A CLINICAL STUDY OF INTRAVENOUS DEXMEDETOMIDINE VERSUS LIGNOCAINE PREMEDICATION FOR ATTENUATION OF HAEMODYNAMIC RESPONSES TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

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ABSTRACT

CONTENT

Direct laryngoscopy and endotracheal intubation are the most stressful periods during induction of anaesthesia. These events can lead to hypertension, tachycardia, arrhythmias and myocardial ischaemia. Dexmedetomidine, an alpha-2 adrenoreceptor agonist, is gaining popularity for its sympatholytic, sedative, anaesthetic sparing and haemodynamic stabilising properties without significant respiratory depression.

AIM

The aim of the study is to compare the efficacy of Dexmedetomidine against Lignocaine in attenuation of haemodynamic response of laryngoscopy and endotracheal intubation.

METHODS

A randomised controlled study was designed with total of 60 patients of which 30 patients received dexmedetomidine (Group D) 1 mcg/kg IV infusion 10 minutes prior to endotracheal intubation and 30 patients received 1.5 mg/kg of lignocaine intravenous (Group L) 3 mins. prior to endotracheal intubation. Inj. Thiopentone was given until eyelash reflex disappeared and intubation was facilitated with succinylcholine. Anaesthesia was maintained with 33:66 Oxygen: Nitrous oxide, halothane, and vecuronium. The patients were evaluated for change in systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) & heart rate (HR) during pre-induction, just prior to induction at 0,1,3,5 & 10 mins. after laryngoscopy & intubation. Any adverse effects of the drugs were noted.

RESULTS

The two groups were comparable regarding age, sex, weight and type of surgeries. The HR, SBP, DBP, and MAP values were significantly lower in Group D at induction and statistically lower at 1, 3, 5, and 10 mins. when compared to Group L.

CONCLUSION

Dexmedetomidine attenuates the haemodynamic stress response to laryngoscopy and intubation more effectively when compared with lignocaine without any adverse effects.

KEYWORDS

Dexmedetomidine, Lignocaine, Laryngoscopy, Intubation, Haemodynamic Stress Response.

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INTRODUCTION: Both laryngoscopy and endotracheal intubation induce a sympathetic response resulting in a rise in serum catecholamines. The rise in serum concentrations of norepinephrine might be up to 147% and that of epinephrine level up to 60% during laryngoscopy and endotracheal intubation.[1] It leads to an increase in heart rate and blood pressure.[2] The change in haemodynamic response is usually transient, variable and unpredictable. The major determinants of myocardial oxygen demand are heart rate (HR) and blood pressure.

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Since endotracheal intubation causes marked increase in arterial pressure and HR, the increase in myocardial oxygen demand must be met by an increase in supply of blood through coronary circulation. This is well tolerated by healthy individuals but may be life-threatening in susceptible individuals.[3] Treatment modalities include topical lignocaine sprays, deeper planes of anaesthesia by inhalational/intravenous (IV) agents or narcotics, calcium channel blockers like verapamil, nicardipine and diltiazem, vasodilators such as sodium-nitroprusside, nitroglycerin, esmolol, magnesium sulphate, gabapentin, etc.[4] have been tried to reduce the pressor response. Alpha-2 adrenergic agonists decrease sympathetic tone and blunt the haemodynamic responses to noxious stimulation and prevent the overall haemodynamic variability.

It also reduces the need for anaesthetics and therefore can be used as an adjunct to general anaesthetics.

Dexmedetomidine, a more specific and selective alpha-2 adrenergic agonist than clonidine has a shorter duration of action.[5] The present study is designed to assess the effects of Dexmedetomidine to attenuate the haemodynamic responses to endotracheal intubation when compared to Lignocaine and to assess the incidence of side effects, that is rebound hypertension, bradycardia and hypotension etc., associated with the use of Dexmedetomidine.

MATERIALS AND METHODS: After institutional approval, written informed consent was obtained from each patient. A total of 60 American Society of Anaesthesiologists (ASA) physical status I and II patients aged between 18 and 60 years undergoing elective surgery under general anaesthesia were enrolled in the study. Patients with hypertension, cardiac, coronary, renal, hepatic, cerebral diseases, and peripheral vascular diseases, bradycardia, obese patients, anticipated difficult airway, pregnant, and nursing women, history suggestive of sensitivity to drugs used during the study and difficult ventilation and/or difficult intubation (more than 15 sec) after induction were excluded from the study. The patients were randomly assigned to one of the two groups. Group D received dexmedetomidine 1 mcg/kg diluted in 100 mL of normal saline IV over a period of 10 min., and the infusion was completed 10 min. before induction. 3 mL of normal saline was injected intravenously 3 mins. before induction to prevent bias. Group L received 100 mL of normal saline 20 min. preoperatively over a period of 10 min., and the infusion was completed 10 min. before induction and 1.5 mg/kg of lignocaine was administered IV 3 min. before intubation.

None of the patients were on any significant drug therapy preoperatively. All patients included in the study were premedicated with tablet alprazolam 0.5 mg and tablet ranitidine 150 mg orally on the night before surgery. The patients were connected to multipara monitor and basal readings of heart rate and blood pressure were noted. IV cannulation was done in the operation theatre. All the patients were premedicated with injection glycopyrrolate 0.01 mg/kg IV, injection ondansetron 0.08 mg/kg IV, injection midazolam 0.02 mg/kg IV, and injection pentazocine 0.5 mg/kg IV before preoxygenation. After preoxygenation for 3 minutes, all patients were induced with injection thiopentone 2.5% solution IV till loss of the eye lash reflex occurred. Endotracheal intubation was facilitated with 2 mg/kg of succinylcholine given IV 1 min. prior to laryngoscopy and intubation. Laryngoscopy was performed using Macintosh laryngoscope, trachea intubated by same senior anaesthesiologist with appropriate size endotracheal tube, and connected to closed circuit. Laryngoscopy and intubation was limited to 15-20 seconds in all patients, failure to intubate within this period were excluded from this study. After confirmation of bilateral equal air entry, endotracheal tube was fixed. No surgical or any other stimulus was applied during 10 min. of study period and vecuronium was the only additional drug given during this period.

Vital parameters such as HR, SBP, DBP and MAP were recorded, at baseline, after study drug infusion, after induction, immediately and at 1, 3, 5 and 10 min after intubation and every 5 min there after using multipara monitor. Anaesthesia was maintained with, 66% N_2O in 33% oxygen and 1% halothane. Bolus IV dose of 0.08 mg/kg vecuronium followed by intermittent dose of 0.02 mg/kg vecuronium was used for muscle relaxation. At the end of the procedure, patients were reversed with an injection neostigmine 0.05 mg/kg IV and injection glycopyrrolate 0.01 mg/kg. IV. Patients were extubated when they regained reflexes and consciousness.

STATISTICAL ANALYSIS: The data are expressed as Mean±Standard deviations. A sample size of 20% patients per group was required to detect a difference of at least 20% between two groups. Demographic data were analysed by student's t-test between the two groups. Statistical analysis was conducted with SPSS using paired and unpaired students t-test. A P-value of less than 0.05 was regarded as statistically significant. A P-value of less than 0.001 was taken as statistically highly significant.

RESULTS: The two groups were comparable in age, sex, weight and types of surgeries (Table 1).

Patients Characteristics	Group - D	Group – L
Age (years)	41 ±12.4	40 ±11.9
Sex (M/F)	16/14	17/13
Weight (kg)	56 ±9.1	54 ±8.1
Type of Surgeries		
Cholecystectomy	11	9
CA breast	4	3
ENT surgery	6	5
Oro-maxillofacial	3	4
Thyroid	2	3
Upper limb surgeries	4	6

Table 1: Demographic profile & Type of surgeries in Dexmedetomidine and Lignocaine groups.

Before administration of the study drugs in the operating room, heart rate and blood pressure values between the two groups did not differ. In group D patients receiving dexmedetomidine loading infusion, a fall in the heart rate and blood pressure was observed, which was not more than 5% of the baseline. Patients were sedated but arousable with Ramsay's sedation score of 3. Heart rate (Table 2) values were statistically significantly lower in the Group D at induction and highly statistically significantly lower at 1, 3, 5 and 10 mins. when compared to the Group L. Systolic blood pressure (Table 3) values were statistically significantly lower in the group D at induction and highly statistically significantly lower at 1, 3, 5 and 10 mins. Diastolic (Table 4) and mean arterial pressure (Table 5) values were highly statistically significantly lower in the group D at 1, 3, 5 and 10 min.

Heart Rate (Beats/min.)	Group D	Group L	P-Value	Significance
Basal	83.50±14.88	90.26±15.50	0.68	NS
Pre-induction	74.42±16.46	88.24±14.46	0.54	NS
Induction	80.46±14.62	104.20±16.96	0.001	HS
Intubation: 0 min.	80.88±16.14	105.04±12.96	0.001	HS
1 min.	80.44±12.38	106.08±11.84	0.001	HS
3 min.	77.82±10.10	98.88±13.26	0.001	HS
5 min.	70.98±11.92	91.16±14.60	0.001	HS
10 min.	78.84±10.66	90.22±12.64	0.001	HS

Table 2: Comparison of Heart Rate in patients of Dexmedetomidine and Lignocaine groups at different intervals.

NS: Not Significant, HS: Highly Significant.

Systolic Blood Pressure(mmHg)	Group - D	Group - L	P-Value	Significance
Basal	120.27±5.45	121.82±9.66	0.96	NS
Pre-induction	126.26±16.03	126.76±12.62	0.57	NS
Induction	120.80±14.62	116.44±5.48	0.001	HS
Intubation: 0 min.	126.22±18.40	166.56±13.40	0.001	HS
1 min.	116.28±11.96	142.80±18.86	0.001	HS
3 min.	112.06±11.82	130.64±16.66	0.001	HS
5 min.	114.36±10.06	126.62±11.80	0.001	HS
10 min.	116.28±14.21	126.62±12.48	0.001	HS

Table 3: Comparison of Systolic Blood Pressure in patients of Dexmedetomidine and Lignocaine groups at Different Intervals.

NS: Not Significant, HS: Highly Significant.

Diastolic Blood Pressure(mmHg)	Group- D	Group- L	P-Value	Significance
Basal	78.16±8.42	76.62±9.64	0.80	NS
Pre-induction	80.10±13.82	75.96±8.62	0.54	NS
Induction	78.06±13.96	77.10±5.18	0.001	HS
Intubation: 0 min.	74.36±6.24	90.66±19.90	0.002	HS
1 min.	76.38±12.66	88.82±10.66	0.001	HS
3 min.	71.24±12.08	82.16±9.96	0.001	HS
5 min.	70.55±11.30	80.16±20.42	0.001	HS
10 min.	71.67±12.85	75.44±9.20	0.001	HS

Table 4: Comparison of Diastolic Blood Pressure in patients of Dexmedetomidine and Lignocaine groups at Different Intervals.

NS: Not Significant, HS: Highly Significant.

Mean Arterial Pressure(mmHg)	Group- D	Group- L	P-Value	Significance
Basal	94.06±10.24	92.96±11.92	1.00	NS
Pre-induction	80.02±11.38	84.70±11.08	0.656	NS
Induction	84.88±11.92	105.88±10.02	0.001	HS
Intubation: 0 min.	86.62±11.24	110.68±12.08	0.001	HS
1 min.	82.64±12.08	106.66±14.98	0.001	HS
3 min.	78.80±11.88	102.62±14.08	0.001	HS
5 min.	76.46±9.62	96.60±12.78	0.001	HS
10 min.	72.26±10.68	98.28±9.84	0.001	HS

Table 5: Comparison of Mean Arterial Pressure in patients of Dexmedetomidine and Lignocaine groups at Different Intervals.

NS: Not Significant, HS: Highly Significant.

There was no case of significant fall in oxygen saturation, hypotension or bradycardia or hypertension in our case series in either group.

DISCUSSION: Laryngoscopy and endotracheal intubation is the most reliable technique of securing the airway and are the most critical events during general anaesthesia. Burstein et al[6] found that the presser response to laryngoscopy and endotracheal intubation was due to an augmented sympathetic activity which was provoked by the stimulation of the epipharynx and the laryngopharynx, which was further confirmed by Prys-Robert. The mechanical stimulation of upper respiratory tract including the tongue, nasopharynx, oropharynx and most importantly the epiglottis results during laryngoscopy. Afferents impulses are carried by the glossopharyngeal nerve and vagus nerve to the cardioaccelerator or vasomotor centre. Sympathetic efferent from this centre results in transient rise in heart rate and blood pressure. Shribman et al[7] demonstrated an increase in serum catecholamine levels during laryngoscopy, with and without concomitant endotracheal intubation, which could be the probable cause of these haemodynamic changes. It has been shown by Kaplan that stress due to sympathetic activation causes myocardial oxygen demand to exceed beyond its coronary supply resulting in parts of myocardium being rendered ischaemic.

Many pharmacological and non-pharmacological techniques have been tried to reduce the sympathetic response to laryngoscopy and intubation. Drugs like topical lignocaine sprays, deepening the planes of anesthesia by inhalational/intravenous (IV) agents or narcotics, calcium channel blockers like verapamil, nicardipine and diltiazem, vasodilators such as sodium nitroprusside, nitroglycerin, esmolol, magnesium sulphate, IV Lignocaine, gabapentin and limiting the period of laryngoscopy and intubation to minimum of 15 – 20 secs have been tried. Lignocaine is one of the cheapest and safest drugs used in many centres to attenuate stress response to intubation as seen in several studies.[8] Several authors.[9,10] have concluded that 1.5 mg/kg of lignocaine suppresses stress response to intubation when given 3 min. before intubation. The alpha adrenoceptors are involved in regulating the autonomic nervous system and cardiovascular systems. Alpha-2 adrenoceptors are located on blood vessels, where they mediate vasoconstriction and on sympathetic presynaptic terminals where they inhibit epinephrine and norepinephrine release.[11] Alpha-2 adrenoceptors are also located within the central nervous system and their activation leads to sedation, a reduction of tonic levels of sympathetic outflow and an augmentation of vagal activity.

This can result in a decrease in HR and cardiac output. Alpha-2 adrenergic drugs, such as clonidine or dexmedetomidine, attenuate these potentially harmful cardiovascular reactions during laryngoscopy and intubation. Alpha-2 agonists produce hyperpolarisation of noradrenergic neurons and suppression of neuronal firing in the locus coeruleus leads to decreased systemic noradrenaline release, results in attenuation of sympathoadrenal responses and haemodynamic stability during laryngoscopy and tracheal intubation.[12] Dexmedetomidine is the new alpha-2 agonist having 8-times more affinity for alpha-2 adrenoceptors as compared with clonidine.

Dexmedetomidine offers a unique pharmacological profile with sedation, sympatholysis, analgesia, opioid and anaesthetic sparing effect, cardiovascular stability and with great advantage to avoid respiratory depression.[13] The mechanism behind the attenuation is inhibition of central sympathetic outflow as well as stimulation of presynaptic alpha-2 receptor, which causes decrease in norepinephrine release, causing a fall in blood in blood pressure and heart rate.[14] The use of alpha-2 agonists in the peri-operative period has been associated with reduced anaesthetic requirements and attenuated HR and blood pressure responses to stressful events.[15] It has been used for adjunctive sedation in alcohol withdrawal, mechanical ventilation in Intensive Care Unit, awake carotid endarterectomy, for bariatric and cosmetic procedures[16] and lowering postoperative delirium after surgery.[17]

Dexmedetomidine has anaesthetic sparing effects and has been widely studied as an anaesthetic adjuvant and in studies by Aho.[18] and colleagues and Aantaa.[19] and co-workers, it has been shown to reduce the isoflurane requirement dose dependently up to 90%. Tanskanen.[20] and co-workers, in their study using dexmedetomidine as an anaesthetic adjuvant for intracranial tumour, concluded that there was increased perioperative haemodynamic stability in patients undergoing brain tumour surgery without postoperative respiratory depression. Also, dexmedetomidine has been studied as a supplement to isoflurane for vitreoretinal surgeries, without causing undue haemodynamic fluctuation, and has been shown to decrease the excitatory response during extubation with acceptable reduction in intraocular pressure.[21]

In our study, we used dexmedetomidine 1 mcg/kg diluted in 100 mL of normal saline and infused over 10 min. for patients in group D. Many authors.[5,22] have used 0.5-1 mcg/kg of dexmedetomidine to attenuate stress response to intubation. The dose of lignocaine used in our study was 1.5 mg/kg IV given 3 min. before intubation. To maintain uniformity and to prevent evaluator's bias, patients in group D received 3 mL of normal saline 3 min before induction and patients in group L received 100 ml of normal saline infusion 10 min. before induction. We did not observed any significant differences in HR and arterial blood pressure values between the baseline and post intubation values in the dexmedetomidine group., the mean percentage variation analysis at the stated moments revealed an absence of any increase in HR, SBP and DBP in dexmedetomidine group suggesting dexmedetomidine as an effective agent for blunting the hemodynamic response to laryngoscopy and tracheal intubation.

Bradycardia and hypotension have been reported in studies pertaining to the effect of dexmedetomidine administration on peri-operative haemodynamics.[23,24] We did not detect any excessive reduction in HR or systemic blood pressure values in the dexmedetomidine group

compared with other group. Moreover, in this study neither bradycardia nor hypotension was observed in the patients.

Prasad SR.[25] et al concluded that Dexmedetomidine when compared to Lignocaine attenuated the stress response to laryngoscopy and intubation more efficiently. Sulhyan SR et al[26] also concluded dexmedetomidine at the rate of 1 mcg/kg prior to induction of anaesthesia is an effective method to attenuate the haemodynamic response to direct laryngoscopy and intubation in elective surgery for off pump CABG. A similar result was found by R. Saraf et al[27] and Sajith Sulaiman et al[28] with low dose (0.6 mcg/kg and 0.5 mcg/kg respectively) dexmedetomidine. Even though the dose was low, the study population was on beta-blocker therapy. Another study done by Ferdi Menda et al[5] also found that dexmedetomidine infusion (1 µg/kg) before the anaesthesia induction blunted the HR and MAP response during laryngoscopy and endotracheal intubation. However, the anaesthetic induction agent etomidate was used in that study. There was a significant decrease in the dose of thiopentone required for induction of anaesthesia in group D compared to group L. Keniya et al,[29] Scheinin et al,[30] Aantaa et al[31] and Bajwa et al[32] reported decreased thiopentone requirement for induction of anaesthesia in the dexmedetomidine group. Dexmedetomidine has also shown to potentiate the analgesic properties of opioids and decrease the dose requirement according to the study conducted by Scheinin B et al.[30] Similar finding were seen in the study conducted by Keniya et al[29].

All patients in group L had sedation score 2 in preinduction period. This was due to injection midazolam used as premedication. Most of the patients in group D had sedation score 3 (responding to verbal commands). None of the patients in group D had respiratory depression or fall in SpO_2. Several authors[29,32] have reported that dexmedetomidine infusion produces sedation which mimics normal sleep, patients are arousable to verbal commands, and it lacks respiratory depression. These properties make dexmedetomidine a better choice of sedation for awake fibreoptic intubation, intensive care unit, post-anaesthesia care unit, magnetic resonance imaging and awake craniotomy.[12] Lignocaine failed to effectively attenuate haemodynamic response to laryngoscopy and intubation. Similar findings were found by many authors.[33,34] who reported that the lignocaine fails to attenuate haemodynamic response and our observations are in accordance with them.

There were few limitations in our study. The effects of dexmedetomidine when used in hypertensive and cardiac patients were not studied as we did not have invasive blood pressure monitoring and advanced cardiac setup in our institute. Also plasma catecholamine levels, which is an objective means of measuring haemodynamic stress response was not measured in our study. Estimating depth of anaesthesia by changes mediated by autonomic nervous system is difficult during dexmedetomidine infusion as it increases the haemodynamic stability. Intraoperative Bispectral Index (BIS) monitoring would have been definitely more objective in deciding the depth of anaesthesia and the requirement of anaesthetic agent. Postoperative analgesic requirement of the patients were not studied in both the groups.

CONCLUSION: This study concluded that dexmedetomidine at the dose of 1 mcg/kg IV infusion for 10 min. attenuates the haemodynamic stress response to laryngoscopy and endotracheal intubation more effectively when compared to lignocaine 1.5 mg/kg IV without any side effects.

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