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Comparison of Conventional Dose *versus* Low-dose Infusion of Dexmedetomidine on Hemodynamic Stress Response: A Prospective Institutional Based Study

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Abstract

Background: Laparoscopic cholecystectomy is one of the most common practiced surgeries for gall bladder disease. Dexmedetomidine is a α2 agonist with sedative, sympatholytic and analgesic properties and hence, it can be a very useful adjuvant in anaesthesia as stress response buster, sedative and analgesic. *Materials and Methods:* The present study was conducted on 90 patients with American Society of Anesthesiologists physical status I to III scheduled for laparoscopic cholecystectomy of both genders. Patients were divided into 3 Group. Group I (Control) patients received normal saline 0.9% infusion, Group II patients received dexmedetomidine infusion 1 mcg/kg/h and Group III patients received dexmedetomidine infusion 0.4 mcg/kg/h. parameters such as duration of anesthesia, duration of surgery, change in heart rate, MAP etc. was compared in both groups. *Results:* ASA I was 25 in Group I, 26 in Group II and 23 in Group III, ASA Grade II was 5 in Group I, 4 in Group II and 7 in Group III. The difference was nonsignificant ($p > 0.05$). Mean duration of anesthesia in Group I was 92.1 minute, in Group II was 98.4 minutes and in Group III was 85.2 minutes, mean duration of surgery in Group I was 77.4 minutes, in Group II was 92.3 minutes and in Group III was 75.1 minutes. The difference was nonsignificant ($p > 0.05$). The mean PR (beats/min) before starting in Group I was 88.3, in Group II was 91.4 and in Group III was 90.3. After 15 minutes was 87.2 in Group I, 82.3 in Group II and 80.4 in Group III. 1 minute after induction was 87.3, 82.5 and 80.6 in groups. MAP before staring was 99.3 mm Hg, 99.2 and 101.4 mm Hg in all groups, after 15 minutes was 98.4, 95.2 and 98.9 in all groups, 1 minute after induction was 98.2, 89.5 and 89.9 in all groups respectively. The difference was nonsignificant ($p > 0.05$). *Conclusion:* Low dose dexmedetomidine infusion in the dose of 0.4 mcg/kg/h effectively attenuates haemodynamic stress response without any adverse events.

Keywords: Dexmedetomidine; Stress Response; Laparoscopic Cholecystectomy.

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Introduction

Laparoscopic cholecystectomy (LC) is most commonly performed procedure for gall bladder disease, it requires small limited incisions, very short hospital stay, faster recovery times; less health care costs which further reduces the hospital stay.1 LC is also associated with stress response induced by surgery; laryngoscopy, tracheal intubation and extubation involve sympathetic stimulation. The

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pneumoperitoneum (PP) and CO_2 insufflation, required in laparoscopic surgeries, lead to increase in plasma nor- epinephrine, epinephrine levels and plasma renin activity.[2] All these changes lead to increase in heart rate, blood pressure, systemic and pulmonary vascular resistance.[1]

Many drugs, namely, alpha-2 adrenergic receptors agonists, high-doses of opioids, and β-blockers have been tried in the past to decrease stress responses during laparoscopic surgery. By reducing the sympathoadrenal and cardiovascular responses caused by noxious surgical stimuli, the alpha-2 agonists inhibit the stress responses mediated by the sympathetic nervous system. Alpha-2 adrenoceptors› activation results in sympatholysis, inhibition of renin release, and decrease in insulin release from the pancreas.[3]

Dexmedetomidine, introduced in 1999 for human use, is a selective α_2 agonist with 8 times more affinity for α_2 adrenergic receptors compared to clonidine and possesses all the properties of α_2 agonist without respiratory depression.[3] Intravenous use of dexmedetomidine in the perioperative period had been found to decrease serum catecholamine levels by 90%, to blunt the hemodynamic response to laryngoscopy, tracheal intubation, pneumoperitoneum and extubation, to provide sedation without respiratory depression and to decrease postoperative analgesic requirements. Dexmedetomidine is a selective and potent α_2-adrenergic agonist. The α_2/α_1 selectivity of dexmedetomidine is 1600 times higher than that of clonidine.[4]

The present study was conducted to compare conventional dose *versus* low-dose infusion of dexmedetomidine on hemodynamic stress response.

Materials and Methods

The present study was conducted in the department of General Surgery and Anesthesiology, Indira Gandhi Madical College and Hospital. Shimla, HP. It comprized of 90 patients with American Society of Anesthesiologists physical status I to III scheduled for laparoscopic cholecystectomy of both genders. All patients were informed regarding the study and written consent was obtained.

Patient information such as name, age, gender etc. was recorded. Patients were divided into 3 group. Group I (Control) patients received normal saline 0.9% infusion, Group II patients received dexmedetomidine infusion 1 mcg/kg/h and Group III patients received dexmedetomidine infusion 0.4 mcg/kg/h. parameters such as duration of anesthesia, duration of surgery, change in heart rate, MAP etc. was compared among the groups. Results thus obtained were subjected to statistical analysis. p - value less than 0.05 was considered significant.

Results

Table 1 shows, that Group I (Control) patients received normal saline 0.9% infusion, Group II patients received dexmedetomidine infusion 1 mcg/kg/h and Group III patients received dexmedetomidine infusion 0.4 mcg/kg/h.

Table 1: Distribution of patients

Groups	Group I	Group II	Group III
Agent	Normal saline 0.9%	Dexmedetomidine infusion 1 mcg/kg/h	Dexmedetomidine infusion 0.4 mcg/kg/h
Number	30	30	30

Table 2 shows, that ASA I was 25 in Group I, 26 in Group II and 23 in Group III, ASA Grade II was 5 in Group I, 4 in Group II and 7 in Group III. The difference was nonsignificant ($p > 0.05$). Mean duration of anesthesia in Group I was 92.1 minute, in Group II was 98.4 minutes and in Group III was 85.2 minutes, mean duration of

Table 2: Comparison of parameters

Parameters	Group I	Group II	Group III	*p* - value
ASA I	25.0	26.0	23	0.12
ASA II	5.0	4.0	7.0	0.06
Duration of anes (min)	92.1	98.4	85.2	0.09
Duration of surg (min)	77.4	92.3	75.1	0.08

surgery in Group I was 77.4 minutes, in Group II was 92.3 minutes and in Group III was 75.1 minutes. The difference was nonsignificant ($p > 0.05$).

Table 3 and Fig. 1 shows, that mean PA (beats/min) before starting in Group I was 88.3, in Group II was 91.4 and in Group III was 90.3. After 15 minutes was 87.2 in Group I, 82.3 in Group II and 80.4 in Group III. 1 minute after induction was 87.3, 82.5 and 80.6 in Groups. MAP before staring was 99.3 mm Hg, 99.2 and 101.4 mm Hg in all groups, after 15 minutes was 98.4, 95.2 and 98.9 in all groups, 1 minute after induction was 98.2, 89.5 and 89.9 in all groups respectively. The difference was nonsignificant ($p > 0.05$).

Table 3: Changes in PR and MAP in groups

Parameters	Group I	Group II	Group III	*p* - value
PR before starting	88.3±3.56	91.4±4.32	90.3±5.32	0.1
After 15 minutes	87.2±2.34	82.3±3.42	80.4±4.68	0.71
1 minute after induction	87.3±3.45	82.5±4.98	80.6±2.43	0.62
10 minutes after insufflation	85.54±2.53	85.0±4.65	79.01±4.67	0.76
30 minutes after insufflation	89.02±4.32	86.05±9.34	85.87±4.89	0.43
5 minutes after desufflation	80.35±4.34	76.23±4.56	75.34±4.89	0.67
MAP before starting	99.3±6.54	99.2±4.78	101.4±9.54	0.14
After 15 minutes	98.4±3.56	95.2±6.54	98.9±7.3	0.87
1 minute after induction	98.2±8.54	89.5±8.54	89.9±3.2	0.58
10 minutes after insufflation	100.1±5.56	92.43±4.34	88.43±3.56	0.36
30 minutes after insufflation	90.34±6.78	96.87±6.45	93.87±3.23	0.37
5 minutes after desufflation	85.43±4.32	82.98±5.45	79.45±7.34	0.56

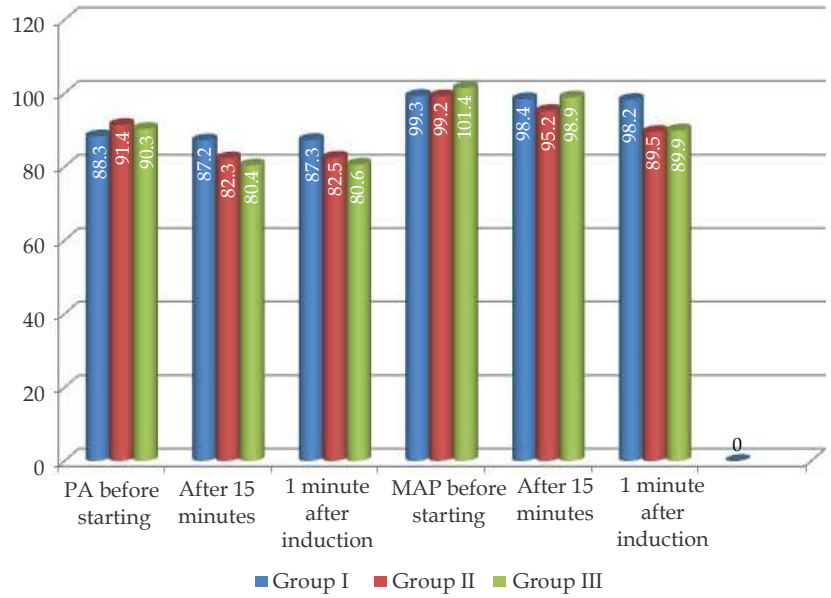

Fig 1: Changes in PR and MAP in groups

Discussion

There has been limited research on evaluating the stress responses during laparoscopic cholecystectomy. There have been evidences that prolonged laparoscopic procedures have been found to be associated with increased stress responses. Dexmedetomidine decreases renin release thereby imparting hemodynamic stability. Cortisol levels have been shown to be decreased by dexmedetomidine.[5]

Perioperative period is a stressful period, and dexmedetomidine is a useful drug to decrease stress responses.[6] Dexmedetomidine has been used by previous researchers as loading dose of 1 mcg/kg over 10 min, followed by maintenance infusion at 0.2–0.7 mcg/kg/h. Our study involves the use of dexmedetomidine in two different doses among

two groups - 1 mcg/kg over 10 min, followed by maintenance infusion at 1 mcg/kg/h or other one being 1 mcg/kg as loading dose followed by maintenance infusion of 0.4 mcg/kg/h. Renal functions in the form of serum creatinine, BUN, and urine output were within normal range in our set of patients.[7] Metabolites of dexmedetomidine biotransformation are excreted in the urine (about 95%). The pharmacokinetics of dexmedetomidine in participants with severe renal impairment (creatinine clearance < 30 ml/min) is not altered relative to healthy controls. Intraoperative use of dexmedetomidine infusion has showed insignificant difference with renal functions on percutaneous nephrolithotomy.[8] The present study was conducted to compare conventional dose *versus* low-dose infusion of dexmedetomidine on hemodynamic stress response.

However, with higher dose infusion of dexmedetomidine, high incidence of adverse cardiac effects have been observed.[9] A biphasic response on blood pressure occurs with a bolus dose.[10] Initially, there occurs hypertension followed by fall in blood pressure. This response is seen often more in young and healthy patients.[9] Stimulation of α2 B receptors in vascular smooth muscles is said to be responsible for this. Low dose infusion of 0.25-0.5 mcg/kg/h results in a monophasic response of 10-15% fall in mean arterial blood pressure and PR.[10] Apart from providing stress response attenuation, the added effects of dexmedetomidine are sedation and analgesia. Sedation produced by α2 agonists is unique in the sense that the patients can be easily aroused to co-operate during procedures and also respond to the verbal commands and then can return to sleep like state when not stimulated.[9]

Manne et al.[11] found that in group NS significant haemodynamic stress response was seen following laryngoscopy, tracheal intubation, creation of pneumoperitoneum and extubation. In dexmedetomidine groups, the haemodynamic response was significantly attenuated. The results, however, were statistically better in Dex 0.4 group compared with Dex 0.2 group. Post-operative 24 hour analgesic requirements were much less in dexmedetomidine groups. No significant side effects were noted.

Conclusion

Low dose dexmedetomidine infusion in the dose of 0.4 mcg/kg/h effectively attenuates haemodynamic stress response without any adverse events.

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