Original Research Article

Indian Journal of Anesthesia and Analgesia
2019; 6(5) (Part - II): 1715-1721
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6519.32

Comparison of Hemodynamic Response Among IV Butorphanol and Dexmedetomidine as a Premedication in Laparoscopic Cholecystectomy

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Abstract

Background: In 1940, Reid and Brace first described the hemodynamic response to laryngoscopy and intubation due to noxious stimuli of the upper airway. To minimize this various drugs have been used. Newer opioids like butorphanol, and dexmedetomidine have significant role to suppress hemodynamic changes during laryngoscopy, intubation and pneumoperitoneum. So we have compared the intravenous butorphanol and dexmedetomidine to reduce stress response during laryngoscopy in laparoscopic cholecystectomy. *Materials and Methods:* The study was carried on 100 patients of both sex with comparable characteristics and of ASA Grade I and II physical status. Patients were allocated into two groups: Group B inj. Butorphanol 30 µg/kg was given 5 minutes before induction and Group D inj. Dexmedetomidine 1 µg/kg diluted in 10 ml normal saline, was given in 10 minutes by infusion pump. *Results:* The rise in heart rate and blood pressure was less in Dexmedetomidine group as compared to Butorphanol. *Conclusions:* Dexmedetomidine is better in attenuating the stress response during laryngoscopy, intubation and pneumoperitoneum as compared to butorphanol.

Keywords: Dexmedetomidine; Butorphanol; Laparoscopic Cholecystectomy; hemodynamic response; pneumoperitoneum; laryngoscopy.

How to cite this article:

Ahmad Waqar Khan, Dheeraj Saxena, Juhi Saran *et al.* Comparison of Hemodynamic Response Among IV Butorphanol and Dexmedetomidine as a Premedication in Laparoscopic Cholecystectomy. Indian J Anesth Analg. 2019;6(5 P-II):1715-1721.

Introduction

In 1940, Reid and Brace first described the hemodynamic response to laryngoscopy and intubation due to noxious stimuli of the upper airway.[1] The rise in Blood pressure and heart rate is usually transient occurring 30 seconds after intubation and lasting for less than 10 minutes.[2] To minimize these adverse effects various drugs have been used as premedicant. Benzodiazepines as anxiolytic, anticholinergic to counteract vagal reflexes and opioids for analgesia are in common practice. The basic physiological or hemodynamic changes occurring during pneumoperitoneum in laparoscopy due to systemic absorption of carbon dioxide (CO_2) and reverse Trendelenburg position. To avoid these hemodynamic changes, different techniques and drugs like opioids, sedatives, beta blockers, iv lignocaine and others have been used with their merits and demerits.[3] Newer opioids like butorphanol, and other drugs like dexmedetomidine have significant role to suppress hemodynamic changes during laryngoscopy and pneumoperitoneum. Butorphanol is a lipid-soluble

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Received on 15.07.2019, **Accepted on** 16.08.2019

narcotic agent with strong κ-receptor agonist and weak μ-receptor agonist/antagonist activity. The above-mentioned narcotic analgesics have been used frequently for postoperative analgesia.[4] The analgesic effect of Butorphanol is influenced by the route of administration. Onset of analgesia is within a few minutes for intravenous administration and within 15 minutes for intramuscular injection. Peak analgesic activity occurs within 30 to 60 minutes following intravenous administration. Dexmedetomidine Is a highly selective α_2 adrenergic receptor agonist with sedative, analgesic, and antianxiety activity.[5,6] Introduced in clinical practice in United States in 1999 and approved by FDA. α_2 adrenergic agonists are used for sedation and premedication prior to general anesthesia in several patients. Racemic medetomidine has a binding ratio of 1620:1 (α_2:α_1) 10 and its d-enantiomer, dexmedetomidine is even more selective. Advantages of α_2-agonists include potent, predictable sedation[7], analgesia, reduced anesthetic requirement, and reversibility.[8] Dexmedetomidine also causes dose-dependent hypotension, bradycardia, and sedation. Dexmedetomidine decreases the heart rate and blood pressure by decreasing plasma levels of norepinephrine and epinephrine.[9] Dexmedetomidine and butorphanol can be used safely and effectively for postoperative analgesia in patients undergoing laparoscopy. The use of Dexmedetomidine 1 μg/kg and butorphanol 30 μg/kg is particularly beneficial in these patients.[10] So in this study we have compared the intravenous butorphanol and dexmedetomidine to reduce the hemodynamic stress response during laryngoscopy, intubation and pneumoperitoneum.

Aims and Objectives

To compare the effect of intravenous butorphanol and dexmedetomidine on the hemodynamic cardiovascular responses as premedication in laparoscopic cholecystectomy.

Following parameters were assessed

Heart rate and Non-Invasive Blood Pressure, SpO_2, $EtCO_2$.

Baseline vitals

Pre-intubation vitals

Post-intubation vitals till the end of surgery at specified intervals

Post-extubation vitals till 10 min after extubation at specified intervals

Materials and Methods

After obtaining ethical committee approval and informed consent from patient, the study entitled "*Comparison of Hemodynamic Response Among Intravenous Butorphanol and Dexmedetomidine as Premedication in Laparoscopic Cholecystectomy*" was carried on 100 patients of both sex with comparable characteristics and group of ASA Grade I and II physical status.

Following patients were excluded from the study

Patients of ASA Class III and above, Age <18 yrs and >60 yrs, Patients with cardiac illness, Patients with pulmonary illness, Patient with nervous system disorders, Pregnant or nursing women, Known hypersensitive to any of the study medication, Patients with anticipated difficult intubation, Duration of laryngoscopy and endotracheal intubation >30 seconds, Chronic narcotic user, Patient refusal.

Anesthesia protocol

All the patients scheduled for laparoscopic cholecystectomy visited a day prior to surgery and a thorough pre-anesthetic examination was done. All routine investigations were done and reviewed. Patients were kept fasting for 8 hrs prior to the surgery. A written and informed consent was obtained from the patients. All patients were premedicated with tab ranitidine 150 mg and tab alprazolam 0.25 mg night before the surgery. The patients were assigned to one of the two groups using a "slips of paper in a box" technique. The grouping is as follows: Group (B) – i.v. Butorphanol (30 μg/kg) Group (D) – i.v. Dexmedetomidine (1 μg/kg) A large bore (18) intravenous canula was inserted for drug and fluid administration. All the patients were premedicated using inj midazolam 1 mg iv, Inj. Ondansetron 0.08 mg/kg IV inj. glycopyrrolate 0.2 mg iv prior to induction of anesthesia. Baseline parameters of hemodynamic and pulmonary status were measured 5 minutes after arrival of patient in the operating room. In Group B inj. Butorphanol 30 μg/kg was given 5 minutes before induction. In Group D inj. Dexmedetomidine 1 μg/kg diluted in 10 ml normal saline, was given in 10 minutes by infusion pump. Patients were induced with inj. propofol 2 mg/kg iv. and inj. succinylcholine 1.5 mg/kg i.v. There after laryngoscopy and tracheal intubation was performed with cuffed endotracheal tube of appropriate size. Anesthesia was maintained with

66:33 (N_2O:O_2) ventilation and isoflurane was used in 0.5–1% concentration. Adequate skeletal muscle relaxation was maintained with loading dose of vecuronium (0.08 mg/kg) followed by intermittent i.v boluses of 0.02 mg/kg. Isoflurane was stopped 10 minutes prior to the end of surgery and N_2O was discontinued after skin closure. At the end of anesthesia, the neuromuscular blockade was antagonized with inj. neostigmine 0.05 mg/kg and inj. glycopyrrolate 0.01 mg/kg intravenously.

Following parameters were monitored at specific intervals

1. Heart rate
2. Systolic blood pressure
3. Diastolic blood pressure
4. SpO_2
5. $EtCO_2$ (after intubation till extubation)

At baseline, Preintubation, 1 min after intubation, 3 min after intubation 5 min after intubation, Every 5 min till 10 min after extubation patients were observed for 1 hour after extubation complications like, bradycardia, hypotension, abnormal ECG, nausea and vomiting were recorded during the study. The results were compared and statistically analyzed.

Statistical Analysis: The results obtained in the study were presented in a tabulated manner as Mean ± SD and were analyzed using with Statistical Package for Social Sciences (SPSS 23.0). The demographic data for categorical variables were done by Independent samples t-test, paired t-test, chi-square test, or suitable stats was used for the purpose of analysis of data. *p* value of <0.05 was considered statistically significant.

Results

Table 1: Distribution of Patients according to their Age and Gender

	Group B (N = 50)	Group D (N = 50)	*p* value
Age (year)	47.64 ± 9.1	46.16 ± 9.3	0.423
Male	22 (44.0)	29 (58.0)	0.161
Female	28 (56.0)	21 (42.0)	

The distribution of patients on the basis of their age and gender in both the groups found to be comparable and statistically insignificant difference ($p > 0.05$) (Table 1).

Table 2: ASA Grade between Two Groups

ASA Grade	Group B (N=50) (%)	Group D (N=50) (%)	*p* value
I	34 (68%)	31 (62%)	0.529
II	16 (32%)	19 (38%)	

The distribution of patients on the basis of ASA grade in both the groups found to be comparable and statistically insignificant difference ($p > 0.05$) (Table 2).

Table 3: Comparison of Mean duration of Surgery in both Groups

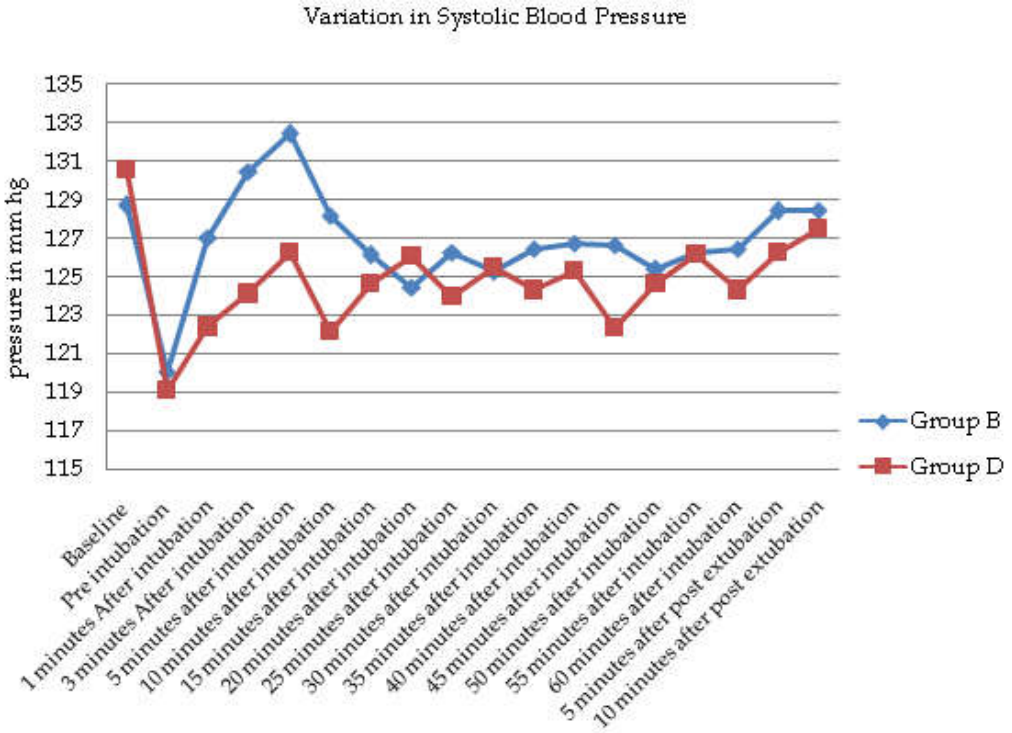
	Group B	Group D	
Duration of surgery (min)	Mean ± SD	Mean ± SD	*p* value
	54.26 ± 4.2	53.02 ± 4.37	0.151

The mean duration of surgery in both groups found to be comparable and statistically insignificant difference ($p > 0.05$) (Table 3).

Table 4: Variation of Systolic (SBP) and Diastolic (DBP) Blood Pressure

		Systolic blood pressure			Diastolic blood pressure		
Time	T	Group B	Group D	*p*-value	Group B	Group D	*p*-value
Baseline	T0	128.70 ± 14.60	130.56 ± 13.03	0.503	82.06 ± 8.18	80.28 ± 7.74	0.266
Pre-intubation		120.08 ± 6.34	119.08 ± 10.59	0.254	74.58 ± 3.68	72.40 ± 5.74	0.326
1 minute after intubation	T1	127.02 ± 14.45	122.40 ± 15.04	0.120	78.30 ± 7.78	79.80 ± 7.61	0.332
3 minutes after intubation	T3	130.44 ± 9.12	124.12 ± 13.71	0.008	82.16 ± 7.91	81.12 ± 8.10	0.017
5 minutes after intubation	T5	132.42 ± 10.00	126.28 ± 17.28	0.032	83.44 ± 8.30	82.16 ± 7.91	0.043
10 minutes after intubation	T10	128.18 ± 14.22	122.18 ± 15.21	0.044	81.32 ± 8.10	80.12 ± 7.98	0.457
15 minutes after intubation	T15	126.12 ± 14.85	124.64 ± 14.31	0.013	81.56 ± 8.83	79.56 ± 6.62	0.023
20 minutes after intubation	T20	124.46 ± 13.29	126.10 ± 16.17	0.058	80.56 ± 7.84	78.20 ± 6.00	0.094
25 minutes after intubation	T25	126.26 ± 13.24	124.0 ± 17.81	0.047	80.12 ± 7.98	78.08 ± 6.41	0.016
30 minutes after intubation	T30	125.26 ± 11.09	125.48 ± 15.73	0.035	79.28 ± 8.86	76.30 ± 6.11	0.043
35 minutes after intubation	T35	126.46 ± 10.48	124.30 ± 14.57	0.039	79.70 ± 9.08	75.22 ± 5.80	0.004
40 minutes after intubation	T40	126.76 ± 10.65	125.34 ± 13.78	0.055	79.22 ± 9.07	76.44 ± 6.32	0.078
45 minutes after intubation	T45	126.66 ± 13.65	122.36 ± 13.73	0.019	78.08 ± 6.41	77.42 ± 5.66	0.586
50 minutes after intubation	T50	125.36 ± 9.96	124.64 ± 14.31	0.770	78.12 ± 6.96	77.18 ± 5.74	0.463

Time	T	Systolic blood pressure			Diastolic blood pressure		
		Group B	Group D	*p*-value	Group B	Group D	*p*-value
55 minutes after intubation	T55	126.24 ± 11.83	126.14 ± 14.18	0.969	77.32 ± 7.83	79.42 ± 6.91	0.158
60 minutes after intubation	T60	126.46 ± 11.70	124.30 ± 11.12	0.046	78.48 ± 7.34	80.06 ± 7.30	0.283
5 minutes after post-extubation		128.40 ± 13.74	126.28 ± 17.28	0.049	80.12 ± 7.98	81.18 ± 7.59	0.001
10 minutes after post-extubation		128.44 ± 14.00	127.48 ± 18.55	0.770	81.32 ± 8.00	80.14 ± 7.76	0.001



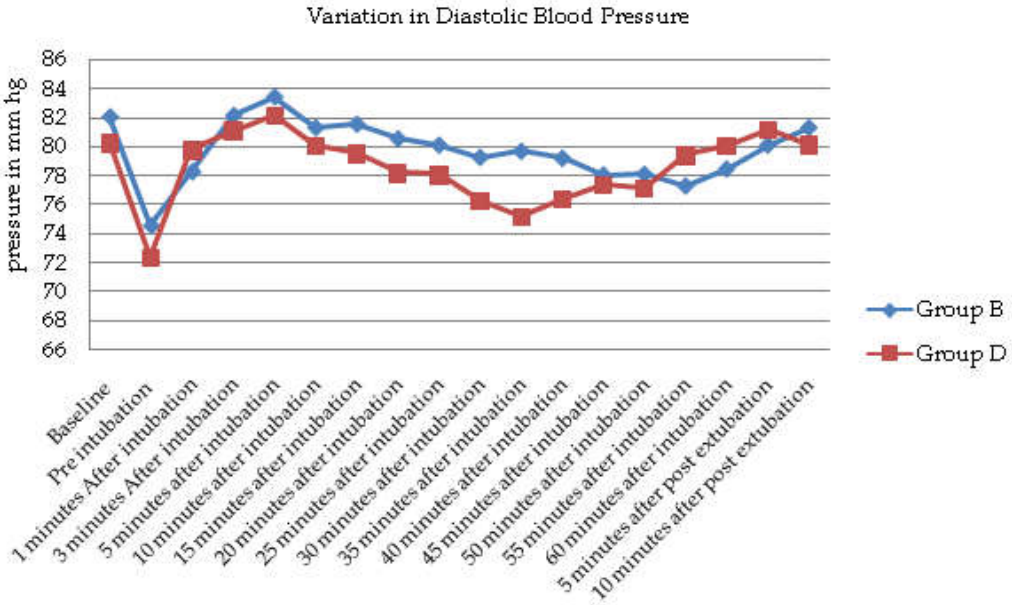


Table 5: Showing Variation in Heart Rate (HR)

Time	T	Group B Mean ± S.D	Group D Mean ± S.D	*p*-value
Baseline	T0	77.34 ± 7.26	77.58 ± 4.12	0.839
Pre-intubation		71.22 ± 13.26	68.76 ± 11.27	0.028
1 minute after intubation	T1	77.42 ± 7.25	69.34 ± 10.25	0.001
3 minutes after intubation	T3	78.56 ± 6.16	73.74 ± 6.65	0.003
5 minutes after intubation	T5	82.84 ± 5.83	75.48 ± 7.41	0.001
10 minutes after intubation	T10	80.34 ± 15.29	73.78 ± 6.64	0.006
15 minutes after intubation	T15	82.24 ± 14.74	74.54 ± 7.09	0.001
20 minutes after intubation	T20	80.56 ± 11.60	75.22 ± 6.32	0.005
25 minutes after intubation	T25	77.42 ± 7.25	75.32 ± 6.32	0.125
30 minutes after intubation	T30	78.54 ± 7.39	74.48 ± 6.78	0.005
35 minutes after intubation	T35	77.42 ± 7.25	75.08 ± 7.41	0.113
40 minutes after intubation	T40	78.20 ± 7.39	73.78 ± 6.64	0.001
45 minutes after intubation	T45	77.10 ± 6.90	74.54 ± 7.09	0.070
50 minutes after intubation	T50	78.32 ± 7.00	75.14 ± 7.87	0.035
55 minutes after intubation	T55	77.42 ± 7.25	77.58 ± 4.12	0.892
60 minutes after intubation	T60	77.88 ± 17.89	76.36 ± 8.12	0.585
5 minutes after post-extubation		78.16 ± 6.87	76.24 ± 7.83	0.015
10 minutes after post-extubation		77.38 ± 7.22	77.22 ± 6.16	0.905

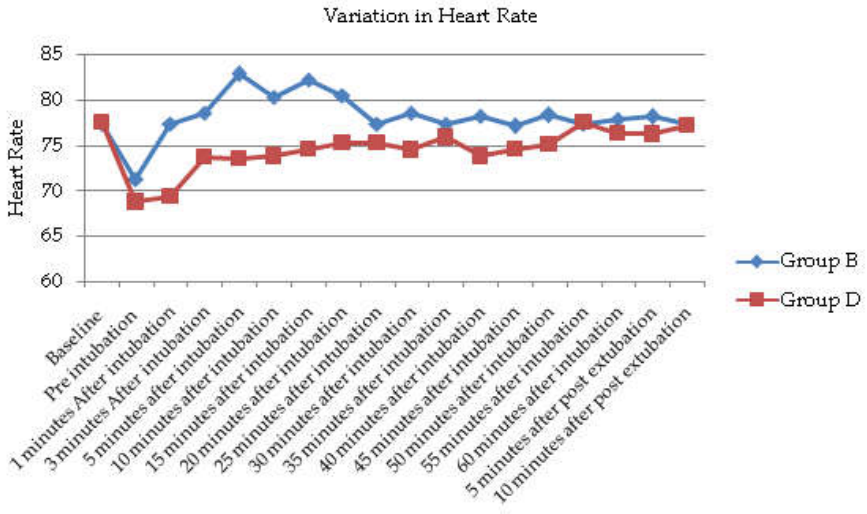


Table 6: Showing Variation in $EtCO_2$ and SpO_2

Time	T	$EtCO_2$			SpO_2		
		Group B Mean ± S.D	Group D Mean ± S.D	*p*-value	Group B Mean ± S.D	Group D Mean ± S.D	*p*-value
Baseline	T0				99.40 ± 0.60	99.46 ± 0.81	0.674
Pre intubation					99.12 ± 0.71	98.86 ± 1.06	0.152
1 minute after intubation	T1	28.08 ± 3.02	28.08 ± 3.67	1.000	99.14 ± 0.78	98.80 ± 1.27	0.109
3 minutes after intubation	T3	29.78 ± 4.40	29.24 ± 3.37	0.492	98.66 ± 1.20	98.44 ± 1.24	0.369
5 minutes after intubation	T5	30.06 ± 2.28	29.58 ± 3.45	0.413	98.58 ± 1.24	98.10 ± 1.31	0.062
10 minutes after intubation	T10	30.74 ± 2.35	29.96 ± 3.03	0.153	98.60 ± 1.24	98.05 ± 1.64	0.061
15 minutes after intubation	T15	31.14 ± 4.14	30.08 ± 3.07	0.149	98.68 ± 1.06	98.34 ± 1.36	0.166
20 minutes after intubation	T20	31.64 ± 5.37	29.88 ± 6.04	0.126	98.66 ± 1.22	98.46 ± 1.40	0.448
25 minutes after intubation	T25	31.90 ± 5.53	29.64 ± 6.86	0.072	98.12 ± 0.98	97.90 ± 1.58	0.404
30 minutes after intubation	T30	32.04 ± 5.30	30.04 ± 7.13	0.059	98.18 ± 0.85	97.88 ± 1.42	0.202
35 minutes after intubation	T35	32.44 ± 6.41	30.04 ± 7.13	0.078	98.28 ± 0.87	97.84 ± 1.54	0.081
40 minutes after intubation	T40	32.52 ± 6.50	31.22 ± 7.22	0.346	98.18 ± 0.87	98.10 ± 1.12	0.690
45 minutes after intubation	T45	32.12 ± 6.24	32.18 ± 7.62	0.965	98.38 ± 0.63	98.78 ± 1.48	0.081
50 minutes after intubation	T50	33.48 ± 3.18	33.26 ± 7.49	0.848	98.08 ± 1.17	98.34 ± 1.35	0.306
55 minutes after intubation	T55	34.52 ± 3.98	34.22 ± 7.41	0.801	98.76 ± 1.29	98.44 ± 1.44	0.244
60 minutes after intubation	T60	35.24 ± 2.79	35.08 ± 6.57	0.874	98.74 ± 1.07	98.52 ± 1.69	0.438
5 minutes after extubation					98.52 ± 1.96	98.30 ± 1.52	0.389
10 minutes after extubation					97.88 ± 1.02	97.50 ± 1.47	0.136

Table 7: Side Effects

Side effects	Group B (%)	Group D (%)	*p* value
Nausea	17 (34)	9 (18)	0.068
Vomiting	12 (24)	3 (6)	0.011
Hypotension	2 (4)	6 (12)	0.398
Bradycardia	3 (6)	5 (10)	0.461

Discussion

Demographic data showed that Group B (butorphanol) and Group D (dexmedetomidine) were comparable in terms of number of patients, age, sex, weight, ASA status, types and duration of laparoscopic surgeries ($p > 0.05$).

Baseline parameters: Present study shows, baseline parameters of hemodynamic like HR, SBP, DBP and SpO_2 were comparable between both groups ($p > 0.05$)

Variation of systolic (SBP) and diastolic (DBP) blood pressure

As shown in table 4 baseline SBP and DBP were comparable between both groups. The blood pressure start to rise during laryngoscopy and intubation. The rise in blood pressure was more in Group (B) as compared to Group (D). Then blood pressure starts declining and at around 10 min come back to baseline value in Group (B) but remain below baseline in Group (D) and below base line during preoperative period. Our result is comparable with Vaswani JP *et al.*[11] they found that there is significantly less increase in blood pressure of dexmedetomidine group after laryngoscopy, intubation, pneumoperitoneum, and in intraoperative period and after extubation. Patel CR *et al.*[12] found lesser increase in SBP, DBP after intubation with dexmedetomidine 1 µg/kg given as loading dose prior to induction. Pandit and Kothary *et al.*[13] compared fentanyl with butorphanol for outpatient laparoscopic procedures. They concluded that butorphanol gives better protection against sympathetic stimulation to tracheal intubation. Rao MH *et al.*[14] observed very minimal changes in pulse rate in both the butorphanol and fentanyl groups. Fall in pulse rate in group butorphanol was more in comparison to fentanyl throughout peri-operative period.

Variation in Heart Rate (HR)

As shown in Table 5 baseline HR was comparable between both groups. The heart rate start to rise during laryngoscopy and intubation. The rise in heart rate was more in Group (B) as compare to Group (D). Then heart rate starts declining and at arround 10 min come back to baseline value in Group (B) but below baseline in Group (D) and remain below baseline during preoperative period. Our result is comparable with Vaswani JP *et al.*[11] in their observation found that there is significantly less increase in heart rate of dexmedetomidine group after intubation, after pneumoperitoneum, in intraoperative period and after extubation. Patel CR *et al.*[12] found lesser increase in heart rate after intubation with dexmedetomidine 1 µg/kg given as loading dose prior to induction. Pandit and Kothary *et al.*[13] compared fentanyl with butorphanol for outpatient laparoscopic procedures. They concluded that butorphanol gives better protection against sympathetic stimulation to tracheal intubation. Rao MH *et al.*[14] observed very minimal changes in pulse rate in both the butorphanol and fentanyl groups. Fall in pulse rate in group butorphanol was more in comparison to Group fentanyl throughout perioperative period.

Variation in $EtCO_2$ and SpO_2

As shown in Table 6 there were no significant changes in $EtCO_2$ and SpO_2 in both the groups in intra and intergroup study. These findings were similar to study was conducted by Rao MH *et al.*[14] where no significant changes were observed in $EtCO_2$ and SpO_2 in butorphanol group. Vaswani JP *et al.*[11] observed that there was no significant difference in pre- and intraoperative SpO_2 and $EtCO_2$ values.

Side Effects

As shown in Table 7 in nausea and vomiting was more in Group (B) as compare to Group (D). But hypotension and bradycardia was more in Group (D). as compare to group (B). Vaswani JP *et al.*[11] used IV dexmedetomidine they found intraoperative hypertension and bradycardia.

Conclusion

We found that butorphanol and dexmedetomidine both provide adequate sedation and analgesia. But patients who received dexmedetomidine as premedication the rise in heart rate and blood pressure after laryngoscopy and intubation was less as compared to the patients who received butorphanol, in which the rise in heart rate and blood pressure after laryngoscopy and intubation was more. So we found that dexmedetomidine is

better in attenuating the stress response during laryngoscopy, intubation and pneumoperitoneum as compared to butorphanol.

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