LOCAL AND SYSTEMIC EFFECTS OF PINDOLOL EYE DROPS

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Local (reduction of intraocular pressure) and systemic (inhibition of exercise-induced tachycardia) effects of 1% and 0.25% pindolol eye drops have been studied in a balanced cross-over double-blind trial in 12 healthy volunteers. Both concentrations produced a comparable reduction in intraocular pressure while the inhibition of exercise tachycardia was significantly less with the lower concentration.

Introduction

β -adrenoceptor blockade is now an established form of treatment for raised intraocular pressure. Pindolol, a β -adrenoceptor blocker, was shown to decrease the intraocular pressure in concentrations of 0.25%, 0.5% (Tyas *et al.*, 1981) and 1% (Rowley *et al.*, 1981) to a comparable degree in normal volunteers. Smith *et al.* (1979) showed that 1% pindolol eye drops produced a significant inhibition of exercise tachycardia and suggested that β -adrenoceptor blocking drugs should not be used in the treatment of glaucoma in patients who also suffer from heart failure.

This study is designed to observe the effects of 0.25% and 1% pindolol eye drops on intraocular pressure and exercise heart rates in normal volunteers.

Methods

The subjects were 12 healthy volunteers (four females and eight males, aged 19–22 years). They attended on three occasions, at least 1 week apart, at the same time of day, for instillation of 1 drop, into the conjunctival sac of the left eye only, of pindolol 1%, 0.25% or saline 0.9% given in a double-blind balanced

design based on four Latin squares.

Intraocular pressure was measured before and 1 h after instillation of the drop using non-contact tonometry (Grolman, 1972; Shields, 1980). Each subject had been screened in preliminary tests to ensure that six consecutive measurements of intraocular pressure showed a difference of less than 3 mm Hg.

Exercise tachycardia was measured 2 h after instillation using an electrically braked bicycle ergometer; each subject had been acquainted with the machine and her/his workload to produce a heart rate of > 160 beats/min in the last 30 s of 3 min exercise was found prior to the study. The exercise heart rates were measured using ECG tracings.

Results

Both 1% and 0.25% pindolol solutions produced a statistically significant reduction of the intraocular pressure in the treated eyes ($P < 0.005$ for both), (Table 1). However, there was not a statistically significant difference between the reductions of intraocular pressure produced by 1% and 0.25% solutions ($t = 1.90$, $P > 0.10$).

Table 1 Reduction in intraocular pressures (IOP) mean $\pm$ s.e. mean). Treatments are instilled into the left eye only.

Solution	Reduction (mm Hg) in IOP		% reduction	
	Left eye	Right eye	Left eye	Right eye
1% Pindolol	2.97 $\pm$ 0.34**	1.47 $\pm$ 0.37*	29.3 $\pm$ 2.58**	13.85 $\pm$ 3.37*
0.25% Pindolol	2.36 $\pm$ 0.37**	0.81 $\pm$ 0.37	22.3 $\pm$ 3.27**	8.30 $\pm$ 3.57
0.9% Saline	0.61 $\pm$ 0.50	0.47 $\pm$ 0.48	4.2 $\pm$ 4.50	3.00 $\pm$ 5.93

* = $P < 0.05$, compared with placebo.

** = $P < 0.005$, compared with placebo.

Pindolol 1% solution caused a significant reduction of intraocular pressure in the untreated eye (Table 1).

Although both 1% and 0.25% pindolol solutions produced a statistically significant inhibition of exercise tachycardia ($P < 0.001$ and $P < 0.005$ respectively) (Table 2), the inhibition with the 1% solution was more than that produced by the 0.25% solution; the difference between them being also significant ($t = 4.03$, $P < 0.005$).

Table 2 Exercise heart rates (EHR) (mean $\pm$ s.e. mean).

Solution	EHR (beats/min)	Reduction from placebo (beats/min)	% reduction
1% Pindolol	139.3 $\pm$ 2.2	14.0 $\pm$ 2.9**	8.7 $\pm$ 1.7**
0.25% Pindolol	147.6 $\pm$ 2.6	5.7 $\pm$ 1.6*	3.5 $\pm$ 1.0*
0.9% Saline	153.3 $\pm$ 3.7		

* = $P < 0.005$, ** = $P < 0.001$

Discussion

The results of this study show that both 0.25% and

1% pindolol solutions produced a similar reduction in intraocular pressure (IOP) after instillation into the conjunctival sac. When the lower concentration was used, the systemic effects, shown here as inhibition of exercise tachycardia, were reduced to a significant degree, while the effect on the IOP was maintained. We are, therefore, still in the plateau stage of the dose-response curve for the local (IOP lowering) effect and are going down the curve for the systemic (inhibition of exercise tachycardia) effect. It is probable that using lower concentrations might enable us to obtain the IOP lowering effect free from systemic β -adrenoceptor blockade.

Other workers have reported a similar reduction in the contralateral eye after local timolol (Zimmerman & Kaufmann, 1977) and pilocarpine (Willets, 1979) and by exerting simple pressure on one eye (Prijet & Stone, 1956). Smith *et al.* (1979) showed that the effect of pindolol on the contralateral eye is unlikely to be due to systemic effect.

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