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Original Research Article

Comparison of hemodynamic responses of intravenous dexmedetomidine and esmolol infusion during laparoscopic cholecystectomy

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ABSTRACT

Background: Laparoscopic cholecystectomy is one of the commonest surgery performed under general anesthesia in this set up but maintaining the hemodynamic stability is challenging in these patients. The present study was conducted to comparatively analyse the hemodynamic variations using intravenous dexmedetomidine and intravenous esmolol during laparoscopic cholecystectomy.
Methods: Study was conducted on 90 adult patients aged 18-60 years, of ASA grade I or II of both gender, scheduled for laparoscopic cholecystectomy under general anesthesia. Patients were randomized into three groups of 30 patients each. Patients of Group A received esmolol infusion (loading: 1mg/kg and maintenance: 5-15µg/kg/min), patients of Group B received dexmedetomedine infusion (loading: 0.7µg/kg and maintenance: 0.4µg/kg/hr) and Group C (control group) received normal saline infusion. Patients were monitored for changes in heart rate, ECG, systemic blood pressure and $EtCO_2$, at baseline, at 5 min and 10 min after giving study drug bolus, after induction, intubation, skin incision and CO_2 insufflation. Thereafter, these changes were recorded at 15 min intervals till the end of surgery.
Results: It was observed that perioperative use of dexmedetomidine and esmolol infusions maintained better hemodynamic stability as compared to the normal saline in control group. Though the patients in esmolol group showed less fluctuations in BP and HR (as compared to control group), but, stability was better in the patients of dexmedetomidine group at all-time intervals.
Conclusions: Dexmedetomidine infusion was a better option for maintaining hemodynamic stability in comparison to emolol infusion during laparoscopic surgeries.

Keywords: Dexmedetomidine, Esmolol, Hemodynamic responses, Laparoscopic cholecystectomy

INTRODUCTION

Laparoscopic surgeries have a number of advantages including reduced blood loss, smaller incision, reduced pain, shortened recovery time and reduced exposure of internal organs to possible external contaminants thereby reduced risk of acquiring infections but these are not completely devoid of disadvantages. Increase in intra-abdominal pressure and volume (pneumoperitoneum), extremes of patient positioning (reverse trendelenberg) and accumulation of carbon dioxide have profound effect on patient's hemodynamic, respiratory and metabolic functions.[1,2] To avoid these disadvantages, we added two adjuvants viz esmolol and dexmedetomedine in the perioperative period and observed their effects on intraoperative hemodynamics.

Dexmedetomidine is a highly selective α2 adrenoreceptor agonist, that dose-dependently reduces blood pressure (BP) and heart rate (HR) and has sedative and analgesic properties without activation of α1 receptors. It also induces a centrally mediated reduction of sympathetic nervous system activity, thus decreasing the hemodynamic and plasma catecholamine response to stressful events of surgery.[3] However, its role in contemporary intraoperative anesthesia practice has not yet been established and there are only few studies on the cardiovascular parameters in humans during continuous infusion of the drug in the perioperative period during laparoscopic surgeries.

Esmolol is the first intravenous titratable β-blocker available for use in surgical settings. It is a cardioselective beta1 receptor blocker with rapid onset, very short duration of action, and no significant intrinsic sympathomimetic or membrane stabilizing activity at therapeutic dosages. In addition to its effect on the sympathetic nervous system, esmolol influences core components of an anesthetic regimen, such as analgesia, hypnosis, and memory function.[4,5] It is a class II antiarrhythmic drug.

The present prospective, randomized study was designed to compare the effect of intraoperative IV esmolol and IV dexmedetomedine on intraoperative hemodynamics, and the incidence of side effects in patients scheduled for laparoscopic cholecystectomy.

METHODS

After getting approval from Ethical Committee, the study was conducted on ASA physical status I and II patients aged 18-60 years of either sex, being admitted for laparoscopic cholecystectomy to be done under general anesthesia. An informed consent was taken from all the patients.

Exclusion criteria included patients having allergy, hypersensitivity or contraindications to anesthetic or analgesic medications, patients with clinically-significant medical conditions, such as brain, heart, kidney, endocrine, or liver diseases, peptic ulcer disease or bleeding disorders, pregnant or lactating women, subjects with a history of alcohol or drug abuse within the past 3 months and any other condition or use of any medication which may interfere with the conduct of the study.

Patients were randomly selected into three groups of 30 each, according to computer generated random number table.

- Group A (esmolol group): Patients received esmolol infusion (loading 1mg/kg and maintenance: 10µg/kg/min)
- Group B (dexmedetomedine group): Patients received dexmedetomedine infusion (loading: 0.7µg/kg and maintenance: 0.4µg/kg/hr)
- Group C (control group): Patients received normal saline infusion.

According to respective groups, infusions were initiated and 10 minutes after the infusion was started, anaesthesia was induced with inj. Propofol (2mg/kg) and inj. Fentanyl (1µg/kg) iv. After induction, succinylcholine was given at a dose of 2mg/kg body intravenously to facilitate intubation. Intraoperative relaxation was achieved by vecuronium 0.05mg/kg. Patient were on controlled mechanical ventilation to maintain $EtCO_2$ at 30 to 40mm Hg.

Patients were intra operatively monitored for heart rate, ECG, systolic blood pressure, diastolic blood pressure, peripheral oxygen saturation and $EtCO_2$ at 5 mins,10 mins, induction, intubation, skin incision, Co_2 insufflation, 5 mins after insufflation, 10 mins after insufflation and thereafter at every 15 mins till the end of surgery.

At the start of surgical wound closure, the study drug infusion was stopped and the neuromuscular block was antagonized with neostigmine (0.04mg/kg) and glycopyrrolate (5 microgram/Kg). Patients were extubated and sent to PACU for further monitoring of vital parameters.

Statistical analysis

Data were tabulated as Mean±SD. One way analysis of variance (ANOVA) and the significance of mean difference between the groups was done by Tukey's post hoc test. Groups were also compared by two factor repeated measures ANOVA using general linear models (GLM) and the significance of mean difference within and between the groups was done by Tukey's post hoc test. Discrete (categorical) groups were compared by chi-square (χ^2) test. A two-sided (α=2) p value less than 0.05 ($p<0.05$) was considered statistically significant. (All analyses were performed on SPSS software (windows version 17.0).

RESULTS

The present study was conducted on 90 patients of either sex between 18-60 years of age ASA Grade I and II undergoing laparoscopic cholecystectomy for cholelithiasis. Out of the 90 patients three patients were excluded from the study (2 from control group and one from dexmedetomedine group) as their laparascopic cholecystectomy was changed to open choleystectomy due to some complication. So, authors had 30 patients in group A, 29 in group B an 28 in group C. Otherwise the three groups were similar to each other on the basis of demographic characteristics. The higher number of female patients in all the three group indicates normal demographic distribution of the disease and its increased prevalence in the female sex.

Table 1: Basic characteristics of three groups.

Characteristics	Group C (n=28) (%)	Group A (n=30) (%)	Group B (n=29) (%)	χ^2/F value	p value
Age (yrs): Mean±SD	39.43±6.87	39.57±9.42	39.83±9.26	0.02	0.984
Sex: Males/ Females	6 (21.4)/22 (78.6)	10(33.3)/20(66.7)	10 (34.5)/19 (65.5)	1.42	0.492
Weight (kg): Mean±SD	57.86±9.25	62.53±9.87	57.66±6.88	2.92	0.059
ASA Grade: I/II	17(60.7/11(39.3)	20(66.7)/10(33.3)	16(55.2)/13(44.8)	0.82	0.664

Table 2: SBP (Mean±SD) of three groups during the surgery.

Observation periods	Time (min)	Group C (n=28)		Group A (n=30)		Group B (n=29)	
		Mean	SD	Mean	SD	Mean	SD
Baseline	0	122.04^{ref}	12.59	121.83^{ref}	9.85	122.00^{ref}	8.49
	5	123.50^{ns}	9.85	122.00^{ns}	11.57	122.28^{ns}	10.62
	10	123.43^{ns}	9.12	121.50^{ns}	12.98	121.83^{ns}	16.41
Induction	1	122.25^{ns}	12.24	121.87^{ns}	14.95	120.69^{ns}	15.60
Intubation	1	127.54^{ns}	8.68	120.97^{ns}	9.80	122.07^{ns}	14.83
	5	123.50^{ns}	9.85	121.00^{ns}	13.07	120.93^{ns}	16.79
Skin incision	5	122.43^{ns}	9.12	121.43^{ns}	12.26	120.93^{ns}	15.42
CO_2 insufflation	1	125.79^{ns}	11.51	121.67^{ns}	15.50	121.97^{ns}	15.37
	5	126.25^{ns}	8.90	123.37^{ns}	15.85	122.59^{ns}	17.46
	10	122.68^{ns}	10.92	122.30^{ns}	14.99	122.17^{ns}	17.42
	30	123.04^{ns}	9.00	122.60^{ns}	13.76	122.97^{ns}	13.54
	45	124.71^{ns}	8.97	123.83^{ns}	12.37	123.31^{ns}	11.25
	60	123.68^{ns}	8.00	122.67^{ns}	10.45	123.31^{ns}	10.40
	75	125.04^{ns}	8.62	123.07^{ns}	11.12	123.76^{ns}	10.83
	90	125.04^{ns}	7.85	123.60^{ns}	10.48	124.79^{ns}	11.78

^{ns}p>0.05- as compared to Baseline (0 min)

Table 3: DBP (Mean±SD) of three groups during the surgery.

Observation periods	Time (min)	Group C (n=28)		Group A (n=30)		Group B (n=29)	
		Mean	SD	Mean	SD	Mean	SD
Baseline	0	78.6	16.41	78.10	10.10	79.38	7.05
	5	82.71	7.33	80.10	12.46	80.28 ^{ns}	7.67
	10	82.96^{ns}	10.88	79.67^{ns}	13.31	79.38^{ns}	5.82
Induction	1	80.25^{ns}	12.10	78.53^{ns}	12.18	79.31^{ns}	5.57
Intubation	1	83.50^{ns}	11.06	81.20^{ns}	9.46	79.10^{ns}	6.11
	5	81.93^{ns}	11.66	79.30^{ns}	10.22	78.07^{ns}	6.36
Skin incision	5	81.57^{ns}	9.95	79.73^{ns}	12.94	78.72^{ns}	5.21
CO_2 insufflation	1	81.75^{ns}	10.02	80.80^{ns}	12.62	77.86^{ns}	6.47
	5	83.50^{ns}	12.34	81.37^{ns}	12.38	80.07^{ns}	4.94
	10	86.86*	13.16	81.93^{ns}	14.62	79.72^{ns}	6.18
	30	85.25^{ns}	11.42	80.03^{ns}	12.78	78.14^{ns}	6.07
	45	86.96*	7.39	80.73^{ns}	11.56	78.07^{ns}	6.69
	60	86.86*	7.20	81.37^{ns}	12.26	80.00^{ns}	7.39
	75	85.61^{ns}	7.49	81.77^{ns}	11.48	79.17^{ns}	5.63
	90	86.50 ^{ns}	7.40	83.20^{ns}	10.49	79.62^{ns}	6.15

^{ns}p>0.05 or *p<0.05- as compared to Baseline (0 min)

Both dexmedetomidine and esmolol, stabilized the systolic blood pressure and reduced the hemodynamic fluctuations during various phases of anaesthesia and laparascopy. Baseline mean SBP was 122.0±12.59, 121.83±9.85 and 122.00±8.49; 127.54±8.68, 120.97±9.80 and 122.07±14.83 at 1 min after intubation; 125.79±11.51, 121.67±15.50 and 121.97±15.37 at 1 min after Co2 insufflation and 126.25±8.90, 123.37±15.85 and 122.59±17.46 at 5 min after CO_2 insufflation in groups C, A and B respectively (Table 2).

Significant stabilization of mean diastolic blood pressure was seen in dexmedetomidine and esmolol after CO_2 pneumoperitoneum as compared to that of control group. Baseline mean diastolic blood pressure was 78.64±16.41, 78.10±10.10 and 79.38±7.05 mm Hg; 86.86±13.16, 81.93±14.62 and 79.72±6.18 mmHg at 10 mins; 86.96±7.39, 80.73±11.56 and 78.07±6.69 mmHg after 45 mins and 86.86±7.20, 81.37±12.26 and 80.00±7.39 mm Hg at 60 mins after Co2 insufflation in groups C, A and B respectively (Table 3).

Table 4: MAP (Mean±SD) of three groups during the surgery.

Observation periods	Time (min)	Group C (n=28)		Group A (n=30)		Group B (n=29)	
		Mean	SD	Mean	SD	Mean	SD
Baseline	0	93.11[ref]	12.99	92.68[ref]	8.95	93.59[ref]	5.05
	5	96.31[ns]	6.23	94.07[ns]	11.52	94.28[ns]	5.93
	10	96.45[ns]	8.58	93.61[ns]	12.75	93.53[ns]	6.98
Induction	1	94.25[ns]	9.28	92.98[ns]	12.45	93.10[ns]	6.92
Intubation	1	98.18[ns]	8.30	94.46[ns]	8.32	93.43[ns]	6.59
	5	95.79[ns]	8.13	93.20[ns]	10.42	92.36[ns]	7.16
Skin incision	5	95.19[ns]	7.19	93.63[ns]	11.75	92.79[ns]	5.94
CO_2 insufflation	1	96.43[ns]	8.54	94.42[ns]	12.02	92.56[ns]	5.74
	5	97.75[ns]	8.85	95.37[ns]	12.17	94.24[ns]	5.55
	10	98.80[ns]	10.22	95.39[ns]	13.77	93.87[ns]	5.23
	30	97.85[ns]	8.96	94.22[ns]	12.47	93.08[ns]	6.35
	45	99.55[ns]	5.75	95.10[ns]	11.09	93.15[ns]	6.44
	60	99.13[ns]	5.49	95.13[ns]	10.84	94.44[ns]	6.36
	75	98.75[ns]	6.49	95.53[ns]	10.30	94.03[ns]	5.23
	90	99.35[ns]	5.19	96.67[ns]	9.62	94.68[ns]	6.47

[ns]p>0.05- as compared to Baseline (0 min)

Table 5: HR (Mean±SD) of three groups during the surgery.

Observation periods	Time (min)	Group C (n=28)		Group A (n=30)		Group B (n=29)	
		Mean	SD	Mean	SD	Mean	SD
Baseline	0	86.75[ref]	17.62	84.97[ref]	10.01	86.10[ref]	15.86
	5	87.36[ns]	17.14	80.73[ns]	9.09	83.52[ns]	14.94
	10	87.96[ns]	17.74	80.03[ns]	8.16	81.59[ns]	13.67
Induction	1	87.32[ns]	15.57	81.30[ns]	8.71	80.45[ns]	11.75
Intubation	1	90.00[ns]	13.66	80.67[ns]	8.40	80.38[ns]	9.11
	5	87.89[ns]	13.22	80.27[ns]	8.48	81.52[ns]	8.53
Skin incision	5	87.32[ns]	17.31	81.37[ns]	8.97	80.31[ns]	9.17
CO_2 insufflation	1	87.71[ns]	14.71	80.00[ns]	6.76	83.31[ns]	10.69
	5	86.46[ns]	11.96	81.13[ns]	5.37	78.48[ns]	7.48
	10	85.82[ns]	12.45	83.37[ns]	6.64	79.52[ns]	8.96
	30	86.46[ns]	13.07	83.90[ns]	6.06	81.55[ns]	12.04
	45	84.93[ns]	12.45	83.40[ns]	6.75	81.55[ns]	11.20
	60	86.75[ns]	13.74	84.17[ns]	6.48	81.97[ns]	10.68
	75	85.14[ns]	13.82	83.03[ns]	6.60	81.48[ns]	10.50
	90	84.68[ns]	12.24	83.90[ns]	6.34	82.38[ns]	12.04

[ns]p>0.05- as compared to Baseline (0 min)

Though increase in mean arterial pressure due to increased response to laryngoscopy, skin incision and CO_2 insufflation was attenuated by both Esmolol and Dexmedetomidine, yet the efficacy of Dexmedetomidine was better than esmolol as the fluctuations in response to sympathetic stimuli were least in group B (Table 4).

Increased heart rate at the time of intubation was attenuated by both the drugs esmolol and dexmedetomidine but it was better in dexmedetomidine group at all periods (Table 5).

Both drugs decreased the incidence of postoperative nausea vomiting.

DISCUSSION

It was observed that perioperative use of dexmedetomidine and esmolol infusion maintained better hemodynamic stability as compared to the control group during laparoscopic cholecystectomy. Though esmolol showed less fluctuations in BP and HR due to attenuation of sympathetic stimuli (as compared to control group), but, the response in dexmedetomedine group was better at all time intervals.

Srivastava VK, et al in their study emphasized the use of dexmedetomidine and esmolol for attenuation of hemodynamic response to pneumoperitoneum in laparoscopic cholecystectomy and concluded that Dexmedetomidine is more effective than esmolol in preventing such hemodynamic responses in laparoscopic surgery. Their results are similar to results of present study. In addition, dexmedetomidine and esmolol also reduce the induction dose of propofol and intraoperative fentanyl requirement.[6]

Bhattacharjee DP et al, conducted a similar study in 60 patients and observed that both esmolol and dexmedetomidine effectively attenuated the increase of MAP and HR during and after pneumoperitoneum and thereby providing hemodynamic stability during laparoscopic surgery. But they did not find any significant difference between the efficacy of esmolol and dexmedetomidine regarding the attenuation of hemodynamic response to pneumoperitoneum in laparoscopic surgeries.[7]

Bhattachargee et al, conducted a study to evaluate the efficacy of dexmedetomidine to provide perioperative haemodynamic stability in patients undergoing laparoscopic cholecystectomy. Their results showed that dexmedetomedine do maintain hemodynamic stability during the intraoperative period of laparoscopic cholecystectomy.[8]

Ghodki et al, conducted an observational study using dexmedetomedine as an anaesthetic adjuvant in laparoscopic surgeries. They monitored the depth of anesthesia (DOA) using entropy to avoid unwanted awareness under anesthesia. 30 patients, American Society of Anesthesiologists grade I and II, aged between 18 to 50 years of either gender undergoing laparoscopic surgeries under general anesthesia were studied. They concluded that dexmedetomidine is an effective anesthetic adjuvant that can be safely used in laparoscopy without the fear of awareness under anesthesia.[9]

Coloma et al, suggested that perioperative esmolol is an effective alternative to remifentanil in gynaecologic laparoscopic surgery. They also observed that esmolol has a role in maintaining the hemodynamic stability during intraoperative period in laparoscopic cholecystectomy.[10]

CONCLUSION

Thus, authors concluded that perioperative use of dexmedetomidine and esmolol infusion maintained better hemodynamic stability as compared to the control group during laparoscopic cholecystectomy. Though esmolol showed less fluctuations in BP and HR due to attenuation of sympathetic stimuli (as compared to control group), but, the response in dexmedetomidine group was better at all-time intervals.

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