

Atenolol versus propranolol

A comparison of ocular hypotensive effect of an oral dose

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Both atenolol and propranolol by mouth reduce ocular tension in normal and glaucomatous eyes (Phillips, Howitt, and Rowlands, 1967; Elliot, Cullen, and Phillips, 1975; Wettrell and Pandolfi, 1975). These drugs are β -adrenergic blockers but propranolol affects both β_1 and β_2 receptors (as well as having a 'membrane' effect), while atenolol is a more specific β_1 receptor antagonist and lacks the membrane-stabilizing activity of propranolol.

Aims

The aim of this study was to compare the ocular hypotensive actions of single oral equipotent doses of atenolol (50 mg) and propranolol (40 mg) in a double-blind cross-over study on 10 patients.

Selection of patients

The 10 individuals were chosen from patients attending glaucoma clinics; they comprised six with open-angle glaucoma, three with chronic closed-angle glaucoma, and one with ocular hypertension. They all satisfied previously-established criteria regarding age and general health—namely, they were aged 70 years or less and had no evidence of cardiorespiratory disease or diabetes, and had normal renal function. Only one eye from each patient, chosen at random, was included in the study.

Details of the patients including previous treatment to the eye examined are given in Table I.

Methods

Conditions were standardized as far as possible. Local treatment to the eye to be examined and systemic carbonic anhydrase inhibitors were stopped 24 hours before test days. Patients attended as outpatients between 9.0 a.m. and 4 p.m. with at least a week between test days. After initial applanation tonometry on the eye

Table I *Details of patients*

Patient	Sex	Age (years)	Diagnosis	Previous treatment
1	Male	66	Open-angle glaucoma	Pilocarpine
2	Male	65	Chronic closed-angle glaucoma	Peripheral iridectomy pilocarpine
3	Female	48	Open-angle glaucoma	Pilocarpine di- chlorphenamide
4	Female	70	Open-angle glaucoma	Pilocarpine
5	Male	62	Open-angle glaucoma (aphakic)	Cyclodialysis pilocarpine
6	Male	52	Chronic closed-angle glaucoma	Sector iridectomy pilocarpine
7	Male	62	Ocular hypertension	Nil
8	Male	62	Open-angle glaucoma	Trephine pilocarpine adrenaline
9	Male	67	Chronic closed-angle glaucoma	Iris inclusion
10	Female	68	Open-angle glaucoma	Pilocarpine

randomly selected for examination, the blood pressure and pulse rate were measured and either 50 mg of atenolol or 40 mg of propranolol was given by mouth. The observers were unaware of which treatment was given and the order of administration was randomized. The same three properties were measured at hourly intervals for seven hours thereafter, by the same examiners. The same procedure was carried out on the second test day with cross-over of the drugs; five patients (at random) had atenolol first and propranolol second, while the other five had the drugs in the reverse order.

Results

OCULAR TENSION

In all 10 patients ocular tension fell after both atenolol and propranolol. For both treatments a significant reduction in mean tensions occurred two hours after administration and was maintained after seven hours. However, at all times the mean fall in ocular tension was greater during treatment with atenolol compared with propranolol, and with the exception of the sixth-hourly reading, these differences were statistically significant, whether or not allowance was made for the slightly different

Table II Comparison of ocular hypotensive effects of atenolol and propranolol based on adjusted mean intraocular pressure in 10 patients

	Hours after treatment							
	0	1	2	3	4	5	6	7
Propranolol								
Means	27.2	26.3	20.7	20.1	18.3	16.7	18.2	19.6
Adjusted Means		25.8	20.2	20.1	18.0	16.6	18.2	19.7
Atenolol								
Means	25.3	22.1	16.7	17.0	15.5	14.7	15.9	16.7
Adjusted Means		22.6	17.2	17.0	15.8	14.8	15.9	16.6
Difference between adjusted means		3.2	3.0	3.1	2.2	1.8	2.3	3.1
SE of difference		0.80	1.12	0.70	0.72	0.74	1.20	0.88
Significance (P)		<0.01	<0.05	<0.01	<0.05	<0.05	NS	<0.05

NS—Not significant

'Adjusted means' have been adjusted for the covariate (pre-dose pressure)

mean starting pressures before the drops were given (Table II).

BLOOD PRESSURE AND PULSE RATE

There was no reduction in diastolic blood pressure after either drug but there were significant falls in systolic pressure 2, 4, 5, and 6 hours after propranolol and three hours after atenolol.

Two hours after treatment by both drugs there

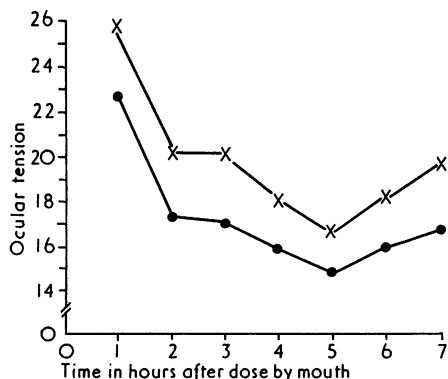


FIGURE Graph showing greater effect on ocular tension of 50 mg atenolol than 40 mg propranolol. Each point represents mean of 10 patients. Means have been 'adjusted' to allow for different starting pressures. All except 'six hour' means were significantly different

● = atenolol × = propranolol

was a significant reduction in pulse rate. This fall was greater with propranolol but the difference was not statistically significant.

Discussion

Two papers have shown the efficacy of systemic atenolol in reducing ocular tension after a single dose (Elliot and others, 1975), and during a period of eight days (Wettrell and Pandolfi, 1975) which confirms that β -adrenergic blockade or, more specifically, β_1 blockade, can produce a net effect of reduction in intraocular pressure. These observations suggest that the membrane-stabilizing effect of propranolol is of negligible importance in lowering intraocular pressure because atenolol 50 mg is more potent than 40 mg propranolol in glaucomatous eyes. This conclusion is supported because Wettrell and Pandolfi (1975) found no significant difference in the ocular hypotensive effect on *normal* eyes of these two drugs which they gave in the above doses twice daily for eight days. This conclusion was predictable from the much greater efficacy of racemic propranolol (that is, a mixture of the dextro- and laevo-rotary form) than dextro-propranolol since the former has 60 \times the β -blocking potency of the latter but the same effect on membrane stability (Vale and Phillips, 1970).

We have no satisfactory explanation for this unexpected effect on intraocular pressure of β -blockers which has been discussed at some length

in the papers already mentioned. It would be biologically consistent if adrenergic stimulation increased outflow commensurately with increased inflow to maintain a steady state. Route of administration may therefore be important—local application affecting outflow and systemic application inflow. Although we suspect that β -blockers given systemically reduce production of aqueous humour, the efficacy of propranolol (as well as practolol) in the form of eye drops (Vale and Phillips, 1973) suggests that an improvement in outflow may also take place. It will be interesting to observe the effect of atenolol eye drops when they become available, not only for theoretical reasons but also because, if the expected fall in

pressure is confirmed, a β -blocking drug suitable for local administration may become available in clinical management of glaucoma.

Summary

In a controlled double-blind cross-over trial in 10 patients comprising six with open-angle glaucoma, three with closed-angle glaucoma, and one with ocular hypertension, a single oral dose of atenolol (50 mg) was significantly more effective than propranolol (40 mg) in reducing ocular tension.

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