Original Research Article

Comparison of conventional dose and low dose infusion of dexmedetomidine on hemodynamic stress response, dose of induction agent and postoperative analgesia in patients undergoing laparoscopic cholecystectomy

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Abstract

Background and Aim: Anesthetic techniques are based on hemodynamic stability during anesthesia and surgery. Dexmedetomidine is centrally acting α_2 agonist with sedative, sympatholytic and analgesic. Aim of this study was to compare effect of conventional dose with low dose infusion of dexmedetomidine on hemodynamic stress response, induction agent requirement & postoperative analgesia.

Materials and methods: Single randomised prospective study done on 100 ASA I and II patients aged 18-65 years scheduled for elective laparoscopy cholecystectomy under general anesthesia. Patients were divided in to two groups of 50 each, **Group A:** 1 µg/kg loading dose of

dexmedetomidine I.V. started 15 min before procedure and infusion. 5 µg/kg/hr after induction and continued till end of surgery. **Group B:** 0.5 µg /kg/hr of dexmedetomidine I.V. started 15 min before procedure and continued till end of surgery.

Results: Hemodynamic stability more in group B by avoiding complications like hypotension and bradycardia (p value < .05). Reduction of induction dose was more in group A than group B as compared to standard doses (P value <0.01). Hypotension and bradycardia were observed in 5 cases after 15 min of infusion in group A (p value <.01). Mean VAS score in Group A was at 330 min was 3.1±0.39 and 3.15±0.94 at 210 min in group B.

Conclusion: Low dose infusion of dexmedetomidine provides more hemodynamic stability. Requirement of induction agent was decreased more in group A than group B. Postoperative analgesia more in group A.

Key words

Laparoscopy cholecystectomy, Dexmedetomidine, General anesthesia.

Introduction

Laparoscopy cholecystectomy (LC) requires small limited incisions, very short hospital stay, faster recovery times; health care costs are reduced as length of hospital stay is decreased with laparoscopic assisted surgery [1].

LC is also associated with stress response induced by surgery; laryngoscopy, tracheal intubation and extubation involve sympathetic stimulation. The pneumoperitoneum (PP) and CO_2 insufflation, required in laparoscopic surgeries, lead to increase in plasma nor-epinephrine, epinephrine levels and plasma renin activity [3]. All these changes lead to increase in heart rate, blood pressure, systemic and pulmonary vascular resistance, and increased cardiac output.

I.V. dexmedetomidine in the preoperative period has been found to decrease serum catecholamine levels by 90% [2], to blunt the hemodynamic response to laryngoscopy, tracheal intubation, PP and extubation [3], to provide sedation without respiratory depression [4] and to decrease post-operative analgesic requirements [5].

So, we designed this study to compare the effect of conventional dose with low dose infusion of dexmedetomidine on hemodynamic stress response, induction agent requirement and postoperative analgesia.

Materials and methods

This study was performed in the Department of Anesthesia, Sardar Patel Medical College and A.G. PBM Hospital after approval by the Institute Ethics Committee. After written informed consent, 100 patients of ASA grade 1 and 11 aged 18-65 of either sex were taken for this controlled randomised prospective study.

Pre-anesthetic check-up was carried out the day before surgery. The procedure of general anesthesia was explained to each patient and a written informed consent was taken from the patient and his relatives in the presence of independent witness. All patients were kept nil by mouth on the night before the surgery.

After noting baseline values of vitals (SBP, DBP, MBP, PR, SPO2), Pre calculated dose of test drug was given to patient intravenously in both groups, 15 min before surgery (In group A loading dose of 1µg/kg and in group B 0.5µg/kg/h till end of surgery by infusion pump). Then again vitals were noted after 15 min of infusion in both groups.

All patients were given Inj. glycopyrrolate 0.2 mg I.V. and Inj. Fentanyl 1µg/kg I.V. as

premedication and preoxygenated with 100% O_2 via face mask with bains circuit. Induction of anesthesia was carried out with Inj propofol I.V till loss of consciousness and Inj. succinylcholine 2mg/kg I.V was given to every patient and appropriate size endotracheal tube placement was done. In group A I.V. infusion of Dexmedetomidine 0.5µg/kg/h was started and continued till end of surgery. Maintenance of anaesthesia was done with inhalational agent sevoflurane, O_2 and inj vecuronium I.V. Vitals were noted after 1 min, 2 min, 3 min of intubation, after creating pneumoperitoneum then at every 15 minutes interval after pneumoperitoneum, at release of pneumoperitoneum and after extubation. Reversal was done with Inj. glycopyrrolate 0.005 mg/kg I.V. and inj neostigmine 0.05mg/kg I.V. Patients were observed for postoperative analgesic requirement and any complication e.g. hypotension, bradycardia, nausea, vomiting. In postoperative period patients were monitored for analgesic requirement, (VAS ≥3) was taken as significant for giving analgesia.

Statical analysis

All the data obtained were analysed using the student T test & SPSS version 10 software used.

In both group female outnumbered males where male to female ratio was 1:9 in both group A and group B.

Results

Patient's characteristics data are present in **Table - 1**. Both groups were comparable with respect to age weight and sex. Female predominance (9:1) was seen in both groups.

Table – 1: Characteristic data of patients.

Characteristics	Group A	Group B
Number	50	50
Gender Ratio M/F	5/45	45/5
Age*	46.62	38.24
Weight*	59.73	58.53

*= Mean

There was highly significant difference in pulse rate between group A and group B at different times intervals ($p<0.001$), especially at 15 min after infusion in group A where decrease in pulse rate was very significant (**Table – 2**).

There was significant difference in M.A.P. in group A and group B ($p <0.005$), especially 15 min after initial infusion where decrease in M.A.P was highly significant in group A (**Table – 3**).

Table – 2: Statistical analysis of Mean Pulse Rate at different time intervals in both groups.

Time Interval	Group A		Group B		T	P
	Mean	SD	Mean	SD		
Base Line	92.80	6.53	91.90	7.63	0.633	0.528
15 Min After Infusion	70.84	5.57	81.82	7.72	8.154	<0.001
1 Min after intubation	74.58	5.74	89.48	7.46	11.189	<0.001
2 Min after intubation	75.18	5.08	88.68	6.64	11.409	<0.001
3 Min after intubation	75.38	4.91	88.04	6.32	11.183	<0.001
1 Min after Creating PP	75.48	5.76	91.34	5.10	14.568	<0.001
15 Min after Creating PP	77.88	6.02	91.28	4.57	12.527	<0.001
30 Min after Creating PP	80.44	5.33	90.10	5.92	8.578	<0.001
45 Min after Creating PP	79.89	5.40	89.90	5.87	8.765	<0.001
60 Min after Creating PP	82.00	0.00	95.67	5.51	2.149	0.165
After Release of PP	75.82	5.64	88.66	6.87	10.208	<0.001
After Extubation	81.60	4.76	95.32	5.67	13.092	<0.001

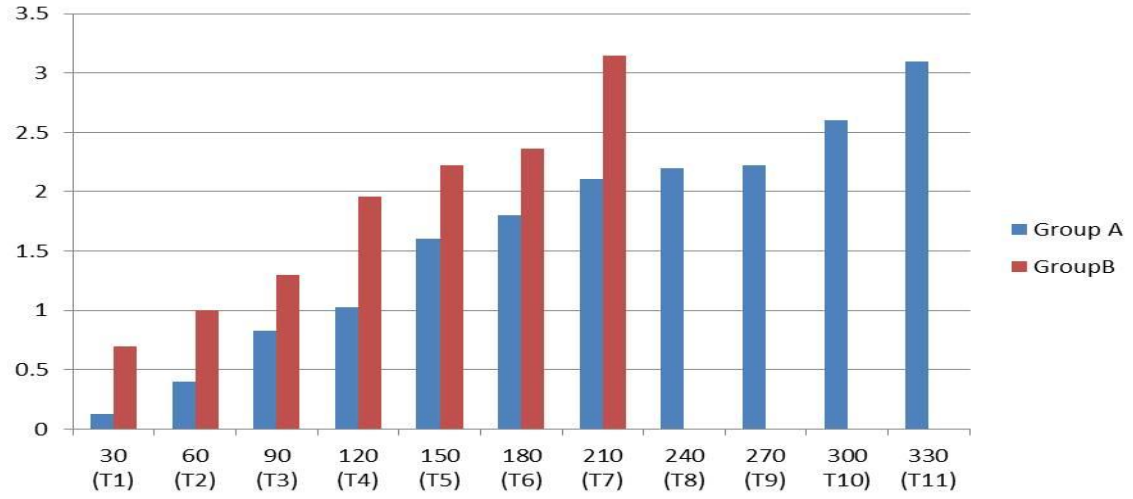
Table – 3: Statistical analysis of Mean Arterial Pressure at different time intervals in both groups.

Time Interval	Group A		Group B		t	P
	Mean	SD	Mean	SD		
Base Line	100.34	5.15	97.56	7.45	2.168	0.033
15 Min After Infusion	80.88	4.93	86.48	6.52	4.839	<0.001
1 Min after intubation	83.90	4.06	89.68	7.65	4.715	<0.001
2 Min after intubation	83.74	3.92	88.54	7.23	4.125	<0.001
3 Min after intubation	83.52	4.30	87.56	7.17	3.414	0.001
1 Min after Creating PP	81.60	6.19	89.54	7.71	5.676	<0.001
15 Min after Creating PP	83.40	5.42	89.66	7.40	4.823	<0.001
30 Min after Creating PP	84.60	5.21	90.24	7.01	4.550	<0.001
45 Min after Creating PP	83.67	13.28	90.32	7.08	3.115	0.002
60 Min after Creating PP	92.00	0.00	92.33	11.93	0.024	0.983
After Release of PP	80.54	4.37	88.40	7.41	6.459	<0.001
After Extubation	86.20	4.40	95.00	7.28	7.304	<0.001

Table – 4: Distribution of cases according to requirement of induction agent in both groups.

Requirement of Induction Agent (mg)	Group A		Group B		Total	
	No.	%	No.	%	No.	%
50	2	4.0	0	-	2	2.0
60	34	68.0	0	-	34	34.0
70	14	28.0	11	22.0	25	25.0
80	0	-	16	32.0	16	16.0
90	0	-	23	46.0	23	23.0
Total	50	100	50	100	100	100
Mean	62.40		82.40			
SD	5.17		7.96			
T	14.884					
P	<0.001					

Figure – 1: Postoperative Mean VAS Score.



Requirement of induction agent was comparatively more in group B than group A, although it decreased in both groups when compared to standard dose (p value<0.001) (**Table – 4**).

Mean VAS score was 3.1± 0.39 in Group A at 330 min while VAS score in group B was 3.15±0.94 at 210 min. Which was highly significant (p value <0.005) (**Figure – 1**).

In group A 5 patients had hypotension +bradycardia while all other patients in group A as well as group B had no complications (p Value<0.01)

Discussion

Laparoscopic cholecystectomy is one of the most commonly practiced surgeries for gall bladder diseases in the present era.

The major sedative and antinociceptive effects of Dexmedetomidine are attributable to its agonism of the Alpha-2 adrenergic receptors located in the locus coeruleus.

In general, presynaptic activation of the Alpha-2 receptor inhibits the release of norepinephrine, terminating the propagation of pain signals and inhibits sympathetic activity and thus can cause decrease in blood pressure and heart rate.

These effects produce analgesia, sedation and anxiolysis. Dexmedetomidine combines all these effects, thus avoiding some of the side effects of the multi-agent therapies.

Low dose dexmedetomidine infusion,blunt the haemodynamic response to critical incidences such as laryngoscopy, endotracheal intubation, creation of pneumoperitoneum and extubation in patients undergoing laparoscopic cholecystectomy and on extubation time, sedation levels, post-operative analgesia requirements and occurrence of adverse effects.

Mane, et al. [6] concluded that low dose dexmedetomidine infusion in the dose of 0.4µg/kg/h effectively attenuates haemodynamic stress response during laparoscopic surgery with reduction in post-operative analgesic requirements.

Preoperative infusion of conventional dose of dexmedetomidine is effective in attenuating sympathoadrenal responses to tracheal intubation. It has significant anaesthetic and opioid sparing effect.
Vora, et al. [7] concluded that dexmedetomidine (conventional dose) as an adjuvant in general anaesthesia for laparoscopic surgeries provided a stable hemodynamic profile in the perioperative period and effectively blunted pressor response to intubation and extubation, leading to minimal requirements for additional analgesics and potent inhalational agents. There were less adverse events.

Ickeringil, et al. [8] Dexmedetomidine was an effective sedative and analgesic in complex surgical and trauma patients with pronounced benefits in cardiac surgery groups. Omitting of loading dose avoided undesirable haemodynamic effects without compromising sedation and analgesia.

Yildiz, et al. [9] preoperatively administration of single dose of dexmedetomidine resulted in progressive increase in sedation, blunted haemodynamic responses to laryngoscopy and reduced opioids and anaesthetics requirements. Furthermore, dexmedetomidine decreased blood pressure and heart rate.

Tufanogullari, et al. [10] observed that dexmedetomidine infusion rate of .2 microgram/kg/hr is recommended to minimize the risk of adverse cardiovascular side effects.

Ickeringill, et al. [11] omitting the loading dose avoids undesirable haemodynamic effects without compromising sedation and analgesia.

Sen, et al. [12] concluded that administration of dexmedetomidine significantly reduces the requirements of propofol while maintaining desired depth of anaesthesia without any significant complication.

Khanduja, et al. [13] concluded that infusion of dexmedetomidine during laparoscopic cholecystectomy decrease requirement of thiopentone and pentazocine and early recovery of patients

Vora, et al. [14] concluded that dexmedetomidine as an adjuvant in general anaesthesia for laparoscopic surgeries provide a stable haemodynamic profile in perioperative period and effectively blunted pressure responses to laryngoscopy, intubation, pneumoperitonium and extubation, leading to minimum requirement for additional analgesics.

Yildz, et al. [9] concluded preoperative administration of single dose of dexmedetomidine, blunted the haemodynamic responses during laryngoscopy and reduced dose of opioids and anaesthethics requirements and dexmedetomidine decreased blood pressure and heart rate.

Jalonen, et al. [15] concluded that pre-treatment with dexmedetomidine attenuates haemodynamic response to tracheal intubation decrease plasma catecholamines concentration during anaesthesia, decrease perioperative requirement of inhaled anaesthetics and opiods and increase the likelihood of hypotension

Our results consistent with most of the trail performed [6, 7, 8, 9, 11, 14, 16].

Conclusion

We concluded that low dose infusion of dexmedetomidine keeps patients more hemodynamically stable by avoiding complications like hypotension and bradycardia. Requirement of induction agent was also decreased as compared to standard doses in both groups but requirement of induction agents was significantly lesser in group A. Patients were pain free in both groups at extubation, but group A seemed to be better as far as post-operative analgesia was concerned.

Limitation

As our study was in small group of patients (100) further studies are required for establishment of low dose infusion of dexmedetomidine as routine infusion in patients undergoing laparoscopy cholecystectomy under General anaesthesia.

References

1. Black TE. Anaesthesia for Laparoscopic assisted surgery. In: Wylie Churchill-Davidson's A Practice of Anaesthesia; Healy TEJ, Knight PR (eds). 7th edition, 2003, p. 1391-1396
2. Aho M, Lehtinen AM, Erkola O, Kallio A, Korttila K. The effect of intravenously administered dexmedetomidine on perioperative hemodynamics and isoflurane requirements in patients undergoing hysterectomy. Anesthesiology, 1991; 74: 997-1001.
3. Isik B, Arslan M, Özsoylar O, Akçabay M. The effects of α2:α1 adrenergic receptor agonist dexmedetomidine on hemodynamic response in direct laryngoscopy. Open Otorhinolaryngol J., 2007; 1: 5-11.
4. Khan ZP, Munday IT, Jones RM, Thrnton C, Mant TG, Amin D. effect of dexmedetomidine on isoflurane requirements in healthy volunteers 1: Pharmacodynamic and pharmacokinetic interactions. Br J Anaesth., 1999; 83: 372-80.
5. Gurbet A, Basagan-Mogol E, Turker G, Ugun F, Kaya FN, Ozcan B. Intraoperative infusion of dexmedetomidine reduces perioperative analgesic requirements. Can J Anaesth., 2006; 53: 646-52.

6. Manne GR, Upadhyay MR, Swadia V. Effects of low dose dexmedetomidine infusion on haemodynamic stress response, sedation and post-operative analgesia requirement in patients undergoing laparoscopic cholecystectomy. Indian J Anaesth., 2014; 58(6): 726-31.
7. Vora KS, Baranda U, Shah VR, Modi M, Parikh GP, Butala BP. The effects of dexmedetomidine on attenuation of hemodynamic changes and there effects as adjuvant in anaesthesia during laparoscopic surgeries. Saudi J Anaesth., 2015; 9(4): 386-92.
8. Ickeringill M, Shehabi Y, Adamson H, Ruettimann U. Dexmedetomidine infusion without loading dose in surgical patients requiring mechanical ventilation: haemodynamic effects and efficacy. Anaesth Intensive Care, 2004; 32(6): 741-5.
9. Yildiz M, Tavlan A, Tuncer S, Reisli R, Yosunkaya A, Otelcioglu S. Effect of dexmedetomidine on haemodynamic responses to laryngoscopy and intubation : perioperative haemodynamics and anaesthetic requirements. Drugs R D., 2006; 7(1): 43-52.
10. Tufanogullari B, White PF, Peixoto MP, Kianpour D, Lacour T, Griffin J, et al. Dexmedetomidine infusion during laparoscopic bariatric surgery: the effect on recovery outcome variables. Anesth Analg., 2008; 106: 1741-8.
11. Ickeringill M, Shehabi Y, Adamson H, Ruettimann U. Dexmedetomidine infusion without loading dose in surgical patients requiring mechanical ventilation: haemodynamic effects and efficacy. Anaesth Intensive Care, 2004; 32(6): 741-5.
12. Sen S, Chakraborty J, Santra S, Mukherjee P, Das B. The effect of dexmedetomidine infusion on propofol requirement for maintenance of optimum depth of anaesthesia during elective spine surgery. Indian J Anaesth., 2013; 57(4): 358-63.
13. Khanduja S, Ohri A, Panwar M. Dexmedetomidine decreases requirement of thiopentone sodium and pentazocine followed with improved recovery in patients undergoing laparoscopic cholecystectomy. J Anaesthesiol Clin Pharmacol., 2014; 30(2): 208-12.
14. Vora KS, Baranda U, Shah VR, Modi M, Parikh GP, Butala BP. The effects of dexmedetomidine on attenuation of hemodynamic changes and there effects as adjuvant in anaesthesia during laparoscopic surgeries. Saudi J Anaesth., 2015; 9(4): 386-92.
15. Jalonen J, Hynynen M, Kuitunen A, Heikkilä H, Perttilä J, et al. Dexmedetomidine as an anesthetic adjunct in coronary artery bypass grafting. Anesthesiology, 1997; 86(2): 331-45.