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A Randomized Double Blind Controlled Study of Attenuation of Hemodynamic Responses to Laryngoscopy and Intubation after Intranasal and Intravenous Administration of Dexmedetomidine

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Abstract: ***Background and aims:*** *Unfavorable hemodynamic responses following during laryngoscopy and intubation (L-I) are common. Preoperative intravenous (IV) Dexmedetomidine (DEX) has been shown to effectively reduce the laryngoscopic stress response. However, severe haemodynamic consequences such as hypotension, bradycardia, and even cardiac arrest may have limited IV DEX's use. Intranasal (IN) administration is more convenient and effective than other methods. The study's aim was to examine hemodynamic responses and other adverse effects between IV and IN DEX.* ***Methods:*** *This was a single centre randomised control study was conducted from Sep 2021 to Feb 2022 in the Department of Anaesthesia at GMC Kota. Individual patients underwent thorough pre-anaesthetic evaluations and investigations. Total 60 patients were separated into two equal groups and randomly assigned using a computer-generated random number table (Group -DIV and Group DIN). SPSS software version 16 was used for statistical analysis and ap value< 0.5 was considered to be statistically significant.* ***Results:*** *A total 60 patients were included. Demographic details and baseline parameters were not significantly different among both groups. There was no statistically significant difference(p->0.05) were noted in pre-induction and post induction HR, SBP, DBP and MAP for all time interval till 40 min.When sedation was compared, it was found that maximum 18 (60%) patients in DIN group remained in RSS stage II and 22 (73.3%) patients in DIV group remained in RSS stage III at 40 min and this difference was found to be statistically significant (p-<0.05).* ***Conclusions:*** *Our study concluded that both intravenous DEX (0.5 µg/kg in 40 minutes) and intranasal DEX (1 µg/kg) given 40 minutes before induction are equivalent efficacious in decreasing haemodynamic surges during laryngoscopy and intubation.*

Keywords: Dexmedetomidine, intravenous, intranasal, laryngoscopy and intubation

1. Introduction

After induction of anesthesia, laryngoscopy and tracheal intubation produce pressure and sympathoadrenal responses, which are assumed to be somatovisceral reflexes generated by stimulation of the epipharynx and laryngopharynx. [1] Laryngoscopy without intubation produces approximately the same pressor response as laryngoscopy with intubation. [2] It begins in 5 seconds, peaks in 1–2 minutes, and then returns to baseline in 5 minutes. [3] Increased circulatory catecholamines, heart rate (HR), blood pressure, myocardial oxygen demand, and dysrhythmias arise from these responses. HR and blood pressure increases are typically temporary, varied, and unpredictable. In order to reduce unfavorable hemodynamic responses following intubation, several approaches have been tested. Increasing the depth of anesthesia with extensive premedication, strong opioids like fentanyl [4], and inhalational anesthetic agents are all common procedures. [5] Others include lignocaine (both IV and topical), clonidine, calcium channel blockers, sodium nitroprusside, beta-adrenergic blockers, and magnesium sulfate, but none are perfect.

DEX is a highly selective, short-acting alpha2-adrenoreceptor agonist that acts as a sedative, analgesic, and anxiolytic without causing respiratory depression. It is an excellent anxiety or nervousness reliever before to anaesthesia. Preoperative intravenous (IV) DEX has been shown to effectively reduce the laryngoscopic stress response. [6] However, severe haemodynamic consequences such as hypotension, bradycardia, and even cardiac arrest may have limited IV DEX's use. The sedative effect of IV DEX has also been linked to a delay in recovery. [7] Alternative approaches to fast intravenous distribution have been explored as a way to reduce the negative effects of DEX. DEX is also efficacious when administered intramuscularly, orally, or intranasally (IN). Intranasal administration is more convenient and effective than other methods. [8] Patient acceptability of intranasal DEX has been demonstrated to be high. Several studies in the paediatric age group have recently demonstrated that intranasal DEX premedication as an alternative to standard premedication has positive perioperative outcomes. [9] To the best of our knowledge, no study has yet been published that compares the efficacy of preoperative IV DEX against IN DEX for reducing haemodynamic reactions during L-I. The study's goal was to examine pre-induction and post-intubation mean arterial pressure (MAP), heart rate, systolic and diastolic blood pressure, sedation scores, and other adverse effects between two groups.

2. Methods

This randomised control study was conducted from May 2020 to April 2021 in the Department of Anaesthesia at GMC Kota.

This study comprised sixty adults with ASA physical status I and II, ranging in age from 18 to 60 years, who were undergoing elective lumbar spine surgery under general anaesthetic with endotracheal intubation. Patients who refused to participate, had a known dexmedetomidine allergy or hypersensitivity, had substantial cardiac or respiratory problems, or were expected to have a difficult airway were excluded from the trial.

Individual patients underwent thorough pre-anaesthetic evaluations and investigations. Patients were separated into two equal groups and randomly assigned using a computer-generated random number table (Group -DIV and Group DIN). After gaining the patient's consent, the list was hidden in opaque sealed envelopes that were numbered and opened sequentially.

On the day of the surgery, all participants were moved to the preoperative area 2 hours prior to the start of the procedure, and baseline hemodynamic measures were recorded in the preoperative room. Group DIV received IV DEX (0.50 g/kg) via an infusion pump 40 minutes before induction [200 g diluted in 50 ml syringe with normal saline (NS) =4 g/ml]. The DIN group received an equivalent volume of NS intravenously. Patients in Group -DIN- received IN DEX (1 g/kg) in an undiluted form made from parenteral preparation (100 g/ml). Intranasal medication was dripped into both nostrils in equal amount using a 1 ml syringe about 40 minutes before induction in a supine head down position. The DIV group received an equivalent volume of NS intranasally. After intranasal medication administration, all patients were told not to suck or sneeze.

A double blinding approach was used during the investigation, in which the person giving the medicine and the patients were both oblivious of the group distribution. Heart rate (HR), mean arterial pressure (MAP), systolic blood pressure (SBP), diastolic blood pressure (DBP), and SpO2 were measured every 10 minutes in the preoperative room until anaesthesia was administered. Haemodynamic values were recorded in the operating room at the time of intubation, then at 1 minute intervals until 5 minutes, 7 minutes, and 10 minutes after intubation. An observer used the Ramsay sedation scale (RSS) to assess sedation status in both groups at baseline and 40 minutes after study medication administration. Throughout the perioperative period, haemodynamic monitoring was continued. All patients were given IV propofol (2 mg/kg) and fentanyl (1 g/kg) after a 3-minute preoxygenation with 100% oxygen. To make tracheal intubation easier, rocuronium bromide (1 mg/kg) was given intravenously. When the train of four (TOF) count was 0, an experienced anaesthesiologist performed laryngoscopy with a Macintosh laryngoscope blade and endotracheal (ET) intubation with an appropriate size cuffed-disposable armoured ET tube. The L-I time restriction was set at 15-20 seconds. If L and I were not completed within 15-20 seconds, the data was removed from the analysis. Surgical intervention could not begin until 10 minutes after intubation. Low flow anaesthesia (50 percent O2 —NO2 at 1 litre/min), propofol infusion (10-15 mg/kg/hr titrated to keep Bispectral Index between 40-60), and intermittent bolus doses of rocuronium (0.1 mg/kg) as needed were used to maintain anaesthesia. Neuromuscular monitoring guided the timing of extubation (TOF watch). The primary result was a comparison of changes in mean arterial pressure (MAP) between two groups from pre-induction to 40 minutes after study medication delivery and from post-intubation to 10 minutes following intubation at frequent intervals. Within the research period, the secondary outcomes were a comparison of HR, SBP, DBP, sedation score, and other side events. When the patient experienced episodes of hypotension (MAP 9, his vitals were monitored for 12 hours on the ward. SPSS software version 16 was used for statistical analysis. Except for RSS and SpO2 data, normality was determined using the Kolmogorov-Smirnov goodness-of-fit test. RSS score 2 (awake, oriented, and cooperative) was deemed satisfactory for statistical analysis. For normally distributed data, the unpaired Students t-test was employed, and for skewed data, the Mann-Whitney U test was utilized. If the data was regularly distributed, repeated measures analysis of variance (ANOVA) with Tukey's test as a post hoc test was used, and for skewed data, Friedman's analysis of variance (ANOVA) with Dunn's test as a post hoc test was used. A P value.

3. Results

In the present study a total 60 patients were included. Demographic details and baseline parameters were not significantly different among both groups. (Table 1)

Our study revealed that there was no statistically significant difference(p->0.05) were noted in pre-induction SBP, DBP and MAP for all time interval till 40 min. All these parameters were significantly decrease from basal to 40 min of induction by using ANOVA test. (Table 2)

Participants among both group were also showed insignificant (p->0.05) difference in HR during pre-induction, however HR was found to be lower in DIV compare to DIN. (Table 2)

There is no statistical significant difference were found in HR, SBP, DBP and MAP, however it was slightly higher in DIV group (p->0.05). (Table 4)

When sedation was compared, it was found that maximum 18 (60%) patients in DIN group remained in RSS stage II and 22 (73.3%) patients in DIV group remained in RSS stage III at 40 min and this difference was found to be statistically significant (p-<0.05).

No participants developed nausea, vomiting or respiratory depression among both groups.

4. Discussion

The effectiveness of preoperative DEX in reducing laryngoscopic stress reactions is well documented. In addition to IV administration, IN DEX is increasingly being used as a premedication, particularly among children. We evaluated the effects of IV and IN dexmedetomidine on L-I stress responses in this study. In our research, we discovered that intranasal 1 g/kg DEX given 40 minutes before induction had an impact comparable to preoperative IV DEX infusion (0.5 g/kg) in preventing L-I stress responses. DEX administered intranasally and intravenously significantly reduced laryngoscopic stress reactions without causing severe hypertension or tachycardia. Before and during L-I, all haemodynamic parameters (HR, SBP, DBP, MAP) were kept within normal limits (20% of basal values) in both groups. The haemodynamic alterations of L-I were initially documented by Raid and Brace. [10] A appropriate sympatholytic drug is required to prevent sympathetic activation.

There was no significant change in haemodynamic parameters between IV and intranasal dexmedetomidine in the current investigation. Dexmedetomine, administered through IV or IN, has been shown to reduce stress reactions, but we found no significant differences in haemodynamics between the two groups. All haemodynamic measures remained within 20% of baseline in both groups, with no notable changes in MAP or HR. Dexmedetomidine used intravenously is considered to offer considerable drowsiness without any respiratory side effects. Another study using intranasal dexmedetomidine as a sedative premedication, on the other hand, found that it generated a favorable perioperative anxiolysis with no delay in anesthesia recovery. [12] Intranasal dexmedetomidine is a safe and effective sedative for dental procedures in children, with good patient compliance and quick recovery. There were no incidences of oxygen deprivation or apnoea recorded. [13-14] In our investigation, the sedation score in the DIV group was considerably higher than in the DIN group after 40 minutes of study medication delivery. The majority of patients in the DIN group were still in RSS stage II, whereas those in the DIV group were still in RSS stage III.

In a study by Li et al. on the pharmacokinetics and pharmacodynamics of intranasal DEX, it was discovered that intranasal dexmedetomidine has a slower and more gradual start than IV dosing.[15] When compared to the IN route, rapid IV delivery leads in substantially greater peak plasma concentrations and early onset. In order to minimize the alpha 1 agonist effects seen with rapid IV delivery, a more delayed start may be preferable (hypertension and bradycardia). Both slow IV DEX infusion and intranasal DEX had similar haemodynamic effects in our research.

According to the findings of this study, both intranasal and intravenous dexmedetomidine can be used as a premedication to reduce haemodynamic surges during L-I with similar efficiency. This result can be explained by the fact that both IV and IN DEX prevent central catecholamine levels from rising.

5. Conclusion

Our study revealed that both intravenous DEX (0.5 g/kg in 40 minutes) and intranasal DEX (1 g/kg) given 40 minutes before induction are equivalent efficacious in decreasing haemodynamic surges during laryngoscopy and intubation.

6. Limitation

The recovery characteristics of both IV and IN DEX in the postoperative phase were not investigated in this research, and only 40 minutes of premedication time were recorded. A large study should be undertaken with these points in mind.

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Conflict of Interest
There is no financial conflict of interest to declare for any of the authors in association with the publication of this manuscript.

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Author Contributions
All authors had access to the study data. contributed to the study concept and design, data collection, data analysis and interpretation, and drafting of the manuscript. Dr Pooja Pahadiya contributed to the data collection, data analysis and interpretation, and drafting of the manuscript. All authors reviewed and approved the final version of the manuscript before submission.

Supplementary Data-No other supplementary data is available.

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Tables:

Table 1: Comparison of demographic and baseline characteristics among both groups.

Parameters	DIV (n=30)	DIN (n=30)	p-value
Age (in years)	38.42±10.24	40.12±12.43	0.782
Gender (F:M)	13/17	14/16	0.673
BMI (in kg/m^2)	22.49±6.89	23.12±5.42	0.532
SBP (in mm hg)	128.42±13.4	129.1±12.24	0.720
DBP (in mm hg)	79.24±8.21	78.34±7.12	0.820
MBP (in mm hg)	94.23±6.28	93.65±7.21	0.798
HR (beats/min)	83.21±7.45	82.14±6.78	0.254

Table 2: Comparison of pre induction haemodynamic parameters among both groups

Group	Basal	At 10 min	At 20 min	At 30 min	At 40 min
SBP					
DIV	128.42±13.4	122.42±11.2	119.12±9.12	116.24±8.23	111.28±6.3
DIN	129.1±12.24	124.1±9.41	120.1±10.32	116.92±9.4	113.42±7.4
p-value	0.720	0.672	0.685	0.508	0.685
DBP					
DIV	79.24±8.21	77.4±9.1	75.2±7.5	72.3±8.1	67.4±5.2
DIN	78.34±7.12	77.4±7.8	74.8±6.9	73.34±7.2	68.3±6.2
p-value	0.820	0.749	0.68	0.76	0.54
MAP					
DIV	94.23±6.28	90.3±6.8	88.3±7.3	85.4±5.8	81.2±6.8
DIN	93.65±7.21	90.6±8.1	87.6±7.1	84.8±6.1	81.7±6.6
p-value	0.79	0.67	0.61	0.59	0.68
HR					
DIV	83.21±7.45	80.3±7.8	72.1`±7.5	70.2±7.45	68.1±7.4
DIN	82.14±6.78	80.1±6.8	72.2±7.8	71.2±6.8	67.13±7.8
p-value	0.25	0.54	0.67	0.82	0.69

Table 3: Comparison of post induction haemodynamic parameters among both groups

Group	Induction	L-I	1 min	3 min	5 min	7 min	10 min
SBP							
DIV	111.2±6.3	120.4±11.4	126.4±13.4	123.2±11.2	120.2±9.2	117.4±8.3	114.8±6.1
DIN	110.4±6.2	121.1±10.8	125.1±10.4	124.1±9.8	120.8±10.2	117.9±8.4	115.4±7.2
p-value	0.72	0.62	0.79	0.72	0.68	0.82	0.85
DBP							
DIV	67.2±7.1	77.3±7.4	80.4±7.2	82.3±8.1	72.2±6.5	72.3±8.2	70.4±6.2
DIN	65.3±6.6	76.6±6.9	80.8±6.7	83.4±7.2	72.8±5.9	73.34±7.4	69.3±6.2
p-value	0.25	0.62	0.87	0.72	0.82	0.77	0.74
MAP							
DIV	79.8±7.4	91.4±6.6	94.3±6.8	92.3±6.6	86.3±7.3	85.6±6.8	82.2±6.4
DIN	80.5±6.8	90.8±6.9	93.5±7.1	91.6±7.1	87.6±7.7	85.8±6.1	81.9±6.2
p-value	0.56	0.81	0.78	0.67	0.43	0.91	0.87
HR							
DIV	68.2±7.1	77.2±7.7	82.2±7.5	80.0±7.2	75.1`±7.5	77.2±7.5	74.1±7.1
DIN	70.3±7.4	78.6±6.9	82.9±6.7	80.8±6.9	77.2±7.8	76.2±6.8	73.13±7.3
p-value	0.48	0.12	0.76	0.54	0.32	0.52	0.58