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Original Research Article

Use of Pre-Operative Clonidine with Calcium Channel Blocker to Reduce the Autonomic Response in a Patient Undergoing Laparoscopic Cholecystectomy Under General Anaesthesia

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ABSTRACT

Introduction: Laparoscopic cholecystectomy done under spinal anaesthesia as a routine anaesthesia of choice that is feasible and safe. Spinal anaesthesia can be recommended to be the anaesthesia technique of choice for conducting laparoscopic cholecystectomy in hospital setups in developing countries where cost is a major factor.

Methods: Twenty patients of ASA-1 weighing about 40- 60 kg were divided into two groups - A and B. All the blood parameters (CBC, RFT, CT, BT, CXR, LFT) are normal. The Group A patients are pre-medicated with inj. Pentazocine 30mg + Glycopyrollate 0.2mg, Pantoprazole 40mg IV, Ondenseteron 4mg IV, Tranexemic Acid 100mg IV and IV antibiotic given one hour prior to surgery given. The Group B are given with Inj. Clonidine 150mcg IV given, Oral Amlodipine 5mg 40 minutes before surgery given. Patients are induced with Inj. Propofol 2mg/Kg body weight, Inj. Suxamethonium 2mg/kg. All patients are monitored, intubated under general anaesthesia. Patient put on supine position and head up position with left lateral position. Laparoscopic Pneumoperitoneum created with various needles 10 mm Trocar in supraumbilical region, three 5mm ports on right flank and two 5mm ports on left flank were analyzed.

Results: During dissection of the Kalleys' triangle, there was a rise of Blood pressure in Group A patients to 30%, which was treated with volatile anaesthetics (Isoflurane/ Sevoflurance and NTG). In Group B patients, blood pressure was stable throughout the surgery.

Conclusion: The usage of calcium channel blockers orally, sublingually is more useful along with IV clonidine in patients undergoing Laparoscopic cholecystectomy.

Keywords: General Anaesthesia, Laparoscopic Cholecystectomy, Pre-Operative Clonidine.

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INTRODUCTION

Laparoscopic surgery aims to minimize trauma of the interventional process but still achieve a satisfactory therapeutic result. It is commonly performed because of various advantages such as reduced postoperative pain, faster recovery and more rapid return to normal activities, shorter hospital stay, and reduced postoperative pulmonary complications. The operative technique requires inflating gas into the abdominal cavity to provide a surgical procedure.[1]

Endotracheal general anaesthesia (GA) is the anaesthetic technique of choice for laparoscopic cholecystectomy (LC). Regional anaesthesia too (spinal/ epidural/ combined spinal epidural) has been reported as a sole technique for performing LC as an alternative to GA for LC. Initially it was reported only for cases who were otherwise high risk candidates for general anaesthesia,[2,3] more recently it has been reported as a routine technique for otherwise healthy patients also.[4,5] It was thought that laparoscopy cholecystectomy necessitates endotracheal intubation. This was to prevent aspiration, abdominal discomfort and hypercarbia which was expected secondary to induction of CO_2 pneumoperitoneum.[1,6]

Laparoscopic cholecystectomy (LC) procedure offers several advantages such as a reduction in stress response, postoperative pain, postoperative wound infection rate, intraoperative bleeding, impairment of respiratory function and pulmonary complications,

short recovery time, and cosmetic appearance.[7,8] LC reduces hospital stay but has no overall effect on postoperative mortality.[9] The risk factors for perioperative complications in patients undergoing LC can be estimated based on patient characteristics, clinical findings and the surgeon's experience.[10] The advantages should to be balanced with potential adverse effects caused by CO_2 pneumoperitoneum. By analyzing the above literatures, the present study aimed to use of pre-operative clonidine with calcium channel blocker to reduce the autonomic response in a patient undergoing laparoscopic cholecystectomy under general anaesthesia

MATERIALS AND METHODS

Study design: This study is a prospective and randomized study. The study was conducted at a rural teaching hospital for the period of 6 months. Twenty patients of ASA-1 weighing about 40-60 kg were divided into two groups - A and B. All the blood parameters including complete blood count (CBC), renal function test (RFT), clotting time (CT), bleeding time (BT), liver function test (LFT), blood pressure (BP) and chest X ray (CXR) are normal.

Inclusion criteria: Consequently newly identified and diagnosed cases of cholelithiasis reported in the department of surgery and who met the following criteria were included.

1. Age between 18 to 80 years
2. The physical status determined by American Society of Anaesthesiologists (ASA)

Exclusion criteria: The patients who are undergoing acute inflammatory process including pancreatitis, cholangitis and cholecystitis, bleeding diasthesis, chronic obstructive pulmonary disease, local spinal deformity, diagnosed psychological morbidity, history of previous open upper abdominal surgery and bile duct stones are excluded from this study. Further, there was not cut off criteria for body mass index was fixed.

Methods: This study was approved and certified by the Institutional ethical committee. All the patients included in this study were explained clearly about the study in their vernacular language and written informed consent was also obtained. All patients were interviewed by the anaesthesiologist in a pre-operative visit who in turn specifically instructed them about possible intraoperative events. As there would be multiple outcomes possible, no separate analysis was undertaken to determine the size of the study groups.

The study patients included in this investigation were randomised to undergo general anaesthesia for the cholecystectomy and the individual resident responsible for post-operative follow-up. The surgery was performed by the same set of consultant surgeons and anaesthesiologists for patients study groups. The post-operative monitoring and data collection was done by an independent observer who had not been involved in either pre-operative or intraoperative course of events.

All the patients included according to ASA guidelines were weighed initially and divided into two groups - A and B. The Group A patients are pre-medicated with inj. Pentazocine 30mg + Glycopyrollate 0.2mg, Pantoprazole 40mg IV, Ondenseteron 4mg IV, Tranexemic Acid 100mg IV and IV antibiotic given one hour prior to surgery given. The Group B are given with Inj. Clonidine 150mcg IV given, Oral Amlodipine 5mg 40 minutes before surgery given. Patients are induced with Inj. Propofol 2mg/Kg body weight, Inj. Suxamethonium 2mg/kg. All patients are monitored, intubated under general anaesthesia. Patient put on supine position and head up position with left lateral position. Laparoscopic Pneumoperitoneum created with various needles 10 mm Trocar in supraumbilical region, three 5mm ports on right flank and two 5mm ports on left flank were analyzed.

Analysis: All the blood parameters including complete blood count (CBC), renal function test (RFT), clotting time (CT), bleeding time (BT), liver function test (LFT) were done as per standard clinical biochemistry procedures. Blood pressure (BP) and chest X ray (CXR) were also checked in all patients throughout the study period.

Table 1: Demographic profile, duration of laparoscopic cholecystectomy

Demographic profile	Control group	Group A	Group B	P value
Age in years	46.32 ± 14.8	42.91 ± 13.3	41.39 ± 11.6	NS
Weight in kgs	63.1 ± 9.6	65.9 ± 11.2	64.7 ± 11.9	NS
Gender (M/F)	7/3	6/4	6/4	NS
ASA (I/II)	6/4	6/4	6/4	NS
Anxiety level	Anxious	Anxious	Anxious	NS
Sedation level	Awake	Awake	Awake	NS
Duration of Laparoscopic cholecystectomy in minutes				
Laparoscopic cholecystectomy	31.96 ± 14.5	36.46 ± 12.6	38.96 ± 12.3	NS
Dissection of adhesions	3.2 ± 0.7	3.7 ± 0.6	3.9 ± 0.5	NS
Elements of Calot's triangle	9.8 ± 3.2	10.6 ± 3.1	10.8 ± 2.9	NS
Gallbladder releasing for its bed	12.8 ± 2.8	13.4 ± 2.6	14.4 ± 2.4	NS
Abdominal cavity lavage and removal of gall bladder from abdomen	6.8 ± 0.9	7.1 ± 0.8	7.3 ± 0.6	NS

RESULTS

A total of 20 patients, 10 in each group were evaluated and a set of 10 subjects were impregnated as control. All groups were comparable with respect to the demographic and operational factors. No significant differences were found between groups with respect to age, gender, weight, time between premedication to anaesthetic induction, duration of Laparoscopic cholecystectomy and surgical procedure time. The duration of anaesthesia did not differ among the study groups (Table 1).

The degree of sedation before pre medication was comparable between the groups, however, they were very anxious at baseline. From this study, it was very clear that there is an increase in

sedation and moderate decreases in anxiety were observed compared to the control groups. Preoperative anxiolysis and sedation was higher in group A as compared with group B is described in table 2.

There was no significant difference in the preoperative heart rate and mean arterial blood pressure values in groups (Table 3). Compared with control and groups, group A showed slight but statistically significant decrease in heart rate before induction. Maximum increase in heart rate from baseline was observed during pneumoperitoneum, it increased in control group, while decrease in group A and B. No significant difference was observed in the arterial blood pressure (ABP) before premedication in groups. Preoperative ABP changes were statistically significant in groups.

Table 2: Comparative analysis of Preoperative anxiolysis and sedation among study groups

Parameters	Group A	Group B
Intra operative analgesic requirement	More	Less
Pulse	More (>30%)	Less
Blood pressure	More (>70%)	Less
Requirement of relaxant	More	Less
Require volatile anaesthetic	More	Less
NTG requirement	More	Cannot be used due to low BP
Bleeding	More	Less

Table 3: Observation of Heart rate (HR) and arterial blood pressure (ABP) changes after laparoscopic cholecystectomy

Observations	Control		Group A		Group B	
	HR	ABP	HR	ABP	HR	ABP
▪ **Premedication**	102.23 ± 6.26	94.39 ± 2.44	93.23 ± 0.96	91.45 ± 1.87	95.26 ± 4.63	91.31 ± 2.52
▪ **Before induction**	107.12 ± 2.13	98.24 ± 2.98	91.26 ± 3.56	89.14 ± 1.52	87.61 ± 4.96	81.47 ± 2.86
▪ **After intubation**	126.34 ± 3.49	107.42 ± 3.96	106.25 ± 3.97	91.57 ± 2.94	89.24 ± 4.94	81.62 ± 3.62
▪ **15 minutes after pneumoperitoneum**	131.46 ± 2.94	111.21 ± 4.83	113.23 ± 3.99	92.35 ± 1.82	94.89 ± 4.81	87.19 ± 3.62
▪ **30 minutes after pneumoperitoneum**	123.21 ± 3.01	104.35 ± 4.17	97.28 ± 4.23	92.56 ± 2.98	82.34 ± 5.11	86.26 ± 2.62
▪ **After release of Co_2**	112.45 ± 3.95	97.23 ± 2.59	98.34 ± 4.12	88.14 ± 3.34	87.33 ± 4.87	81.13 ± 2.32
▪ **After extubation**	120.86 ± 5.16	101.62 ± 3.19	98.10 ± 4.57	92.32 ± 2.12	82.65 ± 5.25	79.14 ± 2.43

DISCUSSION

The present study evaluated the oral premedication with clonidine for hemodynamic stability during laparoscopic cholecystectomy. Further it was observed that the anxiolytic and sedative effects of oral premedicants without any significant respiratory depression. Hemodynamic responses of laparoscopy were attenuated by oral premedication with clonidine.[11] The increase in hemodynamic values in control group may be due to inadequate sedation and analgesia.[12] Near stable hemodynamic variables and absence of any sympatho-somatic response with oral premedication in the present study was an indication of adequate analgesia and sedation. Clonidine effectively attenuated the rise of heart rate and mean arterial blood pressure indicating inactivation of catecholamine.[4,13] In our study, we have used oral premedication with clonidine 200µg and found them to be effective for perioperative hemodynamic stability. The hemodynamic results of our study were in agreement with recent results with clonidine. This drug possess several properties to make them valuable premedicants to attenuate the hemodynamic response.[14]

The use of the intravenous route and the possibility to administer clonidine at the pre-anesthetic preparation room made for a safe administration, which can be done in all outpatients. When it is administered by mouth, it cannot be controlled by the physician, depends on patient compliance, and is associated with an irregular absorption. The intravenous administration of clonidine has a peak of action after 30 minutes and, therefore, can be administered closer to the time of surgery than oral clonidine, whose peak of action is around 2 and 4 hours. Thus, the possible adverse effects would be monitored more safely intraoperatively.[15]

Looking at these pharmacological properties, it has been evaluated in the past to assess its effect on haemodynamic responses in patients undergoing laparoscopic surgeries. The molecule has been used in infusion form with or without bolus dose. However, with higher dose infusion of medicine, high incidence of adverse cardiac effects has been observed. A biphasic response on blood pressure occurs with a bolus dose. Initially, there occurs hypertension followed by fall in blood pressure. This response is seen often more in young and healthy patients.[16]

Clonidine doses have been investigated frequently, though primarily for their anesthetic-sparing effects in the intraoperative period and for their opioid-sparing effects in the postoperative period. We conclude that minimal dose of IV clonidine of 1.5 µg/ kg cause maximum attenuation of pressor response with minimal side effects like hypotension and sedation, and also reduced anesthetic requirements.

CONCLUSION

Laparoscopic cholecystectomy is a common procedure for cholelithiasis patients. Group A patients without calcium channel blocker and clonidine are prone to develop high blood pressure and requires NTG infusion and increased volatile anaesthetics. In Group B, with use of CCB and clonidine, the hypertension response is much decreased and there is much less bleeding and requirement of the intra-op analgesia and volatile anaesthetic and relaxant is also reduced. So, calcium channel blocker and clonidine combination is a very useful in laparoscopic cholelithiasis procedure.

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