Original Research Article

Evaluation of the effect of different doses of dexmedetomidine on induction dose and hemodynamic effects of propofol-a comparative randomised controlled study in orthopedic cases

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Abstract

Dexmedetomidine a potent, highly selective α2n adrenoreceptor agonist possess desirable properties like sedation, analgesia, sympatholysis and reduces the anaesthetic requirement. Bradycardia and hypotension are the most common side effects of dexmedetomidine. Propofol, currently the most popular induction agent due to its beneficial effects such as suppression of airway reflexes, fast recovery etc has the same side effects during induction of anaesthesia. Hence titration of the above mentioned drugs can minimize the adverse and retain the desired effects of their pairing. Various loading dosages of dexmedetomidine ranging from 0.33 to 1 µg/kg have been used pre-induction. Hence this study was conducted with an objective of comparing and evaluating the effects of different doses of dexmedetomidine on induction dose of propofol and hemodynamics.

Key Word: Dexmedetomidine, Propofol, Bradycardia, Comparative randomised controlled study, orthopedic cases.

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INTRODUCTION

Propofol, barbiturates, and benzodiazepines are all associated with profound hemodynamic adverse effects at doses needed to attenuate response to laryngoscopy and intubation. [1]As it is impractical to achieve sufficient depth to prevent sympathetic response to intubation solely with a single agent, adjuvants like opioids, β blockers, calcium channel blockers, vasodilators, etc are used.[2] It is essential to remember that, time of laryngoscopy and intubation should coincide with the peak effect of agents used to minimize hemodynamic stimulation. Opioids are widely used adjuvants and appear to give a graded response in blunting hemodynamic responses. While 2 µg/kg of fentanyl given before induction partially attenuates cardiovascular response, higher doses that prevent a hemodynamic response to intubation are associated with risk of adverse effects. [3]A bolus of 1.5 mg/kg of lignocaine given intravenously adds 0.3 MAC of anaesthetic potency and can blunt hemodynamic responses to intubation. [4]Kasten and co-workers (1986) showed that lignocaine administered (3 mg/kg) 8 intravenously is associated with significant attenuation of hemodynamic response to endotracheal intubation. [5]α2 agonists like clonidine have been used extensively in the past for attenuation of sympathoadrenal stimulation caused by tracheal intubation and surgery. They have the desirable properties of sedation, anxiolysis, and analgesia with no respiratory depression. In addition α2 agonists also have sympatholytic and antinociceptive effects that contribute to hemodynamic stability during surgical stimulation. They also reduce the dose requirement of intravenous and volatile anaesthetics. Dexmedetomidine is a potent and highly selective α2 adreno receptor agonist

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which was approved for clinical use in 1999 and recently introduced in India. It has all the above mentioned properties and can impart significant benefits in the peri-operative use[6,7,8,9]. In spite of the multiple desirable effects of dexmedetomidine, bradycardia and hypotension remain clinically significant adverse effects**.** High doses of dexmedetomidine can result in a decreased heart rate and cardiac output, with a biphasic dose response relation for BP. High doses of dexmedetomidine can also be a cause of systemic and pulmonary hypertension. The most common side effect during induction of anaesthesia with propofol is hypotension. The hemodynamic changes from propofol administration depend on the ability of the compensatory mechanisms to respond to changes and the concomitant use of any other drugs. Since a combination of propofol and dexmedetomidine can cause both beneficial and adverse effects on the patient, it would be ideal to titrate the dosage of dexmedetomidine to retain its desirable effects while negating its side effects. Different doses of dexmedetomidine have been used with an induction agent for attenuation of hemodynamic response to intubation. In this study, we compared and evaluated the different doses of dexmedetomidine for the effect on induction dose of propofol and hemodynamic effects.

AIMS AND OBJECTIVES

To evaluation the effect of different doses of dexmedetomidine on induction dose and hemodynamic effects of propofol-a comparative randomised controlled study in orthopedic cases

MATERIALS AND METHODS

Source of data: This study was conducted on 400 patients posted for elective surgery under general anaesthesia in Sanjay Gandhi Institute of Trauma and Orthopedics, Bangalore. The study was conducted from 1/04/2018 to 1/04/2019.

Inclusion criteria: The following patients were included for the study –

Patients of ASA physical status (PS) I and II scheduled to undergo elective surgery under general anaesthesia Adults aged between 18-60 years

Exclusion criteria: The exclusion criteria for the study are

Known history of sensitivity and contraindications to drugs used in the study History of hypertension

Anticipated difficult airway Patients requiring nasal intubation Patients on long term analgesics, narcotics and antipsychotics Patients who required more than 1 attempt for intubation Patients who were having inadequate depth of anaesthesia during intubation Patients who had bradycardia during the study period and needed atropine for management

Method of collection of data

- Thorough pre-anaesthetic evaluation was done a day before the surgery.
- A written informed consent was taken
- All the patients were kept nil per oral as per standard guidelines
- After shifting the patient to OT, wide bore I.V access was secured and crystalloid infusion was started.
- The study drug was prepared by a designated anaesthesia technician who was not present at the time of administering the drug.
- Patients were randomly allocated to one of the four study groups i.e. group A,B,C,D by computer generated sequence to receive a study drug diluted to 20 ml via an infusion pump over 20 minutes.

Group A received 1 µg/kg of dexmedetomidine.
Group B received 0.6 µg/kg of dexmedetomidine.
Group C received 0.3 µg/kg of dexmedetomidine.
Group D received 20 ml of normal saline.

The parameters of the study such as heart rate, BP (systolic, diastolic, mean),oxygen saturation, propofol dose, Brussels sedation scale was recorded by a person who was unaware of the nature of the study.

RESULTS

All the four groups were comparable in terms of weight. There was no significant statistical difference in between groups (p=0.21). Statistically there were significantly more number of males when compared to females.

Table 1: Gender Distribution

Group	Gender	Frequency	%
Group A	F	37	40.7
	M	54	59.3
Group B	F	22	22.9
	M	74	77.1
Group C	F	35	37.6
	M	58	62.4
Group D	F	42	45.7
	M	50	54.3

There was no statistical difference between groups in terms of ASA PS (p=.708).

Table 2: Age Distribution

Age Distribution				
Group	**Mean(Years)**	**Std. Deviation**	**F**	**Significance(P)**
A	32.03	11.22	2.313	0.076
B	31.07	9.611		
C	32.22	10.643		
D	35	11.342		

There is no significant statistical difference in terms of age in between groups (p=0.076).

Brussels Sedation Scaleat end of 10 minutes showed significantly different scores in the four groups (p<0.001). 2.2% of subjects in group A were deeply sedated and responded only to painful stimuli (score=2) whereas group B, C, D did not have any patient with score of 2 at 10 minutes. 39.6% of people in group A were sedated but arousable with verbal stimuli (score=3), compared to 26% in group B, 9.7% in group C and 2.2% in group D. At the end of ten minutes, 58.2%, 74%, 90.3% , 97.8% of the patient were awake (score=4) in group A, B, C and D respectively. Brussels Sedation Scale 20 minutes post infusion Sedation assessed by Brussels Sedation Scale at the end of 20 minutes, was significantly different in the four groups (p<0.001). In group A, 1.1% of the subjects were not arousable (score=1) whereas none of the subjects in other groups had a score of 1. In group A, 13.2% of subjects and in group B, 5.2% were deeply sedated and responded only to painful stimuli (score = 2). No patients in group C and D had a score of 2. 72.5% of people in group A were sedated but arousable with verbal stimuli (score=3) compared to 65.6% in group B, 18.3% in group C, 3.3% in group D. Number of subject who were awake (score=4) at end of ten minutes were 13.2% in group A, 29.2% in group B, 78.5% in group C and 96.7% in group D. Mean duration of intubation in groups A, B, C and D were 10.91 seconds, 10.687 seconds, 10.602 seconds, 10.59 seconds respectively. There was no statistically significant difference in between groups (p=0.165). There was a significant intragroup (p<0.001) and inter group differences in heart rate during the period of study (p=0.001). Heart rate variations were statistically significant on comparing group D with group A (p<0.001), group B (p=0.32) and group C (p=0.11) during the observation period. There was significant difference in the BP in all groups during the period of study (p<0.001) with a significant inter group differences (p<0.001). The difference was seen between of the groups A and D (p<0.001), B and C (p<0.11), B and D (p<0.001), and C and D (p=0.041). There is significant intragroup difference (p<0.001) and intergroup difference (p<0.001) in diastolic BP during period of study. Significant differences exist between group A and group C (p=0.004), group A and group D (P<0.001), group B and group D (p=0.048), group B and group D (p<0.001). There is statistically significant intragroup (p<0.001) and significant intergroup difference (p=0.001) in mean BP during period of study. Significant differences exist between group A and group D (p<0.001), group B and group C (p=0.034), group B and group D (p<0.001). There was no significant inter and intra group differences seen in saturation during period of observation. There is significant intergroup difference between the four groups for induction dose of propofol(p<0.001). Mean propofol dose for loss of eyelash reflex in the groups A, B, C and D were 48.63 mg, 59.48 mg, 71.51 mg, 88.42 mg. Similarly the mean propofol dose for loss of verbal response in the groups A, B,C and D were 47.97 mg, 58.7mg, 71.72 mg , 88.75 mg. Significant differences existed between all groups(<0.001).

Table 3: Propofol Dose

Propofol dose (mg)	Group	Meaning (mg)	Std. Deviation	Significance(p)
For Loss of eyelash	A	48.63	16.246	<0.001
	B	59.48	21.095	
	C	71.51	25.79	
	D	88.42	20.886	
For verbal Response	A	47.97	15.184	<0.001
	B	58.7	21.067	
	C	71.72	26.728	
	D	88.75	21.299	

DISCUSSION

400 patients of ASA physical status I and II, aged 18 to 60 years, undergoing general anaesthesia requiring oral endotracheal intubation were randomly allocated into 4 groups- Group A, B, C received dexmedetomidine 1 µg/kg, 0.6 µg/kg, 0.3 µg/kg respectively, while group D received normal saline. The study drug was diluted to a 20 ml solution and infused over 20 minutes. The sedation

was assessed using Brussels Sedation Scale during the same period. Anaesthesia protocol included fentanyl 2 µg/kg, propofol infusion at 80 mg/kg/hour, atracurium 0.5 mg/kg, endotrachealintubation, maintenance with oxygen, nitrous oxide and isoflurane. Dose of propofol for loss of eyelash reflex and verbal response, duration of laryngoscopy and number of intubation attempts were noted. Hemodynamics were recorded after shifting the patient to the O.T, 10 minutes after starting the infusion, on completion of the infusion, post induction, post intubation at intervals of 1, 2 , 5 and 10 minutes. Modified Aldrete's Score was noted immediately and 10 minutes after extubation. During the study we noted that 72.5% of subjects in group A and 65.6% in group B were sedated but arousable with verbal stimuli, at end of infusion as compared to 18.3% in group C and 3.3% in group D. We observed a reduction in propofol requirement for the loss of verbal response with dexmedetomidine which was 0.93 mg/kg, 1.08 mg/kg 1.29 mg/kg with group A, group B, group C respectively, while group D (saline) required 1.64 mg/kg propofol. Pressor response to intubation was better controlled in dexmedetomidine groups. We recorded a 8.9% reduction in mean BP compared to baseline at end of one minute post intubation and 15% at end of two minutes post intubation in group A. At the same time intervals we observed a 5.4% and 14% reduction in group B, 0.4% and 9.3% reduction in group C, 1.9% and 5.8% in group D.

CONCLUSION

Dexmedetomidine reduced the induction dose of propofol; a maximum reduction was seen along with 1 µg/kg followed by 0.6 µg/kgand 0.3 µg/kg. Attenuation of hemodynamic response was best seen with 1 µg/kg followed by 0.6 µg/kgwhile hemodynamic profiles of 0.3 µg/kg of dexmedetomidine and placebo group were similar. Hence we conclude that 1 µg/kg and 0.6 µg/kg of dexmedetomidine offer a reduction in anaesthetic requirement along with desirable hemodynamics.

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