CLINICAL STUDY

Comparison of the cardiovascular effects of 2.5% phenylephrine and 10% phenylephrine during ophthalmic surgery

R. MALHOTRA, G. BANERJEE, W. BRAMPTON, N.C. PRICE

Purpose **The recommended concentration of topical phenylephrine for mydriasis is still a matter of debate. Our purpose was to compare the cardiovascular effects of 10% and 2.5% topical aqueous phenylephrine.**
Methods **We carried out a double-masked randomised study on 54 consecutive patients undergoing routine local anaesthetic cataract extraction, comparing the effects on blood pressure and heart rate of either 2.5% or 10% topical aqueous phenylephrine in combination with 1% topical aqueous tropicamide in those with no history of cardiovascular disease.**
Results **No difference was found in the rise in blood pressure produced by 2.5% and 10% topical aqueous phenylephrine. We also found no sustained changes in blood pressure or heart rate after instillation of either 2.5% or 10% topical aqueous phenylephrine.**
Conclusion **We recommend the routine use of 2.5% topical aqueous phenylephrine as a mydriatic agent during cataract surgery and acknowledge the role of 10% topical aqueous phenylephrine as an effective mydriatic agent in cases where 2.5% phenylephrine may not be so effective, such as in subjects with darkly pigmented irides.**

Key words Cataract surgery, Mydriasis, Phenylephrine, Sympathomimetic

Both 2.5% and 10% phenylephrine are used as topical mydriatic agents in combination with topical anti-cholinergic drugs such as 1% tropicamide in ophthalmic surgery. Systemic effects of phenylephrine, which is a sympathomimetic alpha-1 agonist, include peripheral vasoconstriction with a rise in systolic and diastolic blood pressure followed by reflex bradycardia with no inotropic or chronotropic effects.

It has been shown that commercial preparations of aqueous phenylephrine 2.5% and 10% have similar mydriatic effects in the general public and during cataract surgery.[1,2] However, during extracapsular cataract surgery topically applied 10% viscous phenylephrine has been shown to be more effective than 2.5% aqueous phenylephrine in maintaining mydriasis, especially in darkly pigmented irides, with no significant difference in mean blood pressure elevation between the two groups.[3]

One drop of topical 10% aqueous phenylephrine contains between 3.5 and 6.7 mg of the drug. Since in a young healthy adult the upper limit of safety for intravenous administration of phenylephrine is 1.5 mg, the rapid mucosal absorption by the conjunctiva may be at risk of causing excessive systemic effects, especially with repeated applications.[4] Systemic side effects that have been reported include severe hypertension, syncope, myocardial infarction, tachycardia, arrhythmias and fatal subarachnoid haemorrhage.[4,5]

The cardiovascular effects of 10% and 2.5% phenylephrine have been previously investigated with conflicting results. Chin *et al.*[6] showed that 2.5% and 10% topical aqueous phenylephrine produced a significant rise in blood pressure in previously non-hypertensive patients and no significant change in blood pressure in known hypertensive patients. However, no significant difference between the two groups (2.5% vs 10%) was shown.[6] Symons *et al.*[7] recently reported no significant change in the mean systolic and diastolic blood pressure in patients receiving 10% phenylephrine.

As many patients have cardiovascular disease we felt that a further study was needed to confirm that there was no recorded difference in the cardiovascular effects of 2.5% and 10% topical aqueous phenylephrine. We therefore undertook a prospective double-masked randomised study to investigate the effects on heart rate and blood pressure of both 2.5% and 10% topical aqueous phenylephrine in combination with 1% topical aqueous tropicamide during cataract extraction surgery.

R. Malhotra
G. Banerjee
N.C. Price
Department of Ophthalmology
Cheltenham General Hospital
Cheltenham, UK
W. Brampton
Department of Anaesthesiology
Cheltenham General Hospital
Cheltenham, UK
R. Malhotra ✉
Western Eye Hospital
Marylebone Road
London NW1 5YE, UK

Methods

Fifty-four consecutive patients electively undergoing cataract extraction during May and June 1996 were randomly selected. All patients were recruited with informed consent. The study was given approval by the local research ethics committee.

All patients with severe hypertension (systolic blood pressure greater than 190 mmHg and/or diastolic blood pressure greater than 105 mmHg), a known history of ischaemic heart disease (angina or myocardial infarction), cerebrovascular accidents, cardiac arrhythmias (including atrial fibrillation), cerebral or aortic aneurysms were excluded from the study.

All blood pressure and pulse measurements were taken using a Dinamap Vital Sign XL 9301 monitor that was calibrated by the Medical Physics Department at Cheltenham General Hospital. An appropriate cuff size was used for each patient by reference to the size range marked on it.

Prior to instillation of eye drops blood pressure and pulse were measured. Each subject was then randomised, in a double-masked manner, to receive three consecutive drops of either 2.5% phenylephrine (1.25 mg/drop) or 10% phenylephrine (5 mg/drop) together with 1% tropicamide and 0.5% chloramphenicol instilled into the lower conjunctival sac at 1 min intervals. Blood pressure and pulse rate were then measured at 10 min intervals. A pulse oximeter and intravenous access was established once the patient was brought to the anaesthetic induction room.

Due to practical limitations the time between the instillation of drops and the peribulbar injection was not fixed, but was approximately 15 min. A peribulbar regional anaesthesia block was given using 9 ml of 50:50 0.75% bupivacaine and 2% lignocaine with 1:200 000 adrenaline. No intravenous sedation was given at this stage; however, if due to anxiety a patient had required intravenous sedation they would have been excluded from the study. Patients then underwent phacoemulsification cataract extraction. Intraoperative pulse and blood pressure changes were monitored by the Dinamap Vital Sign XL 9301 monitor. Oxygen saturation and ECG changes were monitored by a Datex Cardiocap anaesthetic monitor. In the recovery room, blood pressure and pulse were monitored for up to 80 min in total.

Statistical analysis

To investigate the effect on peak blood pressure changes the maximum increase above control of the systolic and diastolic blood pressure during the 80 min following installation of the drops was compared between the two groups using an analysis of variance. In addition sustained changes in blood pressure and heart rate were investigated by comparing the mean change in systolic and diastolic pressure and pulse rate during the 20–80 min after instillation. Statistical significance was taken as $p \leq 0.05$.

Table 1. *Characteristics of patients: baseline values*

	2.5% Phenylephrine group ($n = 26$)	10% Phenylephrine group (n = 26)
Systolic BP (mmHg)	151.5 ± 17.5	149.3 ± 21 NS
Diastolic BP (mmHg)	80 ± 12.8	79.6 ± 14.5 NS
Heart rate (beats/min)	75.8 ± 11.1	74.3 ± 12.4 NS

Values are the mean ± SD.
BP, blood pressure; NS, not significant at $p \leq 0.05$.

Results

Fifty-four patients were recruited into the study, 56% ($n = 30$) of whom were female. The mean age was 76.1 years (range 55–87 years). Mean weight was not recorded for all patients; however, only patients with an acceptable body mass index (20–30 calculated using the formula: Weight (kg)/Height $(m)^2$) were selected.[8]

Twenty-eight patients received 2.5% phenylephrine and 26 patients received 10% phenylephrine. The incidence of hypertension in the two groups and baseline blood pressure and pulse rate values are shown in Table 1.

Power calculation showed there was a 96% chance of detecting a 20 mmHg difference in blood pressure between the two groups and an 81% chance of detecting a difference of 15 mmHg. There was no difference between the two groups in the mean peak systolic or diastolic blood pressure during the 80 min after instillation of the drops (Table 2). Nor was there any difference between the two groups in the mean change in systolic blood pressure, diastolic blood pressure or heart rate from the baseline during the period 20–80 min after instillation of drops.

As there was no difference between the two groups they were combined for further analysis of mean systolic blood pressure, diastolic blood pressure and heart rate of the whole sample during the period of 20–80 min after instillation of drops. This found no difference when compared with the baseline values (Table 3).

Retrospective analysis of our data found 59% of patients to be hypertensive (9 men, 11 women). Hypertensive patients were defined either as those known to be hypertensive on oral treatment or as those having a baseline systolic pressure greater than 160 mmHg and/or diastolic pressure greater than 95 mmHg.

None of the patients required sedation nor developed severe hypertension or any other untoward event during the intraoperative or post-operative period.

Table 2. *Mean peak rise in systolic blood pressure and diastolic blood pressure during the 80 min after instillation of drops*

	10% Phenylephrine group ($n = 26$)	2.5% Phenylephrine group ($n = 28$)
Systolic BP (mmHg)	18.9 ± 11.2	14.1 ± 11.2 NS
Diastolic BP (mmHg)	9.2 ± 6.6	8.1 ± 6.3 NS

Values are the mean ± SD. NS, not significant at $p \leq 0.05$.

Table 3. *Average change in mean value from baseline during the 20–80 min after instillation of drops*

	Change
Systolic BP (mmHg)	4.3 ± 8.9 NS
Diastolic BP (mmHg)	1.1 ± 6.8 NS
Heart rate (beats/min)	−1.0 ± 6.8 NS

Values are the mean ± SD. NS, no significant difference between these changes and baseline values at $p \leq 0.05$.

Discussion

This study has shown no difference in the rise in blood pressure produced by 2.5% or 10% topical aqueous phenylephrine. In addition there were no sustained changes in blood pressure after instillation of either concentration of phenylephrine.

Whilst 2.5% phenylephrine provides a quarter of the potential systemic dose of the 10% preparation, this study did not show any difference in systemic cardiovascular effects. Peak systolic and diastolic blood pressures were not significantly different for the two concentrations nor was there any sustained change in blood pressure or pulse rate compared with baseline, showing minimal systemic effects in the group as a whole.

The assumption that any rise in blood pressure during surgery is due in some part to phenylephrine is based on the findings of Chin *et al.*,[6] who showed that patients undergoing cataract extraction under local anaesthetic without topical phenylephrine had no rise in blood pressure compared with the group that received either 2.5% or 10% topical aqueous phenylephrine.

The local anaesthetic administered contained adrenaline at a low concentration of 1:200 000. We do not believe that any effect due to phenylephrine would be masked for two reasons. Firstly the concentrations are too low for any significant systemic effect, and secondly the same dose was administered to both groups thereby avoiding any bias.

We have demonstrated that, when combined with tropicamide, neither strength of phenylephrine will routinely cause excessive or prolonged cardiovascular changes. As both strengths of phenylephrine are equipotent mydriatics in most patients, we recommend the routine use of the 2.5% solution during cataract surgery. However, we acknowledge the role the 10% solution in cases where 2.5% phenylephrine may not be so effective, such as in subjects with darkly pigmented irides.

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