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A COMPARATIVE STUDY OF THE EFFECTS OF TWO DIFFERENT CONCENTRATION OF INTRAVENOUS DEXMEDETOMIDINE INFUSION ON HAEMODYNAMIC STRESS RESPONSE, SEDATION AND POST OPERATIVE ANALGESIA REQUIREMENT IN PATIENTS UNDERGOING LAPAROSCOPIC SURGERIES

Anaesthesiology

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ABSTRACT

Introduction:- Laparoscopic surgery is a modern surgical technique involving insufflation of gas (usually CO2) into the peritoneal cavity under pressure to separate the organs from the abdominal cavity. The main cardiovascular changes during laparoscopic surgeries are an increase in systemic vascular resistance, mean arterial blood pressure and myocardial filling pressures. Dexemeditomidine, a highly selective 2-agonist with a relatively high ratio of 2/1-activity promotes cardiovascular stability, sedation, analgesia and lacking respiratory depression making it useful in providing the hemodynamic stability and post operative analgesia. Our study plans to evaluate the effects of two different concentrations of dexmeditomidine infusion on hemodynamic response, sedation levels, post-operative analgesia requirements. **Material and methods:-** This study was conducted at Govt Medical College and Associate group of Hospitals, Kota from june.2019 to jan.2020. We conducted a double blind, prospective, randomized controlled study of 60 adult cases of both sex. We divided the cases into 2 groups of 30 each, as GroupI Dex-0.25 => Patients received dexemeditomidine infusion 0.25 µg/kg/hr. Group II Dex-0.5 => Patients received dexmedetomidine infusion 0.5 µg/kg/hr. Standard protocol followed to administering general anaesthesia. All data were collected and analysed with the help of suitable statistical parameters. **Results:-** Our study results in that Dexemeditomidine administered at an infusion rate of 0.5 µg/kg/hr serve as anaesthetic adjuvant of choice in patients undergoing laparoscopic surgeries.

KEYWORDS

Laparoscopic surgery, general anaesthesia, dexmedetomidine, hemodynamic response

INTRODUCTION

Laparoscopic surgery is a modern surgical technique involving insufflation of gas (usually CO2) into the peritoneal cavity under pressure to separate the organs from the abdominal cavity. The changes in pulmonary function during laparoscopic surgeries include reduction in lung volumes, decrease in pulmonary compliance and increase in peak airway pressure.5 The cardiovascular changes during laparoscopic surgeries are an increase in systemic vascular resistance, mean arterial blood pressure and myocardial filling pressures, with little change in heart rate.6 At intra abdominal pressure levels greater than 15 mmHg, venous return decreases leading to decreased cardiac output and hypotension.[7]

Many factors influence the occurrence, intensity, quality and duration of postoperative pain like the site, nature and duration of operation, type of incision, the preoperative psychological, physical and pharmacological preparation of the patient, added to the anaesthetic management and the quality of postoperative care.[8]

Although general anaesthesia provides hemodynamic stability by rendering patient insensate of pain of surgery and discomfort, it is unable to completely eliminate perioperative stress. Various agents like isoflurane, propofol, β-blockers, and anti-hypertensive medications have been used to reduce hemodynamic changes associated with laparoscopic surgery with variable response. Effects of α2-adrenergic agonist clonidine have also been studied widely.

Likely dexemeditomidine, a highly selective 2-agonist with a relatively high ratio of 2/1-activityinhibits neurotransmitter release leading to decreased neuronal firing causing cardiovascular stability, sedation, analgesia and lacking respiratory depression making it useful in providing the hemodynamic stability and post operative analgesia.9 The primary aim of this clinical study therefore was to evaluate the effects of two different concentrations of dexemeditomidine, infusion on hemodynamic response to critical incidences like laryngoscopy, endotracheal intubation, creation of pneumoperitoneum and extubation in patients undergoing laparoscopic surgeries. The secondary aim was to observe the time of first rescue analgesia, sedation levels, post-operative analgesia requirements, and occurrence of adverse effects.

MATERIAL AND METHOD

This study was conducted at Govt Medical College and Associate group of Hospitals, Kota from june.2019 to jan.2020. This study included Sixty (60) adult patients of either sex scheduled for elective laparoscopic surgery under general anaesthesia were included in the study. Due permission from the institutional ethical committee was obtained.

Study Design: It was a hospital based prospective, randomized, double blind comparative study.

Inclusion criteria:

- All adult patients of both sex [60 patients].
- Patients posted for elective laparoscopic surgery under General Anaesthesia.

Exclusion criteria: Patients suffering from

- Significant cardiovascular and hepatic diseases.
- ASA class III, IV and emergency surgeries.
- Patients requiring chronic analgesic medication for their diseases.
- Patients on drugs like β blockers or calcium channel blockers.
- Contra indications to NSAIDS.
- Patients who are drug and alcohol abuse and with psychological disorders.
- Preoperative hypotension (MAP <60) and bradycardia (<60/min).

The patients were randomly allocated into two groups of 30 patients each

Group	Drug used
Group Dex-0.25 (30 patients)	Patients received dexmedetomidine, infusion 0.25 µg/kg/hr.
Group Dex-0.5 (30 patients)	Patients received dexmedetomidine, infusion 0.5 µg/kg/hr.

METHODS

Pre-anaesthetic assessment:

Standard protocol was followed for Pre-anaesthetic assessment of patients.

Pre-operative fasting:

Solid foods were restricted for 6 hours, milk for 4-5 hours and clear fluids for 2-3 hours prior to surgery.

Pre-medication: All the patients were pre medicated with tablet alprazolam 0.25 mg night before surgery.

Test drug infusion preparation: 200µg/2ml dexemeditomidine in 48mL NS = 50mL solution (4µg/ml) via an infusion pump.

Monitoring: Monitoring included precordial stethoscope, pulse-oximetry, NIBP, respiratory rate, CO2 level by capnograph and ECG.

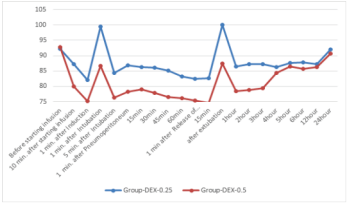
Anaesthesia technique:
Standard procedure was followed. and provision was made for recording and treatment of following side effects-Hypotension, Hypertension, Bradycardia.

After surgery, the following parameters were recorded every hour for the first 6hours and then at 12 hours and 24 hours post operatively in the ward.HR, MAP, SPO2, time to first analgesic demand, VAS and total post operative analgesic requirement in 24hours was also noted and recorded. Sedation was assessed at 0, 15, 30, 60 to 120 min post-operatively using Ramsay sedation score.

Any complications such as laryngospasm, bronchospasm or desaturation (SpO2 <90%), managed according to the standard protocols. Pain was assessed by VAS and Sedation by Ramsay Sedation Scale (RSS).

Statistical analysis: Results were tabulated and statistically analysed using SPSS (Statistical Package for Social Sciences) Software version 15.0. The difference between the two groups was assessed by student's - t test and chi-square test. The results were expressed as mean±standard deviation.For all the tests a 'p' value of 0.05 and less was considered for statistical significance.

RESULTS



Graph 1: Comparision of intra and post operative Mean Arterial Pressure (MAP mmHg) in the two groups

Table 1: Comparision of postoperative Ramsay sedation score in both the groups

Time interval	Group Dex-0.25		Group Dex-0.5		P value
	Mean	SD	Mean	SD	
0 min	2.1	0.45	3	0.47	0.044
15 min	2.0	0.31	2.85	0.44	0.03
30 min	2	0.37	2.65	0.67	0.041
60 min	1.73	0.45	2.14	0.59	0.054
120 min	1.86	0.35	1.96	0.42	0.82

The table shows, sedation scores were higher in group Dex-0.5 as compared to groups Dex-0.25 during the postoperative period. There was statistically significant difference at 0 and 30 minutes (P <0.05).

Table 2: Comparision of the mean postoperative time to first analgesic demand (min) in both the groups

Postoperative time to first analgesicand(min)	Group Dex-0.25		Group Dex-0.5	
	Mean	SD	Mean	SD
	70.8	37.2	131.9	66.4
P value	0.0001			

The table shows, mean post operative time to first analgesic demand in group Dex-0.25 was 70.8 min which was much earlier when compared to group Dex-0.5 (131.9 min). The difference was statistically highly significant (P <0.001).

Table 3: Postoperative Total Analgesic Consumption (INJ. Diclofenac) mg in both the groups

Postoperative Total Analgesic Consumption (INJ. Diclofenac) mg	Group exX-0.25		Group-Dex-0.5	
	Mean	SD	Mean	SD
	170.6	48.6	101.7	36.5
P value	0.0001			

The table shows, mean postoperative total analgesic consumption in (INJ. Diclofenac) mg was 170.6 mg in group Dex- 0. 25 which was much higher when compared to group Dex-0.5 (101.7 mg). The difference was statistically highly significant (P <0.001).

DISCUSSION

The hemodynamic alterations due to intense sympathetic stimulation accompanying laparoscopic surgery, comprising of elevation in heart rate and rise in systolic, diastolic and mean arterial pressure are well known. Various drugs and methods have been studied to prevent hemodynamic alterations due to stress of surgery and anaesthesia. Dexemeditomidine, a highly selective α2 agonist, has been used by many workers likeJalonen J et al45 (1997), Bhattacharjee DP et al50 (2010), Aantaa R et al40 (1990), Kang WS et al59 (2012) and Bajwa SS et al53 (2012) etc for attenuation of hemodynamic responses in various doses. Aho Met al44 (1992) conducted a study in which dexemeditomidine was given, for the first time, to patients undergoing a laparoscopic procedure i.e. gynaecologic diagnostic laparoscopy, and the hemodynamic and endocrine effects of three different doses of dexemeditomidine were compared.

In our study, we observed the effects of dexemeditomidine on hemodynamics during perioperative period in patients undergoing laparoscopic surgeries.

Patients selected in present study were adult patients of both the sex. 60 patients were allocated in two groups, 30 patients in Group Dex-0.25 and 30 patients in Group Dex-0.5.

Mean Arterial Pressure: In group Dex-0.25, the baseline MAP was 92.2±4.3 mmHg and there was a significant decrease in 10 minutes following the drug infusion (87.2±4.3 mmHg). Laryngoscopy and intubation raised the mean MAP (99.5±6.4 mmHg), but this rise (not >20% of baseline MAP) was for a short duration lasting for 5 minutes and then there was a fall in the MAP to less than the preinfusion value. This fall in MAP was statistically significant (P <0.05).

In group Dex-0.5 the mean MAP values were always less than preinfusion values (92.7±5.3 mmHg) at all the points i.e. before induction (87.2±4.3 mmHg), after laryngoscopy and tracheal intubation (86.7±9.1 mmHg), pneumoperitoneum (78.3±6.2 mmHg) and extubation (87.4±6.4 mmHg) (P <0.05). Laryngoscopy & intubation caused a slight increase in mean MAP but the values were significantly (P <0.05) less than the preinfusion values.

MAP was lower than in Group Dex-0.5 as compared to the group Dex-0.25 and significant differences were found at all-time points of the study period (P <0.05). (Graph-1)

Present study is comparable to the studies done by Bhattacharjee DP et al8(2010), Turgut N et al13 (2008), Tufanogullari B et al12 (2008), Kabukcu HK et al14 (2011).

The findings of our study were in agreement with that dexemeditomidine infusion intraoperatively is an effective agent to reduce the hemodynamic fluctuations associated with laparoscopic surgery.

Visual analogue scale (VAS): In the present study, comparing the VAS between the two groups, the mean VAS score was less in group Dex-0.5 than in group Dex-0.25 at all observed time points. The VAS score was statistically significant at 1st, 2nd, 3rd, 12th and 24th hour (P <0.05). The VAS score was not significant at 4th, 5th and 6th hour (P >0.05).

Muslum Cicek et al15 (2006) in their study found that VAS scores for pain were higher at all times in control group than in Group DEX (P <0.05).

Sedation scores: In the present study, comparing the mean postoperative Modified Ramsay Sedation Score in the two groups, the mean sedation score was more in group Dex-0.5 than in group Dex-0.25 at all observed time points but the difference being statistically significant was only till 30 min. None of the patients in either of the groups had sedation scores >4.(Table-1)

Shahbaz R et al16 (2004) showed in their study that the median average sedation scores for the dexemeditomidine and morphine groups were 46 ± 14 and 49 ± 20, respectively.

Post operative analgesic requirement and time to first analgesic demand:

In the present study, the mean total analgesic consumption of inj. Diclofenac in group Dex-0.25 was 170.6±48.6 mg and in group Dex-0.5 it was 101.7±36.5 mg. The total analgesic consumption was higher in the group Dex-0.25, the difference being statistically highly significant (P 0.0001). The mean time to first analgesic demand was later in the group Dex-0.5 group (131.9±66.4 min) as compared to the group Dex-0.25 (70.8±37.2 min), the difference was statistically significant. (P 0.0001). (Table-2 & Table-3)

These findings reflect the point that dexemeditomidine has analgesia-sparing properties and increasing concentrations of dexemeditomidine in humans resulted in progressive increase in analgesia.

Gourishankar Reddy Manne et al17 (2014) in their study concluded that the rescue analgesia was required early (55.5 min) in Group NS compared to dexemeditomidine groups (173 minutes in Dex 0.2 and 249 minutes in Dex 0.4 group). All the patients in group NS (180mg), 15 patients in group Dex 0.2 (115 mg) and 10 patients in group Dex 0.4 group (97. 5mg) required rescue analgesia.

Waleed MA et al18 (2011) in their study found that compared with placebo group, patients in the dexemeditomidine group required 52.7% less PCA morphine during the first 24 hours postoperatively, with significantly better visual analogue scale scores.

Abdullah Tolga et al19 (2010) in their study found thatthetotal remifentanil consumption, additional analgesic requirement, total demand of PCA, total amount of PCA consumption and mean VAS were higher in the control group whereas the first demand time of PCA was longer in the dexemeditomidine group.

Mohamed Khalil et al20 (2012)in their study found that the total morphine consumption was only 7.2±1.14 mg in the Dex Group in comparison to 13.5±2.18 mg in the Control group (P<0.05).

The findings of our study are in agreement with the findings of various above mentioned investigators in that patients who had received dexemeditomidine had a later time to the first analgesic demand and lower cumulative analgesic consumption during the post operative period.

CONCLUSION:

Dexemeditomidine at an infusion rate of 0.5 µg/kg/hr has a better hemodynamic stabilization, smooth emergence and analgesic property when compared to an infusion rate of 0.25 µg/kg/hr, with episodes of transient hypotension, bradycardia, increased postoperative sedation scores, with no serious side effects or adverse reactions.

CONFLICT OF INTEREST: there is no conflict of interest between authors.

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