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Original Research Article.

Comparison of Different Doses of Intravenously Administered Dexmedetomidine with Fentanyl on Haemodynamic Response To Intubation in Patients Undergoing Surgery under General Anesthesia

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ABSTRACT

Background: Laryngoscopy and intubation are associated with a sympathetically mediated circulatory response due to irritation of respiratory tract which is associated with increase in pulse rate and blood pressure that may be dangerous.

Objective: The aim of the present study was to determine and compare of different doses of intravenously administered dexmedetomidine with fentanyl on haemodynamic response to intubation in patients undergoing surgery under general anesthesia.

Methods: 90 patients ASA1, ASA2 scheduled to undergo elective and emergency surgery under general anaesthesia were enrolled in double blind prospective randomized controlled trial. They were randomly allocated to one of the following groups. Group A received 2 micro gram/kg fentanyl intravenously10 minutes before induction. Group B received 2 micro gram/kg fentanyl and 0.5 microgram/kg dexmedetomidine intravenously 10 mins prior to induction. Group C received 2 mico gram/kg fentanyl and 1 microgram/kg dexmedetomidine i.v. 10 minutes prior to induction.

Results: The two groups were comparable in their demographic profiles. Both study groups (B & C) were comparable with respect to their heart rate at base line, 1 minute, 2 minutes, 5 and 10 minutes after inhalation. Group C (Dexmedetomidine 1µg) demonstrated a greater suppression of chronotropic response to intubation as compared together two groups. Both the groups (B & C) were comparable to their SBP at base line, 2, 5 and 10 minutes. Group C demonstrated a better suppression of the pressor response to intubation compared to other two groups.

Key words: Dexmedetomidine, Fentanyl, Hemodynamic response, Laryngoscopy, Intubation.

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INTRODUCTION

The major responsibility of anaesthesiologists towards their patient is provision of patent airway, the most vital element in providing intact functional respiration. The fact that tracheal intubation is gold standard in airway management still holds true, even after advent of an overgrowing treasure of airway devices. Intubation in turn is preceded by laryngoscopy, which is done to visualize the larynx and adjacent structures. However, laryngoscopy and intubation are associated with a sympathetically mediated circulatory response due to irritation of respiratory tract which is associated with increase in pulse rate and blood pressure that may be dangerous. King et al[1] first recognized this phenomenon of reflex increases in circulatory variables way back in 1951.

The hemodynamic changes resulting from airway instrumentation are due to sympatho-adrenal discharge caused by oropharyngeal and parapharyngeal stimulation. To attenuate this pressor response a wide variety of pharmacological and non-pharmacological interventions have been tried, tested, and debated upon in the last 50 years. These include among non-pharmacological methods - smooth swift laryngoscopy and deeper planes of anaesthesia at the time of laryngoscopy. The pharmacological methods are aimed at the efferent, the afferent or both the limbs of responses. One of the most studied drugs to attenuate the hemodynamic response to laryngoscopy and tracheal intubation is fentanyl.[2-5] Fentanyl is a short acting synthetic opioids agonist 75-125 times more potent than

morphine. Several trials have tried varying doses from 2µg/Kg- 8 µg/Kg given 1 minute to 10 minutes before intubation.[6,7] High dose however are fraught with the risk of respiratory depression and the need for postoperative elective ventilation, we therefore used the lower dose range. Dexmedetomidine is another drug which is increasingly being used for the same purpose. It is relatively new alpha 2 agonist approved by FDA (Food and drug Administration) in 1999. Dexmedetomidine is highly selective, short-acting central alpha 2 agonist. It reduces sympathetic responses to airway instrumentation thereby minimizing changes in blood pressure and heart rate during laryngoscopy and intubation. After a bolus of 1µg/kg, a biphasic response is seen. Activation of alpha 2 receptors by dexmedetomidine leads to dose dependant sedation, anxiolysis, analgesia and decrease in plasma catecholamine concentration. It reduces sympathetic responses to airway instrumentation thereby minimizing changes in BP (Blood pressure) and HR (Heart rate) during laryngoscopy and intubation. The present study is aimed to determine and compare different doses of intravenously administered dexmedetomidine with fentanyl on haemodynamic response to intubation in patients undergoing surgery under general anesthesia.

MATERIAL AND METHODS

This study was conducted on 90 ASA physical status grade I and II patients of either sex between 18-60 years of age, undergoing elective surgical procedures. The study was conducted in Department of Anaesthesia, RUHS College of Medical Sciences, Jaipur, Rajasthan. The study population was subdivided using random number tables into three groups with 30 patients in each group, Group A (n=30) – received 2mcg/kg of iv fentanyl and 20 ml of IV Normal Saline administered over 10 minutes, ten minutes before induction of anaesthesia. Group B (n=30) – received 2mcg/kg of iv fentanyl and 0.5 mcg/kg of Dexmedetomidine intravenously 10 minutes prior to induction (made 20 ml with normal saline). Group C (n=30)-received 2 mcg/kg of iv fentanyl and 1 mcg/kg of Dexmedetomidine administered intravenously 10 minutes prior to induction (made 20 ml with normal saline) .

Preanaesthetic Checkup and Preparation

Preanaesthetic evaluation was done a day prior to surgery. It included the following assessments, General condition of the patient, airway assessment using Mallampatti grading and the Rule of 1- 2-3. A general physical examination including the height, weight and the BMI. A detailed examination of the cardiovascular and the respiratory systems. The following investigations were done in patients as required. Heamoglobin estimation, Blood sugars: FBS/PPBS, Blood urea, serum creatinine and electrolytes. Urine examination for Albumin, Sugar and Microscopy. A standard 12 lead ECG and A screening Chest X-Ray. The procedure of general anaesthesia was explained to the patient and written informed consent was taken. Preparation included an overnight fast of 8 hours before the surgery, premedication with Tab Alprazolam 0.25 mg and Tab Ranitidine 150 mg PO night before surgery.

Preparation of the Operation Theatre

The anaesthesia machine was checked. Appropriate sized ET tubes, working laryngoscope with medium and large sized blades and working suction apparatus were kept ready before induction. All anesthetic and emergency drugs were loaded into labeled syringes and kept ready for use.

Anaesthetic Technique

On arrival of the patients to the operating room, they were connected to a multichannel monitor which measures the HR, SBP, DBP, MAP, EtCo2, SpO2 and performs continuous ECG monitoring and the HR, SBP, DBP AND MAP were recorded before administering the study drug. The Cardiac rate and rhythm were also monitored by a continuous visual display of the lead II ECG.

A peripheral line with an 18G IV cannula was secured and an infusion of normal saline was started. Patients were randomly assigned by computer generated random table number to receive either, IV Normal Saline, IV Dexmedetomidine 0.5 µg/kg or IV Dexmedetomidine 1 µg/kg, 10 minutes before induction respectively. IV Dexmedetomidine was administered after diluting the dose to a 20ml volume with normal saline and infusing it over 10 minutes using a syringe pump or a microdrip infusion set. The study drug was prepared by a senior anesthesiologist not involved with the study and the observer was blinded for the study. All the study vital parameters required were recorded at the beginning and at 5 minute intervals from the end of the drug infusion upto the time of induction.

All patients were then premedicated with Inj Fentanyl 2 µg/kg IV and Inj Ondansetron 0.08mg/kg IV and pre-oxygenated with 100% oxygen for 3 minutes before induction with a tight fitting face mask using a closed circuit. After 10 minutes of the administration of the study drug, anaesthesia was induced with Inj. Propofol 1% solution and the dose required to produce loss of verbal response was recorded, Inj succinylcholine 2mcg/kg IV was administered to facilitate intubation and produce muscle relaxation. After 1 minute of the administration of the neuromuscular blocker, laryngoscopy was done. Intubation carried out with an appropriate sized disposable, high volume low pressure cuffed PVC endotracheal tube. After confirmation of tracheal intubation using EtCo2 and auscultation of the chest for bilateral equal air entry, the tube was secured and anaesthesia was maintained with 60% Nitrous oxide, 40% Oxygen and Isoflurane 0.6% with a tidal volume of 8-10 ml/kg and a rate of 10-12 breaths per min. No surgical or other stimulus was applied during the 15 minutes of the study period. At the end of the surgery, the patients were reversed with Inj Neostigmine 0.05mg/kg and Inj. Glycopyrrolate 0.01mg/kg IV. The patients were extubated when awake and breathing adequately and shifted to the recovery. Any untoward effects related to the drug and anaesthesia were noted and attended to appropriately. A fall in MAP by 30% from the baseline was treated with Inj Mephentermine 6mg IV boluses. A fall in the HR to less than 40b/min was treated with Inj Atropine 0.6mg IV. Any hypertension or tachycardia episodes would be treated by Inj Metoprolol 1 mg IV boluses as required. Analgesia if deemed necessary was supplemented with Inj Fentanyl 10-15µg IV boluses. Patients were followed up post-operatively on an hourly basis for 6 hrs from drug administration.

OBSERVATIONS & RESULTS

Both study groups (B & C) were comparable with respect to their HR at base line, 1 minute, 2.5 minutes, 5 and 10 minutes after administration of the study drug. There was a statistically significant difference between the two study groups when compared to the control group with regard to their HR values (p values being <0.01). Group C (Dexmedetomidine 1µg)

demonstrated a greater suppression of chronotropic response to intubation as compared to other two groups.

Both the groups (B & C) were comparable to their SBP at base line 5 and 10 minutes, however there was a statistical significance difference between the two groups with respect to their SBP ($p<0.01$) after intubation. Group C demonstrated a better suppression of the pressor response to intubation as compared to other two groups.

Table 1: Comparison of Heart Rate (BPM) In Three Groups of Patients Studied.

Heart rate	Group A	Group B	Group C	A-B	A-C	B-C
10 min before surgery	84.60±12.73	85.33±13.34	81.13±11.97	0.973	0.543	0.409
Post induction	84.60±12.14	63.07±8.65	62.93±7.14	<0.001**	<0.001**	0.999
1min post induction	102.10±16.04	59.53±7.70	64.10±8.26	<0.001**	<0.001**	0.267
2 minute	97.23±36.76	60.37±8.54	53.73±4.32	<0.001**	<0.001**	0.473
5 minute	85.07±12.96	55.70±5.50	54.83±4.09	<0.001**	<0.001**	0.917
10 minute	82.13±11.29	55.67±4.93	55.20±3.34	<0.001**	<0.001**	0.967
15 minute	77.77±11.92	55.57±4.33	55.67±3.32	<0.001**	<0.001**	0.999
20 minute	78.20±8.66	55.70±3.26	58.23±4.68	<0.001**	<0.001**	0.235

Table 2: Comparison of SBP mm Hg of Three Groups of Patients Studied.

SBP mmHg	GROUP A	GROUP B	GROUP C	A-B	A-C	B-C
10 min before surgery	127.67±11.39	126.53±12.67	126.53±10.57	0.924	0.924	1.000
Before induction	126.67±12.44	99.67±9.22	105.00±8.37	<0.001*	<0.001*	0.111
1 min post induction	150.00±13.61	95.07±7.79	111.20±11.38	<0.001*	<0.001*	<0.001*
2 minute	132.80±15.93	95.00±5.53	98.27±6.30	<0.001*	<0.001*	0.446
5 minute	114.87±20.78	93.53±4.78	96.20±4.11	<0.001*	<0.001*	0.689
10 minute	111.47±17.76	99.53±5.60	96.13±7.20	<0.001*	<0.001*	0.491
15 minute	114.87±13.89	101.87±4.37	100.00±6.45	<0.001*	<0.001*	0.716
20 minute	120.27±13.54	104.87±5.08	107.40±8.54	<0.001*	<0.001*	0.571

DISCUSSION

The pressor response which is part of a huge spectrum of stress response, results from the increase in sympathetic and sympatho-adrenal activity, which is evidenced by increase in plasma catecholamines concentrations in patients undergoing surgery under general anaesthesia.[8-12] Various drug regimens and techniques have been used from time to time for attenuating the stress response to laryngoscopy and intubation, including opioids, barbiturates, benzodiazepines, beta blockers, calcium channel blockers and vasodilators etc.[13-17]

Although the corresponding increases in blood pressure and heart rate are transitory and variable, they are more pronounced and unpredictable in patients with raised intracranial tension, cardiovascular disease like hypertension following laryngoscopy. Consequently, life-threatening complications such as pulmonary edema, cerebrovascular hemorrhage and myocardial infarction are more likely to develop in these groups of patients. Shribman AJ[18] in 1987 found that these responses have two components. The first is the response to laryngoscopy and the other is the response to intubation. Studies have shown that the response to laryngoscopy and intubation is associated with a rise in plasma nor-epinephrine levels by as much as 61%. As our understanding of the causes of this pressor response increased, new methods aimed at the attenuation of these responses also progressively evolved. Various modalities either target the afferent limb or the efferent limb of the pressor effect. The major modalities or agents acting on the afferent limb are smooth and swift laryngoscopy, deep plane of anaesthesia, volatile inhalational agents, lignocaine given topically or 1.5 mg/kg i.v, opioids etc.[19,20] On the other hand, interventions involving the efferent limb include mainly anti-hypertensives and vasodilators like sodium nitroprusside, nitroglycerine, calcium channel blockers and adrenergic blockers to name a few. However long and impressive the list of interventions may be; the success rate of most agents is inconsistent and therefore not dependable.

King et al[1] found that deeper planes of anaesthesia prevented this hemodynamic response but Prys-Roberts et al[21] discovered that 1% halothane given for 5 to 10 minutes could not completely obviate these hemodynamic changes. Stoelting RK also effectively used nitroprusside to overcome this pressor response but found it to be ineffective in controlling the heart rate.[22] Our study was undertaken to determine and compare the efficacy of dexmedetomidine and fentanyl in attenuating the pressor response to laryngoscopy and intubation.

CONCLUSION

Hence we conclude that both doses of dexmedetomidine in group B (0.5 microgram/kg) and group C (1 microgram /kg) were comparable with respect to suppression of haemodynamic response to intubation. We can use both the doses of drug for decreasing heart rate, blood pressure after intubation however group C is better as it causes more decrease in mean systolic and diastolic blood pressure.

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