Effect of the application of acetazolamide soaked contact lenses on intraocular pressure of rabbits

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Abstract. Topical application of acetazolamide has no known effect on intraocular pressure (IOP). We tried to detect the hypotensive effect on IOP of acetazolamide soaked onto soft contact lenses (CL). We applied CLs soaked in either 1%, 3%, or 5% acetazolamide solution onto one eye of 29 rabbits while the contralateral eye served as a control. There was an average 32% reduction of IOP amongst all acetazolamide applied eyes, and an average 19% reduction of IOP amongst all control eyes. Amongst the 1% acetazolamide-CL applied eyes there was a mean 37% reduction of IOP, amongst the 3% acetazolamide-CL applied eyes a mean 36% reduction, amongst the 5% acetazolamide-CL applied a mean 30% reduction, and a mean 19% reduction in control eyes. The longest period of IOP reduction followed the application of 1% acetazolamide-CLs, probably owing to improved drug corneal penetration at this concentration. Our results reveal that the application of acetazolamide soaked soft CLs has a significant hypotensive effect on IOP in both the applied and contralateral control eyes of rabbits.

Introduction

The carbonic anhydrase inhibitors (CAI) were introduced to ophthalmology in 1954 and have been known for the last 38 years as very potent hypotensive agents. Their routine systemic use in the medical management of glaucoma has been severely limited by a variety of side effects: general malaise, gastrointestinal disturbances, weight loss, depression, anorexia, paresthesia, loss of libido, urolithiasis, and blood dyscrasias [1, 2]. A topically administered CAI should, theoretically, avoid the majority of these systemic side effects. Recent studies have explored this concept, and the development of a clinically effective topical CAI would represent a significant advance in the medical treatment of glaucoma.

In the pioneering studies, CAIs were administered topically, but failed to decrease intraocular pressure (IOP) [3–5]. The failure was attributed to inadequate corneal penetration of CAIs due to short corneal surface contact time, rapid tear turnover, and small corneal/conjunctival surface area for drug absorption [2, 6].

Since the failure of topical CAIs in early investigations, many alternative
formulations and delivery vehicles have been proposed to allow an adequate amount of drug to reach the ciliary body following topical administration. Among the latest formulations, MK-927, sezolamide hydrochloride (previously known as MK-417) and MK-507 are the most promising [7, 8]. Alternative vehicles include a gel formulation of CAI or CAI impregnated soft contact lenses (CL) [9-11].

Systemically administered CAI has a well known hypotensive effect on IOP. In this study, we examined the effect on IOP of acetazolamide soaked CLs applied to rabbit eyes.

Materials and methods

We used 1%, 3% and 5% acetazolamide sodium salt solutions (Diamox, Lederle, NC, USA) adjusted to a pH of 9.2 with sodium hydroxide. The sodium salt of acetazolamide was then dissolved in polysorbate 80 (Tween 80) and filtered to remove any precipitate.

High water content soft CLs (Hydrocurve II, Barnes Hind, CA, USA) were soaked in one of the three acetazolamide solutions for 12 hours. Aphakic CLs with powers from +15.0 to +17.0 diopters and a water content of 55% were utilized. Acetazolamide soaked CLs were randomly fitted to one eye of albino rabbits weighing 2 to 3 kg. each. The contralateral eye was fitted with an unsoaked control CL.

IOP measurements were done with a Perkins hand applanation tonometer. Two independent examiners, blind to the location of the acetazolamide CL, measured IOP. The rabbits were restrained and IOP measured after the animal adjusted to handling. Topical 0.5% proparacaine was administered prior to IOP assessment. Rabbits were examined for the presence of irritation and inflammation for the entire duration of the study period. Rabbits were recycled, applying more than one concentration of acetazolamide soaked CL, with a 10 day washout period between applications, to eliminate confounding effects.

Following measurement of baseline IOP, acetazolamide soaked CLs were fitted to one eye of rabbits and remained for two hours. IOP measurements were repeated just after the removal of the CL and 2, 4 and 6 hours later.

Statistical analysis used the mean of two independent examiners, Student's test, and one-way Anova test.

Results

We applied 1%, 3% and 5% acetazolamide soaked soft CLs on one eye of 29 rabbits, while the contralateral eye served as a control. Overall, there was an average 32% reduction in IOP in the CL fitted eyes, while the reduction was only 19% in control eyes.