Piloplex, a new long-acting pilocarpine polymer salt.  
B: Comparative study of the visual effects of pilocarpine and Piloplex eye drops

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SUMMARY  Induced accommodation and changes in vision (distance and near) were measured monocularly and binocularly in 9 young healthy volunteers in a double blind study after administering to them pilocarpine hydrochloride 4%, Piloplex 3-4, and saline eye drop instillations. Piloplex 3-4, a new long-acting pilocarpine polymer salt, and pilocarpine hydrochloride 4% (both contain equal amounts of pilocarpine—3-4%) induced changes in vision and accommodation. These changes were greater with pilocarpine hydrochloride than with Piloplex. The maximum changes occurred half an hour after instillation and the effect vanished after an additional period up to 3 hours. The changes were greater when measured monocularly than binocularly. Piloplex initiates a prolonged hypotensive effect which lasts for 12 hours. Patients with glaucoma are thus able to use Piloplex on a twice-daily schedule. Consequently, visual disturbances occur only once a day in contrast to pilocarpine hydrochloride given 4 times a day, which induces 3 visual disturbances during the day.

The advantage of Piloplex—a new pilocarpine polymer salt—over pilocarpine hydrochloride (PHCl) has been previously presented (Ticho et al., 1978; Blumenthal et al., 1979). Piloplex eye drops were found to have a prolonged and increased hypotensive effect, allowing them to be given on a twice-daily schedule in contrast to a 4-times daily schedule necessary for PHCl. The hypotensive effect of miotic drugs, however, is accompanied by miosis and accommodative spasm, inducing blurred vision. These side effects are predominant in young patients (Place et al., 1975; Brown et al., 1976). Adverse side effects of this nature have not been encountered with Piloplex treatment so far.

This communication reports on a study in which the induced visual effects of pilocarpine hydrochloride and Piloplex were compared in young normal persons.

Patients and methods

Nine medical students who had no record of ophthalmic disturbances were selected for the study.

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On ophthalmic examination before the study all the students had 20/20 visual acuity in both eyes, 4 of them having spectacle corrections. Their informed consent was obtained after a detailed explanation of the study.

The group consisted of 7 men and 2 women, ranging in age from 24 to 31 years. Three of them had green eyes, 3 had brown eyes, 2 had grey-blue eyes, and 1 had hazel eyes. They were examined during 3 daily sessions and were assigned randomly to 3 different eye drop treatments: (1) Pilocarpine hydrochloride 4%; (2) Piloplex 3-4 (Hydrophilics); and (3) isotonic saline. The first 2 eye drop preparations contained equivalent amounts of pilocarpine ion. In each session 1 eye drop was instilled into each eye (both eyes were treated similarly). Successive sessions with different medications were performed 3 or 4 days apart.

All examination sessions included subjects receiving all 3 types of treatments. Subjects were examined in random order. Neither the tested subject nor the examiner knew which of the medications were tested at each examination.

The examinations were of visual acuity and induced accommodation. The visual acuity was determined at 20 ft (6 m) by a Snellen projector
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Fig. 1 Average changes in visual acuity of 9 normal persons after pilocarpine hydrochloride 4%, Piloplex 3-4, and saline eye drops

<table>
<thead>
<tr>
<th>Distinct visual acuity (Snellen)</th>
<th>Hours</th>
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<tbody>
<tr>
<td>20/20</td>
<td>0</td>
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<tr>
<td>20/25</td>
<td>1/2</td>
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<tr>
<td>20/30</td>
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<td>20/60</td>
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<td>20/120</td>
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n=9

Pilocarpine hydrochloride
Saline
Standard error

Discussion

Pilocarpine causes hypotensive and visual effects which can be measured by changes in intraocular pressure, vision (distance and near), refraction, and miosis. Changes in vision and refraction, however, are not directly dose-related to the concentration of pilocarpine in the eye. Thus, constant delivery of...
small amounts of pilocarpine (20 μg/h by Ocusert) produced visual effects—refraction, distance and near vision—which did not substantially differ from those initiated by delivery of 40 μg/h of pilocarpine. Miosis and hypotensive effects were stronger after higher doses (Brown et al., 1976). Thus miosis and ocular hypotension appear to be more sensitive to relatively low doses of pilocarpine than refractive changes and distance and near vision.

Changes in all parameters are reported when the amount of pilocarpine is increased, ranging from 1 to 4%, and the changes were dose-related (Brown et al., 1976). It is expected that saturation of the pilocarpine binding sites will create the maximum visual effect, and higher doses will cause no further changes. Quigley and Pollack (1977) reported experiments with 2 different viscous preparations of PHCl (same pilocarpine dose). Green and Downs (1975) when using these preparations found different pilocarpine levels in rabbit aqueous humour. However, no significant intraocular pressure difference was reported comparing the hypotensive effect of these 2 different preparations in patients (Quigley and Pollack, 1977).

The present study shows that very similar changes in refraction and far and near vision were induced by Piloplex and PHCl, thus hinting that during the first period after instillation of the drug the amount of pilocarpine in the eye is much the same from each of the two pilocarpine preparations. However, the fact that Piloplex causes a longer hypotensive effect than PHCl (Ticho et al., 1978; Blumenthal et al., 1979) suggests that later on after instillation the amount of pilocarpine in the eye from PHCl is no longer sufficient to maintain a hypotensive effect. In contrast, in the later period after instillation of Piloplex there is sufficient pilocarpine in the eye to provide a longer-lasting hypotensive effect but without inducing visual disturbances. A similar situation was reported for Ocusert (Brown et al., 1976).

Piloplex, a salt, releases pilocarpine ion at a sustained rate (Ticho et al., 1978) and initiates a prolonged hypotensive effect lasting 12 hours; it therefore can be given on a twice daily schedule. Since adverse visual effects after evening medication (instilled before night sleep) do not disturb the patient, it could be concluded that Piloplex induces visual disturbances only once a day (after the
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morning medication) in contrast to PHCl on a 4 times daily schedule, which induces 3 disturbances during the daytime.

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References


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