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Incidence of Hypotension and bradycardia with dexemedetomidine and lignocaine in two different doses as premedication for patients undergoing elective surgery - A randomised comparative prospective study

Arathi B H[1], Punita Priya S[2], Yadhuraj M K[3], Nevin Philip[4], V B Gowda[5], Namratha G C[6] , Roopa B O[7]

[1]Associate Professor, Department of Anaesthesia and pain relief, KIDWAI Memorial Institute of Oncology, Bangalore, India.
[2]Assistant Professor, Department of Anaesthesia and pain relief, KIDWAI Memorial Institute of Oncology, Bangalore, India.
[3]Assistant Professor, Department of Anaesthesia and pain relief, KIDWAI Memorial Institute of Oncology, Bangalore, India.
[4]postgraduate student, Department of Anaesthesia and pain relief, KIDWAI Memorial Institute of Oncology, Bangalore, India.
[5]Professor & HOD, Department of Anaesthesia and pain relief, KIDWAI Memorial Institute of Oncology, Bangalore, India.
[6]Assistant Professor, Department of Anaesthesia and pain relief, KIDWAI Memorial Institute of Oncology, Bangalore, India.
[7]Assistant Professor, Department of Anaesthesia and pain relief, KIDWAI Memorial Institute of Oncology, Bangalore, India.

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ABSTRACT

Background: The burden of cancer patients is on an increasing trend globally as well as in India. Systemic chemotherapy is the most common form of treatment for cancer. Laryngoscopy and intubation are nocuous stimuli that can cause intense changes in cardiovascular and respiratory function, through reflex responses. Lignocaine is an amide local anesthetic that reduces the stress response as a result of direct cardiac depression and peripheral vasodilatation. The higher dose of 1 mcg/kg was observed to produce an increased incidence of bradycardia and hypotension. **Methodology:** The study was conducted at a tertiary care centre on 219 patients who fulfilled the inclusion criteria. The duration of the study was from April 2018 to April 2019. Patients were randomly allocated in three groups and were administered their designated drug intravenously. 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. Anaesthesia was maintained. Intraoperative monitoring was consisting of NIBP, continuous ECG, Capnography and SpO_2. **Result:** Hypotension was seen in group B but not in Group A and Group C and this was statistically significant (p value <0.001). Bradycardia was seen in all three groups with highest incidence with group B followed by group A and then group C and this difference in distribution was statistically significant. **Conclusion:** Dexmedetomidine at 1 mcg/kg bolus infusion had more incidences of side effects like bradycardia and hypotension which needed

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intervention whereas the lower dose of 0.5mcg/kg Dexmedetomidine did not require such interventions.

Keywords: Hypotension, bradycardia, oncosurgeries, ECG, intubation.

Corresponding Author: Dr.Nevin Philip , Postgraduate student , Department of Anaesthesia and pain relief, KIDWAI Memorial Institute of Oncology, Bangalore, India.
Email: philvin1991@gmail.com

Introduction

The burden of cancer patients is on an increasing trend globally as well as in India.[1] According to the National Cancer Registry Programme (NCRP), 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. According to Hospital Based Cancer Registries (HCBRs) 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 it has increased the need for oncoanesthesia.[2]

Laryngoscopy, intubation and airway manipulation are nocuous stimuli that can cause intense changes in cardiovascular and respiratory function, through reflex responses. Cardiovascular reflexes are induced due to stimulation of the sensory receptors in the supraglottic region and trachea. These mechanoreceptors located in the airway mucosa comprise of small-diameter myelinated fibers, slowly adapting stretch receptors with large-diameter myelinated fibers, and polymodal endings of non-myelinated nerve fibers. Superficial location of these receptors makes topical local anaesthesia of airway an effective means to blunt cardiovascular responses. The glossopharyngeal and vagal afferent fibers transmit these impulses to the brainstem, which in turn causes widespread autonomic activation through sympathetic and parasympathetic nervous systems. In infants and small children, bradycardia is the autonomic equivalent of the laryngospasm response caused by laryngoscopy or intubation. Although seen only rarely in adults, this reflex is due to increased vagal tone at the sinoatrial node and is a monosynaptic response to a nocuous stimulus in airway. The more common response seen in adults and adolescents to airway manipulation is tachycardia and hypertension mediated by cardio accelerator nerves and sympathetic chain ganglia. This response includes extensive release of norepinephrine from adrenergic nerve terminals and secretion of epinephrine from adrenal medulla. Laryngoscopy and intubation response also includes an increase in electroencephalographic (EEG) activity, cerebral metabolic rate and cerebral blood flow (CBF). 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] 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.[4] 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.[5]

Dexmedetomidine is an α2 adrenoceptor agonist and this action is highly selective and specific. It has central sympatholytic property. Perioperative intravenous infusion of Dexmedetomidine has been shown to decrease plasma catecholamine levels by 90% to blunt the hemodynamic response. Dexmedetomidine does not produce respiratory depression, thus it is a useful and safe adjunct in diverse clinical applications.[6] 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

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an increased incidence of bradycardia and hypotension. It has also been associated with increased sedation.[7]

Keeping the above points in mind our study was designed to analyse and find out the side effects like Hypotension & Bradycardia in two different doses of Dexemedetomidine (0.5/mcg/kg & 1mcg/kg) with lignocaine (1.5/mg/kg) in patients undergoing elective oncosurgeries following laryngoscopy and intubation.

Materials And Methods

This comparative, prospective, randomized study was conducted at tertiary care centre after getting the institutional ethical committee approval. The duration of the study was from April 2018 to April 2019. 219 patients were included for this study who were admitted for undergoing the elective oncosurgery. Patients belonging to17-65 years of age group, belonging to ASA physical status Grade I and Grade II and those who were ready to give consent were included in this study. Whereas, patients having history of allergy to lignocaine and dexmedetomidine, those on calcium channel blockers, beta blockers, ACE inhibitors, having anticipated difficult airway, having more than 2 attempts of intubation, URTI were excluded from the study. Written informed consent was taken from the patients in their local language.

The patients were then randomly allocated to one of the three groups by a computer generated table of random numbers, allotting equal number of patients in each group. All the patients were kept on fasting for 8 hours. Tab. Pantoprazole 40 mg HS and Tab Alprazolam 0.5 mg were administered to the patient one night prior to the surgery. 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 via IV route as follows-

Group A	GROUP B	GROUP C
IV Dexmedetomidine 0.5mcg/kg diluted up to 100 ml with normal saline and given over 10 mins in the OT with all monitors attached and functioning.	IV Dexmedetomidine 1mcg/kg diluted up to 100 ml with normal saline and given over 10 mins in the OT with all monitors attached and functioning.	IV Lignocaine 1.5mg/kg 3 mins before laryngoscopy and intubation.

Premedication of the patients was done with Injection Midazolam (0.02 mg/kg), Injection Ondansetron (0.05mg/kg) and Injection fentanyl (1 mcg/kg). Patients were pre-oxygenated for 3 mins with 100 % oxygen, general anaesthesia was induced with Injection Propofol (1.5 mg/kg) and after confirming adequacy of ventilation, and Injection 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. Anaesthesia was maintained with nitrous oxide 50%, O_2 50% and Isoflurane with Minimum alveolar concentration of 0.8. For maintenance of muscle relaxation injection Vecuronium bromide was given, an initial loading dose of 0.08 mg/kg followed by intermittent doses of injection 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 injection Neostigmine (0.05mg/kg) and injection Glycopyrollate (0.01 mg/kg). Once the patient starts breathing spontaneously and adequately, the patients were extubated and shifted to surgical intensive care unit. Side effects such as hypotension and bradycardia were noted before the administration of drug (baseline), before induction, before intubation 1 min, 3 mins, 5 mins, and 10 mins after intubation.

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Data was entered into Microsoft Excel Data Sheet and was analyzed using SPSS 22 version software. MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

Results

Age Distribution

The study group comprised of patients between the ages 17-65 years.

Table 1: Age distribution among the three groups

	Group						p value	p value b/w A – B	p value b/w B - C	p value b/w A – C
	Group A		Group B		Group C					
	Mean	SD	Mean	SD	Mean	SD				
Age	49.07	10.30	46.47	11.27	49.26	11.13	0.243	0.480	0.480	1.000

In the study mean age of patients in Group A was 49.07±10.30 years, in Group B was 46.47±11.27 years and Group C was 49.26±11.13 years. There was no statistically significant difference seen in mean age distribution among any of the groups.

Gender Distribution

Table 2: Gender distribution among three groups

		Group					
		Group A		Group B		Group C	
		Count	%	Count	%	Count	%
Gender	Female	58	82.86%	64	91.43%	59	84.29%
	Male	12	17.14%	6	8.57%	11	15.71%

In Group A, 82.86% were females and 17.14% were males. In Group B, 91.43% were females and 8.57% were males and in Group C, 84.29% were females and 15.71% were males. There was no significant difference in sex distribution among the three groups.

Weight Distribution

Table 3: Mean weight distribution between three groups

	Group						p value	p value b/w A - B	p value b/w B - C	p value b/w A – C
	Group A		Group B		Group C					
	Mean	SD	Mean	SD	Mean	SD				
Weight	58.27	9.47	57.43	6.99	58.24	8.67	0.799	1.000	1.000	1.000

In Group A, mean weight was 58.27±9.47 kgs. In Group B, mean weight was 57.43±6.99 kgs and in Group C, mean weight was 58.24±8.67 kgs. There was no statistically significant difference seen in the mean weight values among the three groups.

ASA Distribution

Table 4: ASA distribution between three groups

	Group					
	Group A		Group B		Group C	
	Count	%	Count	%	Count	%

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ASA Grade	1	4	5.71%	9	12.86%	4	5.71%
	2	66	94.29%	61	87.14%	66	94.29%

$\chi 2 = 3.2$, df = 2, p = 0.202

In Group A, 5.71% were belonging to ASA 1 and 94.29% were ASA grade 2. In Group B, 12.86% were belonging to ASA 1 and 87.14% were ASA grade 2 and in Group C, 5.71% were ASA 1 and 94.29% were ASA grade 2. There was no statistically significant difference seen in the ASA grading among the three groups.

Table 5: Side effects distribution among the three groups

	Group A		**Group B**		**Group C**		**P value**
	Count	**%**	**Count**	**%**	**Count**	**%**	
Hypotension	0	0%	12	17.2%	0	0%	**<0.001***
Bradycardia	6	8.57 %	22	31.4%	1	1.42%	**<0.001***

SpO_2 Variability Between Three Groups

Table 6: Mean SpO_2 values between three groups at different time intervals

SpO_2	**Groups**						**p value**
	Group A		**Group B**		**Group C**		
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Baseline	98.66	1.11	98.51	1.53	98.30	1.33	0.284
Before Induction	99.40	.97	99.31	1.12	99.16	1.16	0.410
Before Intubation	99.96	.20	99.97	.17	99.96	.20	0.880
1 Min	99.97	.24	99.91	.33	99.91	.33	0.436
3 Mins	99.99	.12	99.91	.37	99.97	.17	0.191
5 Mins	99.97	.17	99.94	.29	99.93	.31	0.619
10 Mins	99.99	.12	99.91	.37	99.96	.20	0.248

Table 6 shows that mean SpO_2 values were comparable at baseline and there was no statistically significant difference between the three groups in mean SpO_2 values at all-time intervals of observation.

Discussion

In our study, all the groups shared similar distribution of age and gender. The mean age in all the groups was fifth decade and female gender predominance was seen in all the groups. Approximately, 85% were female in all three groups. Only ASA 1 and ASA 2 patients were included in the study. Statistically, there was no significant difference in the distribution of the two grades of patients between the groups.

The study population was similar and comparable in terms of demographic parameter to such as age, sex, and ASA physical status. There was no statistically significant difference between the three groups with respect to above parameters. Anesthetic management was also standardized for all the groups. Hence the difference in the various outcome variables can be presumed to be not due to various confounders but attributable to the direct individual pharmacological agents and their effects.

Table 5 shows the side effects distribution among the three groups. Hypotension was seen in group B but not in Group A and Group C and this was statistically significant (p value <0.001). Bradycardia was seen in all three groups with highest incidence with group B followed by group A and then group C and this difference in distribution was statistically significant. In our study, we defined hypotension to be a mean arterial pressure less than 65 mmHg and bradycardia was defined to be a heart rate less than 60 beats per minute. There is a statistically significant difference seen between 0.5 mcg/kg Dexmedetomidine and 1 mcg/kg

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Dexmedetomidine. Although both the doses completely attenuate the stress response to intubation, more incidence of hypotension was seen with the Dexmedetomidine 1 mcg/kg group. Hence, Dexmedetomidine 0.5 mcg/kg attenuated the stress response to intubation completely without the side effect of hypotension, which could be harmful in certain instances. In our study, we used lignocaine 1.5 mg/kg 3 min prior to induction of anaesthesia. Various studies have reviewed the effect of lignocaine to blunt the sympathoadrenal pressure response. **Lev and Rosen[8]** in their study reviewed the use of prophylactic lignocaine as a pre-intubation medication. A dose of 1.5 mg/kg intravenously 3 min prior to intubation was employed and was found to be optimal for attenuation of the sympathoadrenal pressure response to laryngoscopy and intubation without any overt harmful effects. **Gulabani M et al[9]** conducted a similar study where lignocaine was compared with two different doses of Dexmedetomidine in attenuating the stress response to intubation. In patients who received lignocaine 1.5 mg/kg there was an increase in SBP, DBP and MAP at 1 min but then at 3mins, 5 mins and 10 mins there was a fall in SBP, DBP and MAP when compared to pre-intubation values. Hence, lignocaine did not completely blunt the side effects like hypotension and bradycardia also in their study. It was concluded that Dexmedetomidine 1 μg/kg brought upon a maximal reduction in systolic and DBPs at 1-, 3- and 5-min post intubation. Hence, from our study it can be said that in patients undergoing elective oncosurgeries under general anaesthesia and endotracheal intubation, Dexmedetomidine 0.5 mcg/kg can attenuate the stress response completely without the side effect of hypotension.

Conclusion

The present study concluded that Dexmedetomidine is a better premedication when compared to lignocaine, as it completely attenuated the stress response to intubation. But Dexmedetomidine at 1 mcg/kg bolus infusion had more incidences of side effects like bradycardia and hypotension which needed intervention whereas the lower dose of 0.5mcg/kg Dexmedetomidine did not require such interventions. 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 additional benefit of both attenuating the stress response completely as well as having no associated adverse effects when compared to Dexmedetomidine 1 mcg/kg.

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