Original Article

Hemodynamic Alterations With 5% Phenylephrine Eye Drops In Normotensive And Hypertensive Patients Undergoing Cataract Surgery: A Prospective Study

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Abstract

Adequate pupillary dilatation is the prerequisite for ophthalmic examination and surgical procedures. Routinely administered topical phenylephrine is said to cause systemic adverse cardiovascular effects.

Aim

Through our study, we intended to determine the hemodynamic effect of topical phenylephrine (5%) in normotensive and hypertensive patients perioperatively.

Method

The study included 450 patients of ASA Gr I and II undergoing cataract surgery under local anesthesia. They were divided into two groups of normotensive and hypertensive (on medication) patients. These patients were administered with only three drops of topical tropicamide and phenylephrine drug at fixed intervals and the hemodynamic [heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure(MAP)] parameters were monitored perioperatively.

Results

The demographic data were comparable between the groups. We observed slight increase in the mean SBP and MAP in both the groups from the base values and between the groups. The difference was statistically significant but within the permissible limits clinically. Statistically insignificant ($p < 0.05$) variation was observed for mean HR and DBP at various levels from the baseline values and also between the groups. None of the patients in both the groups experienced adverse effects.

Conclusion

Topical phenylephrine (5%) was observed to be safe hemodynamically and effective for pupillary dilatation both in hypertensive and normotensive patients. Avoiding frequent and multiple instillations of the drug and considering hemodynamic monitoring perioperatively is recommended.

Key Words: cataract surgery, mydriasis, phenylephrine, topical, heart rate, blood pressure.

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Introduction

Pupillary dilatation is necessary for patients coming to OPD for ophthalmic examination and for most of the eye surgeries. Phenylephrine hydrochloride and tropicamide is the popular combination used for pupillary dilatation. Tropicamide is a short acting anticholinergic agent used as mydriasis and cycloplegic whereas phenylephrine hydrochloride is a sympathomimetic drug used as mydriatic (without cycloplegia), vasoconstrictor and decongestant. Tropicamide alone cannot provide adequate dilation so the concentration of phenylephrine up to 10% is used in combination. Solutions of 2.5% and 10% of phenylephrine that were used before showed side effects due to systemic absorption, this is why 10% strength was used with caution. Systemic side effects are same as sympathomimetic effects such as tachycardia, arrhythmias, hypertension, headache, sweating, faintness, trembling and pallor.[1] Patients with cataract visiting ophthalmic OPD are above 50 years of age and amongst which 40 % will be with primary hypertension.[2]

The studies that are available in the literature describe about a rise in the blood pressure with topical phenylephrine. The rise in systolic blood pressure (SBP) by 20-40 mmHg and diastolic pressure(DBP) by 10-20mmHg in hypertensive patients with 5% phenylephrine was observed in one study.[1] Whereas, another study mentions about an insignificant increase in blood pressure(BP) both in normotensive and hypertensive patients.[3] There was a need for a larger study with a standardised perioperative procedure and monitoring to reach to a final conclusion about contradictory views.1 In ophthalmic or optometric practice, neither the heart rate (HR) nor the BP is routinely monitored before the administration of topical phenylephrine, which adds to the list of adverse effects of the drug being used. The effect of topical 5% phenylephrine on haemodynamics during the perioperative period was carefully studied in large number of patients (hypertensive and normotensive) undergoing cataract surgery.

Methods and materials

A prospective randomised controlled study was conducted in our hospital after the approval of institutional ethics committee. The study was conducted on 450 patients of ASA Gr I and II who were posted for cataract surgery, between the age of 35-65 years, normotensive and hypertensive (controlled hypertension with BP of < 160/100mm Hg and or on medication) patients and those willing to participate in the study. Patients with complicated cataract, glaucoma, morbid obesity, hypertension (>160 SBP and >100 DBP), secondary hypertension, pregnancy induced hypertension and other cardiovascular diseases were excluded from the study. Those on medications like atropine, βeta blockers and TCA depressants were also not considered. The patients were divided into two groups: **Group I** - 225 normotensive patients. **Group II** - 225 hypertensive patients.

A day prior to the surgery, preoperative visit was made and pre-anesthetic checkup was done. On the day of surgery, patients were checked for basal heart rate (HR) and blood pressure [Systolic Blood Pressure (SBP), Diastolic blood pressure (DBP) and Mean arterial pressure (MAP)] in the supine position in the preoperative room. The commercially available combination of 0.8% w/v tropicamide and 5% w/v phenylephrine was administered to the concerned eye on the lower conjunctival fornix 1 hour before the surgery. The topical instillation was repeated every 15 min for a total of three drops only. A drop of non-steroidal anti-inflammatory agent flubiprofen 0.03% was instilled after each mydriatic drops in all the patients. This is a non mydriatic drug but helps to keep the pupil dilated during surgery. This drug does not affect the results of the study keeps the pupil dilated during surgery. The hemodynamic data were recorded by the electronic monitor and the same monitor was used till the end of the study. Observed data were noted at 5, 10, 15, 20, 30 min and at 1, 2 and 3 hrs.

Minimum of 6mm of pupillary dilation was considered adequate for the study and no extra irrigation with adrenaline was used to keep the pupil mydriatic. Once the adequate pupillary dilation was achieved, peribulbar block was given with a fixed combination dose of lidocaine and bupivacaine without any adrenaline for all the patients. Monitoring of heart rate, blood pressure was continued throughout the surgery and postoperative period.

Any side effects like headache, dizziness, palpitation, tremors and nausea or vomiting were also noted post-operatively.

Statistics

Kolmogorov - Smirnov test was performed to confirm the normal distribution of the data. Numerical data were presented as Mean ± SD. Demographic data like age, height and weight were analyzed by two sample't' test and gender of the patients by Chi-square test. Hemodynamic data of the two groups were compared by ANOVA repeated measures. The categorical data analyzed by Chi-square test and P values of <0.05 was considered as statistically significant. The analysis was performed by NCSS (10) statistical software.[6]

Results

Table 1: Demographic variables

	Group I	Group II	P.VALUE
Age (Mean ± SD)	59.68 ± 9.98	60.80 ± 8.93	0.21
Weight (Mean ± SD)	153.80 ± 8.54	153.65 ± 9.23	0.86
Height (Mean ± SD)	55.28 ± 13.55	57.66 ± 12.64	0.26
Sex (M/F)	107/118	121/104	0.61

***P value ≤ 0.05 is significant**

The demographic data from the patients of two groups are summarised in table 1 and are found to be comparable between the groups.

Table 2 summarises the hemodynamic changes in both the groups during the study period. HR and DBP values were comparable at all the intervals during the study period. SBP and MAP values have shown statistically significant difference at the baseline time and at all the intervals.

Table 2: Heart Rate and Blood Pressure (n= 225) Mean ± SD

Time	Heart Rate			Systolic Blood Pressure			Diastolic Blood Pressure			Mean Blood Pressure		
	Group I	Group II	P value	Group I	Group II	P value	Group I	Group II	P value	Group I	Group II	P value
BS	77.26±13.51	78.62±14.94	0.33	121.51±18.32	128.84±19.93	0.00*	73.25±10.63	75.03±10.07	0.01*	87.54±13.14	91.28±13.21	0.00*
5 MIN	78.94±14.08	77.71±14.59	0.36	123.86±19.07	130.88±19.96	0.00*	75.35±10.72	76.46±09.93	0.26	88.81±13.57	93.71±14.15	0.00*
10 MIN	78.27±14.43	77.11±14.91	0.41	121.39±19.86	128.99±19.61	0.00*	73.84±10.64	75.39±09.92	0.11	87.99±13.56	92.42±13.52	0.00*
15 MIN	77.33±14.13	75.78±14.28	0.23	122.39±18.29	128.28±19.86	0.00*	73.26±10.33	74.82±10.31	0.11	87.36±13.07	90.30±12.84	0.01*
20 MIN	76.79±13.59	75.94±14.84	0.45	121.22±18.49	128.16±19.61	0.00*	73.49±10.42	74.72±10.29	0.21	86.99±13.41	90.73±12.91	0.00*
30 MIN	76.21±13.31	74.85±14.16	0.29	121.76±17.56	127.85±20.11	0.00*	73.14±09.47	74.39±10.16	0.18	86.45±12.62	90.12±13.35	0.00*
1 HOUR	75.82±14.07	74.36±14.57	0.28	124.99±18.80	129.61±19.86	0.00*	74.84±10.53	74.27±10.49	0.83	87.62±13.15	89.99±14.77	0.07
2 HOURS	75.41±14.35	75.84±14.62	0.35	127.81±18.22	134.41±19.55	0.00*	75.28v10.61	75.51±10.85	0.83	88.11±11.84	90.21±12.21	0.02*
3 HOURS	76.26±13.69	76.07±13.81	0.91	128.33±17.73	134.62±19.01	0.00*	76.49±10.44	77.54±10.51	0.31	88.97±12.34	92.21±12.81	0.01*

***P value ≤ 0.05 is significant.**

The mean rise in the heart rate was one beat per minute in group I and a drop of 4 beat per minute in group II from the base values (Fig 1).

SBP increased by 7 mm Hg in group I and 6 mm Hg in group II (Fig. 2).

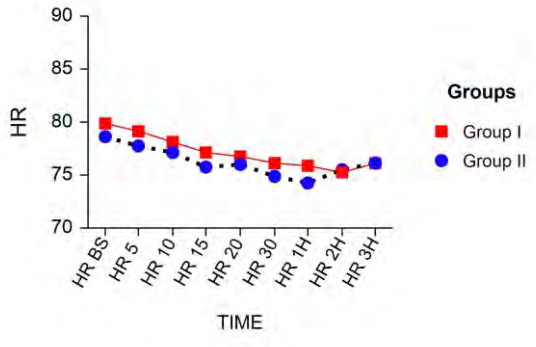

Figure 1 Heart rate per minute observed in the two groups

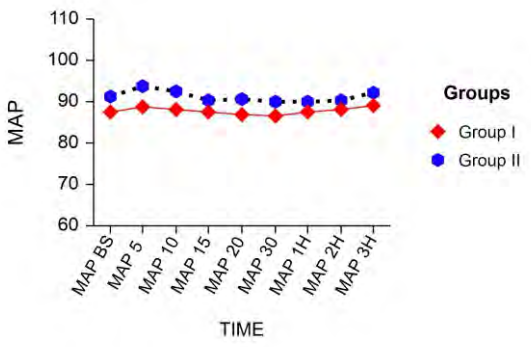

Figure 2 Systolic blood pressure measured in the two groups

The variation in DBP was 3mmHg and 2 mm Hg in group I and group II, respectively from the base values (Fig. 3).

MAP values varied by only 1 mm Hg in both the groups (Fig. 4).

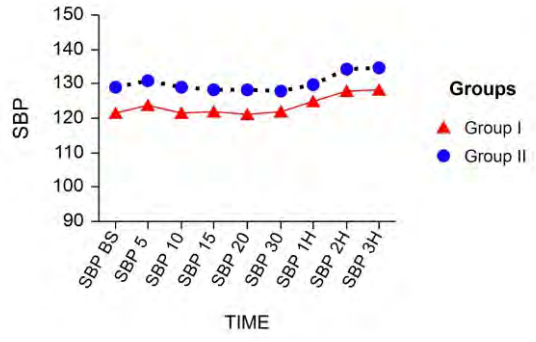

Figure 3 Diastolic blood pressure measured in the two groups

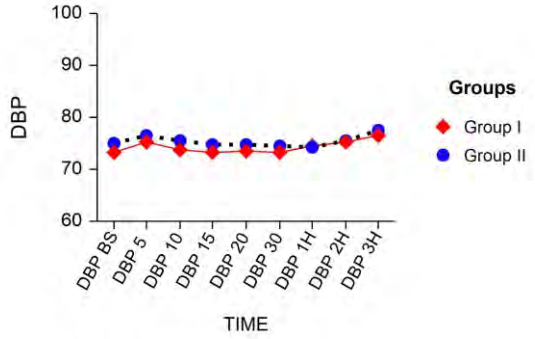

Figure 4 Mean arterial blood pressure measured in the two groups

Table 3 represents the comparisons between the groups at the various time intervals. Between the groups, statistically insignificant change was observed for the mean HR and the mean DBP from the baseline values. Mean SBP and the mean MAP values when compared between the groups was p- 0.000 and p- 0.0012.

Table 3: Heart rate and blood pressure comparison between the two groups (Mean+SD)

	Group I	Group II	P.VALUE
Heart Rate (HR) per minute	77.16±13.69	76.21±14.28	0.45
Systolic Blood Pressure (SBP) mmHg	123.65±18.12	130.18±19.34	0.00*
Diastolic Blood Pressure (DBP) mmHg	74.29±10.63	75.34±10.51	0.221
Mean Blood Pressure (MAP) mmHg	87.75±13.46	91.22±13.52	0.00*

***P value ≤ 0.05 is significant.**

We didn't observe severe hypertension, arrhythmias or ischaemia in any of our patients. No patients from either of the two groups complained of headache, dizziness, palpitation, tremors and nausea or vomiting.

Discussion

Phenylephrine is primarily used as a decongestant, mydriatic, vasopressor and also to relieve hemorrhoids.[5] Unwanted systemic absorption of topical phenylephrine has long been suggested to cause adverse cardiovascular consequences.

This was a prospective randomised study done in 450 normotensive and hypertensive patients, scheduled for ophthalmic surgery with phenylephrine 5% and tropicamide 0.8% for pupillary dilatation.

We did not observe any adverse effects of phenylephrine in the present study. The parameters like HR and DBP showed a statistically insignificant rise from the baseline values. The rise in the mean SBP and MAP showed significant difference statistically from the baseline readings that can be considered clinically insignificant to affect the cardiovascular status. Sander et al. studied the relationship between circadian blood pressure patterns and progression of early carotid atherosclerosis and mentions that systolic blood pressure variation of less than 15 mm Hg as safe and more than that has increased prevalence of coronary artery disease. [6]

Mohammed Ather et al.[2] studied the effect of 5% phenylephrine eye drops on BP in hypertensive patients. They concluded that the rise of SBP was 17.2 mm Hg in hypertensive and 9.2mmHg in normotensive patients. We observed the mean rise of SBP by 7 mm Hg in group I (normotensive) and 6 mm Hg in group II (hypertensive) patients. Similarly pupillary dilatation with 10% phenylephrine eye drops did not significantly increase systemic BP in 87% of normotensive and hypertensive patients.[3] Statistically insignificant rise in the mean SBP was mentioned in patients receiving 10% phenylephrine in different study that is comparable to our study results.[7] In contrast, significant rise in the mean SBP was observed by N B Kenawy et al.[8] with topical 10% phenylephrine. They observed rise in SBP by 34.4 mm Hg and 22.8 mm Hg in normotensive and hypertensive patients respectively. Another study also mentions about an increase in the SBP in both the hypertensive and normotensive patients by 10-40 mmHg. (Samantaray and Thomas).[9]

In our study, the mean rise in DBP was 3mm Hg and 2 mm Hg in group I and group II patients and this was statistically insignificant. McReynolds et al.[10] observed less than 10 mmHg rise in only 6 patients out of total 100 and 94 cases and hypertensive patients had no rise in the BP. DBP was observed to increase by 10-30 mmHg in both the hypertensive and normotensive patients in an old study.[9] Another study by Kenawy et al.[8] concluded that topical 10% phenylephrine increased the DBP by 10.5 mm Hg and 16.8 mm Hg in normotensive and hypertensive patients respectively. But, in a study report by Mohammed Ather et al.,[2] the risk of rise in DBP was 10-20 mm Hg in hypertensive patients and only 4% of normotensive patients with a p value of 0.0028 (topical 5% phenylephrine). In comparison to our study, the above studies showed a slightly higher increase in the DBP.[3,9]

J Skunca et al.[1] compared the cardiovascular effects of 10% and 2.5% topical aqueous phenylephrine and found statistically insignificant difference in the HR and MAP between the hypertensive patients (25) and control patients (24). Similarly, the present study observed statistically insignificant increase in HR between the groups at all the intervals. The HR is expected to increase by 15 beats per minute even in healthy individuals after standing from sitting position. [11] We observed statistically significant increase in the MAP between the hypertensive and normotensive patients, but the increase was less than 10mm Hg so e rise was considered within the clinically limits. This change is considered normal physiological with postural or circadian variations.[12,13] Meta-analysis was done from the related articles to find the cardiovascular adverse effects of topical phenylephrine and they concluded that the change in BP was not clinically relevant with

2.5% phenylephrine and however, with 10% phenylephrine there was a transient rise in the BP that reverted back to normal within 20 minutes.[14]

Fraunfelder et al.[15] had conducted a review study on reported cases of adverse reactions to 10% phenylephrine in 39 cases, in which 15 had myocardial infarction and 11 were fatal. Most adverse reactions occurred approximately 20 minutes after application of the phenylephrine. Case reports mention about the adverse reactions like hypertension and cerebrovascular accidents[16–19] ventricular arrhythmia [20] and sub-arachnoid hemorrhage.[21] Venkatakrishnan[22] and Abdelhalim Ashraf A et al[23] reported (in case reports) about the occurrence of pulmonary edema after topical phenylephrine absorption during pediatric eye surgeries under general anesthesia. A case of cardiac arrest was reported by Samaneah et al.[24] A definite increase in blood pressure was observed with topical phenylephrine in all of their cases as reported by Chin et al.[25] However, in our study of 450 patients (normotensive or hypertensive), none of them complained of any adverse effects and even we didn't observe severe hypertension. The above reports may be because of inadvertently used higher dose when the dilatation is not adequate or when the dilatation is to be achieved faster. This might have resulted in the cumulative effect of the drug.

Systemic absorption of ophthalmic phenylephrine decreases by following the safe measures or strategies.[26]

1. Application of digital pressure on the naso–lacrimal passage immediately for 60s following topical administration of eye drops.
2. The 2.5% topical strengths of phenylephrine is an equipotent mydriatic to 10% phenylephrine so to be preferred.
3. Avoid unnecessary repetition of doses and allow adequate time for the pharmacologic effect to occur,
4. Quick blotting away of excess drops after drug administration and
5. The use of micro drops in infants if possible.
6. Small size drops with increased concentration, improves the therapeutic index of eye drops.

Limitations in our study may be the changes in the haemodynamic parameter that can occur due to the anxiety, discomfort or pain during surgery. This was common in both the groups.

Conclusion

Topical phenylephrine 5% and tropicamide was used for pupillary dilatation in both normotensive and hypertensive patients undergoing cataract surgery. The fixed dose of the drug was used and hemodynamic monitoring was done perioperatively. Statistically insignificant increase in the mean HR and the DBP was observed from the baseline values and between the groups. A slight increase in the SBP and the MAP was observed from the base values in both the groups and between the groups. This increase was clinically negligible and within permissible limits, so it is considered safe clinically. Calculated or fixed doses of topical 5% phenylephrine can be used safely for pupillary dilatation in both hypertensive and normotensive patients undergoing ophthalmic examination/surgery but under guidance and hemodynamic monitoring.

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Conflicts of interest

There are no conflicts of interest.

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