Low-dose combined guanethedine 1% and adrenaline 0.5% in the treatment of chronic simple glaucoma: a prospective study

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SUMMARY This paper reports on the results of a prospective double-blind crossover study, comparing adrenaline 1% with adrenaline 0.5% combined with guanethedine 1% over an 8-week period with each formulation. The guanethedine/adrenaline formulation was found to be the more effective hypotensive agent of the two. This study confirms the potentiating effect of adding guanethedine to adrenaline, and suggests that this combination would be a useful alternative treatment when adrenaline 1% or adrenaline 0.25% with guanethedine 1% is insufficient.

Adrenaline and guanethedine, both alone and in combination, have been known for many years to provide a useful ocular hypotensive effect and have been widely used in the treatment of chronic simple glaucoma.¹⁻⁶ The frequency and severity of side effects of these drugs, and guanethedine in particular, have made their routine use impracticable.

Reduction in the concentration of guanethedine and adrenaline appears to reduce the incidence of these side effects.^{6,7} The ability of low-dose guanethedine (1%) and adrenaline (0.05%-0.5%) to reduce intraocular pressure has already been shown.⁷ More recently 2 prospective double-blind studies compared low-dose adrenaline with guanethedine (0.25% and 1%) and adrenaline 1% and showed a similar hypotensive response.^{8,9} It seemed worthwhile, therefore, to see whether increasing the strength of adrenaline from 0.25% to 0.5% combined with guanethedine 1% produced a greater hypotensive effect than adrenaline 1% alone. We carried out a prospective double-blind crossover study comparing adrenaline 1% with adrenaline 0.5% combined with guanethedine 1% for this purpose. This paper reports the results.

Patients and methods

Patients for the trial were selected from the King's College Hospital Computerised Data Base. Thirteen

patients (26 eyes), 6 men and 7 women, entered the trial. Their ages ranged from 59 to 82 years. One eye was excluded from the trial because of previous filtration surgery. All patients selected had (1) chronic simple glaucoma with anterior chamber depths of >2.5 mm; (2) good intraocular pressure control with pilocarpine drops in 1, 2, 3, or 4%, used 3 or 4 times daily.

The 13 patients received both trial preparations, each acting as his own control. The trial drops were dispensed by Moorfields Eye Hospital in 13 pairs of identical bottles. The identity of the contents was coded by the pharmacy and disclosed only when each patient had completed the trial. Each patient was followed up for two 8-week periods, receiving one trial preparation for the first 8 weeks and then after a 48-hour washout crossing over to the second.

PROTOCOL

Baseline intraocular pressure readings were recorded after an initial washout period of 48 hours, and the first preparation was given. Patients were examined at 2, 4, and 8 weeks on each preparation, at the same time of day. At each visit visual acuity, intraocular pressure, and slit-lamp examination for evidence of conjunctival hyperaemia, papillary and follicular hyperplasia, and corneal epithelial staining were carried out. Each was also questioned about symptoms such as irritation, discomfort, and blurring. The patients' preference for the trial drops over pilocarpine was also recorded. Patients were instructed to instill their drops at 8 am and 8 pm, and were seen as outpatients in the morning.

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Table 1 Mean intraocular pressure (mmHg)

Off treatment	On pilocarpine	Adrenaline	Guanethedine and adrenaline
27.6 SD ± 5.4	17.5	22.2 SD ± 3.55	19.9 SD ± 2.96

Results

All the patients who began the trial completed it. Our findings were considered from 3 standpoints, namely, reduction in intraocular pressure, side effects, and the patient's subjective comments. A summary of the hypotensive action of the drugs is set out in Table 1.

Only 1 patient in the trial showed tachyphylaxis, pressures being adequately controlled initially but going out of control after 4 weeks. This happened on both regimens.

We found that both adrenaline and combined guanethedine and adrenaline produced a noticeable hypotensive effect, though less than that produced by pilocarpine. Because of the sample size and the wide scatter of the pressures off treatment the hypotensive effect of both adrenaline and the combination, although marked (Fig. 1), was not shown to be statistically significant. The combined adrenaline and guanethedine, however, appeared to be more effective as a hypotensive agent, and the difference between the mean pressures of the 2 treatment regimens analysed by Student's *t* test was significant ($0.02 > P > 0.01$).

The relative hypotensive effects of the trial drops, compared to pilocarpine is set out in Fig. 1.

Side effects were few and on the whole not severe. Their incidence was slightly greater in the group on combined drugs and they are set out in Table 2.

Table 2 Side effects seen during the trial

	Adrenaline	Guanethedine and adrenaline
Transient hyperaemia	6	4
Persistent hyperaemia	1	3
Punctate stain	0	0
Blanching	0	0
Ptosis (slight)		2
Blurring	1	1
Headache	2	0
Slight ocular pain	1	2

No case was reported of papillary or follicular hyperaemia or severe allergic reaction. Most patients preferred a twice-daily regimen to pilocarpine 4 times daily.

Conclusions

This study showed that both adrenaline 1% and guanethedine 1% in combination with adrenaline 0.5% applied twice daily, have a useful hypotensive effect, though possibly inferior to pilocarpine. The ocular hypotensive effect of guanethedine 1% together with adrenaline 0.5% would appear to be greater than that of adrenaline 1% alone, and therefore that of guanethedine 1% and adrenaline 0.25%. An increase in adrenaline strength from 0.25% to 0.5% in combination with guanethedine increases the hypotensive effect. Side effects of both preparations are slight, but slightly more common in the preparation containing guanethedine.

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Fig. 1 Hypotensive effects of trial drops compared with those of pilocarpine.

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