The Comparative Efficacy of Intravenous Dexmedetomidine versus Lidocaine in Attenuation of Stress Response during Intubation at Tertiary Care Hospital

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Abstract: Background and Objectives: During induction of general anaesthesia, hypertension and tachycardia caused by endotracheal intubation may lead to cardiac ischemia and arrhythmias. Dexmedetomidine attenuates the hemodynamic response to endotracheal intubation and reduces anaesthetic requirement. The purpose of this study was to evaluate the effect of intravenous dexmedetomidine 1mcg/kg given over 10 minutes before induction of anaesthesia and 0.4mcg/kg/hour as maintenance during the surgery, on haemodynamic stress response resulting from laryngoscopy and endotracheal intubation and the haemodynamic stability during surgery. Materials and Methods: Seventy patients scheduled for elective surgery were randomized into two groups each having thirty five patients-dexmedetomidine group (Group I) and control group (Group II). Group I received 1mcg/kg of dexmedetomidine over 10 minutes before induction of anaesthesia 0.4mcg/mg/hr as infusion before surgery and group II received 1.5mg/kg Lidocaine prior to induction of anaesthesia. Anaesthesia was induced with fentanyl 1.5mcg/kg, propofol 2mg/kg and muscle relaxation with atracurium 0.5mg/kg and endotracheal intubation done under direct laryngoscopy, HR, systolic, diastolic and Mean arterial pressure were recorded before duration and 1, 2, 3, 4, 5, 10 minutes after endotracheal intubation and anaesthesia was maintained with oxygen, nitrous oxide, sevoflurane, atracurium. Any further need for analgesia was supplemented by IV fentanyl.

Statistical Analysis: The data was analysed by SPSS 16.0 with independent t-test. Results: Pretreatment with dexmedetomidine 1 mcg/kg attenuated the cardiovascular and catecholamine responses to tracheal intubation after induction of anaesthesia. In our present study, the rise in heart rate, systolic blood pressure and diastolic blood pressure after intubation, 1, 2, 3, 4, 5 and 10 minutes after intubation was significantly less in the dexmedetomidine group. The patients in dexmedetomidine group also had better haemodynamic stability during surgery. The requirement of opioids and sevoflurane were significantly less in the dexmedetomidine group. Conclusions: Intravenous dexmedetomidine significantly attenuates sympathoadrenal response to laryngoscopy and endotracheal intubation and also cause reduction in intra operative anaesthetic requirement, without affecting intraoperative cardiovascular stability.

Keywords: Dexmedetomidine, endotracheal intubation, premedication, sedation, α2 adrenergic.

INTRODUCTION

Laryngoscopy and endotracheal intubation causes cardiovascular instability in many patients. These stress responses may produce serious cardiovascular and cerebrovascular effects in susceptible cases. Various drugs like beta-blocker, local anaesthetics, vasodilators, etc. are being used to reduce the responses. Dexmedetomidine is a highly selective alpha-2 adrenoceptor agonist and eight times more specific than clonidine. It exerts its major sedative and analgesic effect through stimulation of the alpha-2 adrenoceptor and the locus ceruleus and it also has an advantage of reducing sympathetic activity and analgesic properties without producing significant respiratory depression.
Its analgesic effect is also produced by direct stimulation of the alpha-2 adrenoceptor in the spinal cord. The unique sedative effect of dexmedetomidine that mimics natural sleep makes the post sedative delirium after stopping dexmedetomidine very rare.

Moreover, even on the sedative score, Richmond Agitation Sedation Scale (RASS) 1-2, patients can respond easily to verbal command and go back to sleep. The most commonly reported adverse effects are bradycardia and hypotension.

Dexmedetomidine infusion allows reductions in the amounts of inhalational agent and intraoperative opioid requirements. Dexmedetomidine should be used cautiously because in higher doses and rapid infusion can produce bradycardia and hypotension. Dexmedetomidine provides good sedation throughout the surgery but patient remain arousable and also able to cooperate.

The way of administration of IV dexmedetomidine is initial loading dose followed by an infusion as maintenance dose. The variation in heart rate and blood pressure after intravenous dexmedetomidine varies with each persons. Serum adrenaline and nor adrenaline levels have been drastically reduced to more than 80% with the usage of IV dexmedetomidine.

The advantages of dexmedetomidine include less respiratory depression and it is more cardio protective and Neuro protective. Being more sensitive to alpha 2 receptor dexmedetomidine is devoid of various side effects of clonidine which has additional action on alpha 1 receptor.

In perioperative period dexmedetomidine is used for reducing cardiovascular stress response to intubation because it reduces central sympathetic outflow.

The dose of dexmedetomidine which is used for reducing intubation stress responses nearly about 0.5-1 mcg/kg through intravenous route. Less dosage of dexmedetomidine will not be very effective in the reduction of these responses.

Patients who received dexmedetomidine infusions after surgery in the postoperative have reported less hemodynamic variations and their catecholamines levels are low in plasma.

Lower doses of dexmedetomidine reduced the emergence reaction which usually happens after surgery and it also reduced the requirement of higher doses of analgesics in addition to these there was no delay in recovery from anesthesia. During initial part of infusion with dexmedetomidine there will be a short period of hypertension which leads reflex bradycardia.

Dexmedetomidine exerts its action in the smooth muscles of the blood vessels due to the presence of alpha 2B receptors in it and this causes immediate increase in blood pressure when this drug is given. This response lasts only few seconds because it is compensated by a decrease in blood pressure which is caused by central sympatholysis.

**Aim of the Study**
1. To compare the efficacy and safety of dexmedetomidine versus lidocaine.
2. To demonstrate the dosage of dexmedetomidine in decreasing the stress response and its effect on cardiovascular system during direct laryngoscopy and endotracheal intubation by comparing it with lidocaine.

**Hypothesis and Scientific Justification**

**Hypothesis:**
As compared to lidocaine patients receiving dexmedetomidine have less perioperative cardiovascular stress response.

**Scientific Justification:**
Dexmedetomidine is a good analgesic, sedative and has anesthetic sparing properties without causing significant respiratory depression.

Dexmedetomidine hydrochloride is able to regulate the release of catecholamine by means of negative feedback so as to control blood pressure. Hemodynamic stability was better in the group receiving dexmedetomidine and also had higher incidence of hypotension, bradycardia as side effects.

**MATERIALS AND METHODS**

**Study Design:** Comparative Cross sectional study.

**Study procedure**
This comparative cross sectional study was conducted in Sree Mookambika Institute of Medical Sciences Kulasekharam during the period of January 2017 to June 2018. After obtaining permission from Institutional Human Ethical Committee (IHEC) and Institutional Research Committee (IRC), 70 patients belonging to the American Society of Anaesthesiology (ASA) classification class 1 & 2, of either sex between 18-50 years scheduled for elective surgery under general anaesthesia were included.

Patients who didn’t give valid consent, Age range <18 years >50 years, ASA classification III, IV and V, Allergic reaction to planned medication , Severe bradycardia (heart rate <50/min), Substance abuse were excluded from the study.

Every patient included in the study underwent pre-anesthetic checkup and all patients were reviewed on preoperative day reassured and explained in detail about the procedure, informed consent were obtained, advised fasting regime and given tablet ranitidine.
150mg & alprazolam 0.5mg previous night and T.ranitidine 150mg & T.metoclopramide 10mg on the day 2hrs prior to surgery.

The above selected patients were categorized into two groups of 35 as group I - interventional group (dexametomidine) and group II - control group (lidocaine) based on randomized technique – “slips of paper in a box”.

Patients were shifted to preoperative room and non invasive monitors were connected and baseline recordings were noted, 18G iv cannula secured and Ringer lactate 8ml/kg infusion started. Before inducing, dexametomidine 1 μg/kg was given to the patients in the interventional group I over 10 minutes where as in the control group the patients received lidocaine 2% 1.5 mg /kg bolus intravenously before 90 seconds of intubation. Patients were pre-oxygenated with 100% oxygen for 3 minutes following which Fentanyl 1.5mcg/kg IV given .Induction was done with Inj. Propofol 2mg/kg and muscle relaxation with Inj. Atracurium 0.5mg/kg bag mask ventilation done for 3minutes and patients were intubated with appropriate size laryngoscope blade and endotracheal tube and connected to ventilator after checking bilateral air entry. Maintenance was done with 02: N2O -2:4 liters and sevoflurane 0.5-1%. Inj. Atracurium 0.1mg/kg given for maintenance of muscle relaxation , 0.4mcg/kg of dexametomidine as infusion during surgery for group I patients. Heart rate, systolic blood pressure and diastolic blood pressure were recorded at just before intubation, immediately after intubation 1, 2, 3, 4, 5 minutes after intubation followed by every 5 minutes till the first 45 minutes of surgery. After completion of surgery patient were reversed with Inj. neostigmine 0.05mg/kg and inj. glycopyrrolate 0.004mg/kg and extubated.

RESULTS
Statistical Analysis

Data was entered in Microsoft Excel & statistical analysis was done by SPSS (16.0) version. Statistical analysis of demographic data heart rate changes blood pressure changes were done by Independent t-test. Student's test were used for comparing means of two groups.

P values less than 0.05 (p<0.05) are considered significant at 95% confidence interval p value >0.05 is not significant.

<0.05 is significant
<0.001 is highly significant.

Observation & Results

A sample size of 35 was obtained in each group. The data were collected with the help of a pre-structural profoma.

| COMPARISON OF DEMOGRAPHIC DATA (MEAN ±SD) –TABLE I |
|-------------------------------|-----------------|-----------------|
| PARAMETERS  | GROUP I  | GROUP II |
| AGE         | 36.63 ± 9.65 | 34.23±6.82    |
| SEX(MALE/FEMALE) | 16/19 | 17/18 |
| HEIGHT (cm) | 159.2±5.29 | 160.4±4.68    |
| WEIGHT (Kg) | 57.11±1.123 | 56±1.32       |
| ASA –PS(1/2) | 25/10 | 27/8 |

SD= Standard deviation. ASA -PS – American society of anaesthesiologists physical status

HEART RATE CHANGES
Comparison of heart rate changes between groups at various time intervals

![Fig 1 : Time dependent changes in Heart Rate of Group I & II Patients](image)

There was no difference in the baseline heart rate values. Statistically significant reduction in heart rate occurred in Dexmedetomidine group patients during preinduction, induction, intubation and 1min & 3min after intubation (p value <0.001).
SYSTOLIC BLOOD PRESSURE CHANGES
Comparison of mean systolic blood pressure changes between group

There was no difference in the baseline systolic blood pressure. Statistically significant reduction in systolic blood pressure occurred in Dexmeditomidine group patients during preinduction, induction, intubation and 1min & 3min after intubation (p value <0.001).

DIASTOLIC BLOOD PRESSURE CHANGES:

There was no difference in the baseline diastolic blood pressure and pre induction diatolic BP. Statistically significant reduction in diastolic blood pressure occurred in Dexmeditomidine group patients during induction, intubation and 1min after intubation (p value <0.05) and no difference in diastolic BP 3 min after intubation.

MEAN – ARTERIAL PRESSURE CHANGES

There was no difference in the baseline Mean arterial pressure between the two groups. Statistically significant reduction in mean arterial pressure occurred in Dexmeditomidine group patients during preinduction, induction, intubation and 1min & 3min after intubation (p value < 0.001).
DISCUSSION

Dexmedetomidine is an α2 adrenergic agonist which has highly selective action on its receptors, its action is exerted through three types of α2 receptors like α2 A, α2 B and α2 C. Dexmedetomidine causes conscious sedation, decrease in anxiety, relief of pain and has sympatholytic action by decreasing the catecholamine thereby causing decrease in heart rate and decrease in blood pressure. Dexmedetomidine acts upon the α2 A and α2 C receptors in locus ceruleus in brain and produces sedation.

Dexmedetomidine causes decrease in release of catecholamines by acting upon the alpha 2 receptors in central nervous system and also causes fall in blood pressure and decrease in heart rate. In the spinal cord, it acts upon α2 A and α2 C receptors and causes decrease in pain transmission by decreasing substance P.

The most critical events during general anesthesia are Laryngoscopy and endotracheal intubation. It causes a transient, but pronounced, sympathetic and adrenal response. Larynx, pharynx- and trachea, are extensively innervated by the ANS - During endo tracheal intubation there is activation of these structures leading to increase in BP and tachycardia due to sudden surge of catecholamine release.

Dexmedetomidine is a highly specific, potent, and selective α2-adrenoceptor agonist that causes reduction in the plasma catecholamine levels in patients receiving Dexmedetomidine prior to surgery. And it has been showed that in those patients who received Dexmedetomidine had significantly lower intraoperative catecholamine and cortisol levels when compared to the patients who received lidocaine before surgery.

In the recent years, cytokines and the more accepted stress hormones such as Cortisol and catecholamines acts as mediators of perioperative responses to surgery. A number of studies have proven that pro-inflammatory and anti-inflammatory cytokines are important in the acute-phase of inflammatory and immunologic response after surgical trauma. The important cytokines involved in this response are as follows - TNF-α, IL-6, and IL-10.

Laryngoscopy and endotracheal intubation are considered as the most critical events during general anesthesia. They provoke a transient, but marked, sympathetic and sympathoadrenal response like tachycardia and hypertension increase the risk of cardiovascular instability. Alpha 2 - adrenergic drugs, such as dexmedetomidine, attenuate these potentially harmful cardiovascular reactions during induction of anesthesia. In our study, we compared dexmedetomidine, a newer alpha 2 -agonist with additional properties such as sedation, anxiolyis and sympatholysis for attenuating the hemodynamic response to laryngoscopy and tracheal intubation.

Dexmedetomidine increases the hemodynamic stability by altering the stress-induced sympathoadrenal responses to intubation during surgery and during emergence from anesthesia. Gupreet Singh et al., in their study concluded that Dexmedetomidine has more significant action in reducing the pressor response to laryngoscopy and endotracheal intubation than lidocaine. The dose used for this study was 0.6 mcg/kg/hour, which is almost similar to the dose used by us.

Study conducted by Rasmi and Komala(2016) also showed that 0.6mcg/kg dexmedetomidine obtained the hemodynamic response to laryngoscopy and tracheal intubation.

Sebastian et al(2017) conducted a study to find out the effect of optimal dose of dexmedetomidine on tracheal intubation by comparing two doses along with placebo in decreasing the stress response during laryngoscopy and intubation and the study inferred that dexmedetomidine at the dose of 0.75mcg/kg intravenously is the adequate dosage to attenuate the pressor response during tracheal intubation.

Feng et al(2013) in their study showed that single dose of dexmedetomidine given in induction of GA significantly reduced the stress hormone release in response to tracheal intubation and kept hemodynamics more stable and contributed to perioperative clinical safety. In our study we didn’t measure the plasma concentration of epinephrine and norepinephrine levels.

Sukhminde jit singh bajwa et al (2012) in their study found that IV dexmedetomidine significantly decreased the pressor response during laryngoscopy and intubation and mean dose of fentanyl and isoflurane were also reduced upto 50%. In our study also the dose of fentanyl and sevoflurane requirements were less.

Lawrence et al(1997) found that a single dose of 2 mcg/kg of dexmedetomidine before induction of anesthesia attenuated the hemodynamic response to intubation as well as that to extubation. Bradycardia was observed at the 1st and 5th min after administration. This might have been due to bolus administration of higher dose. The dose of dexmedetomidine in our study was 1 mcg/kg bolus over 10 minutes prior to induction of anesthesia followed by 0.4 mcg/kg as an infusion throughout surgery. Hemodynamic response was better and bradycardia was not observed during in our study.

Sajith Suilaiman et al(2012) conducted a study, 60 patients who were taken up for CABG surgery were allocated into two groups, among which one received dexmedetomidine (0.5 mcg/kg) and other group received normal saline 15 min prior to intubation.
Clinical ravenous A., Scheinin, M., & Fisher, D. e plasma anesthesia in relation to hypertension were not studied. postoperative sedation and hemodynamic variations norepinephrine levels. Secondly, extubation response to endotracheal intubation in patients who are undergoing thyroid surgery. Dexmedetomidine will be a preferred choice high risk patients also.

CONCLUSION Dexmedetomidine has reduced the pressor response during Laryngoendotracheal intubation better than lidocane. This effect of blunting the pressor response to intubation and reducing surgical stress, hence Dexmedetomidine will be a preferred choice in high risk patients also.

BIBLIOGRAPHY