A COMPARATIVE STUDY OF THE EFFICACY OF 2.5% PHENYLEPHRINE AND 10% PHENYLEPHRINE IN PRE-OPERATIVE MYDRIASIS FOR ROUTINE CATARACT SURGERY

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SUMMARY

It is common practice in many ophthalmic units to administer multiple applications of 10% phenylephrine in combination with an anti-cholinergic agent to ensure adequate pupil mydriasis prior to routine cataract surgery. Phenylephrine is a pure α-1 adrenoreceptor agonist known to produce marked systemic vasoconstriction and associated hypertension with occasional profound reflex bradycardia. Many reviews have suggested caution in the use of 10% phenylephrine in the elderly or hypertensive patient. In a prospective, randomised trial we have assessed pupil dilation comparing the efficacy of 10% phenylephrine (53 patients) versus 2.5% phenylephrine (62 patients). When administered in conjunction with 1% cyclopentolate four times over 1 hour pre-operatively, 2.5% phenylephrine was found to be as effective as 10% phenylephrine in the initiation and maintenance of mydriasis during both extracapsular and phacoemulsification cataract extraction.

Phenylephrine acts almost exclusively as a direct α-1 adrenoreceptor agonist and is routinely used to ensure effective pre-operative mydriasis in cataract surgery. In our experience the 10% solution of phenylephrine (Minims) is commonly administered in conjunction with an anti-cholinergic agent (e.g. 1% cyclopentolate) on four occasions over 1 hour pre-operatively. This combination of drugs is thought to ensure maximal stimulation of dilator pupillae while paralysing constrictor pupillae, in the hope of maintaining mydriasis throughout cataract extraction and lens implantation.

The *British National Formulary*[1] recommends caution in the use of 10% phenylephrine in elderly patients and those with hypertension. The Association of British Pharmaceutical Industries,[2] in describing the product licence for phenylephrine, states that the 10% phenylephrine solution is contraindicated in the elderly and in the hypertensive patient even if normotensive on medication. The maximum recommended dose in any patient is one drop per hour.

Our intention in this study was to assess whether the use of 2.5% phenylephrine in pupil dilation prior to routine cataract surgery resulted in a less effective initiation or maintenance of mydriasis per-operatively when compared with the 10% phenylephrine solution.

PATIENTS AND METHODS

One hundred and fifteen patients were operated on by one of four consultant surgeons over a 10 day period as part of a waiting list initiative. Patients presenting for surgery were pre-selected to exclude those with a history of ocular inflammation, pupil abnormality or previous surgery to that eye. All patients in this study were of Caucasian origin with mean age of 77.7 years (range 57–94 years).

All patients received four standard 'Minim' drops of both aqueous phenylephrine and 1% cyclopentolate during the 1 hour preceding surgery. Patients were randomised to receive either 10% phenylephrine (53 patients) or 2.5% phenylephrine (62 patients). Surgery was carried out after peribulbar anaesthesia using a combination of lignocaine, bupivacaine and sodium hyaluronidase. Every patient undergoing phacoemulsification had adrenaline 1:1 000 000 added to the irrigation fluid used per-operatively (Table I). Adrenaline was not added to the infusion fluid of those patients undergoing extracapsular cataract extraction.

All pupil measurements were made by the surgeon with callipers viewed through the operating microscope. The surgeon measuring the pupil diameter

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Table I. Number of patients in each study group

	10% phenylephrine	2.5% phenylephrine
Phacoemulsification	23	20
Extracapsular	30	42
Total	53	62

was not aware of the pre-operative mydriatic drop regime used. Pupil measurements were made immediately before surgery and then repeated following aspiration of lens cortex immediately prior to insertion of the intraocular lens into the capsular bag.

RESULTS

Scattergrams of pre-operative versus post-cortex aspiration pupil diameters are shown in Fig. 1a and 1b for those patients undergoing phacoemulsification, and in Fig. 1c and 1d for those patients undergoing extracapsular cataract extraction.

Table II presents results for mean pre-operative pupil diameter and mean decrease in per-operative pupil diameter. The mean pre-operative pupil diameter achieved in the group of patients receiving 2.5% phenylephrine was 8.0 mm and in those receiving 10% phenylephrine was 8.2 mm. The mean decrease in pupil size per-operatively is presented separately for phacoemulsification and extracapsular techniques. When analysed using Student's *t*-test no statistically significant difference was found between the 10% phenylephrine and 2.5% phenylephrine groups ($p<0.05$) for either phacoemulsification or extracapsular techniques.

The number of patients failing to achieve or maintain a pupil diameter of 6 mm is also shown in Table II. A slightly greater number of patients in the 2.5% phenylephrine group failed to achieve or maintain a pupil diameter of 6 mm. When analysed using the chi-squared test no statistically significant difference was found between the 10% phenylephrine and 2.5% phenylephrine groups ($p<0.05$).

DISCUSSION

In a randomised, prospective trial we have demonstrated that there appears to be no significant difference in the ability of 2.5% and 10% phenylephrine to initiate and maintain pupil mydriasis in both phacoemulsification and extracapsular methods of uncomplicated cataract extraction and lens implantation.

Phacoemulsification causes less operative miosis than extracapsular surgery but it was not determined in this trial whether this was due to decreased iris

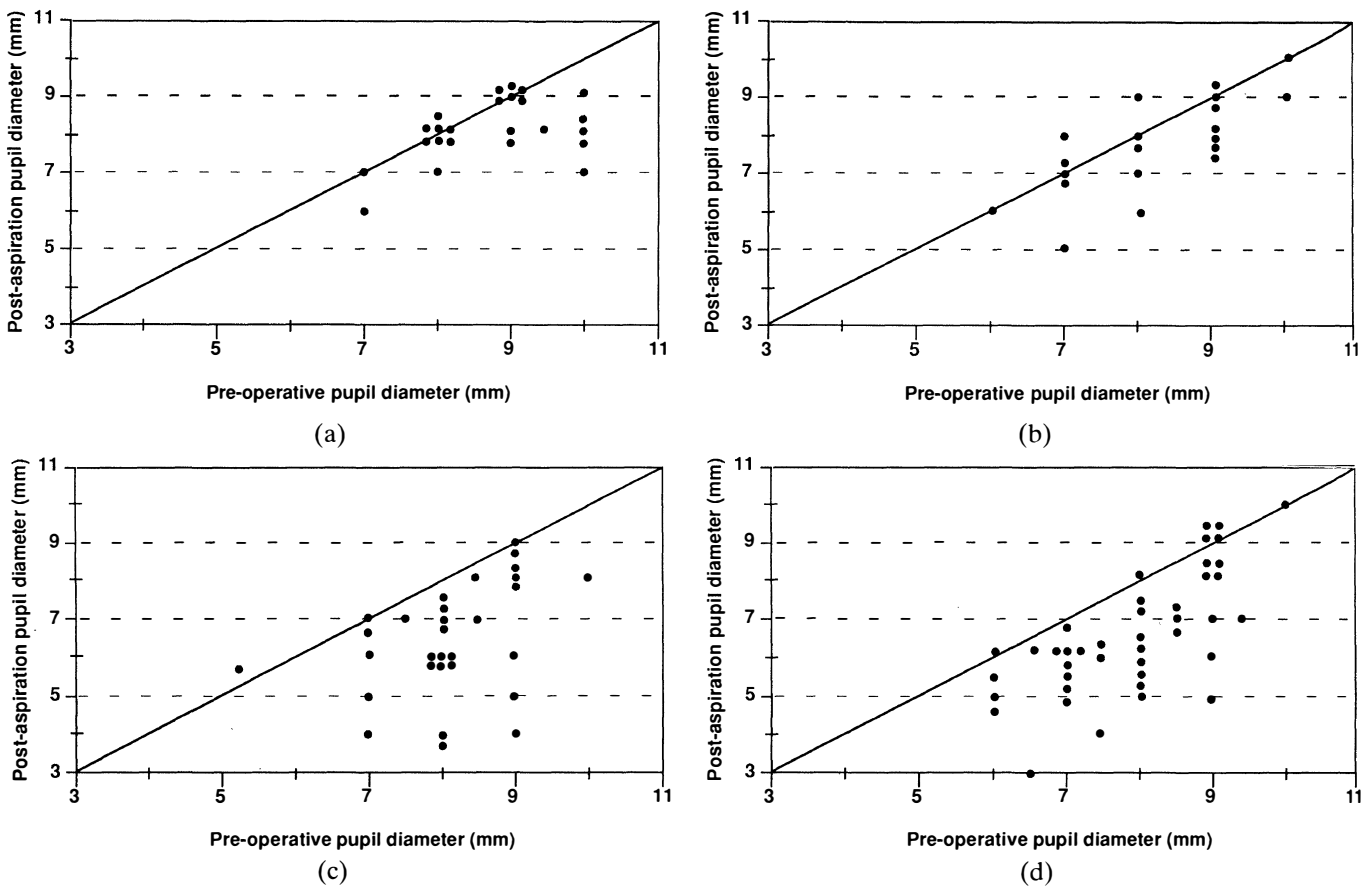

Fig. 1. *Graphical representation of the pre- and per-operative pupil diameters in the four groups of patients: (a) phacoemulsification, 10% phenylephrine; (b) phacoemulsification, 2.5% phenylephrine; (c) extracapsular extraction, 10% phenylephrine; (d) extracapsular extraction, 2.5% phenylephrine.*

Table II. Results for 10% phenylephrine and 2.5% phenylephrine groups

	10% phenylephrine (n = 53)	2.5% phenylephrine (n = 62)
Mean initial pupil size (mm)	8.2	8.0
Mean pupil decrease (mm)		
Phacoemulsification	0.6	0.4
Extracapsular	1.5	1.4
No. pupils initially dilating to 6 mm or less	1	5
No. pupils with decrease to ≤6 mm		
Phacoemulsification	1	3
Extracapsular	15	23

Analysis using chi-squared or Student's t-test demonstrated no statistically significant difference between the groups for each parameter shown ($p<0.05$).

trauma, in particular the avoidance of nucleus expression, or the routine use of adrenaline in the infusion fluid during phacoemulsification – which has been demonstrated elsewhere to maintain mydriasis during cataract extraction.[3] A pupil diameter of 6 mm was considered a clinically relevant size, suitable for comparison of results between the two groups, since below this diameter it becomes impossible to perform a continuous curvilinear capsulorhexis of 6 mm under direct vision. A measured capsulorhexis diameter of 6 mm is subject to corneal magnification and approximates to an actual diameter of 5.0–5.5 mm. We feel this is the minimum size required to facilitate insertion of a non-foldable 5.5 mm intraocular lens as used in phacoemulsification.

Systemic absorption of many drugs applied topically to the conjunctival sac is known to occur via both the conjunctival capillaries and, after passage through the nasolacrimal duct, the nasal mucosa.[4] The predominant α-agonist action of phenylephrine causes a generalised peripheral vasoconstriction with associated elevation of systemic blood pressure and occasionally a marked reflex bradycardia. Many reports exist of adverse systemic reactions to topical 10% phenylephrine through its action on the cardiovascular system, and a few reports exist of cardiovascular reactions to 2.5% phenylephrine.[5]

A review of reported adverse reactions by Fraunfelder *et al.*[6] identified 39 cases of significant reactions to 10% phenylephrine including 15 myocardial infarctions, 11 of which were fatal. Although no proven causal relationship was demonstrated, both the authors and the surgeons who reported the individual cases felt that there was a high probability of the use of 10% phenylephrine contributing to the subsequent cardiovascular event reported. Most adverse reactions occurred approximately 20 minutes after application of the phenylephrine. Other case reports of adverse reactions to 10% phenylephrine include hypertension and cerebrovascular accidents,[7–10] ventricular arrhythmia[11] and sub-arachnoid haemorrhage.[12]

A single 'Minim' eyedrop (approx. 35–50 μl) of 10% phenylephrine contains at least 3.5 mg of active drug (Chauvin Pharmaceuticals Ltd). If used in the treatment of acute hypotension the upper limit of safety for a systemic dose of phenylephrine, in a young adult, has been reported as 1.5 mg by slow intravenous infusion or 10 mg subcutaneously.[1,13] Drugs applied to the conjunctiva are thought to be systemically absorbed almost as rapidly as the equivalent dose given intravenously. Therefore the routine application of four drops of 10% phenylephrine can potentially result in an elderly person receiving up to 9 times the maximum recommended dose of phenylephrine for a young adult. Plasma drug levels following topical administration have been measured by Kumar *et al.*[14] and found to be significantly higher at 20 minutes following application in those receiving 10% as opposed to 2.5% phenylephrine.

Extra caution is required in those taking tricyclic anti-depressants or monoamine-oxidase inhibitors since both drug types are known to potentiate the action of phenylephrine. The 10% phenylephrine solution also causes greater discomfort on application than the 2.5% solution.[15]

A study by Duffin *et al.*[16] of 44 patients receiving 2.5% or 10% phenylephrine prior to extracapsular surgery demonstrated no significant difference in pre-operative mydriasis between the two concentrations regardless of iris colour. This study did, however, find a significant increase in operative miosis in those patients with very darkly pigmented irises if 2.5% phenylephrine was used. Other studies[17,18] assessing pupil dilation for diagnostic purposes tend to support our findings, with no benefit being gained by the use of 10% as opposed to 2.5% phenylephrine. Most patients in our study were elderly Caucasians and it is possible that younger patients, particularly those with a heavily pigmented iris, would demonstrate a greater mydriatic response to the 10% phenylephrine solution.

The infrequency of reported reactions to 10% phenylephrine may be due partly to the fact that maximum plasma concentration of the drug following topical administration occurs 20 minutes after application and then decreases rapidly.[15] In our experience 20 minutes after application of

phenylephrine drops, prior to cataract surgery, most patients would still be on the ophthalmic ward with a minimum of monitoring, allowing hypertensive reactions to pass unnoticed. Phenylephrine also causes marked local vasoconstriction which helps to limit systemic absorption.

The use of topical 10% phenylephrine is already considered to be contraindicated in the newborn due to its systemic hypertensive action,[19,20] and we believe that its use is no longer justified on a routine basis in pupil dilatation prior to uncomplicated cataract surgery in the elderly. We suggest that the use of the commonly available 2.5% solution of aqueous phenylephrine allows a quarter of the potential systemic dose to be given with no significant decrease in degree of mydriasis obtained in most cases.

Key words: Cataract, Mydriasis, Phenylephrine.

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