Comparative Study between Dexmedetomidine and Lignocaine

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Abstract: During induction of general anesthesia hypertension and tachycardia caused by tracheal intubation may lead to cardiac ischemia and arrythymias. Therefore, maintenance of stable haemodynamic parameters during endotracheal intubation under general anaesthesia is crucial to ensure adequate coronary perfusion and prevention of acute rise of blood pressure. To study the hemodynamic response to endotracheal intubation with the new $\alpha2$ agonist dexmedetomidine, This study was carried out in Yashoda Hospital, Hyderabad. A sample size of 60 patients was selected using random sampling 60 patients aged 18 to 60 yrs, belonging to ASA I and II, were included in the study and they were randomly allocated into 2 groups of n=30 each. Group I received lignocaine 1.5mg/kg iv 3min before induction. Group II received 1mcg/kg iv in 100 ml NS over 15 min. before induction.HR, SBP were recorded pre-operatively, 30 sec after intubation, 1 min after intubation , 3min after intubation & 5min after intubation .RPP derived from HR & SBP method. Patient was allocated in one of the group. After Premedication anaesthesia was induced with inj. Thiopentone 5 mg/kg body wt and endotracheal intubation was facilitated with succinylcholine 1.5 mg/kg body wt administered one minute prior to laryngoscopy and intubation. Laryngoscopy was performed by the experienced anaesthetist who was blinded to the groups. Statistically there was no significant difference in two groups regarding the age (p=0.39001) sex (p=0.17) and weight (p=0.33939). In this study, we observed that the increase in the HR at 1 minute after intubation in compared to basal value was statistically significant (p = 0.01439*) in dexmedetomidine group (group 2) but it was less then lignocaine group and it came to base line dramatically. we observed that the decrease in SBP observed at 1 minute and 3 min after intubation with dexmedetomidine when compared with basal value and lignocaine was statistically significant (p < 0.0000***) and (p=0.00004***) respectively. The decrease in RPP at 1 minute & 3 minute after intubation with dexmedetomidine when compared with the basal value and lignocaine was statistically significant (p =0.0000***) & (p=0.01209*) respectively. Need for rescue analgesia did not arise when dexmedetomidine was added (group I) for performing endotracheal intubation, whereas 16% of patients needed rescue analgesia in lignocaine group due to acute increase in SBP.
Keywords: Dexmedetomidine, lignocaine, laryngoscopy, endotracheal intubation and hemodynamic responses.

INTRODUCTION

The placement of endotracheal tube into the trachea stimulates for the release of catecholamines. This is a recognized acute noxious stimulation during intubation and can result in sudden increases in blood pressure (BP) and heart rate (HR) despite apparently adequate depth of anaesthesia. In patients with known coronary artery disease or ischemic heart disease this sympathetic stimulation may cause increases in blood pressure, which can be associated with increased patient morbidity and mortality rates. Hypertension and tachycardia caused by tracheal intubation may lead to cardiac ischemia and arrythymias during induction of general anesthesia. Therefore, maintenance of stable haemodynamic parameters during endotracheal intubation under general anaesthesia is crucial to ensure adequate coronary perfusion and prevention of acute rise of blood pressure.

Many different strategies have been used to minimise the haemodynamic responses to intubation with varying results. The use of large intravenous bolus of opioids before endotracheal intubation to obtund haemodynamic responses secondary to

intubation was associated, in many reports, with increase in blood pressure and may prolong emergence from anaesthesia.

Various adjuvants have been tried with varying results, like lignocaine, esmolol, opioids. Alpha 2 agonists like dexmedetomidine have been used along with opioids and also as premedication to reduce the hemodynamic effects.

A new, potent α2-adrenoceptor agonist Dexmedetomidine is approximately 8 times more selective for the α2-adrenoceptor than clonidine. It has been labelled as "analgesia-sparing" by the FDA. Studies shows that is well tolerated and effective in various neuraxial and regional, general anaesthetics in humans, including during the delivery of intrathecal, caudal, and intravenous (i.v.) regional anaesthesia.

There have been many studies that showed the effectiveness of blunting the hemodynamic response to endotracheal intubation.

We decided to study effect of attenuating the hemodynamic response to endotracheal intubation with the new α2 agonist dexmedetomidine, as α2 agonists are considered to increase the depth of anesthesia.

AIMS & OBJECTIVES
- To compare intravenous dexmedetomidine with intravenous lignocaine for attenuation of hemodynamic responses to laryngoscopy and endotracheal intubation.
- It is a prospective randomized, controlled, double blind study in a groups demographically comparable of patients divided into two groups of 30 patients each.
- To study the effect of laryngoscopy and intubation on changes in the heart rate (HR), Systolic blood pressure (SBP) and Rate pressure product (RPP).

MATERIALS AND METHODS
This study was undertaken in Yashoda Hospital Hyderabad during the year November 2010 to December 2011, after obtaining ethical committee clearance as well as informed consent from all the patients.

The study population were divided into two (2) groups with 30 patients in each group.

- **Group 1** – Received intravenous lignocaine 1.5mg/kg before endotracheal intubation (n=30).

- **Group 2** –Received dexmedetomidine 1mcg/kg before induction of anesthesia (n = 30).

The groups were generated using computer generated random numbers. Person A will inject the drug as per protocol. Person B monitors the heart rate, blood pressure and mean arterial pressure with respect to time and Person C intubate the patient (constant). Persons B and C were blinded.

Inclusion Criteria
- Patients belonging to ASA grade I and II.
- Patients aged between 18 to 60 years undergoing various surgical procedures under general anaesthesia.

Pre-randomisation Exclusion Criteria
- Patients belonging to ASA grades other than I and II.
- Patients of age group below 18years or more than 60 years.
- Pregnant patients.
- Anticipated difficult intubation.
- Allergy or intolerance to study drugs.
- Patient refusal to study.

Post-randomisation exclusion Criteria
- More than two attempts at intubation.
- Inadequate data entry.

Pre-anaesthetic evaluation was done on the evening before surgery. A routine pre-anaesthetic examination was conducted assessing -
- General condition of the patient
- Nutritional status and weight of the patient
- A detailed examination of the cardiovascular system
- A detailed examination of the Respiratory system
- Other associated diseases.

The following investigations were done in all patients
- Haemoglobin estimation
- Urine examination for albumin, sugar and microscopy
- Standard 12- lead electrocardiogram
- X-ray chest/ Screening of chest
- Blood sugar, FBS/PPBS
- Blood urea

All patients were tested for any hypersensitivity reaction to local anaesthetics and an informed consent was obtained from all the patients.

All the patients included in the study were premedicated with Tab. Alprazolam 0.5 mg and Tab. Ranitidine 150 mg orally at bed time the previous day.

On the arrival of the patient in the operating room, a 18-gauge/20-gauge intravenous cannula was inserted. The patients were connected to multichannel monitor which records Heart rate, non-invasive blood pressure (NIBP), end-tidal carbon dioxide concentration (ETCO2), and continuous ECG

monitoring, MAP and oxygen saturation. The baseline blood pressure and heart rate were recorded from the same non-invasive multichannel monitor and cardiac rate and rhythm were also monitored from a continuous visual display of electrocardiogram from lead II.

Inj. Ondansetron 4 mg iv and inj. Glycopyrrolate 0.2 mg i.v. was given to all the patients before induction as premedication. The patients were preoxygenated for three minutes using 100% oxygen by facemask with Bains circuit.

Patients in Group 1 received inj. Lignocaine 1.5mg/kg i.v 3min before induction.

Patients in Group 2 received Inj. Dexmedetomidine 1 mcg/kg i.v. diluted in 100ml NS injected over 15 minutes before induction of anesthesia. The intubating anesthetist was blinded to the study and dilutant procedure.

INDUCTION OF ANAESTHESIA

Inj. Thiopentone 5 mg/kg as 2.5% solution used for induction of anaesthesia and succinylcholine 1.5 mg/kg administered for endotracheal intubation one minute prior to laryngoscopy and intubation. Laryngoscopy was performed by the experienced anaesthetist who was blinded to the groups. The intubating conditions were evaluated and scoring was done according to the four step scale proposed by Goldberg and colleagues by the intubating anaesthetist.

It was graded as follow, Grade I- Excellent, Grade II- Good, Grade III- Poor, Grade IV- Impossible intubating condition. The patients were intubated using appropriate sized cuffed endotracheal tubes. After confirming bilateral equal air entry, the endotracheal tube was secured.

Anaesthesia was maintained using 66% nitrous oxide and 33% of oxygen and isoflurane 0.6 to 0.8%. After the patients recovered from succinylcholine further neuromuscular blockade was maintained with non-depolarizing muscle relaxants. At the end of the procedure patients were reversed with neostigmine 0.05 mg/kg IV and glycopyrrolate 0.008 mg/kg IV.

MONITORING

The following cardiovascular parameters were recorded in all the patients
- Heart rate (HR) in beats per minutes (bpm)
- Systolic blood pressure (SBP) in mm Hg
- Rate Pressure Product (RPP)

The above cardiovascular parameters were noted as below
- Pre-op before giving any study drugs and premedication
- 30 seconds after intubation
- 1 minute after intubation
- 3 minute after intubation
- 5 minute after intubation

Goldberg and colleagues grading of intubating conditions [15]

Grades	Description
Excellent	Easy passage of tracheal tube without coughing, vocal cords relaxed.
Good	Slight coughing, vocal cords relaxed
Poor	Passage of tracheal tube with moderate coughing or bucking, some movements of vocal cords
Impossible	Vocal cords adducted or not visualized, jaw not relaxed.

The results were statistically evaluated using student 't' test & ANOVA test comparing between the groups and within the group respectively.

OBSERVATIONS & RESULTS

It is a prospective, controlled, randomized, double blind study to evaluate the efficacy of intravenous dexmedetomidine 1mcg/kg body weight and intravenous lidocaine 1.5mg/kg on hemodynamic responses to laryngoscopy and endotracheal intubation. It was conducted in the Department of Anaesthesiology, Yashoda Hospital, Hyderabad, between November 2010 to December 2011.Total number of cases allocated to lidocaine group = group i = 30. Total number of cases allocated to dexmedetomidine group = group ii = 30.

Table-1: Frequency distribution of cases according to age

Parameter	Group	N	Mean ± SD	P value
AGE(years)	Group 1	30	35.0667±12.1199	0.39001
	Group 2	30	37.7333±11.7266	

Table-2: Distribution of case according to their sexes

Group 1		Group 2	
Male	Female	Male	Female
18	12	18	12

MALE: FEMALE RATIO

A. percentage of males in Group – I = 60

   Percentage of females in Group – I = 40

B. percentage of males in Group – II = 60

Percentage of female in Group – II = 40

Table-3: Comparison of mean weights (Kgs) between the two groups

Parameter	Group	N	Mean±SD	P value
Weight	Group 1	30	60.8667±7.9989	0.33939
	Group 2	30	63.1667±10.3460	

Table-4: showing changes in mean heart rate

Time	Group 1	Group 2
Pre-op	81.8667±11.5183	89.1667±10.6547
Intubation-30 sec	89.6667±9.3378	95.6667±17.7129
1 min	107.5333±12.2016	97.2000±18.8211
3 min	99.9333±11.9595	96.6000±18.1176
5 min	93.6667±11.8273	91.4000±14.6749

In the group 1(lignocaine group), the basal HR was 81.8667±11.5183 bpm. One minute after intubation, it was 107.5333±12.2016 bpm, representing a rise in HR. Subsequently, the elevated heart rate started settling down. By 3 minute, it was 99.9333±11.9595 bpm and by 5 minute it was 93.6667±11.8273 bpm.

In group 2(dexem group), the basal HR was 89.1667±10.6547 bpm, 1 minute after intubation, it was 97.2000±18.8211.. Subsequently, the elevated heart rate started settling down. By 3 minutes it was 96.6000±18.1176 bpm and by 5 minutes it was 91.4000±14.6749 bpm. The increase in the HR at 1 minute after intubation compared to basal value was statistically significant ($p = 0.01439^{*}$)

Table- 5: Changes in the mean systolic blood pressure (SBP)

Time	Group 1	Group 2
Pre-op	122.6667±11.7248	127.8667±10.2780
Intubation- 30 sec	121.0667±11.4318	118.4667±11.1099
1 min	155.8000±19.3647	122.4000±15.3232
3 min	133.6667±13.7679	119.5000±10.9000
5 min	122.6667±13.1551	117.5333±9.3430

In the group 1 (lignocaine group) the basal value of SBP was 122.6667±11.7248 mm Hg, following 1 min of intubation, the SBP increased to 155.8000±19.3646 mmHg. This elevated pressure started coming down. By 3 minutes it was 133.6667±13.7679 mm Hg and by 5 minutes it was 122.6667±13.1551mmHg.

In group 2 (dexem group) the basal value of SBP was 127.8667±10.2780 mm Hg, 1 minute following intubation the SBP was 122.4000±15.3232 mm Hg,. Afterwards the elevated blood pressure started coming down towards the baseline value. By 3 minutes it was 119.5000±10.9000 mm Hg and by 5 minutes it was 117.5333±9.3430 mm Hg.

The decrease in SBP observed at 1 minute and 3 min after intubation when compared with basal value was statistically significant ($p < 0.0000^{***}$) and ($p=0.00004^{***}$) respectively.

Table 6: Changes in the mean rate pressure product (RPP)

Time	control	Study
Pre-op	10080.0000±1927.8500	11372.9333±1643.4490
Intubation- 30 sec	10866.2667±1615.3050	11370.3000±2713.6160
1 min	16831.2667±3269.5260	11979.3333±3281.5170
3 min	13433.3333±2545.4350	11646.9667±2789.7850
5 min	11504.0000±1978.8220	10750.2000±1851.2400

In the group 1 (lignocaine group), the basal RPP was 10080.0000 ± 1927.8500. One minute after intubation, the RPP increased to 16831.2667 ± 3269.5260. Subsequently the elevated RPP started settling down. By 3 minutes it was 13433.3333 ± 2545.4350 and by 5 minutes it was 11504.0000 ± 1978.8220.

In group 2 (dexem group), the basal RPP was 11372.9333 ± 1643.4490. One minute after intubation, the RPP increased to 11979.3333 ± 3281.5170. Subsequently the elevated RPP started settling down. By 3 minutes, it was 11646.9667 ± 2789.7850 and by 5 minutes it was 10750.2000 ± 1851.2400. The decrease in RPP 1minute & 3 minutte after intubation when compared with the basal value was statistically significant (p =0.^{0000***})
& (p=0.01209*) respectively.

DISCUSSION

Acute increases in heart rate and arterial blood pressure can be deleterious in the patient with cardiac disease like coronary artery disease, hypertension or with cerebral aneurysms.[1] Acute arterial hypertension can further increase ICP with a risk for herniation, and may also result in pulmonary oedema and ruptured cerebral aneurysms.[2] Therefore, prevention of acute hypertension in the neurosurgical patient due to noxious stimuli such as endotracheal intubation would be desirable.

There have been many studies that demonstrate stable hemodynamic parameters during endotracheal intubation with many drugs such as fentanyl, lidocaine, esmolol etc. Various studies have reviewed the effect of lignocaine to blunt these responses.

Some studies note a response of intravenous lignocaine in blunting rises in pulse, blood pressure, intracranial and intraocular pressure. Aouad *et al*. study concluded that lignocaine 2 mg/kg can suppress cough after tracheal intubation. And it also minimizes blood pressure fluctuations after tracheal intubation.

Abou-Madi *et al*. have discussed the possible mechanisms to account for these observations with IV lignocaine. These include a direct myocardial depressant effect, a peripheral vasodilating effect and finally an effect on synaptic transmission.

In our study also lidocaine of 1.5 mg/kg given intravenously 3 minutes before is effective in attenuating the hemodynamic response to endotracheal intubation.

Ebert *et al*. Comparative study concluded that fentanyl decreased the SBP, MAP and DBP significantly below the baseline, while these pressures were either retained at or elevated slightly above control in the esmolol group.There were no complications or ischaemic electrocardiographic changes in any patient.

5 min before tracheal intubation is the most effective time to administer fentanyl to protect circulatory responses to laryngoscopy and tracheal intubation is according to Ko *et al*. Study. However, large doses of fentanyl may cause unwanted side effects. Optimal time administration reduces the dose required.

Dexmedetomidine is a novel alpha2-agonist with potent anxiolytic and sedative properties. The haemodynamic profile of dexmedetomidine was found to be similar to clonidine.

Several studies have found dexmedetomidine to be well tolerated and effective in various neuraxial and regional anaesthetics in humans, including during the delivery of intrathecal[3] caudal[4] and intravenous (IVRA) regional anaesthesia[5].

In a recent animal study, DEX was reported to be well tolerated and it prolonged the duration of sensory blockade effectively when injected perineurally in the peripheries [6].

The mechanism of action of α2-adrenoceptor agonists in peripheral nerve blocks is not understood fully.

Proposed mechanisms include central analgesia, vasoconstriction, and anti-inflammatory effects [7]. However; none of these mechanisms can explain fully the synergistic effect of α2-adrenoceptor agonists when added to a local anaesthetic in peripheral nerve blocks.

The direct action of α2-adrenoceptors on the peripheral nerve may be mediated through an increase in hyperpolarization of the after-potential that follows a single compound action potential[8].

It is well known that in peripheral myelinated and nonmyelinated fibres, membrane hyperpolarization develops during and after stimulation and mainly results from the activation of the sodium–potassium pump after the transient influx of sodium ions[9].

Dalle *et al*. [10] found that clonidine increases the hyperpolarization that develops during low-frequency stimulation by inhibiting the hyperpolarization-activated cation (Ih) current. The Ih current is activated during the hyperpolarization phase of an action potential and acts to reset a nerve for subsequent action potentials. Thus, clonidine enhances the level of hyperpolarization by blocking the Ih current and thus inhibits subsequent action potentials.

Dexmedetomidine may enhance the sensory blockade in a manner similar to clonidine.

Dexmedetomidine is a highly selective α2-adrenoceptor agonist; however, the analgesic effect of α-adrenoceptor agonists may not be mediated via the α2-adrenoceptor [11].

The safety of perineural administration of dexmedetomidine has not been well studied in humans. Accordingly, we developed a cautious study design, using a dose of dexmedetomidine (1mcg/kg) as has been done.

Dexmedetomidine is a preservative-free solution and contains no additives or chemical stabilizers. More recently, data from an animal study[26] showed that high doses of DEX (up to 40 mcgkg_1) had no effect on either nerve axons or myelin sheaths and might even attenuate the acute perineural inflammation that is induced by bupivacaine without causing nerve damage[6].

The main result of our study is that, dexmedetomidine group showed maximum attenuation of haemodynamic responses (HR, SBP, and RPP) to endotracheal intubation when compared to lidocaine group.16 % of the study patients needed rescue analgesia with fentanyl but dexmedetomidine group not needed rescue analgesia

CONCLUSION
Findings from our study suggest that, dexmedetomidine 1 mcg/ kg iv 15 min before induction in ASA grade I and II patients is a simple, effective and practical method of blunting cardiovascular responses to tracheal intubation, not associated with any adverse effect and provided good analgesic effect.

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