ORIGINAL ARTICLE

Phenylephrine Eye Drops in Ophthalmic Surgery - A Clinical Study on Cardiovascular Effects

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Summary

Phenylephrine in concentrations of either 2.5% or 10% is widely used as a mydriatic agent in ophthalmic surgery. Its potential cardiovascular effects are seldom recorded as ophthalmic surgery is not usually monitored by an anaesthetist. A prospective randomised double blind study was carried out in 89 consecutive cases of uncomplicated cataract surgery in the presence of an anaesthesiologist ensuring the continuous monitoring of blood pressure, heart rate, electrocardiography and pulse oximetry. All these patients were given a drop of either normal saline, 2.5% or 10% phenylephrine in addition to mydriacyl prior to surgery. Blood pressure readings were found to be significantly higher in non-hypertensive patients receiving phenylephrine at the start of the operation and at five, 10, 15 and 20 minutes intra-operatively and the first three hours post-operatively. Blood pressure readings in hypertensive patients, on the other hand, were also found to increase after phenylephrine administration, though not statistically significant. 10.3% of the 10% phenylephrine group and 3% of the 2.5% phenylephrine group required intraoperative intravenous hypotensive agent to control the blood pressure. There were no arrhythmias or ischaemic changes observed intraoperatively. None of the patients complained of palpitation, headache or chest discomfort. There was no oxygen desaturation observed. We concluded that significant hypertensive effects can arise after phenylephrine eye drop administration. Hence, it should be used cautiously with intraoperative monitoring of the cardiovascular status during cataract surgery.

Key Words: Sympathomimetic, Phenylephrine, Cataract extraction

Introduction

The cardiovascular effects of phenylephrine applied topically was first described by Heath[1] He applied the drug in powder form to the dog cornea and found a sudden and marked increase in systemic blood pressure. Subsequently, extensive reports had been published regarding marked increases in blood pressure, syncope, myocardial infarction, tachycardia, arryhthmia, acute pulmonary edema and fatal subarachnoid haemorrhage after topical application of phenylephrine[2-8]. However most of these are anecdotal reports. A review of the literature revealed few randomised controlled studies on phenylephrine during cataract surgery[9]. The extent of cardiovascular stimulation and

its prevalence when used during cataract surgery remained ill-defined. Therefore we designed a randomised double blind prospective study comparing the pressor effects of 2.5% and 10% phenylephrine.

Material and Methods

Eighty-nine consecutive patients undergoing cataract extraction were enlisted into the study. All patients with known history of cerebrovascular accidents, myocardial infarction, cerebral or aortic aneurysms were excluded from this study. Informed consent was obtained from the patients or their immediate relatives one day before the procedure.

All patients received premedication comprising Tab Diazepam 5 mg one hour prior to surgery whilst in the wards. A drop of mydriacyl was instilled into the lower conjuctival sac at this time. The patients were then brought into the operating room where intravenous lines and monitors were set up. The monitors included the following: a Critikon Dinamap tm 1846sx vital signs monitor with recording of blood pressure and pulse rate with a printout set at five minute intervals, continuous electrocardiographic monitoring by Siemens Sirecust 404-1 ECG monitor with CM5 leads for detection of ischaemia or arryhthmia, and a pulse oximeter (Omeda Biox 3700e). The baseline blood pressure and pulse rate readings were taken.

An O'Brien facial nerve block and a retrobulbar regional anaesthesia were given, using 1.5% plain lignocain, by either the surgeon or anaesthetist. A drop of either 0.9% saline, 2.5%(1.25mg of phenylephrine/drop) or 10% phenylephrine (5mg of phenylephrine/drop) was randomly assigned and instilled into the eye about five minutes before the start of surgery by an assistant in a double blind fashion. All procedures were performed by the same surgeon. Any intraoperative ECG changes or oxygen desaturations were recorded.

Intravenous hydrallazine in 5mg incremental doses was administered in cases of severe hypertension which is defined as a sudden increase of 20% or more above the baseline. In the recovery room, blood pressure and pulse rate were monitored at an hourly interval for three hours and the same repeated the next day. The patients were instructed to complete a questionnaire one day after the procedure. Specific questions in relation to symptoms of palpitation, headache and chest discomfort were asked.

All data obtained were stored in a Lotus programme and analysed using Student's t-test, Chi-square test with Yate's correction and ANOVA where appropriate. Differences were considered significant if the probability value was less then 0.05.

Results

Eighty-nine patients were enlisted into the study. Male to female sex ratio was 1:1.1. Mean age was 69.7 years (range 45-91 years). Mean body weight for 2.5% group was 50.5 kg (range 40-65 kg) and for 10% group was 52 kg (range 42-67 kg). Based on baseline blood pressure recordings, patients were classified as hypertensive if systolic pressure exceeded 160 mmHg and/or diastolic pressure exceeded 95 mmHg. Patients were allocated to either 0.9% saline, 2.5% or 10% phenylephrine group (Table I). The 2.5% group received 0.024mg/kg and 10% group 0.096mg/kg of phenylephrine respectively.

Mean baseline systolic and diastolic blood pressure and pulse rates were not significantly different for the three treatment groups within their respective blood pressure classifications as defined by ANOVA, hence demonstrating the effectiveness of randomisation. Unpaired t-test did not reveal any statistical significance between both sexes.

Analysis of variance showed a significantly higher systolic blood pressure at the start of surgery and at five, 10, and 15 minutes and at one, two and three hours post-operatively for the non-hypertensive group. Systolic pressures for the hypertensive group were also higher for the phenylephrine groups as compared to the control group. However, no statistical significance could be attached to it. (Table II)

Table I
Patients data

	Non-hypertensives	Hypertensives	Total
Normal saline group	17	13	30
2.5% phenylephrine group	14	15	29
10% phenylephrine group	15	15	30

Table II
Mean systolic blood pressure for three treatment groups: hypertensive and non-hypertensive patients
(P value for significance between groups)

	Mean Systolic Blood Pressure							
	Non-Hypertensive				Hypertensive			
	0%	2.5%	10%	P	0%	2.5%	10%	P
Base	137.7	143.6	149.3	NS	166.8	179.1	177.1	NS
O'	131.0	146.9	155.0	<0.05	153.8	173.8	180.1	NS
5'	133.0	150.6	158.1	<0.05	156.2	174.2	185.0	<0.05
10'	134.9	150.6	160.7	<0.05	163.4	178.1	144.6	NS
15'	140.7	151.7	169.5	<0.05	170.7	182.7	182.4	NS
20'	137.3	150.3	166.1	NS	170.6	181.7	188.7	NS
1 Hour	118.1	139.4	134.2	<0.05	144.8	142.9	152.6	NS
2 Hours	117.9	129.6	135.3	<0.05	148.1	140.0	142.2	NS
3 Hours	117.8	138.9	130.9	<0.05	136.7	138.3	140.3	NS
1 Day	138.9	144.2	136.1	NS	150.0	158.2	136.7	NS

NS: Statistically not significant

Table III
Mean diastolic blood pressure for three treatment groups: hypertensive and non-hypertensive patients
(P value for significance between groups)

	Mean Diastolic Blood Pressure							
	Non-hypertensive				Hypertensive			
	0%	2.5%	10%	P	0%	2.5%	10%	P
Base	79.0	80.1	83.1	NS	91.1	93.5	93.7	NS
O'	74.3	77.1	81.1	NS	85.4	93.3	93.4	NS
5'	73.9	78.3	81.6	NS	81.1	92.2	100.0	<0.05
10'	75.6	79.2	80.5	NS	80.2	96.0	97.3	NS
15'	77.6	80.2	84.1	NS	88.9	98.4	96.7	NS
20'	76.7	82.0	88.9	<0.05	89.6	99.5	96.2	NS
1 Hour	78.4	81.4	82.5	NS	83.8	84.3	91.4	NS
2 Hours	74.8	80.0	80.9	NS	87.5	83.6	82.7	NS
3 Hours	75.4	81.7	80.9	NS	82.3	85.0	84.3	NS
1 Day	79.4	78.3	75.3	NS	81.0	88.2	83.3	NS

NS: Statistically not significant

Significantly higher diastolic pressure readings were obtained for the phenylephrine groups at five minutes for the hypertensive patients, and at 20 minutes for the non-hypertensive patients. No significant difference was found in the intraoperative and post-operative diastolic pressures for both the hypertensive and non-hypertensive groups at the other time intervals. However, readings for the phenylephrine treated groups tend to be higher than the control group. (Table III).

While pulse rates tend to be higher in the phenylephrine groups, statistically significant difference was not obtained in the intraoperative period (Table IV). In the phenylephrine groups, 42 patients had more than 10 mmHg systolic blood pressure elevation. Seventy-four per cent of these patients had maximum systolic blood pressure changes 10-20 minutes after the administration of phenylephrine eye drops.

None of the patients within the control group developed severe hypertension during surgery. Four of the 30 patients in the 10% group and one of the 29 patients in the 2.5% group developed severe hypertension which required intravenous hydrallazine for management. All these five patients had baseline hypertension.

There were no intraoperative arrhythmia or ischaemia observed in all patients. None of the patients had oxygen desaturation or complained of palpitation, headache or chest pain.

Table IV
Mean pulse rate for three treatment groups: hypertensive and non-hypertensive patients
(P value for significance between groups)

	Mean Pulse Rate							
	Non-hypertensive				Hypertensive			
	0%	2.5%	10%	P	0%	2.5%	10%	P
Base	74	71	77	NS	70	78	74	NS
O'	68	69	73	NS	68	76	77	NS
5'	68	71	74	NS	69	76	73	NS
10'	70	71	76	NS	68	78	78	NS
15'	72	73	77	NS	70	80	78	NS
20'	69	72	76	NS	70	79	77	NS
1 Hour	74	77	80	NS	78	80	87	<0.05
2 Hours	72	78	81	<0.05	77	80	84	NS
3 Hours	73	80	80	NS	79	77	86	<0.05
1 Day	72	74	78	NS	74	82	83	NS

NS: Statistically not significant

Discussion

Phenylephrine HCL is a direct acting synthetic sympathomimetic amine. It acts mainly on the alpha-adrenergic receptors with minimal effects on the beta-receptors. Its peripheral alpha effects result in peripheral vasoconstriction causing a rise in both the systolic and diastolic blood pressure when given parenterally. Therefore it is used in the management of hypotension and shock. In ophthalmology this topical sympathomimetic amine is used as a vasoconstrictor and a mydriatic.

A significant amount of topically applied phenylephrine can be absorbed into the circulation via the conjuctival and episcleral vessels and the nasal and oral mucosa. Plasma drug level from musocal absorption can rise as rapidly as intravenous administration as evidenced by reports of marked increase in blood pressure, syncope, myocardial infarction, tachycardia, arrhythmia, acute pulmonary edema and fatal subarachnoid haemorrhage occurring in patients given topical administration of phenylephrine[2-8].

Our study has demonstrated that both the 2.5% and 10% solutions could cause cardiovascular stimulation. The 2.5% solution seems to be as capable as the 10% solution to cause excessive increase in blood pressure as shown in this and other studies[10].

The period of maximal systolic blood pressure rise is around 10-20 minutes after the administration of phenylephrine which corresponds to the time of maximal plasma phenylephrine level as demonstrated by other authors[11]. Therefore, care should be taken in the pre-operative period within

minutes after application of the topical phenylephrine to observe for any cardiovascular stimulation that may occur during this period which is usually not monitored by the anaesthetist inspite of the adverse effects.

There is still a definite role for phenylephrine in maintaining pupil diameter during cataract surgery. In view of its potential cardiovascular effects, monitoring during ophthalmic operation is strongly recommended.

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