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Comparative study of two different doses of Dexmedetomidine (0.5/mcg/kg & 1mcg/kg) with lignocaine (1.5mg/kg) as IV premedication on hemodynamic parameters in patients undergoing elective oncosurgeries following laryngoscopy & intubation

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Abstract

Background: Lung, oral, oesophageal, stomach and nasopharyngeal cancers are the most common cancers in men, whereas cancers of the breast, cervix and uterus are the most common cancers in women. Although systemic chemotherapy is the most common form of treatment for these cancers, the incidence of surgeries for the same have been on the increasing trend and therefore the need for oncoanesthesia has increased. **Methodology-** The study was conducted in Department of Anaesthesiology and Pain relief at Kidwai Memorial Institute of Oncology, Bangalore. duration of the study was from November 2019 to November 2021. 210 patients fulfilling the inclusion criteria were included in the study. Patients were divided into 3 groups and randomly allocated to each of them. Designated drug was administered via IV route. Oral intubation with proper cuffed endotracheal tube and its position was confirmed by bilateral five-point auscultation and was connected to volume controlled mode of mechanical ventilation. Monitoring of NIBP, continuous Ecg, Capnography and SpO2 was done. **Result-** In our study, there was no statistically significant difference in the mean baseline heart rates between the three groups. There is a decrease in mean heart rate after administration of study drug till the time interval before intubation when compared to the baseline heart rate. In our study, there was no statistically significant difference in the mean baseline SBP, DBP and MAP between the three groups. **Conclusion-** Dexmedetomidine is a better premedication when compared to lignocaine, as it completely attenuated the stress response to intubation.

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Introduction

Cancer patients tend to have associated co-morbidities that remain under-diagnosed and asymptomatic prior to surgery. Most common among them are Hypertension, Diabetes Mellitus, Ischemic heart disease, Chronic obstructive pulmonary disease.[1] Stressful responses such as laryngoscopy and intubation can lead to complications that will have an influence on perioperative outcome and long term hospital stay. Hence, attenuation of stress responses in cancer patients needs to be addressed. Laryngoscopy and orotracheal intubation are potent stressful stimuli that causes hemodynamic responses which can lead to myocardial ischemia, ventricular arrhythmias, left ventricular failure and cerebral haemorrhage. The proposed mechanisms are somatovisceral reflexes.[2] Stimulation of proprioceptors in the base of tongue during laryngoscopy induces impulse dependent increase of systemic blood pressure, heart rate and plasma catecholamine concentrations. Successive orotracheal intubation will stimulate additional receptors which produce the increased hemodynamic and epinephrine responses along with some vagal inhibition of heart.[3] These changes are dangerous to patients with reduced myocardial reserve as in coronary artery disease, cardiac dysrhythmias, cardiomyopathy, congestive heart failure, hypertension, geriatric population and in patients with past history of chemotherapy with cardiotoxic agents.[4] In infants and small children this autonomic stimulus may cause bradycardia.[5] Lignocaine is an amide local anesthetic that reduces the stress response as a result of direct cardiac depression and peripheral vasodilatation. It also has antiarrhythmic and analgesic properties.[6] Recent studies have shown that lignocaine could decrease cancer recurrence due to its direct effect on tumor cells and immunomodulatory properties in the stress response.[7]

Dexmedetomidine has analgesic, sedative and anaesthetic sparing property.[8] Pre-treatment with Dexmedetomidine attenuates hemodynamic response to laryngoscopy and intubation.[9] Perioperative intravenous infusion of Dexmedetomidine has been shown to decrease plasma catecholamine levels by 90% to blunt the hemodynamic response. Some researchers have used Dexmedetomidine in doses of 0.5 mcg/kg and 1 mcg/kg and have observed that it attenuates the stress response to laryngoscopy and orotracheal intubation. The higher dose of 1 mcg/kg was observed to produce an increased incidence of bradycardia and hypotension. It has also been associated with increased sedation.[10] Studies on Dexmedetomidine being used as bolus infusion preoperatively to attenuate hemodynamic responses of laryngoscopy and endotracheal intubation in cancer patients are not available. However, studies on Dexmedetomidine infusions being used intraoperatively for stable hemodynamics, opioid sparing anaesthesia and reduced usage of inhalational agents in cancer patients are available.

The above study was carried out to study the effects of intravenous Dexmedetomidine with two different doses of 0.5 mcg/kg and 1 mcg/kg given as a preoperative bolus dosing while comparing it with preoperative administration of intravenous lignocaine for the attenuation of hemodynamic stress response to laryngoscopy and intubation.

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Materials & Methods

A comparative, analytical, prospective, randomized single blinded study was conducted in Department of Anaesthesiology and Pain relief at Kidwai Memorial Institute of Oncology, Bangalore, after obtaining the institutional ethical committee approval. The duration of the study was from November 2019 to November 2021. The sample size taken for the study was 210 patients. Patients aged between 18-65 years, belonging to ASA physical status Grade I and Grade II and those who are ready to give consent were included for the study. Patients having history of allergy to study drug, those on calcium channel blockers, beta blockers, ACE inhibitors, those who had more than two attempts at intubation, having history of cerebrovascular accident, ischemic heart disease, systemic hypertension, chronic obstructive lung disease, upper respiratory tract infections, impaired liver and renal function test were excluded from the study.

Informed written consent was taken. Patients posted for elective oncosurgeries underwent pre-anaesthetic check-up and all necessary investigations were carried out. The patients were then randomly allocated to one of the three groups. Patients were kept fasting for 8 hours. Patients were given Tab. Pantoprazole 40 mg HS and Tab Alprazolam 0.5 mg on the night prior to the surgery. On arrival to preoperative room, NPO status was confirmed and patient was shifted to the operation theatre. After shifting patient to operation table, routine monitoring was commenced which included electrocardiogram, pulse oximetry, non-invasive blood pressure (NIBP). Patients allotted to their group were given their designated drug intravenously.

Group A: Patients will be given IV Dexmedetomidine 0.5mcg/kg diluted upto 100 ml with normal saline and given over 10 mins in the OT with all monitors attached and functioning.

Group B: Patients will be given IV Dexmedetomidine 1mcg/kg diluted upto 100 ml with normal saline and given over 10 mins in the OT with all monitors attached and functioning.

Group C: Patients will be given IV Lignocaine 1.5mg/kg 3 mins before laryngoscopy and intubation.

All patients were then pre-medicated with Inj. Midazolam (0.02 mg/kg), Injection Ondansetron (0.05mg/kg) and Inj. fentanyl (1 mcg/kg). Patients were pre-oxygenated for 3 mins with 100 % oxygen, general anesthesia was induced with Inj. Propofol (1.5 mg/kg) and after confirming adequacy of ventilation, and Inj. Succinylcholine (2 mg/kg) was administered. Patients were intubated orally with appropriate cuffed endotracheal tube and tube position was confirmed by bilateral five-point auscultation and then connected to volume controlled mode of mechanical ventilation. Anesthesia was maintained with nitrous oxide 50%, O_2 50% and Isoflurane with Minimum alveolar concentration of 0.8. For maintenance of muscle relaxation. Inj. Vecuronium bromide was given, an initial loading dose of 0.08 mg/kg followed by intermittent doses of Inj. Vecuronium (0.01mg/kg). Intraoperative monitoring was consisting of NIBP, continuous ECG, Capnography and SpO_2. At end of surgery neuromuscular blockade was reversed with Inj. Neostigmine (0.05mg/kg) and Inj. Glycopyrollate (0.01 mg/kg). Once the patient starts breathing spontaneously and adequately, the patients were extubated and shifted to surgical intensive care unit. Hemodynamic parameters such as heart rate, systolic, diastolic and mean arterial blood pressures were recorded before the administration of drug (baseline), before induction, before intubation, 1 min, 3 mins, 5 mins, and 10 mins after intubation. Data was entered into Microsoft Excel Data Sheet and was analyzed using SPSS 22 version software.

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Results

Heart Rate Variability

Table 1: Heart rate variability between three groups at different intervals of time

HR	Group						p value
	Group A		Group B		Group C		
	Mean	SD	Mean	SD	Mean	SD	
Baseline	91.41	10.60	90.49	9.40	90.19	12.03	0.779
Before Induction	82.14	9.33	78.57	8.48	89.09	10.81	< 0.001*
Before Intubation	77.99	8.66	72.37	7.07	87.87	10.79	< 0.001*
1 Min	73.36	8.36	66.16	7.24	91.43	12.00	< 0.001*
3 Mins	71.30	7.61	64.27	7.81	89.03	11.08	< 0.001*
5 Mins	70.99	7.89	64.59	8.27	88.64	11.00	< 0.001*
10 Mins	72.19	6.72	65.76	8.07	87.34	10.92	< 0.001*

Table 1 shows the mean heart rate comparison between the three groups at different time intervals. The baseline heart rate was comparable between the three groups without a statistically significant difference among them (p value = 0.779). From the time interval of before induction till up to 10 mins after intubation, the mean heart rate was highest with group C when compared to group A with the lowest mean rate rates seen with Group B. There was a statistically significant difference seen between the three groups in the mean heart rate comparison (p value < 0.001) before induction, before intubation, 1 min after intubation, 3 mins, 5 mins and 10 mins after intubation.

Table 2: Comparison of p-values between the groups for heart rate variability at different time intervals

p-values	Group A vs Group B	Group B vs Group C	Group A vs Group C
Baseline	1.000	1.000	1.000
Before induction	0.086	< 0.001	< 0.001
Before intubation	0.001	< 0.001	< 0.001
1 min	< 0.001	< 0.001	< 0.001

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3 min	< 0.001	< 0.001	< 0.001
5 min	< 0.001	< 0.001	< 0.001
10 min	< 0.001	< 0.001	< 0.001

In the mean heart rate comparison between group A versus Group B, there was no statistically significant difference seen in the baseline values (p value =1.000) between the two groups, but higher mean heart rates were seen with Group A and this difference was statistically significant in the time intervals from before intubation (p value =0.001) till 10 mins after intubation (p values <0.001). In the mean heart rate comparison between group B versus Group C, there was no statistically significant difference seen in the baseline values (p value = 1.000) between the two groups, but higher mean heart rates were seen with Group C and this difference was statistically significant in the time intervals from before induction (p value <0.001) till 10 mins after intubation (p values <0.001).
In the mean heart comparison between group A versus Group C, there was no statistically significant difference seen in the baseline values (p value = 1.000) between the two groups, but higher mean heart rates were seen with Group C and this difference was statistically significant in the time intervals from before induction (p value <0.001) till 10 mins after intubation (p values < 0.001).

Dbp Variability Between Three Groups

Table 3: DBP comparison between three groups at different time intervals

DBP	Group						p value
	Group A		Group B		Group C		
	Mean	SD	Mean	SD	Mean	SD	
Baseline	82.49	7.57	81.30	6.95	83.70	8.04	0.172
Before Induction	77.39	7.07	74.54	8.94	81.57	7.14	< 0.001*
Before Intubation	73.70	7.34	69.23	8.76	80.17	7.06	< 0.001*
1 Min	67.87	6.84	61.67	8.24	82.33	8.99	< 0.001*
3 Mins	64.59	6.91	58.34	8.26	81.13	9.57	< 0.001*
5 Mins	64.56	6.95	60.17	7.09	80.99	9.10	< 0.001*
10 Mins	65.77	6.91	61.87	6.52	81.66	7.71	< 0.001*

Table 3 shows the mean DBP comparison between the three groups at different time intervals. The baseline DBP was comparable between the three groups without a statistically significant difference among them (p value = 0.172). From the time interval of before induction till upto

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10 mins after intubation, the mean DBP was highest with group C when compared to group A with the lowest DBP was seen with Group B. There was a statistically significant difference seen between the three groups in the mean DBP comparison in the time intervals from before induction (p value <0.001) till 10 mins after intubation (p value <0.001) .

Table 4: Comparison of p-values between the groups for DBP variability at different time intervals

p-values	Group A vs Group B	Group B vs Group C	Group A vs Group C
Baseline	1.000	0.183	1.000
Before induction	0.094	< 0.001	0.005
Before intubation	0.002	< 0.001	< 0.001
1 min	< 0.001	< 0.001	< 0.001
3 min	< 0.001	< 0.001	< 0.001
5 min	0.003	< 0.001	< 0.001
10 min	0.004	< 0.001	< 0.001

In the mean DBP comparison between group A versus Group B, there was no statistically significant difference seen in the baseline values (p value =1.000) between the two groups, but higher mean DBP was seen with Group A and this difference was statistically significant in the time intervals from before intubation (p value =0.002) till 10 mins after intubation (p value = 0.004).

In the mean DBP comparison between group B versus Group C, there was no statistically significant difference seen in the baseline values (p value = 0.183) between the two groups, but higher mean DBP was seen with Group C and this difference was statistically significant in the time intervals from before induction (p value <0.001) till 10 mins after intubation (p values <0.001).

In the mean DBP comparison between group A versus Group C, there was no statistically significant difference seen in the baseline values (p value = 1.000) between the two groups, but higher mean DBP was seen with Group C and this difference was statistically significant in the time intervals from before induction (p value <0.001) till 10 mins after intubation (p values < 0.001).

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Map Variability Between Three Groups

Table 5: MAP comparison between three groups at different time intervals

MAP	Groups						p value
	Group A		Group B		Group C		
	Mean	SD	Mean	SD	Mean	SD	
Baseline	98.93	7.58	97.31	7.07	101.11	10.23	0.187
Before Induction	92.54	8.06	89.00	9.97	98.36	9.01	< 0.001*
Before Intubation	88.37	8.17	83.24	8.94	95.87	8.36	< 0.001*
1 Min	81.31	6.20	74.37	7.94	98.20	9.19	< 0.001*
3 Mins	78.07	6.02	71.39	7.49	96.74	9.90	< 0.001*
5 Mins	78.11	6.73	72.37	6.34	96.97	8.70	< 0.001*
10 Mins	79.10	5.75	74.37	5.77	96.90	8.26	< 0.001*

Table 5 shows the mean MAP comparison between the three groups at different time intervals. The baseline mean MAP was comparable between the three groups without a statistically significant difference among them (p value = 0.187). From the time intervals of before induction till upto 10 mins after intubation, the mean MAP was highest with group C when compared to group A with the lowest MAP was seen with Group B. There was a statistically significant difference seen between the three groups in the mean MAP comparison in the time intervals from before induction (p value <0.001) till 10 mins after intubation (p value <0.001)

Table 6: Comparison of p-values between the three groups for MAP variability at different time intervals

p-values	Dexmedetomidine 0.5 mcg/kg vs Dexmedetomidine 1 mcg/kg	Dexmedetomidine 1 mcg/kg vs Lignocaine 1.5 mg/kg	Dexmedetomidine 0.5 mcg/kg vs Lignocaine 1.5 mg/kg
Baseline	0.915	0.205	0.205
Before induction	0.065	< 0.001	0.001
Before intubation	0.001	< 0.001	< 0.001
1 min	< 0.001	< 0.001	< 0.001
3 min	< 0.001	< 0.001	< 0.001

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5 min	< 0.001	< 0.001	< 0.001
10 min	< 0.001	< 0.001	< 0.001

In the mean MAP comparison between group A versus Group B, there was no statistically significant difference seen in the baseline values (p value = 0.915) between the two groups, but higher mean MAP was seen with Group A and this difference was statistically significant in the time intervals from before intubation (p value =0.001) till 10 mins after intubation (p value < 0.001). In the mean MAP comparison between group B versus Group C, there was no statistically significant difference seen in the baseline values (p value = 0.205) between the two groups, but higher mean MAP was seen with Group C and this difference was statistically significant in the time intervals from before induction (p value <0.001) till 10 mins after intubation (p values <0.001).

In the mean MAP comparison between group A versus Group C, there was no statistically significant difference seen in the baseline values (p value = 0.205) between the two groups, but higher mean MAP was seen with Group C and this difference was statistically significant in the time intervals from before induction (p value = 0.001) till 10 mins after intubation (p values < 0.001).

Discussion

In our study, there was no statistically significant difference in the mean baseline heart rates between the three groups. There is a decrease in mean heart rate after administration of study drug till the time interval before intubation when compared to the baseline heart rate:

The mean heart rate values was significantly higher in Group C or lignocaine 1.5mg/kg group (91.43±12, 89.03±11.08, 88.64±11 and 87.34±10.92 at 1, 3, 5 and 10mins after intubation respectively) when compared to Group A or Dexmedetomidine 0.5 mcg/kg group (73.36±8.36, 71.30±7.61, 70.99±7.89 and 72.19±6.92 at 1, 3, 5 and 10 mins after intubation respectively) and Group B or Dexmedetomidine 1 mcg/kg group (66.16±7.24, 64.27±7.81, 64.59±8.27 and 65.76±8.07 at 1, 3, 5 and 10 mins after intubation respectively). Thus, Dexmedetomidine helps in attenuating the hemodynamic response to intubation.

Jarineshin H et al[11] (2015) compared two different doses Dexmedetomidine in attenuating the cardiovascular responses to laryngoscopy and endotracheal intubation with a control group of normal saline in 90 patients with 30 in each group, and concluded that Dexmedetomidine significantly and effectively attenuates cardiovascular and hemodynamic responses during laryngoscopy and endotracheal intubation. In addition, 0.5 mcg/kg Dexmedetomidine properly decreased the cardiovascular responses, but, a significant difference was not observed between 0.5 mcg/kg Dexmedetomidine group and 1 mcg/kg of Dexmedetomidine group in reducing HR. In our study, it was found that there was a statistically significance between 0.5 mcg/kg Dexmedetomidine and 1 mcg/kg of Dexmedetomidine in the mean heart rate parameter with a greater decrease in mean heart rate seen with 1 mcg/kg Dexmedetomidine.

In our study, there was no statistically significant difference in the mean baseline SBP, DBP and MAP between the three groups. After administration of study drugs, there was a decrease noted in mean SBP, DBP and MAP values till prior to intubation. Till time interval of prior to intubation, the lowest mean SBP, DBP and MAP values were seen with Dexmedetomidine 1 mcg/kg group followed by Dexmedetomidine 0.5 mcg/kg and Lidocaine 1.5 mg/kg. After

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intubation there was an increase in the mean SBP, DBP and MAP seen with the lidocaine 1.5 mg/kg group when compared to pre-intubation values in all time intervals of 1 min, 3 mins, 5 mins and 10 mins, and it was statistically significant. Whereas, no such increase in mean SBP, DBP and MAP was seen with the Dexmedetomidine 0.5 mcg/kg group or the Dexmedetomidine 1 mcg/kg group at all-time intervals from before induction to 10 mins after intubation. There was a decrease in mean SBP, DBP and MAP in both the Dexmedetomidine 0.5 mcg/kg and Dexmedetomidine 1 mcg/kg groups at all-time intervals from before induction till 10 mins after intubation. In our study it was observed that Dexmedetomidine 0.5 mc/kg completely abolished the stress response at all points post intubation. Dexmedetomidine 1 mcg/kg also abolished the stress response completely but in 17.32% of the participants a fluid bolus of 200 ml was needed to keep MAP above 65 mm Hg. Hence, from our study it can be said that in patients undergoing elective oncosurgeries under general anesthesia and endotracheal intubation, Dexmedetomidine 0.5 mcg/kg can attenuate the stress response completely.

Sebastian B et al[10] in their study used intravenous Dexmedetomidine 0.5 mcg/kg, Dexmedetomidine 0.75mcg/kg as infusion over 10 min and saline in control group. They observed a statistically significant difference between Dexmedetomidine and intravenous normal saline in HR, SBP, DBP, and MAP at all-time points after tracheal intubation with intravenous Dexmedetomidine 0.75mcg/kg being most effective.[20] Our study also showed a statistically significant difference between the Dexmedetomidine groups and lidocaine in SBP, DBP and MAP after intubation and intraoperatively. However, we observed that both IV Dexmedetomidine 0.5 mcg/kg and IV Dexmedetomidine 1 mcg/kg were effective doses required to attenuate hemodynamic stress response to intubation. They observed no adverse cardiovascular or respiratory effects in their study. But, in our study we observed hypotension in the Dexmedetomidine 1 mcg/kg having an incidence of 17.2% of hypotension. Hence, in our study, it can be said that 0.5 mcg/kg Dexmedetomidine is appropriate dose to totally blunt stress response to intubation.

Conclusion

The present study concluded that Dexmedetomidine is a better premedication when compared to lignocaine, as it completely attenuated the stress response to intubation. Patients undergoing elective oncosurgeries are at high incidence of developing anxiety which when coupled with the stress response to intubation can lead to unwanted complications for which Dexmedetomidine can be used as a premedication preoperatively. Dexmedetomidine at a dose of 0.5 mcg/kg has the benefit of attenuating the stress response.

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