Original article

Comparative Evaluation of two different doses of Intranasal Dexmedetomidine in elderly hypertensive patients undergoing cataract surgery under peribulbar block: A prospective double blind randomised controlled study

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Abstract

Background: Dexmedetomidine is an alpha-2 agonist which has been extensively used intravenously for sedation. However, the safety and efficacy of its intranasal formulation has not been studied in the geriatric population. The purpose of this study is to compare the safety and efficacy of two different doses of intranasal Dexmedetomidine (0.25 µg/kg vs 0.5µg/kg) as a premedication for elderly patients with grade-2 hypertension (white coat hypertension) undergoing elective cataract surgery under peribulbar block.

Materials and methods

This is a prospective double blinded randomised controlled study conducted at our hospital. Seventy elderly hypertensive patients who were undergoing cataract surgery under peribulbar block were randomly allocated into two groups of 35 each. Patients in Group A received 0.25µg/kg and Group B received 0.5µg/kg intranasal Dexmedetomidine single dose through an atomiser. Vital signs and sedation Modified Observer's Assessment of Alertness and Sedation [MOAA/S] were measured for two hours after administration. Peribulbar block was administered 15 minutes after the administration of the intranasal Dexmedetomidine and surgery was commenced after adequate anaesthesia was achieved.

Results

Heart rate, systolic and diastolic blood pressures were significantly lower in the Group B compared to Group A ($p< 0.05$). Systolic blood pressure decreased >30%, lasting more than 5mins in 40% (n= 14)of the patients in Group B as compared to 8.57% (n=3) in Group A.

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None of the patients had any clinical signs of hypoperfusion. MOAA/S score were comparable in both groups.

Conclusion

Intranasal Dexmedetomidine premedication at the dose of 0.5µg/kg produces acceptable reduction in blood pressure and heart rate when compared to dose of 0.25µg/kg in elderly patients.

Keywords

Intranasal Dexmedetomidine, cataract, peribulbar, sedation

Introduction

Cataract surgeries are commonly performed under locoregional anaesthesia. The prevalence of unoperated cataract has been reported as 58% in North India and 53% in South India.[1] Modern phacoemulsification procedure is now considered the safest and preferred method of cataract surgery.[2] Patients undergoing cataract surgery are usually elderly (>60yrs) and present with a variety of systemic comorbidities including hypertension. The Perioperative Quality Initiative (POQI), an international, multidisciplinary organization, recommends that elective surgery should not be cancelled based solely on preoperative blood pressure.[3] Dexmedetomidine is an alpha 2 agonist which is commonly used for procedural sedation.[4] It has a central sympatholytic action which helps to overcome the cardiovascular stress response (tachycardia and hypertension).[5]

There is growing evidence that Dexmedetomidine also reduces the occurrence of post-operative delirium in elderly patients.[6] Intranasal Dexmedetomidine has not been extensively studied in the elderly population. Cataract surgeries can be done under peribulbar block, however, mild sedation will improve the operating conditions by reducing the stress response to surgery and decreasing the intra ocular pressure. Hence, Dexmedetomidine may be an ideal drug for procedural sedation in elderly patients with grade 2 hypertension coming for cataract surgery. Intranasal Dexmedetomidine has been studied in this cohort of patients previously by Clemens et al.[7] They found that doses above the range of 0.5µg/kg was associated with significant hemodynamic changes precluding its use as a premedication in elderly patients.[7] However, the study wasn't limited to ophthalmic patients, who require to be fairly conscious and responsive to commands during the surgery.

The aim of the study was to compare the safety and efficacy of two different doses of intranasal Dexmedetomidine (0.25µg/kg vs 0.5µg/kg) as a premedication for elderly patients with grade-2 hypertension (white coat hypertension) undergoing elective cataract surgery under peribulbar block. The primary objective was to compare the efficacy of two different doses of intranasal Dexmedetomidine in controlling white coat hypertension.

The secondary objective was to compare the safety of two different doses of intranasal Dexmedetomidine in the elderly population with co-morbidities posted for elective cataract surgery.

Materials & Methods

This double blind prospective randomised controlled study was performed in accordance with the Declaration of Helsinki, in compliance with Good Clinical Practice and the applicable regulatory requirements. Approval from the Institutional ethics committee was obtained. The study was registered in the Clinical Trial Registry of India (CTRI/2022/04/041910). The present study included 35 patients in the age group of 60 to 75yrs of ASA grade 2-3, body weight >50 kg having grade 2 hypertension (ACC/AHA guidelines 2017) (white coat hypertension) posted for cataract surgery under peribulbar block. Patients were randomly allocated into one of the 2 groups during the study period of 2 months from April 2022 to June 2022.

Exclusion criteria

Patient refusal, low baseline HR <50bpm, age lesser than 60 years or more than 75 years, heart block of any degree, known valvular heart disease, known history of renal or hepatic impairment, severe left ventricular dysfunction, obesity BMI >30kg/m.^{2}

Thorough pre-anaesthetic evaluation was done for all the patients. All the patients who were found to have stage 2 hypertension as per the ACC/AHA guidelines (SBP>140 and DBP> 90mmHg) were recruited for the study. Patients were randomly allocated into one of the 2 groups: patients in Group A received 0.25µg/kg nasal Dexmedetomidine and Group B received 0.5µg/kg nasal Dexmedetomidine using an online randomisation programme (www.randomization.com). The list was concealed in opaque sealed envelopes that were numbered sequentially and opened after obtaining the patients' consent by a nurse not involved in the study. All patients were pre-medicated with 0.25mg alprazolam and 40mg pantoprazole oral tablets. They were then transferred to a quiet pre-operative room with a low ambient light half an hour before the start of the surgery. The appropriate drug dose was drawn into a 1ml syringe and diluted to 1ml by the same nurse in order to ensure that the anaesthetist and the patient remained blinded to the randomisation. Emergency drugs and equipment needed to treat hypotension, bradycardia and airway compromise were kept ready. Pre procedure vital parameters like HR, systolic blood pressure (SBP), diastolic blood pressure (DBP) SpO2, Respiratory rate (RR), ECG, Modified Observer's assessment of alertness/ sedation scale (MOAA/S) were noted. Oxygen was administered via a nasal cannula at 2 litres /min. Intravenous line access was established. Dexmedetomidine was administered intranasally using the MAD Nasal (Intranasal Mucosal Atomisation Device, Teleflex Medical, India).

The correct dose volume was filled in the syringe depending on the group that the patient was allocated. Patient was made to lie in the bed at angle of around 45 degree in a semi recumbent position and the head was tilted backwards during administration of the drug. Single dose was divided equally between the 2 nostrils After the drug was administered the patient was instructed to stay in bed and not to move out of bed and to avoid talking. Vitals and MOAA/S scale was continuously assessed at 2.5 minute interval for the first 15 minutes. Peribulbar block was performed with 8ml of local anaesthetic agents (3ml of 0.5% bupivacaine, 5ml of 2% lignocaine) with hyaluronidase (15IU/ml) and surgery commenced after achieving adequate anaesthesia. Vital parameters HR, SBP and DBP, RR, SpO_2 and level of sedation (MOAA/S) was noted every 5 min until the end of 2 hours after administration of the drug. Patients were discharged when the criteria for home readiness was achieved.

The primary outcome was >30% decrease in SBP and DBP with signs of hypoperfusion necessitating the use of vasopressors; the number of patients experiencing symptomatic bradycardia (HR<40bpm) needing treatment. We also measured the maximum change of these variables from the baseline in each patient (percentage change). The secondary outcome was the maximum sedation levels being achieved in these patients, [excessive sedation (MOAAS/S </= 3); hypoventilation with RR<8/min; drop in SpO2 to <92% and the need for airway support; nausea and vomiting within 6 hours of administration of Dexmedetomidine]; time taken to achieve the maximum sedation level.

Sample size determination

The sample size was determined from data available from previous studies in the cohort of elderly patients and from our experience in using similar doses intravenously.[8] Clemens R. M. Barends et.al [7] reported mean percentage decrease in SBP after surgery in 0.5 μg/kg dose of Dexmedetomidine group is 19.1%±10.3. Expecting a 7% lesser decrease in SBP percentage in Group A and assuming a pooled standard deviation of 10.3 with 5% level of significance and 80% power, a sample size of 34 in each group was required.

Statistical Methods

Data was analyzed using R software version 4.1.0. All categorical data was presented using frequency and percentages, all continuous data was described using mean and standard deviation or Median and inter quartile range based on the distribution. To assess the clinical parameters between the two groups, independent sample t-test or Mann Whitney U test was applied for the continuous measurements after checking normality assumption. Chi-square test or Fisher's exact test was applied for the categorical observations based on the expected frequency. P-value of < 0.05 was considered significant level of significance for all comparisons.

In the Month of April and May 2022, 142 patients were eligible for the inclusion based on the initial screening, pre-anaesthetic evaluation and planning for surgery. Figure 1 shows the Consolidated Standards for Reporting Trial diagram of the recruitment process.

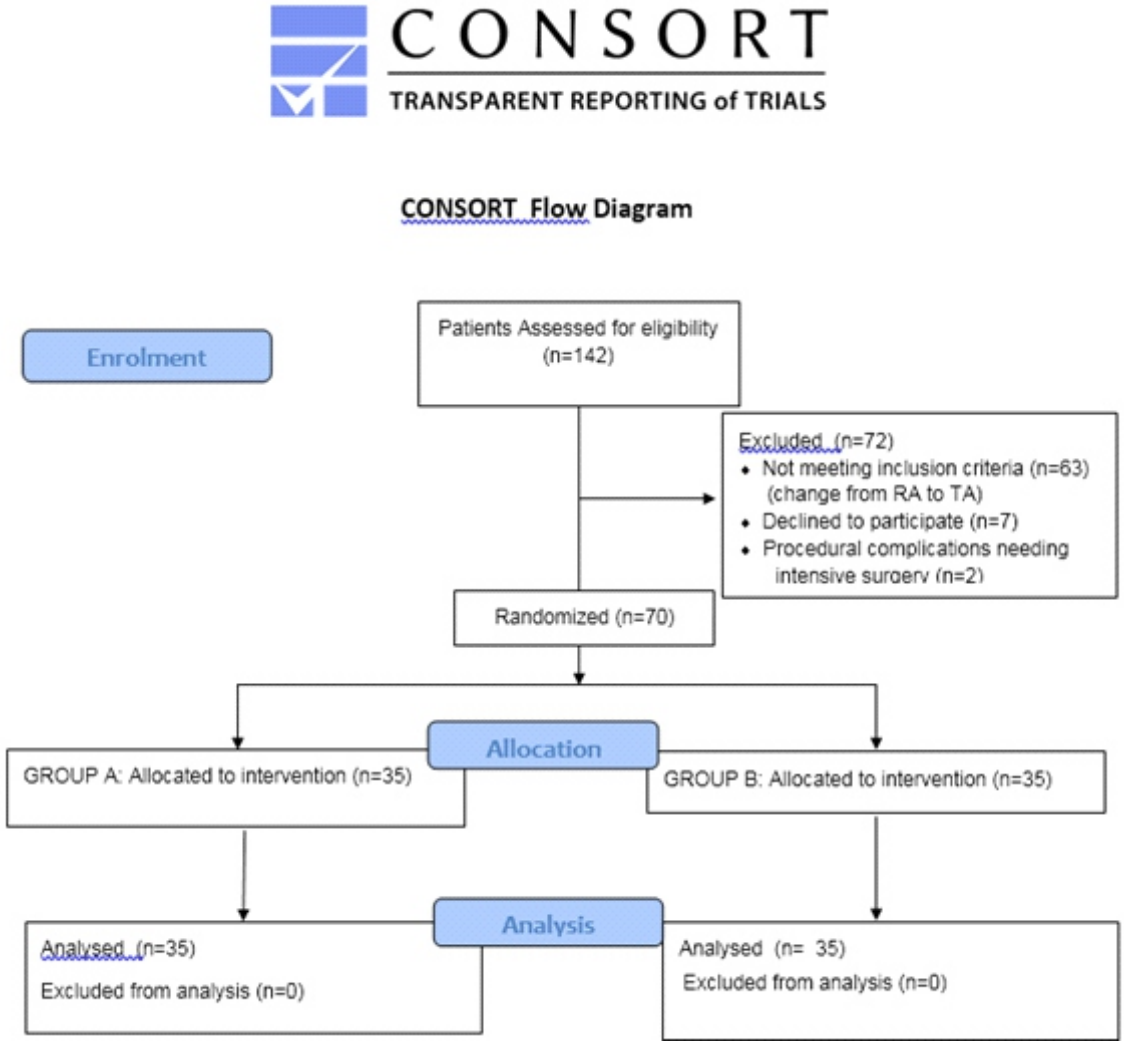

Figure 1 : CONSORT diagram for the recruitment of patients for the trial.

Results

None of the subjects recruited in the study met the critical values of the vital parameters. All patients tolerated the intranasal Dexmedetomidine well and experienced no discomfort during administration and they underwent surgery uneventfully.

Baseline data/ demographics data are demonstrated in Table 1.

There was no statistically significant difference in the age, gender, weight and mean duration of surgery between the 2 groups.

Table 1: Table showing the demographics distribution in the two groups, values are in Mean ± SD, n (%)

	Group A (n=35)	Group B (n=35)	P Values
Age (years)	66.4 ± 3.93	66.09 ± 4.73	0.763
Gender: Male/Female	16 (46%) / 19 (54%)	17 (49%) /18 (51%)	0.811
Weight (kgs)	65.42 ± 9.86	63.11 ± 9.78	
Duration of surgery (mins)	24.29 ± 7.49	24 ± 7.36	0.872

Primary outcomes

Hemodynamic response in both the groups is summarised in Table 2. HR, SBP and DBP were significantly lower in Group A compared to Group B, P<0.006. None of the patients in both the groups had any clinical signs of hypoperfusion needing treatment or clinically symptomatic bradycardia.

Table 2: Table showing the effects of Dexmedetomidine on the blood pressure and heart rate in the two groups

Parameter	Group A (n=35)	Group B (n=35)	P Values
No. of patients with SBP decline >30%	4 (11%)	14 (40%)	0.006
No. of patients with SBP decline <30%	31 (89%)	21 (60%)	
No. of patients with SBP/DBP decrease >30% showing signs of hypoperfusion	0	0	
No. of patients with DBP decrease >30%	2 (5.71%)	6 (17.14%)	
Maximum % decrease in Heart rate, mean±SD	14.03±7.79	18.36±8.83	0.032
Time to lowest reading, (mins)(median,IQR)	70 (35,100)	95(70,105)	0.017
Maximum % decrease in SBP, mean±SD	19.13±8.55	28.59±7.98	<0.001
Time to lowest reading (mins) (median,IQR)	70 (30,105)	105 (80,115)	0.002
Maximum % decrease in DBP, mean±SD	19.16±8.61	26.58±8.44	<0.001
Time to lowest reading, (mins) (median, IQR)	75 (35,105)	95 (50,115)	0.103

The maximum percentage of change in HR, SBP and DBP is further summarised in Figure2, 3 and 4.

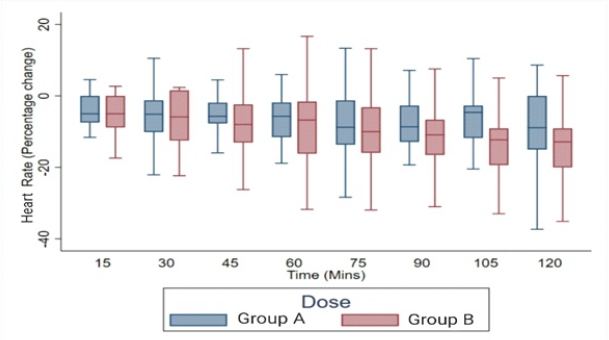

Figure 2: Percentage change in Heart Rate in the groups

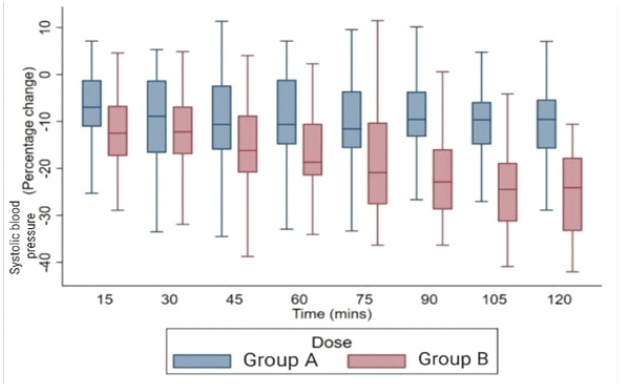

Figure3: Percentage change in Systolic Blood Pressure in the groups

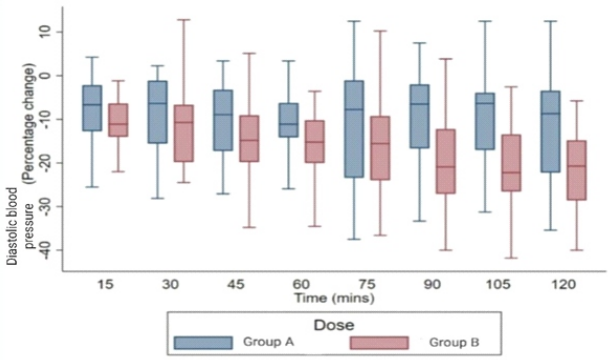

Figure 4: Percentage change in Diastolic Blood Pressure in the groups

Secondary outcomes

Respiratory rate and SpO2 remained relatively unaffected. In Group A, six patients had snoring and small self-limiting decreases in SpO2 which was not clinically significant. None of the patients needed any airway support at any time. All patients had MOAA/s score of 5 at the start of the study period. Group A patients were more sedated than Group B patients. The lowest MOAA/s score achieved in both the groups was 4.

The lowest MOAA/s score and the mean time to achieve the lowest MOAA/s score is shown in Table 3.

Table 3: Sedative effects of Dexmedetomidine

Lowest MOAA/S score (number of patients	Dose group		P Values
	Group A	Group B	
5	20	13	0.094
4	15	22	
3	0	0	
2	0	0	
1	0	0	
0	0	0	

Discussion

Cataract surgeries are mostly carried out in the geriatric population, who tend to have multiple systemic comorbidities, most commonly hypertension. White coat hypertension is a common occurrence in treated hypertensives and blood pressure recordings in the immediate pre operative period is usually higher in patients when compared to their usual BP measurements. Agrawal et al concluded that isolated elevated BP recording in the immediate preoperative period does not increase the risk of perioperative complications during procedures under local anaesthesia.[9] White coat hypertension can be countered using adequate anxiolysis. The data on the safety and efficacy of intranasal Dexmedetomidine

for premedication in the elderly population is limited. Clemens et al studied the safety and efficacy of intranasal Dexmedetomidine premedication in the elderly population.[7] They found that the doses required to induce moderate sedation (i.e., 1.0 – 2.0μg/kg) had a high incidence of profound and sustained hypotension, which can be associated with increased risk of perioperative myocardial and renal damage.[7] Ramaswamy et al have found that lower IV loading doses of 0.25μg/kg and maintenance at 0.25μg/kg/hr was better suited for ophthalmic procedures from both patient and surgeon satisfaction point of view.[8]

White coat hypertension often leads to unnecessary cancellations or postponement of surgery. In our study, we found that the intranasal 0.5μg/kg Dexmedetomidine was more effective in reliably countering white coat hypertension and bringing the BP down to acceptable levels. None of the patients had symptomatic hypotension or bradycardia needing treatment.

In the present study, more patients in the 0.5μg/kg dexmedetomidine group achieved MOAA/S score of 4 which is ideal for cataract surgery as the patient remains calm but is responsive to verbal commands and hence can follow surgeons instructions during the surgery. Any deeper level of sedation for cataract surgery as a day case procedure would be counter-productive, as the patients can cause untoward movement and may not follow commands.

None of the patients recruited for this study had any incidence of post operative nausea and vomiting. This can be explained by the antiemetic properties of Dexmedetomidine due to its effect of reducing the noradrenergic activity.[10]

The limitation with intranasal administration of any drug is that variable amount of the administered drug may reach the pharynx during atomisation and may be swallowed by the patients and affect the bioavailability of the drug. The bioavailability of Dexmedetomidine after intranasal administration has been found to be 65%.[11] Further in order to ensure blinding of the anaesthetist and the patient, we administered a fixed volume of 1ml (by diluting the calculated dose of Dexmedetomidine for each patient to 1ml with saline), but this leads to concentration of the administered Dexmedetomidine formulation to vary between patients.

The patients underwent peribulbar block and the surgery during the period of observation of this study. The painful stimulus from the peribulbar block offset the fall in blood pressure in some of the patients. However, in-spite of a temporary surge in pressure during the block administration, the patients receiving 0.5μg/kg Dexmedetomidine had an acceptable fall in blood pressure with no untoward side effects or clinical signs of hypoperfusion. The effect of intranasal Dexmedetomidine on haemodynamics of patients undergoing the cataract surgery under topical anaesthesia will require further studies for evaluation.

Conclusion

Intranasal administration of 0.5µg/kg Dexmedetomidine premedication produced more consistent fall in blood pressure as compared to 0.25µg/kg to alleviate white coat hypertension in patients undergoing cataract surgery under peribulbar block. We suggest that intranasal Dexmedetomidine 0.5µg/kg premedication can be used safely for elderly patients with white coat hypertension undergoing cataract surgery as a day case procedure.

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Conflict of interest

NIL

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