</td>
<td>15.30±3.22</td>
<td>15.95±1.37</td>
<td>0.13</td>
</tr>
</tbody>
</table>

IOP: intraocular pressure.

*No therapy was given to the rabbits in the control group.

**Figure 1:** Shows the mean IOP for right and left eyes before and after therapy with right and left mean IOP for control group.

**Figure 2:** Shows the mean IOP of the right and left eyes before and after therapy with mean IOP for control group in all observations.

R.IOP-1: right eye intraocular pressure before therapy.

R.IOP-2: right eye intraocular pressure after therapy.

L.IOP-1: left eye intraocular pressure before therapy.

L.IOP-2: left eye intraocular pressure after therapy.

R.IOP-C: right eye intraocular pressure for the control group.

L.IOP-C: left eye intraocular pressure for the control group.
REFERENCE


18- Vizzioli K, Köller AU, Spolid E, Bohm AG, Pillunat LE. Intraocular pressure measurement during the day and night for glaucoma patients and normal controls using Goldmann and Perkins applanation tonometry. Ophthalmologe 2006;103(12):1027–31.

