Original Research Article

Effects of Intravenously Administered Dexmedetomidine and Clonidine on Haemodynamic Response and Post Operative Analgesia in Laparoscopic Surgery: An Observational Study

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Abstract

Introduction: Laparoscopic surgery is become the normal now due to its advantages. To counter its disadvantages on haemodynamics, α-2 receptor agonists clonidine and dexmedetomidine are increasingly being used during laparoscopic procedures. **Aim:** To compare the haemodynamic response, perioperative analgesia, and sedative effects of intravenous dexmedetomidine versus intravenous clonidine given as premedication among patients receiving general anaesthesia for elective laparoscopic surgeries. **Materials and methods**: The study was an observational, prospective, comparative study in which **Group D** was given Injection dexmedetomidine 1 µ/kg in 100 ml of normal saline intravenously and Group C was given Injection clonidine 2µ/kg in 100ml of normal saline intravenously before induction of general anaesthesia. **Results:** Data was calculated as mean, median, and standard deviation. Any statistical difference between the two proportions was estimated using the Chi-square test and any statistical difference between had better hemodynamic control and post-operative analgesia. Both dexmedetomidine and clonidine attenuated the cardiovascular and pressor response to intubation. Dexmedetomidine caused deeper sedation and better analgesia in comparison to clonidine. **Conclusion:** Alpha 2 agonist dexmedetomidine and clonidine provide haemodynamic stability among patients undergoing laparoscopic surgery. Dexmedetomidine provided much better cardiovascular stability and superior analgesia.

Keywords: Laproscopic Surgery, Dexmedetomidine, Clonidine, Haemodynamic Response.

Introduction

Laparoscopy surgery has the advantage of minimal tissue damage, reduced recovery time and reduced postoperative pain leading to shorter hospital stay. The physiologic derangements due to positional changes during the procedure, increase in intraabdominal pressure due to carbon dioxide insufflation, and systemic effects secondary to absorption of gas in the body challenge the anaesthetic management of laparoscopic surgery.[1-3]

The pathophysiologic effects of laparoscopic surgery are secondary to (i) carbon dioxide insufflation, (ii) increased intraabdominal pressure (IAP) (iii) positioning. These factors cause an alteration in physiology and put a significant strain on the cardiovascular and pulmonary system. [3-5]

Pneumoperitoneum causes hypercarbia, hypoxemia, reduction in pulmonary compliance, and subcutaneous emphysema. Hypercarbia and acidosis cause hemodynamic alternation during laparoscopy by the directly affecting cardiovascular system and secondly by stimulating the sympathoadrenal system. Common side effects observed are hypertension, hypotension, arrhythmias, and cardiac arrest due to sudden increase in vasovagal tone (caused by sudden peritoneal distension) and gas embolism. Newer agents like α-2 receptor agonists clonidine and dexmedetomidine are being used during laparoscopic procedures to modify these deleterious pathophysiological change.[3-6]

Materials and Methods

The study was designed as an observational, prospective, comparative study. It was conducted in the Department of Anesthesiology, LN Medical College Bhopal between December 2018 to August 2020. After approval from institutional ethical committee, 60 patients of ASA class 1 and 2 between 18 to 50 years of age undergoing elective laparoscopic surgeries were included in the study.

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Inclusion Criteria

- 1.Patients of ASA physical status I & II scheduled for elective laparoscopic surgeries.
- 2.Patients aged between 18 to 50 years.

Exclusion Criteria

- Patient refusal to give consent for the study.
- Patients with ASA physical status III or more
- Patients with a history of alcohol or drug abuse.
- Patients on any opioid or any sedative medication in the week before surgery.

Patients were divided into two groups with 30 patients in each group . Drug was given at the discretion of attending anesthetist. **Group D:** Injection dexmedetomidine 1 µ/kg in 100 ml of normal saline was given intravenously. **Group C:** Injection clonidine 2µ/kg in 100ml of normal saline was given intravenously.

After written informed consent, selected patients underwent pre-anaesthetic check-up and advise. In the operation theatre, monitor (Philips MP 20®) was attached to the patients. Patients were given the study drugs before induction over 10 minutes at. General anesthesia was induced with Inj. Midazolam 0.05mg/kg IV, Inj.Fentanyl 2μg/kg IV, Inj.Propofol 1.5-2.5mg/kg IV and tracheal intubation facilitated by Atracurium 0.5mg/kg IV. Patients were put on intermittent positive pressure ventilation with tidal volume 8-10ml/kg and respiratory rate 12-14/minute adjusted to maintain End tidal carbon dioxide (EtCo2) between 35-45 mm Hg. Anesthesia was maintained with N_2O:O_2 mixture in a 60:40 ratio and isoflurane 0.5%-1%. Heart rate, non invasive blood pressure (NIBP), arterial oxygen saturation(SpO_2) were recorded before giving study drugs, before intubation, after intubation every

minute for first 5 minutes, every 5 minutes for next 15 minutes, and than 15 minute subsequently till the end of surgery. In post-operative period recording was done every 30 minutes for first 2 hour .

Hypotension (mean arterial pressure decreased more than 20% from baseline or systolic pressure was less than 90 mmHg)was treated with intravenous mephenteramine dose titrated according to response. Bradycardia (heart rate less than 50 beats/min) was treated with intravenous atropine in boluses of 0.6 mg.The time for the first request for postoperative analgesia and the number of patients who required supplemental analgesia was recorded. Pain intensity was assessed by using Visual analogue scale (VAS). When VAS≥ 4 study was terminated. Inj. Diclofenac 75mgIM was given as rescue analgesic.

Level of sedation was assessed post operatively using Ramsay Sedation Score. Any respiratory or cardiovascular complications, nausea vomiting and headache was noted

Observation Chart

Table 1: Demographic Data and Duration of Surgery

Demographically both groups were similar. There was no statistically significant difference between the two groups in terms of duration of surgery (Table 1).

Parameter	Group D n=30	Group C n=30	P value
Age(Years) mean±SD	42.47 ±9.87	44.30 ±9.21	0.460
Weight	58.87 ±10.02	57.83 ±9.76	0.687
GenderM:F	15:15	16:14	0.796
ASA grading I ASA grade II	18(60%) 12(40%)	19(63.3%) 11(36.7%)	0.791
Duration of surgery(hours) mean (±SD)	1.79±0.67	2.54 ±1.66	0.074

Table 2: Vas Score

VAS Score numbers (%)	Group D	Group C	P value
≤ 3	27(90)	10(33.3)	
4-5	3(10)	13(43.3)	
≥6	0(0)	7(23.3)	
Mean (±SD)	2.17(±1.12)	4.13(±1.31)	<0.001
Median (IQR)	2(1-3)	4(3-5)	
Range	1-5	2-6	

Difference in mean, median VAS scores between groups was statistically significant. Patients having VAS score > 4 were significantly higher in group C. (Table 2).

Table 3: Sedation score

Sedation score	Group D n=30	Group C n=30	X^2	P value
1	0	4 (13.3%)		
2	9 (30.0%)	14 (46.7%)	9.949	0.014
3	17 (56.7%)	12 (40.0%)		
4	4 (13.3%)	0		

Median sedation score in Group D was statistically higher as compared to group C (p value 0.014)(Table 3). 33.3% of the participants in group C needed repeat dose of Fentanyl 25µgm intraoperatively. In group D 10.0% of the participants were given repeat dose of Fentanyl.

Table 4: Haemodynamic Changes in Two Groups

Hemodynamics Parameters Studied Intraoperatively						
PARAMETER	**GROUPS**				**P VALUE(Wilcoxon- Mann- Whitney U Test)**	
Time	D (MEAN SD)		C (MEAN SD)		P value of heart rate	P value of MAP
	Heart rate (bpm)	MAP (mmhg)	Heart rate (bpm)	MAP (mmhg)		
Pre-Operative	81.77 (10.11)	94.30 (8.96)	78.47 (7.85)	94.77 (6.85)	0.100	0.635
Before Induction	81.17 (10.01)	95.33 (9.28)	79.63 (8.90)	96.10 (6.40)	0.221	0.529
After Induction	76.13 (12.18)	88.37 (8.38)	77.33 (8.70)	92.00 (8.66)	0.657	0.073
Before Intubation	75.23 (11.29)	85.27 (8.96)	78.53 (11.16)	90.50 (12.08)	0.242	0.153

After Intubation	75.20 (9.69)	84.77 (9.69)	78.93 (11.15)	91.33 (13.51)	0.111	0.077
1 Minute	74.20 (9.35)	82.07 (9.77)	79.33 (10.06)	90.97 (12.82)	0.033	0.009
3 Minutes	72.63 (9.32)	80.77 (7.41)	79.83 (8.32)	94.67 (12.41)	<0.001	<0.001
5 Minutes	72.83 (9.51)	80.90 (6.78)	81.60 (8.08)	96.20 (11.95)	<0.001	<0.001
10 Minutes	73.50 (9.48)	80.80 (6.39)	82.43 (7.86)	96.23 (10.94)	<0.001	<0.001
15 Minutes	72.20 (9.44)	81.63 (6.34)	84.00 (8.42)	95.07 (9.70)	<0.001	<0.001
35 Minutes	73.33 (8.07)	83.43 (7.24)	82.70 (8.00)	95.40 (9.88)	<0.001	<0.001
60 Minutes	74.67 (8.21)	83.33 (8.10)	82.87 (6.39)	95.90 (9.94)	<0.001	<0.001
80 Minutes	73.54 (8.85)	83.71 (8.12)	81.83 (6.54)	97.52 (10.05)	<0.001	<0.001
120 Minutes	75.00 (8.81)	82.79 (8.05)	84.52 (7.73)	100.43 (10.47)	<0.001	<0.001
180 Minutes	79.78 (10.97)	85.50 (7.23)	85.73 (7.97)	101.40 (11.20)	0.384	0.003
P Value (within each group - Friedman Test)	0.069	<0.001	0.043	<0.001		

Results

The MAP declined in both groups immediately after induction until 1 minute after intubation. Thereafter, the MAP continued to decline in the group D whereas it started to increase among participants in group C. Following induction, in Group D, the mean MAP (mmHg) increased from the baseline value of 94.30 to a maximum of 95.33 just before induction and then declined by about 7 points to a value of 88.3 just after induction, thereafter MAP continued to decline throughout the period of observation to reach a minimum value of 80.77 mm Hg 3 minutes after intubation.

In Group C, the mean MAP (mmHg) decreased from 94.77 at baseline to a minimum of 90.50 just before intubation and then increased to 101.40 mm Hg at 180 Minutes after surgery. The difference in change in heart rate and mean arterial pressure between the two groups was statistically significant at all time point except for baseline and endline.(Table:4)

In Group D, increase in heart rate following the intubation was not seen. the maximum change (- 10.2%) from the pre-operative timepoint was observed at 80 Minutes after surgery. Participants in group C had a slight increase in heart rate just after the intubation. In Group: C, the mean HR decreased from 79.63 just before induction to a minimum of 77.33 immediately after induction and then increased to 85.73 at 180 Minutes after surgery. This difference in HR between baseline and end-line was statistically significant (Friedman Test: p = 0.043). Even though the heart rate was higher in group D participants at baseline, comparatively, throughout the observed period, the mean heart rate was lower in group D in comparison to group C participants. Moreover, this difference was statistically significant at 1 minute after intubation and remained statistically significant until 180 minutes after surgery. None of the participants in our study had an episode of bradycardia.

Table:4 illustrates the change in Mean Heart rate and mean arterial pressure among the participants in the two groups. At baseline, the mean heart rate was slightly lower in group C participants, however, this difference was not statistically significant (P-value-0.10). In Group: D, the Heart Rate declined from 81.77 at induction to a minimum of 72.20 at 15 minutes and the MAP declined in both groups immediately after induction until 1 minute after intubation. As can be inferred, the MAP in the two- study group was almost the same (P-value =0.635) at the baseline.

Statistical Analysis

Data collected was coded and analyzed using Stata 15.1 version. For the continuous data, the mean, median, and standard deviation were calculated. Discrete data was expressed as frequency, proportion, and percentage. Statistical difference between the two proportions was estimated using the Chi-square test . Statistical difference between the two means was estimated using the T-test. Non-Parametric test (Friedman test) were used to make a statistical inference in case the data were not normally distributed [31].Analysis of VAS score was done using Wilcoxon Mann Whitney U test.

Discussion

For several reasons discussed earlier, laparoscopic surgeries have replaced convectional surgeries as the new norm for various elective procedures. Several pharmacological agents have been tested to attenuate the hemodynamic responses to tracheal intubation and the creation of pneumoperitoneum hence in this regard, α -2 adrenergic agonists have become very popular in the practice because of their numerous remarkable properties, and minimal adverse effect profile. These include cardiovascular stability, opioid, and anaesthetic sparing effect without causing respiratory depression. Two of the most widely used alpha agonists used for this purpose are clonidine and dexmedetomidine. In the present study. it compares the effect of intravenous clonidine or dexmedetomidine on the hemodynamic response, sedation, analgesia and additional medication requirements, among a total of 60 patients undergoing elective abdominal laparoscopic surgery.[5-8]

Sedation score The sedative effect of α 2 adrenergic agonists is mediated through the locus ceruleus in the brain stem by reducing the sympathetic outflow and increasing parasympathetic outflow. This sedative effect may result in delayed recovery time as measured by a variety of parameters.

Comparatively, in the present study, among the two study groups, the median and the mode sedation score was higher among subjects belonging to the dexmedetomidine group. Overall, it was observed that a maximum of 46.0% participants in Group C had a sedation score of 2 and a maximum of 56.0% of the participants in Group D had sedation score 3. Moreover, the difference in the sedation score was statistically significant between the two study groups. In our study, subjects in the dexmedetomidine group were more sedated in comparison to the clonidine group. Similar to our results, Anjum N et al. reported a delayed recovery among all patients receiving alpha-2 agonist in comparison to the control group. Kumar Setal. reported that- sedation score at the end of the surgery were higher in dexmedetomidine in comparison to the clonidine group, this difference was both clinically as well as statistically significant. Trikhatri Y et al. observed that participants -were more sedated in dexmedetomidine group than control group till 30minutes after the surgery, however, all participants recovered 45 minutes postoperatively.[6-8]

VAS score Analgesic effects attributed to α_2-agonists are believed to be mediated by α_2-receptor located in the central nervous system and spinal cord. Also, it is postulated that the dexmedetomidine has anti-nociceptive effects on both somatic and visceral pain. In our study, both the mean and median VAS score was higher among participants receiving clonidine. The mean VAS score in Group D and Group C was 2.17 and 4.13, respectively. The median VAS score in Group D and Group C was 2 and 4, respectively. The VAS score in the Group D ranged from 1 – 5 and the VAS in the Group C ranged from 2 -6. The difference in the mean VAS score among the participants in the dexmedetomidine and clonidine group was statistically significant. Gautam P et al. also concluded that dexmedetomidine is far better and longer-acting analgesic property in comparison to clonidine.[8-12]

Hemodynamic Stability

In the present study, at baseline, the mean heart rate was slightly lower in group C participants, however, this difference was not statistically significant and in Group D, the mean Heart Rate decreased from 82 bpm at induction to a minimum of 72 bpm 15 minutes after infusion, thereafter the heart rate gradually increased to 79, 3 hours after surgery. In Group C, the mean Heart Rate decreased from 80 bpm before induction to a minimum of 77bpm immediately after induction and then increased to 86 bpm at 180 Minutes after surgery. The mean heart rate was lower in group D in comparison to group C participants but higher in group D in postoperative period. Moreover, this difference was statistically significant at several observation points. The difference in change in heart rate between the two groups was statistically significant at all time point except for baseline and end line. Hussain et al. noted that -heart rate declined by 15 and 6 beats respectively in the dexmedetomidine and the clonidine group. They also observed that the maximum decline in heart rate in the group receiving dexmedetomidine was 30 bpm and in the clonidine group was 20bpm[23].Very similar to our findings ,Hussain et al. noted that a minute after intubation, mean heart rate in dexmedetomidine group did not change much from baseline value and in clonidine group, the heart rate increased by an average of 5 bpm. Kumar S et al. reported that throughout the surgical procedure the HR was higher in clonidine group in comparison to dexmedetomidine. They further report that the in comparison to baseline, the heart rate was significantly lower at the end of the observation period in both groups and it was statistically significant.[12-14]

In the present study, the MAP in the two groups was almost the same at the baseline. Following induction, in Group D, the MAP inclined from the before induction (94.30) to a maximum of 95.33 just before induction and then declined by about 7 points to a value of 88.3 mm of Hg just after induction. Throughout the observed postoperative period, the MAP remained below the baseline level and it was 85.50 mm of Hg at the end of observation. This difference in the MAP value between the baseline and the end line was statistically significant. Comparatively, in Group C, the MAP decreased from 94.77 at baseline to a minimum of 90.50 just before intubation and then increased to 101.40 mm Hg at the end of the observation period. Similar to group D, this difference between the MAP between the baseline and the end line was statistically significant.[15-17]

Several of the previously conducted studies agree with the findings of the present study. Agarwal S et al. noted a decrease in systolic, diastolic, and mean blood pressure after induction in both groups, though, the decline was greater among patients receiving dexmedetomidine as premedication. Anjum N et al. (2015) reported that both the dexmedetomidine and Clonidine caused a decrease in MAP during laparoscopic cholecystectomy. Tripathi et al. demonstrated 2μg/kg dose of clonidine was more effectivethan1μg/kg for achieving hemodynamic stability. Similar to our findings, they observed that comparatively, dexmedetomidine provided better hemodynamic stability.[18-20]

In the present study, among participants in group D, a maximum of 14 % decline in the MAP was observed around 5-10 minutes after the intubation. The maximal decline in MAP in group C participants was only 3.7% and it lasted till just after intubation. At the end of the observation period, the MAP in group D was -11.6% and it was +7.6% in group C participants. At each observation time point during the surgery and postoperative period, the MAP was comparatively higher among group C participants than group D participants. Similarly, to our results, Kumar Set al., also reported that the Blood pressure lower with dexmedetomidine at intubation, extubation and postoperatively period than clonidine group.[21-24]

Similar to our study, Sharma et al. compared dexmedetomidine and clonidine and concluded that dexmedetomidine attenuated the cardiovascular response more effectively. Selvaraju et al. reported that immediately following intubation all the parameters of hemodynamic stability i.e., heart rate, SBP, and DBP increased in both groups, however, the increment was greater among patients of clonidine group in comparison to the dexmedetomidine group. Hypotension and bradycardia are the two major serious side effects of α2 agonists. In the present study, none of the participants in both the comparison groups experienced either hypotension or bradycardia. Agarwal S et al. reported that 1 subject (%) dexmedetomidine group and 2 subjects (%) in the clonidine group experienced bradycardia after intubation which responded to a single dose of intravenous atropine. This could be attributed to the preloading of patients with normal saline before induction.[25-31]

Conclusion

Dexmedetomidine had more analgesic effectiveness in comparison to clonidine. Dexmedetomidine considerably reduced the need for additional analgesic medication during the post- operative period. Further, dexmedetomidine provided much better control over all the cardiovascular parameters viz. Heart Rate, Systolic, Diastolic and Mean arterial Blood Pressure Dexmedetomidine attenuated the cardiovascular and pressor response to intubation. Dexmedetomidine had profound sedative action in comparison to clonidine.

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