Original Article

STUDY ON ROLE OF ORAL CLONIDINE IN LAPAROSCOPIC CHOLECYSTECTOMY SURGERY – A COMPARATIVE STUDY

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SUMMARY

Laparoscopic surgical techniques have been rapidly accepted by the surgeon worldwide e.g. especially laparoscopic cholecystectomy, with published reports describing the benefits of less postoperative pain, reduced hospital stay and an earlier return to work. The hall mark of laparoscopic surgery is the creation of pneumoperitoneum with pressurized CO_2. The high solubility of CO_2 increases systemic absorption by the vasculature of the peritoneum. This, combined with smaller tidal volumes because of poor lung complication, leads to increased arterial CO_2 levels which is known as hypercarbia. If hypercarbia allowed to develop, will stimulate the sympathetic nervous system and thus increase heart rate, blood pressure, and the risk of dysrhythmias. These effects can prove especially challenging in patients with restrictive lung disease, impaired cardiac function, or intravascular volume depletion [1].

The present study was to evaluate the role of oral clonidine and atenolol in controlling tachycardia and hypertension associated with pneumoperitoneum with CO_2 during laparoscopic cholecystectomy under general anaesthesia and also to find out the best premedicant in controlling heamodynamic instability in laparo-scopic cholecystomy. 75 patients schedule for laparoscopic cholecystectomy were randomly selected by blind envelop method. Patients were divided equally into three groups, which were Group-I: Oral clonidine(150ìgm), Group-II: oral atenolol(25mg) and Group-III: placebo (vitamin-c tablet), twenty five patients were in each group.

The mean difference of pulse rate at different times was significant ($p<0.05$), however just before induction, just after skin incision and just after insufflations CO_2 were not significant ($p>0.05$). The mean differences of systolic, diastolic BP at different times were not significant ($p>0.05$), however BP was almost stable just before induction to the end of the operation in group I patients. The mean difference of SPO_2 at different times was not significant($p>0.05$) but just after intubations (99.6%±0.5% in group I, 99.3% ±0.5% in group II and 98.7%±1.1% in group III) and just after skin incision (99.5%±0.6% in group I, 98.9%± 0.6% in group II and 98.3% ±0.9 % in group III) was significant ($p<0.05$). The mean difference of $ETCO_2$ at different times was not significant ($p>0.05$) however after 5 minutes insufflations (35.8±0.8 mmHg in group I, 36.5±0.5 mmHg in group II and 35.5±0.8 mmHg in group III) was significant ($p<0.05$). The mean (±SD) halothane intake of group I patients was 0.49±0.06%, 0.56±0.10% in group II and 0.66±0.09% in group III. The mean (±SD) duration of first analegesic demand of the patents was 90.8±8.5 minutes in group I, 74.0±8.5 minutes in group II and 72.2±8.7 minutes in group III. The mean difference of halothane requirement & duration of first analegesic demand were significant ($p<0.05$). The aldrete recovery status of original criteria were almost similar in three groups ($p>0.05$).

We can conclude that oral clonidine and atenolol to control heart rate & haemodynamic instability in laparoscopic cholecystectomy under general anaesthesia is better than placebo.

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INTRODUCTION

Laparoscopic surgery, also called minimally invasive surgery (MIS), bandaid surgery, keyhole surgery, or pinhole surgery is a modern surgical technique in which operations in the abdomen are performed through small incisions (usually 0.5-1.5cm) as compared to larger incisions needed in traditional surgical procedures. Laparoscopic surgery includes operations within the abdominal or pelvic cavities, whereas keyhole surgery performed on the thoracic or chest cavity is called thoracoscopic surgery. Laparoscopic and thoracoscopic surgery belong to the broader field of endoscopy [2].

Laparoscopy (or peritoneoscopy) procedure allowing endoscopic access to the peritoneal cavity after insufflation of a gas (CO_2) to create space between the anterior abdominal wall & the viscera. The space is necessary for the safe manipulation of instruments and organ. Laparoscopic surgery can also be extraperitoneal. It can also be gasless with abdominal wall retraction, and, more recently it may be hand assisted [3]. The choice of anaesthe-tic technique for upper abdominal laparoscopic surgery is mostly limited to GA because of patients discomfort associated with creation of pneumoperitoneum and the extent of position changes associated with the procedure. Cuffed endotracheal tube placement will minimize the risk of acid aspiration if reflux occurs. Controlled ventilation is recommended because several factors may induce hypercarbia. In general, local or regional anaesthetic techniques have not been advocated for laparoscopic cholecystectomy or other upper abdominal laparoscopic procedures [4].

Today, as equipment and techniques improved and a greater number as well as more involved types of surgery are performed using laparos-copy. As a result of the frequency and complexity of much of this surgery, it is imperative that the anaesthesiologist has a clear understanding of the procedure, the physiologic changes and the potential complications. Clonidine is an imidazo-line compound and a selective α_2 adrenoceptor agonist. It is currently the only drug in this group available for use in anaesthetic practice. Clonidine is lipid soluble and is absorbed rapidly and almost completely after oral administration with peak plasma concentrations occurring 60-90 minutes. The cardiovascular effects of clonidine probably involve both α_2 - adrenonecptors & imidazoline receptors, administration leads to a decreased HR and arterial pressure. Clonidine decreases the requirements for both IV and volatile anaesthetics. Clonidine produces sedation and anxiolysis.

Atenolol is a β-adrenoceptor blocking agent with a cardioselective action i.e. $\hat{a}_1$ βselective, on CVS- It produces negative inotropic effect i.e. decrease force of contraction and negative chronotropic effect i.e. decrease heart rate, as a result decrease blood pressure. It also decreases myocardial O_2 consumption. It has no sympathomimetic action and no membrane stabilizing effect on cardiac muscle. patients were selected for laparoscopic cholecyst-ectomy, age 30 to 60 years and weight 50-60 kg of either sex. Patients who had bronchial asthma, COPD, diabetes mellitus, hypertension, IHD and who had H/O hypersensitivity reaction to study drugs were excluded from the study. After taking informed written consent, patients were randomly divided into three groups, twenty five patients were in each group. A total number of 75 cards, 25 in each group was prepared in a white envelop by another person who is not involved in the study. Each patient selected for study was allowed to draw one card and grouped accordingly. Group-I: received oral clonidine 150ìgm, Group-II: received oral atenolol 25mg, Group-III: received placebo i.e. oral vitamin-c tablet lhr before induction of anaesthesia.

On arrival of the patients in the operation theatre an IV line was inserted and heart rate, blood pressure and respiratory rate were recorded. Before induction of anaesthesia 10ml/kg body weight of Lactate Ringer's solution was infused. Oxygen saturation was observed by pulse oxymeter. One hour before induction group-I got oral clonidine 150ìgm, group-II got oral atenolol 25mg and group-III got placebo i.e. oral vitamin-c tablet. Patient pre-oxygenated with 100% O_2 for 5 mimutes, receiving Inj. Fentanyl (1.5µg/kg body weight) then given IV induction agent Inj. thiopental sodium (3-5mg/kg/ body weight). Endotracheal intubation was facilitated by Inj. Succinylcholine (1-1.5 mg/kg/body weight). Anaesthesia was maintained by Halothane 0.5% and Nitrous oxide 66% in oxygen. Controlled mechanical ventilation was maintained for all study patients. Muscle relaxation was achieved by Inj. Vecuronium (0.lmg/kg body weight). Intra operative proper hydration was maintained with Lactate

Ringer's solution. Time of surgery was within 1 hour. Tracheal extubation was perform-ed with reversal of neuromuscular blocking by Inj. Neostigmine (0.04mg/kg body weight) and Inj. Atropine (0.02mg /kg body weight).

STATISTICAL ANALYSIS:

The data were compiled and analyzed by using statistical software SPSS (ver. 12.0) significance test performed by ANOVA. Only p value <0.05 was considered statistically significant.

MATERIALS AND METHODS

This randomized prospective placebo control study, was carried out in the Department of Anaesthesiology & ICU, Dhaka Medical College Hospital, during the period of January, 2006-December, 2007. ASA class I and class II adult

RESULTS

No significant mean age, weight, BP, heart rate and Hb% differences were found among three groups. Female patients were predominant in the study groups and no significant differences were found among the three groups.

MEAN PULSE AND BP

The mean difference of pulse rate at different times were statistically significant ($p<0.05$) except just before induction, just after skin incision and Just after insufflations of CO_2 ($p>0.05$) (Table II).

The mean difference of systolic and diastolic blood pressure at different times were not statistically significant ($p>0.05$) (Table III). The mean difference of average mean BP at different times were not significant ($p>0.05$) (Table IV).

Table I

Demographic and baseline characteristics of the study subjects

Variables	Group I (n=25)	Group II (n=25)	Group III (n=25)	p value
Age (years)	38.0 ±10.6	38.4 ±15.3	40.5 ±16.3	0.125
Weight (kg)	55.3 ±3.1	56.7 ±4.3	55.1 ±2.9	0.970
Male/Female	7 /18	5 /20	6 /19	0.803
Systolic BP (mmHg)	110.9 ±10.4	116.9 ±7.5	119 ±9.9	0.410
Diastolic BP (mmHg)	70.5 ±8.5	75.6 ±6.2	75.5 ±12.1	0.285
Heart rate (/min)	80.5 ±8.3	81.1 ±7.2	79.0 ±13.1	0.658
Hb%	56.1 ±36.6	52.6 ±34.4	54.6 ±36.8	0.445

Values are expressed as mean±SD, Age and weight analysis done by ANOVA test and sex analysis done by Chi square test Value are regarded significant if $p<0.05$.

Group I: Oral clonidine 150 μgm

Group II: Oral atenolol 25 mg

Group III: Placebo

ns=not significant, n=number of subjects

Table II

Mean pulse at different times in group three groups

Pulse	Group I (n=25)	Group II (n=25)	Group III (n=25)	p value
Just before induction	91.3 ±15.9	83.4 ±12.8	90.5 ±13.2	0.258
Just after intubations	91.8 ±14.9	75.8 ±9.4	92.6 ±11.4	0.019
Just after skin incision	80.5 ±09.3	71.1 ±6.7	78.5 ±11.1	0.056
Just after insufflations of CO_2	81.0 ±08.5	71.9 ±8.2	80.2 ±9.8	0.142
5 min. after insufflations of CO_2	81.2 ±11.4	64.4 ±7.0	77.6 ±13.4	0.003
10 min. after insufflations of CO_2	82.0 ±10.4	62.6 ±5.1	73.9 ±11.2	0.047
15 min. after insufflations of CO_2	81.6 ±10.0	60.8 ±7.9	75.2 ±8.5	0.022
20 min. after insufflations of CO_2	81.0 ±09.0	63.3 ±3.9	75.6 ±9.7	0.013

Table III

Mean systolic and diastolic blood pressure at different times in three groups

Systolic BP (mmHg)	Group I (n=25)	Group II (n=25)	Group III (n=25)	p value
Just before induction	121.3 ±18.1	125.5 ±18.9	135.0 ±18.4	0.568
Just after intubations	123.8 ±28.0	126.4 ±9.2	133.5 ±22.1	0.595
Just after skin incision	120.0 ±20.0	117.3 ±18.5	131.0 ±19.1	0.516
Just after insufflations of CO_2	121.3 ±17.2	128.2 ±12.5	135.0 ±19.1	0.819
5 min. after insufflations of CO_2	121.3 ±14.7	131.8 ±11.3	129.0 ±17.3	0.344
10 min. after insufflations of CO_2	122.1 ±12.3	131.4 ±18.7	132.0 ±25.3	0.915
15 min. after insufflations of CO_2	125.0 ±11.2	124.5 ±23.8	127.2 ±14.8	0.972
20 min. after insufflations of CO_2	127.5 ±18.4	117.8 ±12.6	126.9 ±17.1	0.464
Diastolic BP (mmHg)				
Just before induction	78.8 ±11.9	79.5 ±12.7	82.0 ±14.0	0.954
Just after intubations	81.3 ±18.0	83.6 ±08.3	94.0 ±13.5	0.438
Just after skin incision	85.6 ±22.4	70.0 ±10.5	86.0 ±22.2	0.84
Just after insufflations of CO_2	87.5 ±08.5	90.5 ±08.9	97.5 ±09.8	0.292
5 min. after insufflations of CO_2	85.6 ±11.4	89.1 ±06.2	93.0 ±11.6	0.338
10 min. after insufflations of CO_2	82.9 ±10.1	90.5 ±12.5	91.0 ±08.4	0.608
15 min. after insufflations of CO_2	85.0 ±07.6	85.5 ±17.3	88.9 ±07.0	0.692
20 min. after insufflations of CO_2	87.5 ±05.2	83.8 ±09.6	87.5 ±08.0	0.397

Table IV

Mean blood pressure at different times in three groups

Mean BP (mmHg)	Group I (n=25)	Group II (n=25)	Group III (n=25)	p value
Just before induction	92.9 ±13.7	94.8 ±14.3	99.8 ±13.6	0.794
Just after intubations	95.5 ±20.8	98.7 ±09.4	109.5 ±15.1	0.529
Just after skin incision	96.1 ±13.8	91.1 ±12.6	105.1 ±11.6	0.144
Just after insufflations of CO_2	99.1 ±12.6	101.5 ±09.2	110.1 ±12.5	0.462
5 min. after insufflations of CO_2	98.8 ±12.8	102.6 ±06.8	105.3 ±13.5	0.568
10 min. after insufflations of CO_2	96.4 ±10.1	104.0 ±14.4	100.5 ±08.2	0.572
15 min. after insufflations of CO_2	98.3 ±08.3	97.7 ±19.3	100.4 ±07.6	0.868
20 min. after insufflations of CO_2	101.8 ±07.9	97.3 ±10.2	99.8 ±09.0	0.721

Table V

Mean SPO_2(%) at different times in three groups

SPO_2(%)	Group I (n=25)	Group II (n=25)	Group III (n=25)	p value
Just before induction	99.2 ±0.6	98.4 ±0.7	98.2 ±1.3	0.061
Just after intubations	99.6 ±0.5	99.3 ±0.5	98.7 ±1.1	0.810
Just after skin incision	99.5 ±0.5	98.9 ±0.6	98.3 ±0.9	0.150
Just after insufflations of CO_2	99.1 ±0.7	98.9 ±0.6	98.1 ±1.4	0.276
5 min. after insufflations of CO_2	99.2 ±0.8	98.9 ±0.6	98.1 ±1.4	0.199
10 min. after insufflations of CO_2	99.2 ±0.8	98.9 ±0.7	98.0 ±1.6	0.226
15 min. after insufflations of CO_2	98.9 ±0.7	98.3 ±1.7	98.2 ±1.4	0.143
20 min. after insufflations of CO_2	98.8 ±1.0	98.8 ±1.0	98.1 ±1.8	0.373

SPO_2 (%) AND $ETC0_2$

The mean difference of SPO_2 at different times were not statistically significant ($p>0.05$) except just after intubations and just after skin incision were statistically significant ($p<0.05$) (Table V).

The mean difference of $ETCO_2$ at different times were not statistically significant ($p>0.05$) except after 5 minutes insufflations was significant ($p<0.05$) (Table VI).

Table VI

Mean $ETC0_2$ at different times in three groups

	Group I (n=25)	Group II (n=25)	Group III (n=25)	p value
Just before induction	35.3 ±0.8	35.4 ±0.9	34.8 ±1.0	0.647
Just after intubations	36.0 ±0.9	35.9 ±0.6	35.5 ±1.0	0.606
Just after skin incision	35.5 ±1.1	35.6 ±0.7	35.2 ±0.8	0.918
Just after insufflations of CO_2	36.3 ±0.8	36.4 ±0.7	36.1 ±0.7	0.927
5 min. after insufflations of CO_2	35.8 ±0.8	36.5 ±0.5	35.5 ±0.8	0.90
10 min. after insufflations of CO_2	35.5 ±0.9	36.1 ±0.4	35.4 ±1.5	0.933
15 min. after insufflations of CO_2	35.7 ±0.8	36.3 ±0.5	35.1 ±0.8	0.431
20 min. after insufflations of CO_2	35.6 ±0.7	36.3 ±0.5	35.3 ±0.7	0.647

Table VII

Halothane and analegesic requirement of the patients

	Group I (n=25)	Group II (n=25)	Group III (n=25)	p value
Halothane (%)	0.49 ±0.06	0.56 ±0.10	0.66 ±0.09	0.001^s
First demand of analegesic (min)	90.8 ±8.5	74.0 ±8.5	72.2 ±8.7	0.001^s

Table VIII

Post operative anaesthetic aldrete recovery score of the patients

Recovery status Original criteria	Group I (n=25)	Group II (n=25)	Group III (n=25)	p value
Color	1.8 ±0.1	1.3 ±0.6	1.2 ±0.2	0.462^{ns}
Respiratory	1.6 ±0.5	1.8 ±0.7	1.7 ±0.1	0.449^{ns}
Circulation	1.6 ±0.5	1.9 ±0.7	1.5 ±0.2	0.137^{ns}
Consciousness	1.2 ±0.5	1.5 ±0.5	1.4 ±0.5	0.327^{ns}
Activity	1.5 ±0.3	1.2 ±0.4	1.2 ±0.5	0.324^{ns}

Halothane and analegesic requirement

The mean difference of halothane requirement and duration of first analegesic demand were significant ($p<0.05$).

Post operative anaesthetic Aldrete recovery score

The Aldrete recovery status of original criteria was were almost similar in three groups ($p>0.05$).

DISCUSSION

This prospective placebo control study was carried out with an aim to evaluate the oral clonidine and atenolol in controlling tachycardia & hypertension associated in pneumoperitoneum with CO_2 during laparoscopic cholecystectomy under general anaesthesia and also to find the best premedicant in controlling heamodynamic instability in laparoscopic cholecystomy.

Regarding sex incidence of laparoscopic cholecystectomy surgery in the present study it was higher in female. In this study mean age of patients in three groups were within 40 years ranging from 25 to 60 years and no significant difference was found among the three groups. Baseline characteristics, systolic BP, diastolic BP, heart rate, Hb% and platelet count were almost consistent among the three groups ($p>0.05$).

The mean pulse rate was comparatively higher in group I than group II and group III since just before induction to 20 minutes after insufflations except just after intubations where group III was higher. However in group I was almost stable but group II significantly ($p<0.05$) declined just after intubations, where the mean(±SD) pulse rate was 92.6±11.4 / min in group III, 91.8±14.9 /min group I and 75.8±9.4 /min in group II. Just after skin incision pulse rate consequently decreased in all the three groups, where the mean pulse rate more decreased in group III followed by group I and group II. Just after skin incision the mean (±SD) pulse rate was 80.5±9.3 /min in group I, 71.1±6.7 /min in group II and 78.5±11.1 /min in group III. However pulse rate became static just after skin incision to the end of the surgery, where the pulse rate was 80 - 82 /min in group I, whereas in group III the pulse rate varied from 74 to 80/min, but more variation was observed in group II, where the pulse rate varied from 60 to 71/min. The pulse rate difference were significant ($p<0.05$) from just after skin incision to the end of the surgery. Yu et al. (2003)[5] done a study to investigate the clinical efficiency of oral clonidine premedication in anaesthesia and analgesia. Anaesthesia and analgesia in patients undergoing laproscopic cholecstectomy on 32 patients, out of which 16 patients received oral clonidine 150 µg and rest 16 placebo control received oral antacid (alugel hydroxide 300 mg) before anaesthesia and they found oral clonidine preserved the heart rate control, which is consistent with the present study. Cevheroglu, Ozcan and Bilgin (1999)[6] observed that heart rate decrease in preoperative period, 2, 4 and 6 minutes after intubation and in postoperative period in the clonidine group, where 150µgm received oral clonidine in group I, 10mg oral diazepam in group II and oral placebo in group III were used for premedication. The results of the above authors are similar with the present study. Naris et al. (2004)[7] followed a standard anesthetic protocol and observed a significant difference in overall mean heart rate between the placebo and beta-blocker groups. Zaugg et al. (2003)[8] evaluated the effects of preoperative atenolol administration. The perfor-mance of routine anesthetic depth indicators were analyzed in 45 patients undergoing abdom-inal surgery: group I(n=12), isoflurane/fentanyl/ nitrous oxide in oxygen anesthesia; group II (n=16) isoflurane/fentanyl/ nitrous oxide in oxy-gen with 10mg atenolol intravenously prior to anesthesia; group III (n=17) isoflurane/fentanyl/ nitrous oxide in oxygen with a maximum end-tidal isoflurane concentration of 0.4 vol.% and incremental doses of atenolol (5mg intravenously stepwise) enously prior to anesthesia. In all groups, BP was maintained within ±20.0% of preoperatively defined baseline BP and heart rate between 50 to 80 beats/minute. The perfor-mance of haemodynamic variables was moderate even at critical intraoperative events but unaffected by atenolol, which are comparable with the present study.

The mean systolic blood pressure was compara-tively higher in group III followed by group I and group II just before induction. But just after intubations the mean systolic blood pressure increased in all the three groups and also declined in all the three groups just after skin incision and the decline was higher in group III followed by group II and group I. Just after skin incision the mean(±SD) systolic BP was 120.0± 18.5 mmHg in group I, 117.3±20.0mmHg in group II and 131.0±19.1 mmHg in group III. The mean systolic blood pressure became almost stable just after skin incision to the end of the surgery and the systolic blood pressure was 120 – 128 mmHg in group I, whereas in group III the systolic blood pressure varied from 127 to 135 mmHg, but more variation was observed in group II, where the systolic blood pressure varied from 118 to 132 mmHg. There was no significant (>0.05) difference in systolic blood pressure just before induction to the end of the operation in the present study, whereas systolic blood

pressure was found moderately higher in group III than other two groups. Cevheroglu, Ozcan and Bilgin (1999)[6] observed in their study that systolic blood pressure significantly decreases in the preoperative, after induction, during the operation and in postoperative period. Similarly, Yotsui (2001)[9] has observed that systolic blood pressure was lower in the clonidine group than in the placebo control group immediately after endotracheal intubation and extubation, where the control and clonidine groups received placebo on clonidine 4 microg/kg orally 2 hours before the induction of anesthesia, which are almost similar with the present study.

In the present study diastolic blood pressure was almost similar just before induction. But just after intubations the mean diastolic blood pressure increased in all the three groups and also declined in group I and group II, however in group I increased. Just after skin incision the decline of diastolic blood pressure was higher in group II and than group III. The mean(±SD) diastolic blood pressure was 85.6±10.5mmHg in group I, 70.0±22.4 mmHg in group II and 86.0±22.2 mmHg in group III just after skin incision. The mean diastolic blood pressure became invariable just after skin incision to the end of the surgery and the diastolic blood pressure was 83 – 88 mmHg in group I, whereas in group III the diastolic blood pressure varied from 86 to 97 mmHg, but more variation was observed in group II, where the diastolic blood pressure varied from 70 to 91 mmHg. There was no significant ($p>0.05$) change in diastolic blood pressure just before induction to the end of the operation in the present study. The diastolic blood pressure was also found reasonably higher in group III than other two groups. Same authors Cevheroglu, Ozcan and Bilgin (1999)[6] also observed that diastolic blood pressure decreased after intubation and 2, 4 and 6 minutes after intubation. Yotsui (2001)[9] also observed that the diastolic blood pressure was in the clonidine group than in the placebo control group, which is also comparable with the present study. Zaugg et al. (2003)[8] found blood pressure maintained ±20.0% preoperatively defined baseline blood pressure in their comparative study, which is similar to the present study.

Regarding the mean blood pressure of the current study it was found comparatively higher in group III followed by group I and group III just before induction. But just intubations the mean blood pressure increased in all the three groups and also declined in group II and group III just after skin incision and the decline was higher in group II and group, however in group I slightly increased. Just after skin incision the mean(±SD) mean blood pressure was 96.1±13.8 mmHg in group I, 91.1±12.6 mmHg in group II and 105.1±11.6 mmHg in group III. The mean blood pressure became almost stable just after skin incision to 10 minutes after insufflations but during the end of the surgery three was a little increase and the average blood pressure was 96 – 102 mmHg in group I, whereas in group III the mean blood pressure varied from 100 to 110 mmHg, but more variation was observed in group II, where the systolic blood pressure varied from 91 to 104 mmHg. There was no significant ($p>0.05$) change in mean blood pressure just before induction to the end of the operation, whereas mean blood pressure was found higher in group III than others two groups. In another study Sung et al. (2000)[10] investigated the clinical efficiency of oral clonidine premedication in anesthesia and analgesia in patients undoing laproscopic cholecstectomy. One hundred and ten patients randomly allotted to the placebo group (n=65) were premedicated with oral antacid (alugel hydroxide 300 mg) and clonidine group (n=45) were premedicated with oral clonidine 150 micrograms prior to anesthesia and found in clonidine received patients displayed greater haemodynamic stability preoperatively and the isoflurane requirement also reduced (30.0% less) in comparison with the placebo group. As regard to the haemodynamic parameters, results obtained in the present study were comparable with the findings of the mentioned above authors. The value of mean heart rate and mean arterial pressure in the present study strengthened by similar observation made by Howie et al. (1996)[11].

Howie et al. (1996)[11] had done a double blind, placebo controlled study on 54 patients under-going elective coronary artery bypass graft (CABG) surgery. Patients received approximately 5 micrograms/kg of oral clonidine or a placebo together with 40 micrograms/kg lorazepam 90 minutes prior to titrated sufentanil induction of anesthesia. Thirty minutes prior to cardiopulmo-nary bypass, a second dose of either approxima-tely 5 micrograms/kg of oral clonidine or placebo was given as a slurry via a nasogastric tube and observed heart rate and mean arterial pressure

within 15% of baseline without significant diff-erence in other vasoactive drugs. Pawlik et al. (2005)[12] conducted a prospective study in 30 adult patients with obstructive sleep apnea, under-going elective ear-nose throat surgery. The patients were randomly assigned to receive placebo or clonidine (2 μg/kg oral) the night before & the next morning 2 hours before surgery & the investigators observed consistent heart rate and blood pressure in oral clonidine. Yamakage et al. (2004)[13] investigated the effect of oral premedication with atenolol on volatile anesthetic induction with sevoflurane by monitor-ring the cardiac output (CO) and bispectral (BIS) index. Twenty four patients undergoing general anesthesia with endotracheal intubation were randomly divided into two groups: a control group (n=12) & a â blocker group (n=12). Each patient in the â blocker group was premedicated with oral atenolol 25mg 1 hour before the induction of anesthesia. Anesthesia was induced by repeated vital capacity technique with 5% sevoflurane and 66% nitrous oxide as well as the authors observed the haemodynamic changes caused by endotracheal intubations were inhibited in the â blocker group but not in the control group, on effect of oral atenolol on volatile anesthetic induction with sevoflurane in adults.

The mean SPO_2 was comparatively higher in group I followed by group II and group III just before induction. But just after intubations the mean SPO_2 increased in all the three groups and also declined in all the three groups just after skin incision and the decline was higher in group III and group II and lesser in group I. Just after skin incision the mean(±SD) SPO_2 was 99.5±0.6% in group I, 98.9±0.6% in group II and 98.3 ±0.9 % in group III. The mean SPO_2 of group I was comparatively higher from just before induction to the end of the operation and became stable just after insufflations to the end of the surgery. On the other hand the mean SPO_2 of group III was comparatively lesser from just before induction to the end of the operation and group II became stable just after skin incision to 10 minutes after insufflations and became unstable after 10 minutes after insufflations. The mean SPO_2 at different times were significant ($p>0.05$), however just after intubations and just after skin incision the mean SPO_2 was significant ($p<0.05$). The mean difference of $ETCO_2$ was 36.5 ± 0.5 in group II and 35.5±0.8 mmHg in group III. The mean (±SD) halothane intake of group I patients was significantly ($p<0.05$) higher in group III and lesser in group II where the mean (±SD) halothane intake of group I patients was 0.56± 0.10 %, 0.49±0.06 % in group II and 0.66±0.09 years in group III. Regarding the mean (±SD) duration of first analegesic demand of group I patients significantly ($p<0.05$) delayed, which was 90.8±8.5 minutes, however in group II and group III were 74.0±8.5 minutes and 72.2±8.7 minutes respectively after the end of the operation. The aldrete recovery status of original criteria was almost similar in the three groups and no statistical significant ($p>0.05$) difference was found among the groups.

CONCLUSION

Under the condition of the present study, we can conclude that oral clonidine and atenolol to control heart rate and haemodynamic instability in laparoscopic cholecystectomy under general anaesthesia is better than placebo. On the other hand, when compared oral clonidine with atenolol as premedicant in laparoscopic cholecystectomy surgery, clonidine is superior in controlling heart rate.

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