International Journal of Medical and Health Research
ISSN: 2454-9142
Impact Factor: RJIF 5.54
www.medicalsciencejournal.com
Volume 4; Issue 9; September 2018; Page No. 178-181

Intravenous administration of dexmedetomidine in patients undergoing laparoscopic surgery under general anaesthesia

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Abstract
This study was carried out in Department of Anaesthesiology, Krishna institute of Medical sciences, Karad during a period of 2011-2013. All patients received premedication in form of inj. glycopyrrolate & Inj fentanyl IV; Inj ranitidine & Inj ondansetron IV. General anaesthesia was given in conventional manner using inj. thiopentone sodium, Inj succinylcholine, O2 + N2O, Inj Vecuronium. The patients of group Dex had optimum sedation as assessed by Ramsay Sedation Score, the mean score being around 3(patient sleepy but responds to verbal commands), unlike those of group NS who had scores around 1(anxious, agitated or restless or both). The incidence of intraoperative & postoperative complications in patients of our study. Hypotension, tachycardia & hypertension in 1, 1 & 2 patients of group Dex respectively. In group DEX bradycardia occurred in 1 patient. Dryness of mouth was seen in one patient of each of two Groups.

Keywords: pneumoperitoneum, dexmedetomidine, laryngoscopy, anaesthesia, laparoscopic surgery, DEX bradycardia

1. Introduction
Minimal access surgery (laparoscopic surgery) has been proved to be a successful surgical technique with added advantage in day care surgery. Anaesthetic maneuvers like direct laryngoscopy, tracheal intubation and even extubation involve severe sympathetic stimulation leading to increase in serum catecholamine and norepinephrine levels. Moreover, the reverse trendelenburg position and pneumoperitoneum associated with laparoscopic surgery further make the problem accentuated. Pneumoperitoneum is produced by administration of carbon dioxide in to peritoneal cavity. Pneumoperitoneum and carbon dioxide, both, cause adverse cardiovascular effects [1]. Immediately after neither pneumoperitoneum plasma levels of nor epinephrine, epinephrine and plasma renin activity increases [2]. Dexmedetomidine is being considered as an adjunctive agent for intraoperative use since it blunts the stress response to surgery via sympatholysis, decreases opioid consumption, causes sedation and does not produce respiratory depression [3].

Aims and Objectives
To study the effect of intravenous infusion of dexmedetomidine in patients undergoing laparoscopic surgery under general anaesthesia. To study the effect of dexmedetomidine on hemodynamic parameters during perioperative period in patients undergoing laparoscopic surgery. To study the postoperative sedation score and analgesic requirement in patients receiving dexmedetomidine.

Review of Literature
Laparoscopic surgery is associated with haemodynamic stress induced by surgery and anaesthesia, the two leading to an endocrine response starting adrenaline and noradrenaline secretion by the stimulation of sympathetic nervous system [4]. Pneumoperitoneum is produced by administration of carbon dioxide in to peritoneal cavity. Pneumoperitoneum and carbon dioxide, both, cause adverse cardiovascular effects [1]. Immediately after pneumoperitoneum plasma levels of nor epinephrine, epinephrine and plasma renin activity increases [2]. Among the α2 agonist, two drugs have been commonly used, these being Clonidine and Dexmedetomidine [5]. Dexmedetomidine first administered epidurally in 1997, combined with 1.5% lignocaine for patients undergoing hysterectomy. Dexmedetomidine was used for the first time in spinal anaesthesia in 2006, combined with 0.5% bupivacaine for patients undergoing urological procedures.
Dexmedetomidine minimally affects the cortical evoked potential amplitudes and latencies during neurophysiological monitoring and abalates memory in a dose dependent manner [6]. The incidence of Hypotension, profound bradycardia and occasionally sinus arrest/pause can be minimized by omitting the loading dose or not giving more than 0.4μg/kg. Giving the loading dose over 10-15 minutes also minimizes the initial transient hypertensive response64. Most episodes of bradycardia resolve spontaneously or are readily treated with anticholinergic without adverse outcome [7, 8]. Studies have demonstrated a beneficial effect of Dexmedetomidine on the ischaemic myocardium by decreasing the O2 consumption and producing a favourable redistribution of coronary blood flow from the non ischaemic to the ischaemic myocardium [9].
Dhuroji Prasad Bhattacharjee, *et all* in 2010 [10] did a randomized double blind prospective clinical study conducted on 60 patients, the maintainance of perioperative hemodynamic stability by dexmedetomidine intravenous infusion was studied in patients undergoing laparoscopic

cholecystectomy. Burcu Tufanogullari *et al*l in 2008 [11] found that as an adjunct dexmedetomidine infusion (all three dex groups) decreased fentanyl use, antiemetic therapy, & length of stay in PACU, but requirement of PCA Morphine on post of Day 1 & 2 was not different. It was concluded that 0.2mcg/kg/hr dose is recommended for early postoperative recovery while minimizing cardiovascular side effects. Bhakhamees HS *et al* in 2007 [12] carried out with 40 patients received normal saline & 40 patients received dexmedetomidine infusion 0.8mcg/kg bolus followed by 0.4mcg/kg/hr. Dexmedetomidine group showed significant decrease in intra & postoperative MAP, HR, postoperative PCA score & morphine use, total requirement of propofol & fentanyl with better recovery score. No difference in PONV incidence was noted between both groups. Martina *et al* in 1999 [13] studied the effects of two doses of dexmedetomidine (0.3 or 0.6 mcg/kg), fentanyl 2mcg/kg or saline as a single intravenous bolus administered 10 mins prior to induction of anaesthesia were assessed in 96 women undergoing abdominal hysterectomy. single iv bolus dose of dex0.6mcg/kg before induction of anaesthesia reduced increase in HR than saline group (p=<0.01) in response to tracheal intubation, & decreased isoflurane requirements. In patients receiving 0.3mcg/kg, the increase in HR & BP did not differ from that of saline group.

Material and Methods

The prospective study was carried out with 40 patients in Department of Anaesthesiology, Krishna institute of medical sciences, Karad during a period of 2011-2013. The study was conducted after approval from the ethical committee and with the informed consent given by the patient.

All the patients underwent a pre-anaesthetic evaluation which consisted of detailed history regarding present complaints, past medical history, physical examination and routine investigations including complete haemogram, urine examination, blood urea, serum creatinine, random blood sugar, X-ray chest PA view and electrocardiogram. All the patients were kept nil by mouth from 10 p.m. a day before surgery. Tab. Diazepam 10 mg was given orally to provide a nice sleep on the previous night of operation.

Observations and Results

The subjects were divided into two groups according to the randomization number used by chief resident which was decoded during the time of analysis of the data as, GROUP ns and group DEX

Group NS: Patients received Inj. Normal Saline infusion IV started 10 min. before the induction of anaesthesia till the end of the surgery.

Group DEX: Patients received Inj. Dexmedetomidine 1mcg/kg/hr IV infusion as a loading dose started 10 min. before induction and later with maintenance dose of 0.5mcg/kg dexmedetomidine given till the end of surgery.

Table 1: Demographic Data

	Group NS (n=20)	Group DEX (n=20)	T value	Inter group p value
Age in years (mean ±SD & range)	31.3±11.04 (19-63)	33±8.92 (18-48)	t value 0.5357	>0.05
Gender : Male Female	07 (35%) 13 (65%)	06 (30%) 14 (70%)	X^2 value 0.1140	>0.05
Weight in kg (mean ±SD & range)	61.1±9.08 (45-78)	62.9±7.70 (48-75)	t value 0.6762	>0.05
ASA:12	18 (90%) 02 (10%)	16 (80%) 04 (20%)	X^2 value 0.1961	>0.05

As shown in the table no. 1, the mean age of patients in Group NS was 31.3±11.04 years and in group Dex it was 33±8.92. The minimum age was 19 years and maximum age was & 63 yrs. Mean weight in case of group NS was 61.01±9.08 kg and in case of group Dex it was 62.9±7.06 kg. The minimum weight was 45 kg and maximum weight was 78 kg. In group NS 7 patients were male and 13 were females compared to 6 males and 14 females in group Dex. In group NS 18 patients were of ASA grade I and 2 patients was of grade II in comparison to 16 patients of ASA grade I and 4 patients of ASA grade II in group Dex. All the two groups were comparable to each other with respect to age, sex, weight, ASA grade.

Table 2: Comparison of Mean Pulse Rate BPM (Mean±SD)

Time		Group NS	Group Dex	t value	Intergroup p value
Before IV infusion		84.7±12.4	87.5±9.69	0.7957	>0.05
10 min After starting infusion		80.6±10.4	72.9±7.7	2.661	<0.05*
After Induction		77.7±8.5	70.2±7.8	2.9.7	<0.001**
After laryngoscopy & Intubation	1 min	92.6±8.8	75.6±6.5	6.949	<0.001**
	3 min	91.9±6.5	68.4±3.8	13.95	<0.001**
	5 min	88.7±2.8	70.3±6.1	12.26	<0.001**
After Pneumoperitoneum	1 min	86.8±4.7	66.3±7.8	10.06	<0.001**
	15 min	84.3±7.3	65.5±4.9	9.563	<0.001**
	30 min	83.8±8.8	67.1±8.5	6.104	<0.001**
	45 min	81.2±6.7	68.4±8.7	5.213	<0.001**
	60 min	81.4±8.2	69.8±5.2	5.343	<0.001**
After extubation	1 min	90.6±6.2	74.7±5.6	8.511	<0.001**
	15 min	84±5.0	75.1±4.3	0.2713	>0.05
	30 min	81±4.2	74±3.8	5.527	<0.001**
	45 min	81±6.5	75.2±4.9	3.187	<0.01*
	60 min	77.6±6.0	75.3±5.7	1.386	>0.05

This table no. 2 shows changes in mean pulse rate. The mean pulse rate before starting the infusion was comparable in both the two groups. After starting the infusion, the mean pulse rate in group NS did not show any significant change till laryngoscopy and intubation. The pulse rate increased highly significantly after laryngoscopy & intubation, and also highly significantly after creation of pneumoperitoneum and extubation. The values came down to near pre infusion level by 60 min. after extubation. In group Dex there was a highly significant decrease in pulse rate following the drug infusion. Even after laryngoscopy & intubation and also after creation of pneumoperitoneum there was highly significant difference in dex group compared to NS group. Immediately after extubation there was highly significant difference and later was significant. There was no difference in both the groups after 60 minutes of extubation.

Table 3: Comparison of Mean Systolic Blood Pressure Mm Hg (Mean ± SD)

Time		Group NS	Group DEX	T value	Inter-group p value
Before IV infusion		125.5±7.9	120.7±27.3	0.755	>0.05
10 min After starting infusion		123±6.6	118±6.7	2.378	<0.05*
After Induction		119±6.5	112.1±9.4	2.700	<0.05*
After laryngoscopy & Intubation	1 min	138.7±4.2	116.1±11.6	8.192	<0.001**
	3 min	133.2±7.5	116.1±6.4	4.591	<0.001**
	5 min	131.7±4.3	112.5±11.2	4.528	<0.001**
After Pneumoperitoneum	1 min	128.9±6.4	116.3±10.0	4.068	<0.001**
	15 min	127.1±9.9	115.6±10.4	3.582	<0.001**
	30 min	124±8.2	115.1±10.6	2.970	<0.05*
	45 min	123.8±5.4	118±9.7	2.336	<0.05*
	60 min	124.1±5.3	119.6±13.2	1.415	>0.05
After extubation	1 min	133.8±5.2	123.4±9.4	4.330	<0.001**
	15 min	129.6±1.2	123.9±8.8	2.870	<0.05*
	30 min	127.8±2.9	120.4±7.5	4.116	<0.001**
	45 min	123.8±6.2	121.7±7.6	0.9575	>0.05
	60 min	121.2±6.8	114.9±24.4	1.112	>0.05

This table no. 3 shows the changes in mean systolic blood pressure. The values for mean systolic blood pressure before starting the infusion were comparable in both the two groups. After starting saline infusion the mean systolic blood pressure in group NS did not show any significant change till laryngoscopy & intubation. The mean systolic blood pressure showed a highly significant rise at laryngoscopy, intubation, and creation of pneumoperitoneum and after extubation. The values came down to preoperative level by about 45 minutes after extubation. On the other hand, in group Dex there was a significant decrease in mean systolic blood pressure following the drug infusion. The mean systolic blood pressure showed highly significant decrease after Laryngoscopy & intubation, after creation of pneumoperitoneum and even after extubation there was highly significant decrease in mean systolic blood pressure. The values came down to pre-infusion level after 45 minutes of extubation. i.e. control was better with dex group.

Table 4: Changes In Mean Systolic Blood Pressure %Wise From Pre-infusion Values

Time	Group NS	Group Dex
After drug infusion	2% fall	2.3 % fall
After laryngoscopy & intubation	10.5 % rise	3.9 % less
After Pneumoperitoneum	2.70 % rise	3.6 % less
After extubation	6.6 % rise	2.2 % less

This table no. 4 shows the changes in mean systolic blood pressure % wise from the pre- infusion values. After drug infusion, in group NS, there was fall in mean SBP by 2% were as in group fall in mean SBP was 2.3%. The laryngoscopy & intubation caused a rise in mean SBP by 10.5 % in group NS but in group there was fall in mean SBP by 3.9%. Pneumoperitoneum and extubation both caused a rise in mean SBP in Group NS by 2.70% and 6.6 % respectively, but in group Dex, mean SBP was less by 3.6%and 2.2% respectively compared to pre-infusion values.. The control over mean SBP was better in group Dex compared to group NS.

Table 5: Perioperative Adverse Effects

Adverse effects	Group NS	Group Dex
Bradycardia	Nil	2
Hypotension	Nil	01(%)
Tachycardia	07 (35%)	01 (5%)
Hypertension	06 (30%)	02 (10%)
Arrhythmias & ST–T changes	Nil	Nil
Excessive sedation (grade 5 & 6)	Nil	Nil
Dryness of mouth	01 (5%)	01 (5%)
Respiratory depression	Nil	Nil
Nausea & vomiting	Nil	Nil

This table no. 5 shows the incidence of perioperative adverse effects in patients of our study. Tachycardia & hypertension occurred in 7 & 6 patients of Group NS respectively. Hypotension, tachycardia & hypertension were seen in 1, 1 & 2 patients of group Dex respectively. In group Dex bradycardia occurred in 2 patient. Dryness of mouth noted in one patient each of Group NS and Group Dex.

Discussion

Tracheal intubation, pneumoperitoneum, carbon dioxide insufflation, reverse trendelenburg position and extubation, all cause significant haemodynamic alterations in laparoscopic

surgeries. Normal heart can cope up with these alterations in haemodynamics. Effects on haemodynamics are mediated by inhibition of central sympathetic outflow. Various studies like those of Bhattacharjee DP *et al* 2010 [10], Keniya VM *et al* 2011 [14]. have confirmed the efficacy of intravenous Dexmedetomidine in controlling the haemodynamic response to tracheal intubation and pneumoperitoneum. We therefore carried out this study with the primary aim of assessing the haemodynamic response and secondary aims of assessing sedation, analgesia and extubation time i.e. recovery following intravenous perioperative infusion of Dexmedetomidine in patients undergoing laparoscopic surgery. Our study was randomized prospective double blind clinical study. All the patients were within 23-60 years of age. None of the patients were underweight or overweight and were free of any severe systemic illness. One of the main advantage of dexmedetomidine is that though it possesses sedative & analgesic effects, but it lacks serious respiratory depression (Ebert T J *et al* 2000 [6], Hall J E *et al* 2000 [15]. In our study also we did not find any respiratory depression as assessed by oxygen saturation in any of the patients. The mean oxygen saturation values were normal & comparable within all the three groups.

Conclusion

Dexmedetomidine infusion in the dose of 1mcg/kgwt as bolus and 0.5 mcg/kg/hr as maintenance controlled the haemodynamic response to critical incidence and maintained haemodynamic stability perioperatively in patients undergoing laparoscopic surgery. Dexmedetomidine infusion, in the doses used in our study, did not make the patient heavily sedated. Dexmedetomidine increased the pain free period post-operatively and helped in reducing the total analgesic requirement thereafter. The infusion of Dexmedetomidine did not precipitate any serious side effect during the period of study. Hence this can be concluded that Dexmedetomidine infusion in the dose of 1mcg/kgwt as bolus and 0.5 mcg/kg/hr as maintenance can serve as a very useful anaesthesia adjuvant for control of haemodynamic stress response to critical incidences and reduction in postoperative analgesic requirements without producing any significant adverse effects.

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