Concentration of timolol in aqueous humour

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Accepted 15 August 1991

Key words: Timolol, topical administration, intraocular penetration, aqueous humour concentration

Abstract. Two groups of twenty patients who were to undergo a routine c.c.e. applied eye-drops containing timolol 0.1% or 0.5% twice daily during the week preceding their operation. A third group of twenty patients, using placebo drops, served as control. During the cataract surgery a sample of aqueous was collected. The samples from the timolol 0.1% patient group contained a significantly lower concentration of timolol than those from the timolol 0.5% patient group, but there was considerable overlap.

Introduction

There is only a slight difference in pressure-lowering effect between eye drops containing timolol 0.1%, 0.25% or 0.5%. This raised the question: What would be the level of timolol in the aqueous humour after a standardized application of eye drops containing timolol in these three concentrations?

Materials and methods

Sixty patients who were to undergo a routine extracapsular cataract extraction with implantation of a posterior chamber lens gave their informed consent and joined in the study. During the week preceding their cataract surgery they applied eye drops, and they agreed to the taking of a sample of aqueous humour during the operation. The study was approved by the Medical Ethical Committee of the hospital.

Criteria for admission to the study were senile cataract and a deep anterior chamber. Ophthalmological criteria for exclusion from the study were glaucoma, inflammation, trauma or surgery within three months prior to the start of the study, contact lenses and corneal, conjunctival or retinal abnormalities. Systemic criteria for exclusion from the study were diabetes mellitus, cardio-pulmonary disease, the use of beta-blockers and contraindications to the use of timolol or beta-blockers.
Table 1. Composition of the patient groups*

<table>
<thead>
<tr>
<th>Kind of eye drops</th>
<th>Patients</th>
<th>Age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>M</td>
</tr>
<tr>
<td>Timoptol 0.1%</td>
<td>19</td>
<td>9</td>
</tr>
<tr>
<td>Timoptol 0.5%</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>Placebo</td>
<td>20</td>
<td>9</td>
</tr>
</tbody>
</table>

*The three patient groups show a symmetrical distribution over the sexes (M = Male; F = Female) and there is no statistically significant difference in age (p = 0.11, Coneway variance analysis).

The patients were randomly divided into three groups. Twenty patients applied Timoptol 0.1% eye drops, twenty patients applied Timoptol 0.5% and twenty patients used a placebo. The Timoptol eye drops were supplied by Merck Sharp and Dohme, Haarlem, the Netherlands.

The patients were asked to apply these drops twice a day during the week preceding their operation. One hour before entering the operation theatre the patients received the last drop of the experiment. Half an hour later the premedication and local anaesthesia were given. These procedures and the operation were so planned that the collection of the aqueous humour sample took place one-and-a-half hours after the application of the last experimental drop. The sample was immediately stored at −10 °C.

The timolol concentration in the samples was analysed by Pharma Bio-Research, Assen, the Netherlands, without knowledge of the kind of eye-drops the patients had used. High performance liquid chromatography and UV detection were used, after sample clean-up by protein precipitation.

The composition of the patient population is shown in Table 1. The aqueous sample of one patient who had applied Timoptol 0.1% was lost. The distribution over the sexes is symmetrical and there is no significant difference in age between the three patient groups (p = 0.11; Coneway variance analysis).

Results

Timolol was demonstrated in the samples of all patients who had applied Timoptol 0.1% or 0.5%. In the Timoptol 0.1% group the concentration of timolol in the aqueous was between 0.09 and 0.97 mg/L. In the Timoptol 0.5% group the lowest concentration was 0.29 mg/L and the highest was 2.11 mg/L. In the patients who had used placebo eye drops the timolol concentration in the aqueous samples was below the level of detection of 0.03 mg/L (Fig. 1).