The 12-hour control of intraocular pressure on carteolol 2% twice daily

G R DUFF¹ AND R G NEWCOMBE²

From the ¹Department of Ophthalmology, University Hospital of Wales, and the ²Department of Medical Computing and Statistics, University of Wales College of Medicine

SUMMARY In a 15-week double-blind, placebo-controlled, crossover study both carteolol 2% and timolol 0.5% produced a significant reduction in intraocular pressure. Twelve hours after administration the reduction in pressure on carteolol was significantly less than that obtained on timolol.

Carteolol is a non-specific beta-blocking agent used in the treatment of glaucoma. The literature on the effect of carteolol on intraocular pressure is not extensive. Previous publications have demonstrated a significant reduction in pressure at peak effect¹ and for up to six² and eight³ hours. In this placebo controlled study the 12-hour control of intraocular pressure of carteolol 2% and timolol 0.5% are compared.

Material and methods

Twenty-five subjects between the ages of 45 and 80 years were recruited for this trial, 16 male and nine female. All had a mean intraocular pressure of 21 mmHg or more recorded on at least two occasions before the trial began. Exclusion criteria were: open-angle or closed-angle glaucoma, visual field defects detectable with the Friedman analyser, visual acuities of less than 6/12, asthma, cardiac failure, or any other medical condition in which treatment with a beta-blocking agent would be contraindicated. Ethical approval was obtained from the local hospital ethics committee.

At enrolment each patient filled out a medical questionnaire and gave written informed consent. Corrected visual acuities were measured with a Snellen chart, and visual fields were assessed with a Friedman visual field analyser. All subjects on prophylactic ocular hypotensive therapy had this stopped one month before the start of the trial.

Subjects were randomly allocated among six treatment groups, representing all six possible sequences

of the three treatments carteolol, timolol, and placebo. The order of administration of the three treatments for each group are given in Table 1.

The study was performed double-masked; the three treatments were presented in identical glass bottles with sterile droppers. Each treatment was instilled into both eyes 12-hourly for one week. There was a four-week washout period between the treatment periods. Intraocular pressures were measured at the beginning of each treatment period, to allow an estimate of the carry-over effect, and 12 hours after the last dose at the end of the treatment period. All measurements were made at the same time of day (to within 14 minutes for each subject) by the same observer.

The intraocular pressures obtained on each of the three treatments were compared by analysis of variance, and pairwise differences between treatments were then identified.

Results

Two subjects failed to complete the study: one completed one treatment period, the other completed two treatment periods. One subject was withdrawn from the study after one week's treatment

Table 1 The order of administration of treatments in each of six treatment groups

Group	1	2	3	4	5	6
Treatment 1	T	C	P	T	C	P
Treatment 2	C	T	C	P	P	T
Treatment 3	P	P	T	C	T	C

Carteolol=C. Timolol=T. Placebo=P.

Correspondence to G R Duff, Department of Ophthalmology, University Hospital of Wales, Heath Park, Cardiff CF4 4XW.

Table 2 Comparison of the effects of carteolol, timolol, and placebo on intraocular pressure; adjusted for carry-over; 25 subjects, both eyes averaged. Adjusted means in mmHg: carteolol 17.2, timolol 15.7, placebo 19.9

Comparison	Estimate	SE	95% confidence interval	% reduction	t	p
C vs P	-2.67	0.72	-4.12 to -1.22	-13.4	-3.72	<0.001
T vs P	-4.22	0.73	-5.70 to -2.74	-21.2	-5.75	<0.001
C vs T	+1.55	0.73	+0.07 to +3.03	-	+2.11	<0.05

Carteolol=C. Timolol=T. Placebo=P.

with carteolol and a one-month washout owing to the development of a unilateral uveitis and a consequent reduction of visual acuity in the affected eye to 6/24.

The results of the comparison of the effects of carteolol, timolol, and placebo on intraocular pressure are summarised in Table 2. The analysis of variance was performed with the post-treatment intraocular pressure (average of both eyes) as the dependent variable and subject, period, and treatment as the explanatory factors. There was a linear period effect, a reduction of the order of 1.3 mmHg per treatment period. Adjustment for carry-over had very little effect on the results owing to the balanced design of the study.

There was a highly significant reduction in intraocular pressure on both carteolol and timolol. After one week's therapy the reduction in pressure obtained 12 hours after the administration of carteolol 2% was significantly less than that obtained on timolol 0.5%. In the analysis incorporating adjustment for carry-over there was a 13.4% reduction on carteolol and a 21.2% reduction on timolol compared with the mean pressure on placebo.

Discussion

Carteolol is a non-specific beta-blocking agent recently licensed in the UK for use in the treatment of glaucoma. Though the manufacturers suggest a twice daily regimen, there is no satisfactory information so far on the control of intraocular pressure over a 12-hour period.¹

There is no doubt that at peak effect carteolol 2% does produce a significant reduction in intraocular pressure.¹⁻³ The difference between the effects of carteolol 1% and carteolol 2% is small and did not reach significance in a crossover study.⁴ When comparing the pressures obtained on carteolol with those on placebo (rather than comparing pressures on carteolol with pretreatment pressures, and ignoring the effect of diurnal variation) Kitazawa *et al.* demonstrated a significant reduction in intraocular pressure for up to six hours.²

In an open study on eight patients with ocular hypertension and glaucoma Horie *et al.*⁵ demonstrated a greater reduction in intraocular pressure on

timolol 0.5% than on carteolol 2%. In the same publication the authors reported a failure to demonstrate a difference between timolol 0.5% and carteolol 2% in a double-blind study on 10 subjects. This might have been due to the small sample size or to the study design, in which the two treatments were administered in succession (for one month each) without an intervening washout period.

The present study is the first placebo-controlled, double-masked trial to show a significant reduction in intraocular pressure 12 hours after the administration of carteolol 2%. It also shows that the reduction on carteolol 2% is significantly less than that obtained on timolol 0.5%.

The results presented here apply to 'glaucoma suspects' who have had one week's treatment with carteolol and with timolol. Further work is needed to determine the reduction in pressure obtained over longer treatment periods, and, more important, to determine the long term effects of carteolol on the visual field of glaucoma patients. Until the initial studies on the effect of carteolol on differential light threshold are confirmed,⁶ carteolol, in terms of its ocular effect, does not appear to offer any significant advantage over timolol. In terms of the 12-hour control of intraocular pressure carteolol appears to be less effective than timolol.

References

- 1 Duff GR, Graham PA. A double-crossover trial comparing the effects of topical carteolol and placebo on intraocular pressure. *Br J Ophthalmol* 1988; 72: 27-8.
- 2 Kitazawa Y, Azuma I, Takase M, Komemushi S. Ocular hypotensive effects of carteolol hydrochloride in primary open angle glaucoma and ocular hypertensive patients. *Nippon Ganka Gakkai Zasshi* 1981; 85: 798-804.
- 3 Negishi C, Ueda S, Kanai A, *et al.* Effect of beta-blocking agent, carteolol on healthy volunteers and glaucoma patients. *Nippon Ganka Gakkai Zasshi* 1982; 85: 57-66.
- 4 Duff GR. A double-blind crossover study comparing the effects of carteolol 1% and 2% on intraocular pressure. *Acta Ophthalmol (Kbh)* in press.
- 5 Horie T, Takahashi O, Shirato S, Kitazawa Y. Comparison of ocular hypotensive effects of carteolol eye drops and timolol eye drops. *Jpn J Clin Ophthalmol* 1982; 36: 1065-70.
- 6 Flammer J, Drance SM. The effect of a number of glaucoma medications on the differential light threshold. In: Greve EL, Heijl A, eds. *Fifth international visual field symposium, Sacramento 1982*. The Hague: Junk, 1983: 153-6.

Accepted for publication 30 September 1987.