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Original Article

Anaesthesia Section

Comparison of Intranasal Dexmedetomidine with Intravenous Dexmedetomidine as Premedication in Patients undergoing Laparoscopic Surgeries under General Anaesthesia: A Randomised Controlled Trial

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ABSTRACT

Introduction: The sympathetic stress response due to pneumoperitoneum during laparoscopic surgeries necessitates a balanced anaesthesia technique. Dexmedetomidine (DEX) has emerged as a promising option. While intravenous (i.v.) DEX is well established in attenuating the haemodynamic stress response to pneumoperitoneum, the Intranasal (IN) route remains underexplored for this purpose.

Aim: To compare the efficacy and safety of IN and i.v. DEX in attenuating the haemodynamic stress response to pneumoperitoneum.

Materials and Methods: In this randomised triple-blind controlled trial which was conducted at Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun, Uttarakhand, India. A total of 75 adults classified as American Society of Anaesthesiologists (ASA) physical status I or II, scheduled for elective laparoscopic surgery, were randomly allocated to one of three groups (25 in each group): control, IN DEX (IN group), and i.v. DEX (i.v. group). DEX was administered at a dose of 1 µg/kg via the IN or i.v. route before induction. Heart Rate (HR) and Mean Arterial Pressure (MAP) were monitored until 10 minutes postextubation at appropriate time intervals, along with preoperative sedation scores and any side-effects. All statistical calculations were performed using Statistical Package for the Social Sciences (SPSS) 21.0 version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

Results: Patients were comparable with respect to age (p-value=0.769), gender (p-value=0.321), and weight (p-value=0.672). HR and MAP were significantly lower in the IN and i.v. groups compared to the control group during pneumoperitoneum, but were comparable between the IN and i.v. groups. Both of these groups had better sedation scores compared to the control group. None of the groups experienced any significant side-effects.

Conclusion: Both IN and i.v. DEX have similar efficacy and safety in alleviating the haemodynamic stress response to pneumoperitoneum. Side-effects such as bradycardia, hypotension, nausea, vomiting and shivering were comparable among the three groups. Both IN and i.v. DEX provided comparably satisfactory preoperative sedation, which was significantly better than that of the control group.

Keywords: Alpha 2 agonists, Balanced anaesthesia, Laparoscopy, Pneumoperitoneum

INTRODUCTION

Laparoscopic procedures are well established in surgical practice. They are associated with less tissue injury, pain, early discharge and ambulation, which warrants balanced anaesthesia [1,2]. Pneumoperitoneum during laparoscopic surgeries poses significant challenges to anaesthesiologists by inducing a neuroendocrine sympathetic response, manifesting as tachycardia, hypertension and increased levels of cortisol, catecholamines and blood glucose [3,4]. Many pharmacological agents and anaesthetic techniques are known to attenuate the stress response, such as deepening the plane of anaesthesia, administration of opioids, beta-blockers, calcium channel blockers, magnesium sulphate, lignocaine and alpha-2 agonists [1,5,6].

DEX is a potent, short-acting and highly selective α-2 agonist. It has anxiolytic, sedative, analgesic and sympatholytic effects. The i.v. and IN routes of DEX administration have been reported to attenuate the haemodynamic stress response to laryngoscopy and intubation [5,7,8]. Intravenous DEX has also been shown to effectively reduce the haemodynamic stress response to pneumoperitoneum [9,10]. However, i.v. DEX is associated with significant bradycardia and hypotension; therefore, it needs to be administered via infusion with meticulous monitoring and titration [5]. There is a scarcity of literature on IN DEX for attenuating the haemodynamic stress response to pneumoperitoneum. Nebulisation causes drug loss, is time-consuming, cumbersome and may not be acceptable to many patients. IN administration by the drop method overcomes some of these disadvantages, as it is easy to administer, convenient, more acceptable and does not lead to drug loss. However, there is a paucity of studies comparing the efficacy and safety of i.v. DEX and IN DEX by the drop method for attenuating the haemodynamic stress response to pneumoperitoneum [9]. Therefore, this study was designed to compare the efficacy and safety of i.v. DEX and IN DEX by the drop method in attenuating the haemodynamic stress response to pneumoperitoneum.

MATERIALS AND METHODS

This parallel-group randomised triple-blind controlled trial was conducted at Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun, Uttarakhand, India. The study duration was from April to October 2021, following approval from the Institutional Ethics Committee (IEC) (SGRR/IEC/04/20) and registration with the Clinical Trials Registry-India (CTRI/2021/03/032009). Written informed consent was obtained from all participants.

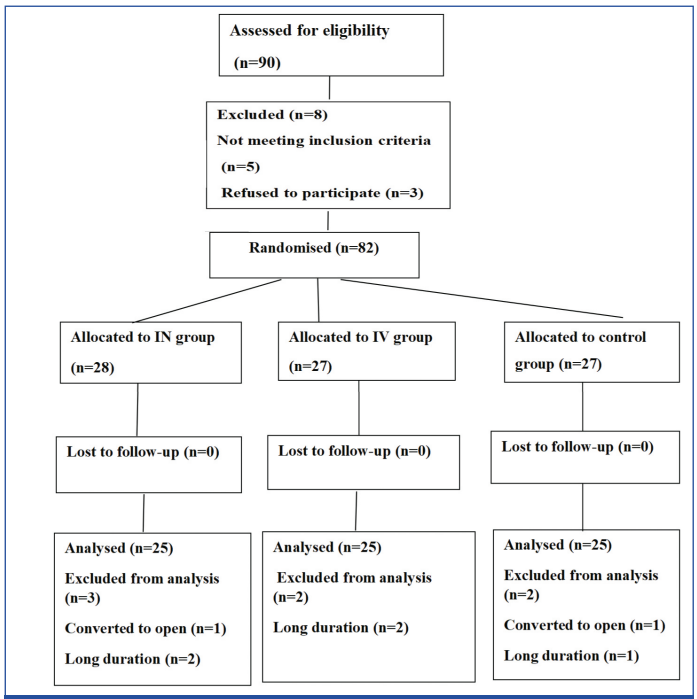
Inclusion criteria: Seventy-five patients, aged 18-60 years, of either gender, with ASA physical status I or II for elective laparoscopic surgery, were included in the study.

Exclusion criteria: Pregnant or lactating females, individuals with an anticipated difficult airway, ejection fraction < 40%, BMI > 30 kg/m², valvular dysfunction, insulin-dependent diabetes, renal or hepatic dysfunction, respiratory diseases, a history of Coronary Artery Bypass Grafting (CABG), those taking clonidine or α-methyldopa, and patients for whom the intubation time exceeded 20 seconds and/or the duration of surgery was more than 90 minutes were excluded from the study.

Sample size estimation: The sample size was calculated based on the difference in MAP between the IN and i.v. groups in the postintubation period at three minutes (MAP being 86.40±7.53 and 86.89±7.69 in the i.v. and IN groups, respectively) in the study by Niyogi S et al., [7]. The sample size was estimated at a 5% level of significance and with 80% power to conclude the equivalence design. The sample size was determined to be 17 in each group. Keeping a 10% dropout rate in mind, a sample size of 20 was taken in each group. When comparing these two groups with the control, using Basunia SR and Mukherjee P, a sample size of 60 patients (20 in each group) provided 80% power to conclude clinical superiority, applying a one-sided 5% significance level and a clinically acceptable margin of nine [11]. Assuming a dropout rate of 10% resulted in a required sample size of 75 patients (25 in each group).

Study Procedure

A total of 90 patients were screened for participation in the study. Five participants did not meet the inclusion criteria, and three refused to participate. Eighty-two patients were randomised into three groups. Of the 82 patients, seven were excluded for the reasons outlined in the CONSORT flow diagram [Table/Fig-1]. This resulted in 75 patients (n=25 in each group) being included in the analysis.



[Table/Fig-1]: Consort flow diagram.

The patients were randomly allocated using a computer-generated random number list to one of three equal groups: Control group: 1 mL Normal Saline (NS) intranasally (IN) 40 minutes prior to induction and 100 mL NS intravenously (i.v.) 20 minutes prior to induction; IN group: IN DEX 1 μg/kg diluted to 1 mL in NS 40 minutes prior to induction and 100 mL NS i.v. 20 minutes prior to induction; i.v. group: IN NS 1 mL 40 minutes prior to induction and i.v. DEX 1 μg/kg diluted in 100 mL NS 20 minutes prior to induction [4,7]. The IN drug was prepared in identical 1 mL syringes containing either 1 μg/kg DEX diluted to 1 mL in NS (IN Group) or only NS (i.v. and Control Groups) and labelled as the IN drug. The i.v. drug was prepared in identical 100 mL NS bottles with (i.v. Group) or without 1 μg/kg DEX (IN and Control Groups) and labelled as the i.v. drug. The IN drug was administered in both nostrils in the recumbent position in the preoperative room, with vital signs monitored including HR, Pulse Oximetry (SpO_2), and MAP. This was followed 40 minutes later by the administration of the i.v. drug.

The allocation was concealed using serially numbered sealed opaque envelopes, which were opened sequentially after the trial participants reached the preoperative room and just before the preparation of the study drug solution. Once opened, the allocation was irrevocable. The study drugs were prepared by an anaesthesiologist not further involved in the study. The anaesthesiologist administering the drugs and monitoring the patients, as well as the patients themselves and the statistician, were blinded to the group allocation. No other premedication was given to the patients. Induction was performed using i.v. fentanyl 2 μg/kg and i.v. propofol 1.5-2 mg/kg. Muscle relaxation was achieved with i.v. vecuronium 0.1 mg/kg. The trachea was intubated with an appropriately sized endotracheal tube. Ventilation was adjusted to maintain End-Tidal CO_2 ($ETCO_2$) between 35-40 mmHg. HR, MAP and SpO_2 were recorded at baseline, at 5-minute intervals preoperatively until 60 minutes (t5-t55 and t propofol), and at 0, 1, 5, and 10 minutes after induction, followed by every 15 minutes until extubation (Ti1-Ti90), and at one, five and ten minutes post extubation. Ti10 to Ti90 marked the time of pneumoperitoneum. Intra-abdominal pressure was maintained between 12-15 mmHg. Any episodes of bradycardia (HR <50), hypertension (increase in MAP by 30% of preoperative value for 1 minute), hypotension (decrease in MAP by 30% of preoperative value for 1 minute), and tachycardia (HR > 100) were recorded. Episodes of nausea, vomiting and shivering were noted in the postoperative period. Bradycardia was managed with i.v. atropine 0.6 mg. Hypotension was treated with i.v. ephedrine 5 mg boluses, while hypertension was managed using nitroglycerine infusion. Neuromuscular blockade was reversed with neostigmine and glycopyrrolate.

Sedation was assessed using the Modified Observer's Assessment of Alertness/Sedation (OAA/S) scale: 6=appears alert and awake, responds readily to name spoken in a normal tone; 5=appears asleep but responds readily to name spoken in a normal tone; 4=lethargic but responds to name spoken in a normal tone; 3=responds only after name is called loudly or repeatedly; 2=responds only to shaking; 1= does not respond to shaking; and 0=does not respond to noxious stimulus [12]. A sedation score of five was considered satisfactory. The primary outcome was to compare the haemodynamic stress response to pneumoperitoneum at different time intervals. Secondary outcomes included sedation score, incidences of nausea, vomiting, shivering and extubation response.

STATISTICAL ANALYSIS

Data were described in terms of range, mean ± standard deviation (SD), frequencies (number of cases), and relative frequencies (percentages) as appropriate. The Kolmogorov-Smirnov test was used to assess the normal distribution of the data. Comparison of quantitative variables between the study groups was performed using Analysis of Variance (ANOVA) and the Kruskal-Wallis test, along with post-hoc Tukey's test for independent samples for parametric and non parametric data, respectively. For comparing categorical data, the Chi-square (χ^2)test was utilised. A probability value (p-value) of less than 0.05 was considered statistically significant. All statistical calculations were conducted using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA) statistical programme for Microsoft Windows.

RESULTS

The groups were comparable concerning demographic variables and the type of surgery [Table/Fig-2]. Baseline HR and MAP were comparable among the three groups. HR was statistically lower from time t45 until the completion of surgery (Ti90) in the i.v. and IN groups compared with the control group; however, HR

was comparable between the i.v. and IN groups [Table/Fig-3]. HR was also comparable among the IN, i.v., and control groups postextubation [Table/Fig-3].

Variable	Control	IN group	i.v. group	p-value
Age, years (Mean±SD)	32.44±8.00	30.64±9.59	32±9.76	0.769
Sex (F:M)	10:15	9:16	14:11	0.321
Weight, Kg (Mean±SD)	54.04±7.88	55.92±6.04	54.88±8.25	0.672
Surgery				
Lap cholecystectomy	23	20	20	0.103
Lap appendicectomy	0	2	0	
Lap herniorrhaphy	2	3	2	
Diagnostic laparoscopy	0	0	3	

[Table/Fig-2]: Demographic characteristics and type of surgery.
Lap= Laparoscopic; F:M= Female:Male ratio

Heart rate	IN group Mean±SD	i.v. group Mean±SD	Control Mean±SD	IN vs i.v. p-value	IN vs control p-value	i.v. vs control p-value
HR basal	91.92±20.04	89.56±16.28	84.24±14.81	0.629	0.118	0.118
HR t5	89.16±19.53	88.08±15.21	83.88±11.65	0.810	0.241	0.350
HR t10	83.92±19.72	86.44±15.05	82.24±9.55	0.563	0.700	0.337
HR t15	81.36±19.73	85.20±13.92	83.04±9.71	0.369	0.694	0.613
HR t20	79.88±17.69	84.08±12.17	80.56±10.30	0.284	0.862	0.368
HR t25	80.36±17.53	86.36±15.05	78.40±11.69	0.160	0.644	0.064
HR t30	77.20±19.27	85.00±14.83	78.96±10.66	0.076	0.686	0.168
HR t35	77.08±15.59	85.92±14.92	79.86±10.75	0.028	0.492	0.125
HR t40	81.76±19.09	84.88±15.89	82.52±7.63	0.465	0.858	0.580
HR t45	79.88±19.87	77.12±14.90	86.08±4.65	0.506	0.049	0.033
HR t50	71.32±18.01	69.60±16.15	85.08±5.42	0.672	0.001	0.001
HR t55	69.24±23.32	67.44±15.04	80.92±6.31	0.700	0.014	0.005
HR tpropofol	66.36±20.34	66.52±13.04	83.36±6.58	0.969	0.001	0.001
HR Ti 1	81.16±19.28	80.76±13.94	96.56±7.39	0.922	0.001	0.001
HR Ti5	75.68±15.75	72.20±11.63	106.40±8.72	0.32	0.003	0.001
HR Ti10	74.48±8.23	70.32±12.21	91.80±8.02	0.133	0.009	0.001
HR Ti15	74.80±7.82	73.20±16.00	92.40±6.60	0.607	0.001	0.001
HR Ti30	78.92±14.10	75.12±10.52	100.3±9.25	0.246	0.001	0.001
HR Ti45	79.68±9.21	76.44±7.10	98.92±6.54	0.141	0.001	0.001
HR Ti60	74.48±9.76	76.84±6.26	82.48±4.93	0.255	0.001	0.008
HR Ti75	76.52±6.77	74.84±8.50	82.04±8.87	0.466	0.019	0.019
HR Ti90	70.56±9.43	84.80±7.12	100.3±9.25	0.246	0.001	0.001
HR ext1	101.60±20.82	92.92±13.41	112.80±8.83	0.114	0.108	1.000
HR ext5	89.40±20.06	86.04±14.49	100.76±7.60	0.707	0.945	0.507
HR ext10	81.84±19.89	81.20±15.49	96.32±4.15	0.987	0.387	0.475

[Table/Fig-3]: Comparison of heart rate among the three groups.

MAP was statistically lower from time t45 until 10 minutes post extubation in the i.v. and IN groups compared to the control group, but it was comparable between the i.v. and IN groups [Table/Fig-4]. The incidence of nausea and shivering was comparable among the three groups. None of the patients experienced bradycardia, hypotension, or vomiting [Table/Fig-5].

A sedation score of 5 was considered satisfactory. The median Interquartile Range (IQR) sedation score at t60 was comparable between the IN {5 (5,5)} and i.v. {5 (5,5)} groups (p-value=0.187). The median (IQR) sedation score at t60 was statistically lower in both the i.v. {5 (5,5)} and IN groups {5 (5,5)} compared to the control group {6 (6,6)} (p-value=0.001) [Table/Fig-6a].

Upon arrival in the Operating Theatre (OT) (t60), 25 (100%), 23 (92%), and none (0%) of the patients in the IN, i.v., and control groups, respectively, had a satisfactory sed ation score [Table/Fig-6b].

Map	IN group Mean±SD	i.v. group Mean±SD	Control Mean±SD	IN vs i.v. p-value	IN vs control p-value	i.v. vs control p-value
MAP basal	101.45±7.94	98.92±6.03	98.93±4.83	0.166	0.168	0.994
MAP t5	95.35±6.16	96.29±4.52	98.88±7.04	0.582	0.043	0.135
MAP t10	92.96±6.95	94.49±6.99	94.4±2.86	0.363	0.384	0.968
MAP t15	97.28±7.64	96.40±6.38	98.39±8.67	0.684	0.609	0.360
MAP t20	95.61±7.07	95.27±5.14	97.05±6.37	0.845	0.417	0.315
MAP t25	95.28±8.12	95.64±5.88	94.83±7.12	0.858	0.822	0.687
MAP t30	95.44±7.79	94.12±5.37	96.85±8.50	0.527	0.498	0.192
MAP t35	95.92±7.29	94.76±5.95	96.09±8.10	0.569	0.932	0.513
MAP t40	96.79±7.25	94.71±3.52	98.27±3.71	0.155	0.310	0.056
MAP t45	89.55±8.71	90.36±5.47	98.63±2.88	0.642	0.001	0.001
MAP t50	91.07±6.74	91.27±9.50	99.11±5.42	0.924	0.001	0.001
MAP t55	85.24±6.28	86.49±11.05	99.21±4.90	0.575	0.001	0.001
MAP t propofol	85.13±13.75	83.81±12.70	99.07±5.65	0.680	0.001	0.001
MAP Ti1	96.44±15.33	92.20±15.03	107.60±4.94	0.243	0.003	0.001
MAPTi2	89.97±7.45	90.24±14.27	115.17±7.66	0.927	0.001	0.001
MAP Ti5	87.75±11.08	80.63±12.26	112.01±8.02	0.051	0.001	0.001
MAP Ti10	81.87±9.13	79.88±9.52	98.65±8.84	0.446	0.001	<0.001
MAP Ti15	90.12±11.9	88.03±11.05	122.25±6.88	0.471	0.001	<0.001
MAP Ti30	97.61±8.37	99.84±17.67	111.01±12.00	0.554	0.001	0.004
MAP Ti45	94.76±9.10	93.96±6.64	108.9513.78	0.784	0.001	0.001
MAP Ti60	96.11±7.63	94.77±6.17	108.28±6.05	0.481	0.001	0.001
MAP Ti75	95.63±7.26	92.61±5.11	107.09±6.43	0.097	0.001	0.001
MAP Ti90	90.59±7.16	91.67±5.83	108.95±13.78	0.765	0.001	0.001
MAP ext1	106.31±10.60	107.07±11.95	116.1±11.33	0.813	0.003	0.006
MAP ext5	95.7±5.51	98.93±4.49	107.5±8.90	0.333	0.001	0.001
MAP ext10	96.47±7.15	93.72±4.62	103.9±5.91	0.109	0.001	0.001

[Table/Fig-4]: Comparison of Mean Arterial pressure (MAP) among the three groups.

Side-effect	In group	i.v. group	Control	p-value
Nausea	0	2 (8%)	0	0.128
Shivering	4 (16%)	0	1(4%)	0.062

[Table/Fig-5]: Side-effects.

Saturation (SpO_2) was comparable at all time intervals among the three groups, remaining above 98% at various time points [Table/Fig-7].

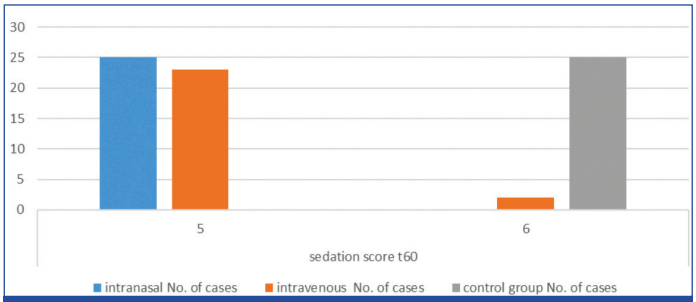
DISCUSSION

DEX is a centrally acting alpha-2 agonist with sympatholytic, sedative and anxiolytic properties that do not produce respiratory depression. The sympatholytic activity of DEX is explained by the central activation of alpha-2 adrenoreceptors, which leads to a reduction in sympathetic tone. Its peripheral action results in a decrease in norepinephrine release from nerve endings to blood vessels, consequently causing a reduction in vascular tone [7].

The present study concluded that DEX, whether administered via the i.v. or IN route, is equally effective in attenuating the haemodynamic stress response to pneumoperitoneum, with no increase in the incidence of perioperative side-effects (nausea, vomiting, shivering, hypotension and bradycardia). Both IN and i.v. DEX significantly reduced the haemodynamic stress response to laryngoscopy, endotracheal intubation, pneumoperitoneum and surgery, with HR and MAP being statistically lower compared to the control group starting from 45 minutes and five minutes after the administration of IN and i.v. DEX, respectively, and extending until the completion of surgery. HR was comparable among the IN, i.v., and control groups postextubation. MAP was significantly lower in the IN and i.v. groups compared to the control group

Sedation score	IN group		i.v. group		Control		IN vs i.v.	IN vs control	i.v. vs control
	Median	IQR	Median	IQR	Median	IQR	p-value	p-value	p-value
sed t0	6.00	6-6	6.00	6-6	6.00	6-6	1.000	1.000	1.000
sed t15	6.00	6-6	6.00	6-6	6.00	6-6	1.000	1.000	1.000
sed t30	6.00	5.5-6	6.00	6-6	6.00	6-6	1.000	1.000	1.000
sed t45	6.00	6-6	6.00	6-6	6.00	6-6	1.000	1.000	1.000
sed t60	5.00	5-5	5.00	5-5	6.00	6-6	0.187	0.001	0.001

[Table/Fig-6a]: Comparison of sedation score preoperatively.



[Table/Fig-6b]: Sedation score on arrival in operation room.

SpO_2	IN group	i.v. group	Control	IN vs i.v.	IN vs control	i.v. vs control
	Mean±SD	Mean±SD	Mean±SD	p-value	p-value	p-value
SpO_2 t0	99.00±0.00	99.00±0.76	99.08±0.70	1.000	0.885	0.885
SpO_2 t5	98.96±0.84	99.00±0.76	99.08±0.70	0.982	0.847	0.929
SpO_2 t10	98.96±0.84	99.00±0.76	99.08±0.70	0.982	0.847	0.929
SpO_2 t15	98.96±0.84	99.08±0.81	99.24±0.78	0.860	0.445	0.766
SpO_2 t20	98.96±0.84	99.28±0.89	99.44±0.82	0.384	0.121	0.785
SpO_2 t25	99.28±0.98	99.64±0.49	99.64±0.49	0.165	0.165	1.000
SpO_2 t30	99.24±0.80	99.08±0.81	98.92±0.81	0.452	0.135	0.452
SpO_2 t35	99.00±0.82	99.00±0.76	98.92±0.81	1.000	0.933	0.933
SpO_2 t40	99.00±0.82	98.76±0.66	98.60±0.81	0.481	0.137	0.721
SpO_2 t45	98.68±0.56	98.72±0.68	98.96±0.54	0.813	0.100	0.158
SpO_2 t50	99.04±0.20	99.04±0.45	98.96±0.54	1.000	0.782	0.782
SpO_2 t55	99.08±0.28	99.12±0.33	99.12±0.33	0.895	0.895	1.000
SpO_2 t propofol	99.08±0.28	99.12±0.33	99.12±0.33	0.895	0.895	1.000
SpO_2 Ti1	99.08±0.28	98.92±0.70	98.76±0.66	0.595	0.132	0.595
SpO_2 Ti2	98.80±0.65	98.84±075	98.60±0.71	0.978	0.574	0.451
SpO_2 Ti5	98.76±0.60	98.64±0.64	98.48±0.51	0.749	0.214	0.599
SpO_2 Ti10	98.80±0.65	98.92±0.70	98.92±0.57	0.787	0.787	1.000
SpO_2 Ti15	98.76±0.66	99.12±0.67	99.20±0.71	0.154	0.064	0.909
SpO_2 Ti30	99.32±0.48	99.04±0.84	99.20±0.71	0.330	0.813	0.693
SpO_2 Ti45	98.76±0.78	98.60±0.71	98.60±0.71	0.442	0.442	1.000
SpO_2 Ti60	99.20±0.76	99.13±0.61	99.16±0.37	0.666	0.816	0.840
SpO_2 Ti75	99.04±0.45	99.21±0.43	99.33±0.52	0.489	0.339	0.853
SpO_2 Ti90	99.12±0.33	99.00±0.00	99.16±0.37	0.813	0.895	0.158
SpO_2 ext1	98.68±0.56	98.72±0.68	98.96±0.54	0.813	0.100	0.158
SpO_2 ext5	98.96±0.84	99.00±0.76	99.08±0.70	0.982	0.847	0.929
SpO_2 ext10	98.96±0.84	99.08±0.81	99.24±0.78	0.860	0.445	0.766

[Table/Fig-7]: Comparison of SpO_2 amongst the three groups.

postextubation. This can be explained by the pharmacodynamics and pharmacokinetics of DEX. The route, timing and dose of drug administration influence effects such as sedation, bradycardia and hypotension. The onset of action of i.v. DEX is five minutes, lasting approximately two hours after a single dose [9]. In contrast, IN DEX begins to take effect between 10 and 33 minutes, with a duration of action extending up to 55 to 100 minutes due to its slow release into the systemic circulation from the mucosa [9,13-15]. The bioavailability of i.v. and IN DEX is 100% and 40.6-82%, respectively [16,17].

Both IN and i.v. DEX have been widely studied as premedication for anxiolysis, sedation and for attenuating the haemodynamic stress response to laryngoscopy and intubation [5,7,8,11,18-24]. Present study results are consistent with those of Padmasree MK and Nelamangala K; and Niyogi S et al., who also reported that both i.v. DEX and IN DEX are equally effective in attenuating the pressor response to laryngoscopy and endotracheal intubation. However, they did not specify the types of surgeries included or the effect on the haemodynamic stress response to pneumoperitoneum and the adverse effects of the study drugs [5,7]. Present study found that both i.v. DEX and IN DEX are equally effective in mitigating the stress response to pneumoperitoneum at a dose of 1 µg/kg. Authors noted that there was no instance of bradycardia, hypotension, or vomiting. Nausea and shivering were not significant among the three groups. Authors observed that the IN and i.v. DEX groups had better sedation scores preoperatively.

Similarly, Shankar K et al., compared the effects of i.v. and nebulised DEX at a dose of 1 µg/kg in ASA I and II adult patients undergoing laparoscopic surgeries. They found nebulised DEX to be a useful alternative, as it had a dose-sparing effect on opioid and propofol consumption while demonstrating similar efficacy in attenuating the haemodynamic stress response to pneumoperitoneum compared to i.v. DEX [9]. However, they did not comment on side-effects (bradycardia, hypotension, nausea, vomiting) or sedation scores.

A number of studies have compared the efficacy of i.v. DEX with other intravenously administered drugs in attenuating the stress response to pneumoperitoneum. Hazra R et al., compared i.v. clonidine at a dose of 1 µg/kg and i.v. DEX at a dose of 1 µg/kg in patients undergoing laparoscopic cholecystectomy and found that i.v. DEX was more effective than i.v. clonidine in blunting the haemodynamic response to pneumoperitoneum, although it was associated with a greater chance of developing hypotension and bradycardia [10]. Jaiswal S et al., reported that i.v. DEX at a dose of 1 µg/kg was better than i.v. magnesium sulphate at a dose of 50 mg/kg in attenuating the stress response to laparoscopy [4]. Gupta K et al., found that i.v. DEX at 1 µg/kg was better than i.v. fentanyl at a dose of 2 µg/kg in modulating the neuroendocrine stress response to laparoscopy [25]. Bhattacharjee DP et al., reported that an i.v. DEX bolus of 1 µg/kg followed by a continuous infusion of 0.2 µg/kg/hr was as effective as an i.v. esmolol bolus of 500 µg/kg followed by a continuous infusion of 100 µg/kg/min in attenuating the haemodynamic stress response to pneumoperitoneum during laparoscopic surgeries [6].

Although the studies mentioned above have found i.v. DEX to be either superior or equally effective compared to other intravenously administered drugs, none have compared i.v. DEX with IN DEX.

To address this gap in the existing literature, present study compared the efficacy and safety of IN and i.v. DEX on the stress response to pneumoperitoneum as the primary aim and found both methods to be equally effective and safe. The doses for both IN and i.v. DEX were selected based on previous studies [6,9,26-28]. Kochar A et al., reported that, while comparing IN DEX at doses of 2 µg/kg and 1 µg/kg for attenuation of the haemodynamic stress response to laryngoscopy and intubation, the higher dose produced significant bradycardia without any difference in efficacy [27]. Therefore, present study chose the lower dose of 1 µg/kg for IN DEX. Ankita et al.,

compared IN and i.v. DEX at a dose of 1 µg/kg for the attenuation of the haemodynamic response to laryngoscopy and intubation in lumbar spine surgery and found the two routes to be comparable [28]. Present study administered the same doses of IN and i.v. DEX and found the two groups to be comparable, but superior to the control group in attenuating the haemodynamic stress response to pneumoperitoneum.

Present study found that IN and i.v. DEX were equally effective in producing satisfactory sedation, defined as a sedation score of 5 (indicating that the patient appears asleep but responds readily to their name spoken in a normal tone), which was observed in 100% of patients in the IN group and 92% in the i.v. group. The sedation scores were significantly better in the IN and i.v. groups compared to the control group, where a sedation score of 6 (indicating that the patient is awake) was observed. IN DEX has previously been reported to be more effective in achieving satisfactory sedation and attenuating the laryngoscopic response compared to IN clonidine at a dose of 3 µg/kg [26]. Present study found IN DEX to be as effective as i.v. DEX at a dose of 1 µg/kg in providing satisfactory sedation and in blunting the stress response to laryngoscopy and pneumoperitoneum. In contrast, Niyogi S et al., and Ankita et al., reported the sedation score to be significantly better in the i.v. DEX group [7,28].

Laparoscopic surgeries pose many challenges, one of which is the sympathetic response to pneumoperitoneum, leading to increased HR, MAP and a decrease in cardiac output. Modifying the anaesthetic technique, deepening the plane of anaesthesia, maintaining eucapnia and using low intra-abdominal pressure during pneumoperitoneum, as well as gasless laparoscopic surgeries, are some strategies to reduce the incidence of hypertension and tachycardia during pneumoperitoneum [3]. Many pharmacological agents are also used to attenuate the pressor response, including esmolol, labetalol, propofol, clonidine and DEX. However, the efficacy of DEX via the intranasal route in attenuating the haemodynamic stress response to pneumoperitoneum is under-researched.

A strength of this study was that, to the best of the authors' knowledge, it was the first Randomised Controlled Trial (RCT) comparing a single dose of IN and i.v. DEX at 1 µg/kg for preoperative sedation, as well as for the attenuation of the stress response to laryngoscopy, endotracheal intubation, pneumoperitoneum and extubation. As the intranasal route is more acceptable, easier to administer, and associated with fewer side-effects, and given that there is currently no literature comparing IN and i.v. DEX for modulating the sympathetic stress response to laparoscopy, authors chose to undertake this comparison.

Limitation(s)

This study had some limitations. Plasma drug concentrations were not measured, so data on drug bioavailability could not be produced. Due to resource limitations, serum biochemical markers of the stress response were not measured. However, only adult ASA I and II patients undergoing laparoscopic surgeries were included in the study. The IN route may prove to be more advantageous for neurologically challenged, uncooperative adult patients with difficult i.v. access, as it offers a non invasive and more acceptable means of premedication. More studies will be required to assess the safety and efficacy of DEX in other patient groups and types of surgeries where the sympathetic response is more detrimental, such as neuro- and cardiac surgeries. Author limited present study to short laparoscopic surgeries; therefore, further research is needed to evaluate the effects of a single dose of DEX in prolonged laparoscopic procedures.

CONCLUSION(S)

Present study conclude that both IN and i.v. DEX at a dose of 1 µg/kg are equally effective in attenuating the haemodynamic stress response to laryngoscopy, endotracheal intubation and pneumoperitoneum, with no increase in the incidence of perioperative side-effects compared to the control group. Both IN and i.v. DEX provided comparable satisfactory preoperative sedation, which was significantly better than that of the control group. Thus, IN DEX can be considered an effective and safe alternative to i.v. DEX for attenuating the haemodynamic stress response in laparoscopic surgeries.

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