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Effectiveness of intranasal versus intravenous dexmedetomidine for attenuation of hemodynamic responses of laryngoscopy and endotracheal intubation in patients undergoing general anaesthesia: Randomized controlled trial

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ABSTRACT

Aim and Objective: Attenuation of hemodynamic responses to laryngoscopy and intubation is major concern during conduct of general anaesthesia. This study compared the efficacy of intranasal versus intravenous Dexmedetomidine for attenuation of these hemodynamic responses.

Materials and Methods: Prospective double blind randomized controlled study was conducted on 90 participants randomized in 2 groups - Group DIN (n=45) received Intranasal Dexmedetomidine (1 μg/kg of 100μg/ml preparation) 40 minutes preinduction and Group DIV (n=45) received Intravenous Dexmedetomidine (0.5μg/kg of 200μg in 40 ml normal Saline infusion) 10 minutes preinduction.

Primary objective was to compare hemodynamic parameters in both groups every 10 min from drug administration till induction, at intubation and till 30 min postinduction. Secondary objective was to compare postoperative sedation in both groups at variable intervals. Data was analysed in statistical software Epi Info Software version 7.

Results: No significant hemodynamic response to laryngoscopy and intubation seen above baseline values in both groups. Group DIV showed lower values than DIN at laryngoscopy-intubation (P=0.0095) and postintubation phase till 7min (P=0.0016) in terms of MAP. No significant difference in postoperative sedation in both groups.

Conclusion: Intravenous and intranasal Dexmedetomidine equally attenuate hemodynamic responses to laryngoscopy and intubation during general anaesthesia with similar postoperative sedation. Intranasal Dexmedetomidine had steadier hemodynamics than intravenous Dexmedetomidine.

1. Introduction

Laryngoscopy and endotracheal intubation during general anaesthesia cause strong nociceptive stimuli, leading to unintended sympathetic nervous system stimulation[1] through release of catecholamines noradrenaline immediately after laryngoscopy. This result in hypertension, tachycardia, laryngospasm, bronchospasm, raised intracranial pressure and intraocular pressure.

This reflex hemodynamic pressor response arises 30 seconds post-laryngoscopy and intubation and reverses back to baseline within 5–10 minutes.[2] In some patients, exaggerated hemodynamic alterations may lead to fatal complications like myocardial ischaemia or secondary brain damage.[3] Hence it is one of the crucial step to supress these pressor responses effectively.

Different types of drug combinations to alleviate these sympathetic responses are currently in use like – opioids,

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benzodiazepines, barbiturates, beta blockers, alpha agonists, calcium channel blockers, vasodilators etc. with variable pros and cons. Dexmedetomidine (Dexmed) is an ideal alternative anxiolytic for anaesthesia with properties like analgesia, anxiolysis and central sedation without any known respiratory depression.[4] The different routes of Dexmed are available, such as intravenous, intramuscular, oral and intranasal route. As of today, it is well studied that preoperative intravenous (IV) Dexmed effectively supress the reflex hemodynamic laryngoscopy and intubation response.[5] But IV Dexmed has adverse hemodynamic complications like hypotension, bradycardia, cardiac arrest and delayed recovery from sedative effect,[6] limiting its widespread use.

The intranasal Dexmedetomidine (IN Dexmed) is painless, tasteless and odourless with more patient compliance. Several paediatric studies reported good outcomes of IN Dexmed premedication as an alternative to previously used premedication.[7] There is paucity of literature of effectiveness of IN Dexmed for suppression of laryngoscopy-intubation pressor response and recovery of postoperative sedation in adult Indian population.

Hence primary aim of this study was to compare the effectiveness of IN Dexmed over IV Dexmed for attenuation of hemodynamic effects of laryngoscopy and endotracheal intubation in terms of Heart Rate, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP) and Oxygen Saturation (SpO2). While postoperative sedation in terms of Ramsay sedation score was kept as a secondary objective.

2. Materials and Methods

This double blind, randomised control study was carried out at a tertiary care teaching institute from November 2022 to May 2024, after the approval of the Institutional Ethics Committee (ECR/88/Inst/MH/2013RR/19). Written informed consent was obtained from each study participant. The convenience sampling was done and randomization by block method, 15 blocks of size 6 each was done. Sequentially numbered, sealed, opaque envelopes were used. ASA (American Society of Anaesthesiologists) physical status I and II patients between age of 18 and 60 years posted for elective surgery under general anaesthesia were included in this study after thorough clinical and laboratory workup along with written informed consent from each patient. Patients who refused to participate, had known allergy or hypersensitivity to study drug, predicted difficult airway, nasal ulcers/polyps, nasal septal deviation were excluded from study. Participants were blinded to treatment allocation and drug was administered by one anaesthesiologist and operative room monitoring was done by another anaesthesiologist who was blinded to the drug administered.

After obtaining Written informed consent, detailed medical history and required investigations from each patient; thorough physical examination, detailed pre-anaesthetic evaluation was done and ASA physical status was determined. The convenience sampling was done and randomization by block method, 15 blocks of size 6 each was done. Sequentially numbered, sealed, opaque envelopes were used. Randomisation was done into two groups - Group DIN (study group) Intranasal Dexmedetomidine and Group DIV (control group) Intravenous Dexmedetomidine with 45 patients in each group. Each patient was kept fasting as per ISA NPO guidelines.

On operative day, all the participants were shifted to preoperative area 2 hours before surgery. All standard monitors like pulse oximetry, non-invasive blood pressure (NIBP), electrocardiogram (ECG) were attached to record baseline hemodynamic parameters in preoperative room. Baseline RSS score was noted for each patient before administration of study drug. IV Ringer's lactate solution was administered as maintenance fluid through 20G peripheral venous canula.

Group DIV (Control Group) patients received intravenous Dexmedetomidine (0.50 μg/kg) [200 μg diluted in 40 ml syringe with normal saline (NS) through an infusion pump over 10 min before induction. The Normal saline was dripped into both nostrils in equal volume using a 1 ml syringe in supine head down position about 40 min before induction.

Group – DIN (Study Group) patients received intranasal Dexmedetomidine (1 μg/kg) in undiluted form which was prepared from available parenteral preparation (100 μg/ml). Intranasal drug was dripped into both nostrils in equal volume using a 1 ml syringe in supine head down position about 40 min before induction. 40 ml volume of Normal saline was administered through an infusion pump over 10 min before induction.

In the preoperative room, hemodynamic parameters like heart rate (HR), mean arterial pressure (MAP), systolic blood pressure (SBP), diastolic blood pressure (DBP), and SpO2 were noted at every 10 min intervals till induction of anaesthesia. Sedation status in both groups was assessed by an observer using the Ramsay sedation scale (RSS) at before drug administration. In the operative room, hemodynamic parameters were noted at the time of intubation, thereafter every 1 min interval till 5 min, then at 7th, 10th, 15th, 20th, 25th and 30th minute after intubation. Ramsay sedation scale (RSS) after extubation followed by at 1hour, 2hours (hrs), 3hrs, 4hrs, 6hrs, 8hrs, 10hrs, 16 hrs and 24hrs post extubation were noted.

After shifting the patient in operative room, standardized general anaesthesia techniques were maintained for both the groups. Monitors were reattached and intraoperative monitoring was done and hemodynamic monitoring was continued throughout the perioperative period.

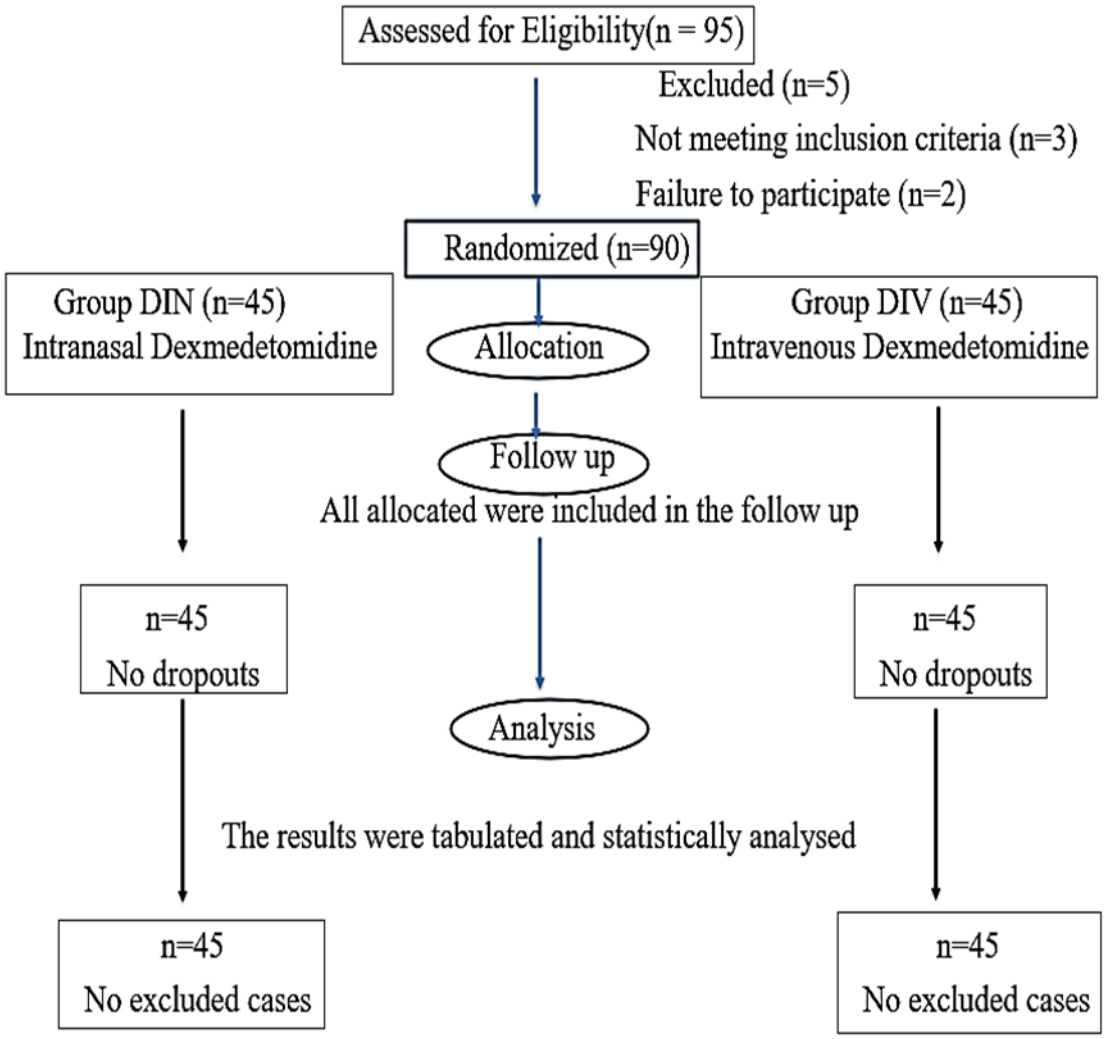


Figure 1: Consort flow diagram

Premedication was done with Inj Glycopyrolate 0.004mg/kg IV, Inj Midazolam 0.03mg IV and Inj Fentanyl 2μg/kg IV. After preoxygenation with 100% oxygen for 3 min, all patients were induced with Inj Propofol (2 mg/kg) IV. Inj Vecuronium (0.1 mg/kg) IV was administered to facilitate tracheal intubation. Laryngoscopy was performed with appropriately sized Macintosh laryngoscope blade and endotracheal (ET) intubation was done with appropriately sized cuffed Endotracheal tube. No surgical intervention was allowed till 10 min after intubation. Anaesthesia was maintained and repeated intermittent bolus doses of Vecuronium were given as and when needed. All patients were ventilated on volume-controlled ventilation using a closed circuit (Dragger) and end tidal CO2 was maintained 35-45 mm of Hg.

Extubation timing was guided by clinical parameters. After completion of surgery, neuromuscular block was reversed with appropriate dose of IV Neostigmine and Glycopyrolate. After adequate recovery, the patient was shifted to the postoperative care unit or recovery room. The primary outcome of interest was comparison of changes in heart rate along with systolic, diastolic and mean arterial pressure in both groups before induction, at induction and postinduction till 30 minutes. The secondary outcome of interest was recovery from sedation post-extubation.

2.1. Statistical analysis

Statistical Epi Info Software version 7 was used. Sample size was estimated to be total 90 which was calculated based on article by Niyogi S et al. 2019.[8] with mean heart rate at 40 minutes (71.23±9.48) in group DIN (intranasal Dexmedetomidine) and (66.60±5.55) in group DIV (intravenous Dexmedetomidine) with α error 0.05, power = 80% and level of significance < 0.05.

For qualitative data frequency and percentage was calculated and for quantitative data, mean and standard

deviation was calculated. Unpaired t test was applied. Repeated measure one way ANOVA followed by Tukey Test was used.

3. Results

The demographic characters like age, sex and BMI were comparable in both groups (Table 1). Baseline heart rate and blood pressure values were almost similar in both groups.

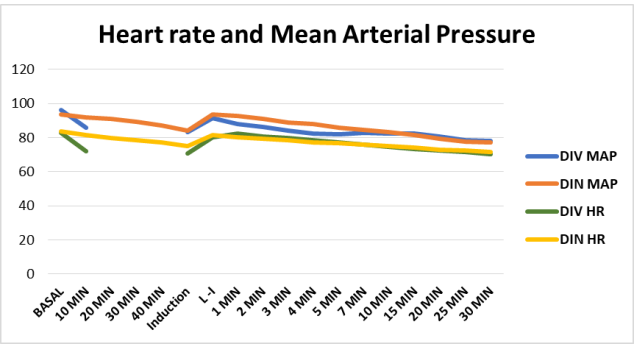
Table 1: Comparison of demographic variables in both groups

Variables	Group DIN (n=45)	Group DIV (n=45)
Age (years) (Mean±SD)	40.26±11.65	40.73±11.98
Sex, n(%)		
Male	13 (28.89%)	13 (28.89%)
Female	32 (71.11%)	32 (71.11%)
BMI (kg/m2) (Mean±SD)	22.05±2.09	22.55±2.67

[BMI – Body Mass Index]

There was statistically significant difference in mean HR at 10 minutes pre induction and at induction (p=<0.0001). Rest, at all intervals, no significant changes in mean HR was seen in both groups. (Table 2)

There was statistically significant difference in mean SBP at 10 minutes preinduction, at laryngoscopy-intubation and post induction from 1 minute till 7 minutes (P=<0.05). Rest at all intervals, no significant changes in mean SBP was seen in both groups. There was statistically significant difference in mean DBP at 10 minutes preinduction, at laryngoscopy-intubation tube and post intubation from 1 minute till 7 minutes (p=<0.05). Rest at all intervals, no significant changes in mean DBP was seen in both groups. There was statistically significant difference in mean MAP at 10 minutes preinduction, at laryngoscopy intubation and post intubation from 1 minute till 7 minutes (p=<0.05). (Table 3)



Graph 1: Comparison of heart rate and mean arterial pressure in both groups

There was no significant difference in the Ramsay sedation scores between the two groups (Table 4). Additionally, no episodes of side effects, such as bradycardia or hypotension, were observed.

4. Discussion

Laryngoscopy and intubation stress response is always a challenge to anaesthesiologist. Different proven pharmacological modalities are available at present to supress these hemodynamic responses and some are still evolving.[9,10] Out of which, intravenous Dexmedetomidine has been proven to be effective in attenuation of stress response to laryngoscopy and intubation but with common adverse effects like hypotension, bradycardia, making it of limited use in cardiac compromised patients.[6] In recent times intranasal premedication of Dexmedetomidine is quite popular for sedation, analgesia and hemodynamic stability in paediatric population. While in adult Indian population, there is scarcity of intranasal Dexmedetomidine studies for effective suppression of this pressor response. In our study, we have studied effectivity of intranasal Dexmedetomidine in comparison with intravenous Dexmedetomidine for attenuation of hemodynamic response to laryngoscopy and intubation.

Laryngoscopy and intubation Stimulates Mechanoreceptors in larynx which carries afferent stimulus through Glossopharyngeal and Vagus nerve to relay at caudal and posterior part of brainstem medulla. This results in sympathetic activation of vasomotor centre releasing catecholamines.[11] Through Adrenal medulla causing resultant Tachycardia, Hypertension and Raised intracranial and intraocular pressure. The reaction starts after five seconds of laryngoscopy, reaching its peak after one to two minutes, and recovers to normal levels within five to ten minutes.

Dexmedetomidine is a centrally acting α 2 agonist with sympatholytic property along with sedative, hypnotic, anxiolytic, antisecretory and analgesic property. Dexmedetomidine blocks α 2 receptor by inhibits presynaptic release of noradrenaline at central locus ceruleus and produces drowsiness and hypnosis while postsynaptic inhibition results in tachycardia and hypertension. Both Intravenous and intranasal routes of Dexmedetomidine carry out this sympatholysis, thus resulting in attenuation of hemodynamic stress response of laryngoscopy and intubation. Dexmedetomidine has all in one i.e. analgesic, drowsiness and anxiolysis property. Thus, reducing the need of many medications and less possibility of adverse reactions. It produces dose-dependent cooperative sedation, enabling early communication and postoperative neurological testing. Atipamezole, is available antagonist of Dexmedetomidine.[12] Dexmedetomidine is available in intravenous as well as intranasal preparation. Because of larger surface area of the nasal cavity and the high vascularisation of the nasal mucosa, intranasal route of administration received increasing popularity for systemic

Table 2: Comparison of changes in mean heart rate in both groups

Time (minutes)	Heart rate		Unpaired t Test p Value
	DIN group Mean ± SD	DIV group Mean ± SD	
Preinduction			
Basal	83.56±6.48	82.82±3.99	0.51
10 min	81.26±6.45	72.13±4.27	<0.0001*
20 min	79.73±6.25	Not recorded	-
30 min	78.53±6.09	Not recorded	-
40 min	77.13±5.89	Not recorded	-
At induction	74.97±5.91	70.48±3.57	<0.0001*
at Laryngoscopy-Intubation	81.46±5.85	80.20±4.01	0.23
1 min	80.27±5.61	82.24±4.09	0.059
2 min	79.44±5.85	80.80±3.87	0.19
3 min	78.35±5.71	79.60±3.68	0.22
4 min	77.33±5.73	78.26±3.82	0.36
5 min	76.62±5.67	77.02±3.67	0.69
7 min	75.64±5.75	75.80±4.13	0.87
10 min	74.91±5.63	74.44±3.94	0.64
15 min	73.93±5.24	73.24±3.80	0.47
20 min	73.02±5.11	72.22±3.74	0.39
25 min	72.53±4.44	71.40±3.69	0.19
30 min	71.53±4.09	70.33±3.47	0.87

[DIN: Intranasal Dexmedetomidine, DIV: Intravenous Dexmedetomidine, P<0.05 significant]

drug delivery. The faster onset of action, non-invasiveness, easy administration and effective action make this route an effective option with less exposure of drug to vital organs, thus decreasing its chances of abrupt side effects which are seen with intravenous administration.

Currently, it is well established that preoperative intravenous dexmedetomidine effectively suppresses the hemodynamic responses associated with laryngoscopy and intubation. However, this comes with potential drawbacks, including adverse hemodynamic effects such as hypotension, bradycardia, cardiac arrest, and delayed recovery from sedation,limiting its widespread use.[6] While the intranasal route Dexmedetomidine is painless, tasteless and odorless with more patient compliance. Several paediatric studies reported good outcomes of IN Dexmedetomidine premedication as an alternative to traditional premedication.[10] But there is paucity of literature of effectiveness of IN Dexmedetomidine for effective suppression of laryngoscopy-intubation pressor response in grown up Indian population.

Both the groups in this study were comparable in terms of age, sex, BMI and ASA status. The demographic parameters were standardised for both groups. Basal HR, SBP, DBP, MAP and SpO2 in both groups do not show any significant difference. (Tables 1, 2 and 3)

HR, SBP, DBP, MAP show significant difference in Group DIN (Study Group) and DIV (Control Group) at 10th minute post drug administration (P<0.0001) (Tables 2 and 3). This difference may have occurred due to difference in time of drug administration. DIV group was given Intravenous Dexmedetomidine infusion (0.50 μg/kg) 10 minutes prior to induction. While the DIN (Study Group) group received Intranasal Dexmedetomidine (1μg/kg) 40 minutes prior to induction.

Numerous studies have demonstrated the effectiveness of intravenous dexmedetomidine in attenuating the stress response to laryngoscopy and intubation in the adult population. Tanskanen et al. concluded that administering intravenous dexmedetomidine 20 minutes prior to induction, achieving a plasma concentration of 0.4 ng/ml in the DEX 0.4 group, is an effective adjunct in elective supratentorial brain tumor surgeries.[13] This approach significantly reduces cardiac variability, such as hypertension and tachycardia, during intubation and extubation, as well as lowers intraoperative opioid consumption compared to a placebo group. While there was an increase in systolic blood pressure (SBP) following laryngoscopy and intubation across all groups, the post-extubation rise in SBP was more effectively managed in the dexmedetomidine groups (P<0.01). Furthermore, heart rate (HR) increases were better controlled in both the post-laryngoscopy-intubation and post-extubation phases in the dexmedetomidine groups compared to placebo (P<0.01).

Similarly, Keniya et al. found that administering an intravenous dexmedetomidine infusion of 1 μg/kg over 10 minutes prior to induction, followed by a maintenance dose of 0.2–0.7 μg/kg/hr, effectively attenuated the sympathetic response to tracheal intubation.[14] In this study, the maximal rise in HR and blood pressure occurred immediately after intubation, but increases in HR, SBP, and diastolic blood pressure (DBP) post-intubation were significantly lower in the dexmedetomidine group (7%, 8%, and 11%,

Table 3: Comparison of changes in SBP, DBP and MAP in both groups

Time	SBP			DBP			MAP		
	DIN group Mean ± SD	DIV group Mean ± SD	Unpaired t Test p Value	DIN group Mean ± SD	DIV group Mean ± SD	Unpaired t Test P Value	DIN group Mean ± SD	DIV group Mean ± SD	Unpaired t Test P Value
Basal	120.38±5.36	120.22±4.51	0.94	80.13±5.08	81.91±4.02	0.06	93.54±5.15	93.04±4.08	0.82
10 min	118.67±5.06	112.91±3.10	<0.0001*	78.71±4.92	71.96±3.59	<0.0001*	91.98±4.93	85.56±2.91	<0.0001*
20 min	117.05±5.02	NIL	NIL	77.68±5.12	NIL	NIL	90.80±4.91	NIL	NIL
30 min	115.56±4.69	NIL	NIL	76.04±4.99	NIL	NIL	89.21±4.71	NIL	NIL
40 min	113.72±4.57	NIL	NIL	73.91±4.08	NIL	NIL	88.17±4.11	NIL	NIL
Induction	110.31±4.54	109.87±3.08	0.58	71.22±3.99	70.04±2.71	0.10	84.27±4.15	83.18±2.50	0.13
At L - I	121.11±4.66	121.22±3.90	0.90	79.73±4.11	76.73±3.09	0.0002	93.58±4.14	91.62±2.71	0.0095*
1 min	121.07±4.33	120.47±3.35	0.46	78.60±3.76	71.49±3.21	<0.0001*	92.76±3.91	87.80±2.54	<0.0001*
2 min	118.71±4.08	116.78±2.69	0.0094	76.98±3.43	70.67±2.68	<0.0001*	90.87±3.63	86.02±1.98	<0.0001*
3 min	116.82±3.98	112.38±3.82	<0.0001*	74.87±3.76	69.67±1.93	<0.0001*	88.93±3.73	83.96±2.01	<0.0001*
4 min	115.11±3.61	109.51±3.89	<0.0001*	74.24±3.38	68.58±2.29	<0.0001*	87.82±3.41	82.22±2.17	<0.0001*
5 min	113.24±3.72	108.67±2.79	<0.0001*	71.93±3.30	68.58±1.48	<0.0001*	85.71±3.42	81.96±1.49	<0.0001*
7 min	111.93±4.04	110.27±3.29	0.03	70.84±3.33	68.76±1.76	0.0003	84.53±3.45	82.62±1.89	0.0016
10 min	110.18±3.87	108.98±2.47	0.08	69.60±2.74	68.82±2.06	0.13	83.13±2.95	82.11±1.99	0.057
15 min	108.38±3.96	109.33±2.93	0.19	67.87±3.52	68.53±2.58	0.30	81.40±3.56	81.96±2.70	0.40
20 min	106.48±3.72	107.95±3.58	0.05	65.84±3.19	66.67±2.16	0.15	79.38±3.38	80.20±2.64	0.20
25 min	104.75±3.62	106.11±3.73	0.08	63.87±2.79	64.80±3.07	0.13	77.53±3.09	78.53±3.27	0.13
30 min	103.04±3.61	104.53±3.70	0.05	64.42±2.59	64.64±3.53	0.73	77.29±2.62	77.94±3.58	0.32

[DIN: Intranasal Dexmedetomidine, DIV: Intravenous Dexmedetomidine, SBP – systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, P<0.05 significant]

Table 4: Comparison of changes in mean Ramsay sedation score in both groups

Time (minutes)	Mean Ramsay Sedation Score	
	DIN group Mean ± SD	DIV group Mean ± SD
Basal	2.00±00	2.00±00
At extubation	3.00±00	3.00±00
Post Extubation		
30 min	2.04±0.20	2.08±0.28
2 hours	2.00±00	2.00±00
6 hours	2.00±00	2.00±00
8 hours	2.00±00	2.00±00
12 hours	2.00±00	2.00±00
16 hours	2.00±00	2.00±00
24 hours	2.00±00	2.00±00

[DIN: Intranasal Dexmedetomidine, DIV: Intravenous Dexmedetomidine]

respectively) compared to the control group (21%, 40%, and 25%, respectively).

In a study by Sulaiman et al., intravenous dexmedetomidine at a dose of 0.5 μg/kg administered 10 minutes before induction in cardiac patients undergoing elective off-pump coronary artery bypass surgery also effectively mitigated the sympathetic response during laryngoscopy and intubation.[15] The HR, SBP, and DBP post-intubation remained within 20% of baseline values and were significantly lower in the dexmedetomidine group, aligning with our findings.

Additionally, a comparative study by Jarineshin et al. assessed two different doses of intravenous dexmedetomidine (0.5 μg/kg versus 1 μg/kg) administered over 10 minutes pre-induction, concluding that the 0.5 μg/kg dose effectively inhibited tachycardia and hypertension responses to endotracheal intubation.[16] In our study, the control group received the lowest effective dose of dexmedetomidine (0.5 μg/kg) over 10 minutes before induction.

IV Dexmedetomidine rapid infusion dose of more than 0.5μg/kg is associated with more negative effects with drowsiness and hemodynamic instability.[13,17] Also, IV Dexmedetomidine is associated with more sedative action than analgesic effectand have side effects like severe bradycardia and hypotension which are dose dependant.[18] Intranasal route being easy to administer, more patient compliant and bypassing of first pass metabolism has been good alternative. Intranasal Dexmedetomidine as premedication has been studied in various paediatric studies. The crossover study by Yuen et al. compared intranasal Dexmedetomidine 1μg/kg and 1.5 μg/kg in paediatric population aged 1-12yrs, posted for elective surgery; which concluded that both doses have effective sedation with reduced bispectral index, BP and HR with onset time of 45 min (peak at 90 – 150 min).[19] In a pharmacokinetic and pharmacodynamic comparative study for 1 μg/kg Dexmedetomidine on adult population by Li A et al., as 3 different routes: intravenous, intranasal by atomiser, intranasal by drops, the average onset time of sedation found with intravenous route(15 min) faster than intranasal atomiser (47 min) and intranasal drops (60 min).[20] Sedation duration was longer with intravenous (200.4 min) than Intranasal atomizer (147.5min) and drops (170 min). This difference in time of onset of action in intravenous and intranasal route has specific reason. In intravenous route of drug administration, drug enters directly into blood stream and produce immediate effects after injected as bolus or infusion in one of the superficial veins; thus, carrying more risk of exposure of vital organs to high concentrations of the drug.[21] While intranasal drug first cross nasal barriers (Mucus layer, Epithelial layer and Capillary endothelium) to get absorbed in systemic circulation, resulting in delayed action compared to intravenous route. Depending on differences in bioavailability, 0.5 μg/kg IV Dexmedetomidine is equivalent to 1μg/kg Intranasal Dexmedetomidine as stated by Singh V et al.[22]

In our study, on endotracheal intubation there is slight rise in heart rate but not more than the basal mean heart rate values in both groups (Basal 83.56±6.48 to 81.46±5.85 in DIN) (basal 82.82±3.99 to 80.20±4.01 in DIV). This indicates adequate attenuation of tachycardia response to laryngoscopy and intubation. In group DIV, comparatively lower values of HR are seen. Similar trends in HR were noted in study by Niyogi S et al. which concluded that there was equal and effective attenuation of stress response in terms of HR by both - intravenous (0.5 μg/kg) and intranasal (1μg/kg) Dexmedetomidine administered 40 min preinduction in patients undergoing elective lumbar spine surgery.[8] Statistically significant difference in mean HR was seen only during preinduction 30^{th} and 40^{th} minute after drug administration. While in IV group, heart rate was lower at time of intubation compared to IN group.

In another study by Lu et al., intranasal Dexmedetomidine (1 μg/kg 45–60 min preinduction) group recorded significant decrease in the HR at preinduction phase compared to placebo group.[23] There were no significant differences in groups for episodes of bradycardia

and hypotension. But, in the placebo patients, episodes of tachycardia and hypertension were significantly more after tracheal intubation(P=0.037) and extubation (P=0.022) compared to IN Dexmedetomidine group.

In our study, on laryngoscopy and intubation, rise in SBP, DBP and MAP was noted which was not more than basal values in either group.(Table 3) This hypertensive response was settled in postintubation phase with significant lower values in DIV group at postintubation 2,3,4,5 and 7 minutes. The changes in blood pressure were more gradual and stable in DIN (Study Group). Recent study by M.K Padmasree et al. showed similar trends for blood pressure.[24]

In a study by Jayaraman et al., intranasal dexmedetomidine (1 μg/kg based on ideal body weight) was compared with oral alprazolam (0.5 mg) administered 45 minutes prior to elective surgery in morbidly obese patients (BMI > 35). The study concluded that intranasal dexmedetomidine was inadequate for attenuating the hypertensive pressor response to laryngoscopy and intubation, as measured by mean arterial pressure (MAP). However, the tachycardia response was well controlled with this dose of dexmedetomidine (P = 0.022).[25]

In our study, three cases of DIV (CONTROL GROUP) had prolonged postoperative sedation (RSS 3) at 30 minutes but both groups had no statistically significant difference in terms of postoperative Ramsay sedation scores. In a study by Prasad et al. it was concluded that Dexmedetomidine IV infusion (0.5 μg/kg/h) provide adequate postoperative sedation for mechanical ventilation.[26] Intranasal Dexmedetomidine is now being used to provide effective method of sedation for CT scan in paediatric age groups.[27]

There was no episode of any side effects like bradycardia or hypotension seen in our study. In a study by Keniya VM et al. where IV Dexmedetomidine infusion [1μg/kg over 10 min before the induction followed by maintenance dose 0.2–0.7μg/kg] was compared with placebo normal saline.[15] Bradycardia (HR up to 42/min) was observed in two patients in Dexmedetomidine group intraoperatively which was treated by Inj. Atropine 0.6 mg IV. While in a study by Patel CR et al., dexmedetomidine was administered prior to induction and significantly reduced the stress response during intubation, resulting in lower increases in heart rate and blood pressure compared to fentanyl. However, bradycardia was noted as a potential concern, necessitating careful monitoring, especially in patients with pre-existing cardiac conditions.[28]

This study demonstrates that both intranasal and intravenous dexmedetomidine are equally effective in attenuating the hemodynamic stress response to laryngoscopy and intubation. However, intranasal dexmedetomidine has a slower and more gradual onset of action compared to the intravenous route. Future research should explore the use of an atomizer for drug administration or varying concentrations of intranasal dexmedetomidine to expedite its onset time.

In routine clinical practice, administering intranasal dexmedetomidine drops from available parenteral preparations at a dose of 1 μg/kg, given 40 minutes prior to laryngoscopy and intubation during general anesthesia, presents an effective, convenient, and patient-compliant alternative to intravenous dexmedetomidine. This approach also offers hemodynamic feasibility, making it a viable option for managing pressor responses.

5. Limitations of Study

This study did not assess the effects of intranasal and intravenous dexmedetomidine on analgesic and anesthetic requirements or opioid consumption during the intraoperative and postoperative periods. Additionally, we were unable to measure circulating catecholamine levels to compare the suppression effects of both routes due to the unavailability of specialized equipment. These factors may limit the comprehensive understanding of the drugs' overall impact on analgesia and stress response.

6. Conclusion

Intranasal Dexmedetomidine (1μg/kg) 40 minutes before induction and intravenous infusion (0.5 μg/kg) 10 minutes before induction, are equally effective for attenuation of hemodynamic response to laryngoscopy and intubation. Intranasal Dexmedetomidine can also be used as a safer alternative for adequate stable control of hemodynamic responses in terms of heart rate and blood pressure during laryngoscopy and endotracheal intubation.

7. Source of Funding

Nil.

8. Conflicts of Interest

There are no conflicts of interest.

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References

1. Kazama T, Ikeda K, Morita K. Reduction by fentanyl of the Cp50 values of propofol and hemodynamic responses to various noxious stimuli. *Anesthesiology*. 1997;87(2):213–27.
2. Reid LC, Brace DE. Irritation of the Respiratory Tract and Its Reflex Effect upon Heart. *Surg Gynecol Obstet*. 1940;70:157–62.
3. Kovac AL. Controlling the hemodynamic response to laryngoscopy and endotracheal intubation. *J Clin Anesth*. 1996;8(1):63–79.
4. Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: a novel sedative-analgesic agent. *Proc (Bayl Univ Med Cent)*. 2001;14(1):13–21.
5. Sebastian B, Talikoti AT, Krishnamurthy D. Attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation

with intravenous dexmedetomidine: A comparison between two doses. *Indian J Anaesth*. 2017;61(1):48–54.
6. Bharati S, Pal A, Biswas C, Biswas R. Incidence of cardiac arrest increases with the indiscriminate use of Dexmedetomidine: A case series and review of published case reports. *Acta Anaesthesiol Taiwan*. 2011;49(4):165–7.
7. Talon MD, Woodson LC, Sherwood ER, Aarsland A, Mcrae L, Benham T. Intranasal Dexmedetomidine premedication is comparable with midazolam in burn children undergoing reconstructive surgery. *J Burn Care Res*. 2009;30(4):599–605.
8. Niyogi S, Biswas A, Chakraborty I, Chakraborty S, Acharjee A. Attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation with dexmedetomidine: A comparison between intravenous and intranasal route. *Indian J Anaesth*. 2019;63(11):915–23.
9. Khan FA, Ullah H. Pharmacological agents for preventing morbidity associated with the haemodynamic response to tracheal intubation. *Cochrane Database Syst Rev*. 2013;7:CD004087.
10. Figueredo E, Garcia-Fuentes EM. Assessment of the efficacy of esmolol on the haemodynamic changes induced by laryngoscopy and tracheal intubation: a meta-analysis. *Acta Anaesthesiol Scand*. 2001;11(8):1011–22.
11. Joffe AM, Deem SA. Physiologic and pathophysiologic responses to intubation. In: Benumof J, Hagberg CA, editors. Benumof and Hagberg's Airway Management. Philadelphia: Elsevier Saunders; 2012. p. 184–95.
12. Karhuvaara S, Kallio A, Salonen M, Tuominen J, Scheinin M. Rapid reversal of alpha 2-adrenoceptor agonist effects by atipamezole in human volunteers. *Br J Clin Pharmacol*. 1991;31(2):160–5.
13. Tanskanen PE, Kyttä JV, Randell TT, Aantaa RE. Dexmedetomidine as an anaesthetic adjuvant in patients undergoing intracranial tumour surgery: A double-blind, randomized and placebocontrolled study. *Br J Anaesth*. 2006;97(5):658–65.
14. Keniya VM, Ladi S, Naphade R. Dexmedetomidine attenuates sympathoadrenal response to tracheal intubation and reduces perioperative anaesthetic requirement. *Indian J Anaesth*. 2011;55(4):352–7.
15. Sulaiman S, Karthekeyan RB, Vakamudi M, Sundar AS, Ravullapalli H, Gandham R. The effects of dexmedetomidine on attenuation of stress response to endotracheal intubation in patients undergoing elective off-pump coronary artery bypass grafting. *Ann Card Anaesth*. 2012;15(1):39–43.
16. Jarineshin H, Baghaei AA, Fekrat A, Kargar A, Abdi N, Navabipour S, et al. Comparison of two different doses of Dexmedetomidine in attenuating cardiovascular responses during laryngoscopy and endotracheal intubation: A double blind, randomized, clinical trial study. *J Med Life*. 2015;8(4):45–51.
17. Isik B, Mustafa A, Ozsoylar O, Akcabay M. The Effects of α2-Adrenergic Receptor Agonist Dexmedetomidine on Hemodynamic Response in Direct Laryngoscopy. *Open Otorhinolaryngol J*. 2007;1:5–11.
18. Sağıroğlu AE, Celik M, Orhon Z, Yüzer S, Sen B. Dıfferent doses of Dexmedetomidine on controlling hemodynamic responses to tracheal intubation. *Internet J Anesthesiol*. 2010;27(2):1–5.
19. Yuen VM, Hui TW, Irwin MG, Yao TJ, Wong GL, Yuen MK. Optimal timing for the administration of intranasal Dexmedetomidine for premedication in children. *Anaesthesia*. 2010;65(9):922–9.
20. Li A, Yuen VM, Goulay-Dufaÿ S, Sheng Y, Standing JF, Kwok PCL, et al. Pharmacokinetic and pharmacodynamic study of intranasal and intravenous Dexmedetomidine. *Br J Anaesth*. 2018;120(5):960–8.
21. Tripathi KD. Essentials of medical pharmacology. 8th ed. New Delhi, India: Jaypee Brothers Medical; 2018.
22. Singh V, Pahade A, Mowar A. Comparison of Intravenous Versus Nebulized Dexmedetomidine for Laryngoscopy and Intubation-Induced Sympathoadrenal Stress Response Attenuation. *Anesth Pain Med*. 2022;12(5):e132607.
23. Lu C, Zhang L, Zhang Y, Ying Y, Li L, Xu L, et al. Intranasal Dexmedetomidine as a Sedative Premedication for Patients Undergoing Suspension Laryngoscopy: A Randomized Double-Blind Study. *PLoS One*. 2016;11(5):e0154192.
24. Padmasree M, Nelamangala K. A Comparative Study Between Intranasal and Intravenous Dexmedetomidine and Hemodynamic Responses During Endotracheal Intubation. *Cureus*. 2023;15(2):e35196.
25. Jayaraman L, Sinha A, Punhani D. A comparative study to evaluate the effect of intranasal Dexmedetomidine versus oral alprazolam as a premedication agent in morbidly obese patients undergoing bariatric surgery. *J Anaesthesiol Clin Pharmacol*. 2013;29(2):179–82.
26. Prasad SR, Simha PP, Jagadeesh AM. Comparative study between Dexmedetomidine and fentanyl for sedation during mechanical ventilation in post-operative paediatric cardiac surgical patients. *Indian J Anaesth*. 2012;56(6):547–52.
27. Mason KP, Zgleszewski SE, Dearden JL, Dumont RS, Pirich MA, Stark CD, et al. Dexmedetomidine for pediatric sedation for computed tomography imaging studies. *Anesth Analg*. 2006;103(1):57–62.
28. Patel CR, Engineer SR, Shah BJ, Madhu S. Effect of intravenous infusion of Dexmedetomidine on perioperative hemodynamic changes and postoperative recovery: A study with entropy analysis. *Indian J Anaesth*. 2012;56(6):542–6.

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