Original Article

Effect of Oral Clonidine as Premedication on Perioperative Haemodynamic response for Patients undergoing Laparoscopic Cholecystectomy

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ABSTRACT

Back ground and Aim: Clonidine (a2 adrenergic agonist), it has an anti hypertensive properties and augments the effects of anaesthesia, hence it is considered to be an ideal agent to contain the stress response to pneumoperitoneum. The aim of this study was to evaluate the effect of oral clonidine as premedication on perioperative hemodynamic response for patients undergoing laparoscopic cholecystectomy compared with control group.

Materials and Methods: A randomised, prospective single blind study was conducted on 60 American society of Anaesthesiologists grade I and II patients of age between 20 to 60 years both males and females, scheduled for laparoscopic cholecystectomy surgeries. These patients were randomly allocated to receive premedication with either oral clonidine 150 µg (Group I, n=30) or placebo (Group II, n=30) 90 minuts prior to induction. These two groups were compared with respect to haemodynamic parameters, requirement of isoflurane concentration.

Results: Administration of oral clonidine 150 µg as a premedicant in patients undergoing laparoscopic cholecystectomy results in improved perioperative haemodynamic stability and a reduction in intra-operative anaesthetic requirements compared to control group.

Conclusion: Premedication with oral clonidine was found to be significantly better in maintaining haemodynamic stability and it also having an isoflurane sparing effect in patients undergoing laparoscopic cholecystectomy surgeries.

Keywords: Clonidine, laparoscopic, pneumoperitoneum, stress response

INTRODUCTION

Phillipe Mouret was introduced the Laparoscopic cholecystectomy in 1987.[1] Since then, it quickly became apparent that laparoscopy results in multiple benefits. Compared with open procedures, laparoscopy is characterized by better maintenance of homeostasis.[2]

The hallmark of laparoscopy is creation of carbondioxide (CO_2) pneumoperitoneum and change in positioning of patient from Trendelenberg to reverse Trendelenberg. It also results in stress hormone responses (cortisol, epinephrine and nor-epinephrine) especially when CO_2 pneumoperitoneum is used concomitantly.[3]

Clonidine is an alpha–2 adrenoreceptor agonist. It exerts central sympatholytic effect and has a half life of 9-12 hours.[4] Premedication with oral clonidine blunts the stress response to surgical stimuli and the requirement of narcotic and anaesthetic doses are also reduced. In addition, clonidine increases cardiac baroreceptor reflex sensitivity to increase in systolic blood pressure, and thus stablises, blood pressure.[5]

These characteristics suggest that clonidine may be useful in the anaesthetic management of patients undergoing laparoscopic surgeries. Accordingly, the purpose of study was to evaluate the effects of oral clonidine premedication on haemodynamic response in patients undergoing laparoscopic surgeries.

MATERIALS AND METHODS

After approval from the Institute ethical committee, CAIMS, Karimnagar a prospective, randomized, single-blind,comparative study was conducted on adult patients undergoing laparoscopic surgeries. Randomization was done using a computer generated random number table.

The study was conducted on 60 adult patients cases randomly divided into two groups of 30 each.

Group I patients were given clonidine 150 µg orally 90min before induction.

Group II patients were given Vitamin C tablets 100 mg orally 90min before induction.

Inclusion criteria

ASA grades I and II, both males and females, adult patients aged 20 to 60 years, with scheduled Laparoscopic cholecystectomy surgeries.

Exclusion criteria

Patient not fulfilling eligibility criteria, lack of patient consent, hypertensive and diabetic patients, drug dependence, history of bronchial asthma, patients allergic to clonidine, severe coronary insufficiency, recent myocardial infarction, concomitant use of monoamine oxidase inhibitors, tricyclic antidepressants or opioids.

During pre-anaesthetic assessment, a detailed history and examination of each patient was carried out prior to surgery. In the operating room, all patient's pulse oximetry, ECG and non-invasive blood pressure was recorded and a wide bore intravenous line established. End tidal carbon dioxide (EtCO2), inspired and expired concentration of isoflurane was also measured intraoperatively.

The patients were pre-medicated with intravenous metoclopramide 0.1 mg/kg, ranitidine 1 mg/kg and fentanyl 2 µg/kg. General anaesthesia was induced with thiopentone 5 mg/kg and vecuronium 0.1 mg/kg and maintained with isoflurane in 60% N2O/40%O2 mixture.

Controlled mechanical ventilation was applied to maintain endtidal CO2 between 30-40 mmHg. The mean arterial blood pressure (MABP) was maintained at 20% above or below the pre-operative value by adjusting the isoflurane concentration.

In case of severe haemodynamic fluctuations, medical intervention other than adjustment of isoflurane was applied. For bradycardia (heart rate less than 60 bpm), atropine 0.6 mg i.v. was administered. Hypotension (MABP <60 mmHg) was managed with fluid challenges and/or i.v.mephentermine 6 mg bolus.

Hypertension (MABP > 110 mmHg) was treated with inj. nitroglycerine 0.5-5µg/kg/min i.v. Haemodynamics and isoflurane concentration was recorded. Prior to induction, 1 min after endotracheal intubation, 5 min after endotracheal intubation, at skin incision, start of pneumoperitoneum, 15 and 30 min after intubation of CO_2 pneumoperitoneum and 15 min after release of pneumoperitoneum .

STATISTICAL ANALYSIS

The statistical significance for categorical variables was determined by chi-square test. Fisher exact test was used in case one or more expected cell count was less than 5. For continuous variables two sample t-test was applied. Non paramertric "Mann whitney" test was used for data that did not follow a normal distribution. Results were expressed as Mean ± SD (standard deviation). A p-value < 0.05 was considered statistically significant.

Demographic data (age, weight, height), haemodynamic data (Heart rate, Mean arterial pressure [MAP]), isoflurane requirement were subjected to statistical analysis using two sample t-tests. Sex was analysed by chisquare test.

RESULTS

There were no differences between the clonidine and placebo groups regarding age, sex and weight [Table 1].

The basal heart rate was not comparable. There was a increase in pulse rate post intubation the difference being statistically significant only at 5 min after intubation. The mean heart rate was lower in group I as compared to group II perioperatively.

In group I, Mean heart rate ranged from 78.08 ± 10.62 to 84.74 ± 11.22. whereas, in group II it is ranged between 82.70 ± 13.86 to 99.02 ± 13.18.

At skin incision, following start of pneumoperitoneum and 15 min after pneumoperitoneum changes in mean heart rate between the two groups was statistically significant (p value < 0.05) [Table 2].

Table 1: Demographic data

	Clonidine (n=30)	Placebo (n=30)
Sex (M/F)	8(32%), 17 (68%)	5(20%), 20(80%)
Age (Yr)	35.02± 11.45	34.57± 6.94
Height (cm)	164.8 ± 2.42	163.08 ± 2.83
Weight (kg)	60.65 ± 6.21	60.06 ± 5.27

Table 2: Heart Rate

	Group I Mean ± SD	Group II Mean ± SD	P Value
Baseline	82.7±13.71	86.3±14.32	0.32
1 Min after intubation	84.74±11.22	99.02±13.18	0.32
5 min after intubation	80.66±9.72	91.46±9.94	0.001
Skin incision	78.26±11.56	89.20±10.59	0.001
Start of Pneumoperitoneum	78.20±14.89	88.06±12.64	0.006
15 min	78.24±11.86	87±15.17	0.02
30 min	78.16±10.62	82.70±13.86	0.15
15 min after release	80.21±11.60	85.02±12.00	0.08

The basal MAP of the two groups were not comparable. The maximum rise in MAP was noted at 1 minute after intubation and at start of pneumoperitoneum in both groups. Perioperatively, the MAP was lower in group I compared to group II. In group I, MABP ranged from 87.66 ± 9.10 to 101.31±11.45, whereas In group II it ranged from 95.89±7.47 to 113.80±15.08. The difference in the MAP value between the two groups was significant at all time points except at 15 min after the release of pneumoperitoneum when it became not significant [Table 3].

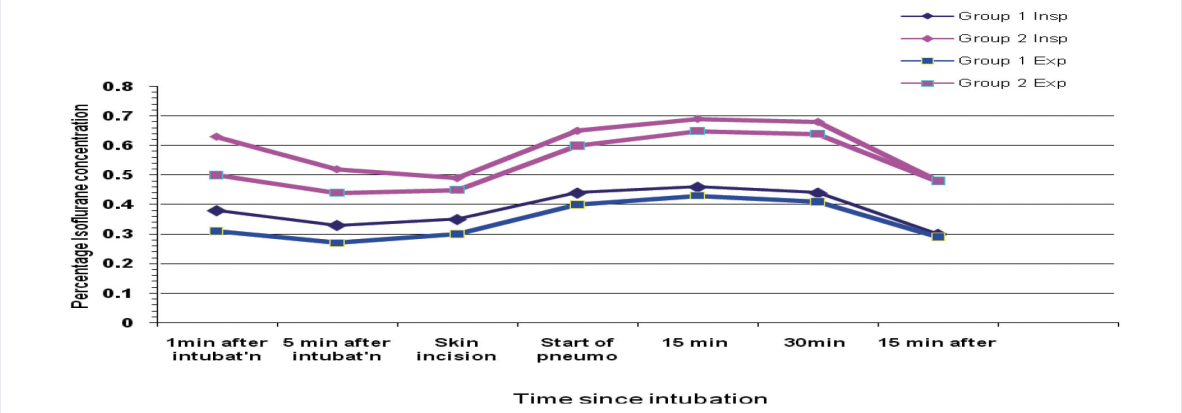
The isoflurane concentration requirement at 1 and 5 min post-intubation was higher in group II than group I; the difference being statistically significant. During the rest of perioperative period isoflurane concentration required for maintaining acceptable haemodynamics was reduced in group I than group II and comparable ($p<0.05$).

DISCUSSION

During laparoscopic surgical procedures changes in the

Table 3 : Mean arterial Blood Pressure

	I (Mean ± SD (mm Hg)	Group II (Mean ± SD (mmHg)	P Value
Baseline	100.41±9.26	99.20±9.28	0.606
1 Min after intubation	100.82±11.55	113.80±15.08	0.001
5 min after intubation	86.51±9.46	95.89±7.47	0.001
Skin incision	87.66±9.10	96.28±11.04	0.001
Start of pneumoperitoneum	101.31±11.45	108.69±12.37	0.002
15 min	99.64±7.70	106.54±9.48	0.002
30 min	96.16±7.20	105.15±8.77	0.001
15 min after release	98.01±5.95	100.29±5.82	0.1



patient's position and surgical stress, especially following pneumoperitoneum cause labile haemodynamics. The choice of anaesthetic technique for upper abdominal laparoscopic surgery is mostly limited to general anaesthesia with muscle paralysis, trac heal intubation and intermittent positive pressure ventilation.[6]

This study was conducted in 60 adult patients belonging to ASA physical status I and II, to evaluate the effect of oral clonidine premedication on haemodynamic response associated with laparoscopic cholecystectomy. After oral administration clonidine is rapidly and completely absorbed and reaches peak plasma concentrations within 60-90 min. In our study, tablet clonidine was given 90 min before scheduled laparoscopy.

Hypertension and tachycardia were noted during the application of CO2 pneumoperitoneum in the placebo group. Premedication with clonidine had more stable haemodynamics than those pre-treated with placebo. Clonidine premedication effectively blunted the cardiovascular response to surgical stress,especially pneumoperitoneum.

Compared with the baseline measurements, there was significantly less increase in heart rate and MAP in the clonidine group compared to the placebo group.Tablet clonidine premedication in the dose of 150 mcg orally has been used by other authors who have documented maintenance of stable haemodynamics intraoperatively and during pneumoperitoneum.[7-9]

Higher doses (5 µg/kg) have also been used with a significant attenuation of responses to hypercapnia.[10] In our study, we have also used 150 µg of clonidine orally. A reduction of isoflurane requirement was observed in our patients who were premedicated with clonidine. They maintained stable haemodynamics at significantly lower concentrations of isoflurane.

Our findings were in concordance with other studies in which there was decrease in MAC and inhalational agent requirement.[11,12] In another study, the preoperative use of oral clonidine (3.5 µg/kg) followed by IV infusion postoperatively was found to improve the haemodynamic profile associated with anaesthetic discontinuation, thus further proving its anaesthetic sparing effect.[13]

CONCLUSION

The administration of oral clonidine 150 µg as a simple and cost effective form of premedication in patients undergoing laparoscopic cholecystectomy results in improved perioperative haemodynamic stability and reduction in anaesthetic requirements.

CONFLICT OF INTEREST :

The authors declared no conflict of interest.

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