ISSN- O: 2458 - 868X, ISSN –P: 2458 - 8687

International Journal of Medical Science and Innovative Research (IJMSIR)

IJMSIR : A Medical Publication Hub

Available Online at: www.ijmsir.com

Volume – 2, Issue –6, November – December - 2017, Page No. : 461 - 466

Comparasion of oral clonidine and oral atenolol as premedication in patients posted for laparoscopic cholecystectomy under general anaesthesia

Vijay Patil, Assistant Professor, GMC, Nagpur, India

Correspondence Author: Vijay Patil, Assistant Professor, GMC, Nagpur, India

Conflicts of Interest: Nil

Abstract

Aim and Objectives: To assess the effect of oral clonidine and oral atenolol as premedication on hemodynamic stability and side effects if any in patients undergoing laparoscopic cholecystectomy. **Material and Methods:** The study included total 50 patients of (age 15 – 50 years) ASA grade I and II were randomly divided into two groups of 25 each. Patients received oral clonidine 5mcg/kg in group C and oral atenolol 1mg/kg in group A, 90 minutes prior to induction. Induction and maintainence of general anaesthesia was performed by the same standard protocol for both groups. Various study parameters i.e. hemodynamic effect (PR, SBP, DBP & MAP) and side effects were recorded and statistically analyzed. **Results:** Better hemodynamic stability was obtained in clonidine group compared to that of atenolol group & there were no serious side effects both in the groups. **Conclusion:** We conclude that oral clonidine is better than atenolol in terms of hemodynamic stability without any side effects.

Keywords: Atenolol, Clonidine, hemodynamic stability, laparoscopic Cholecystectomy.

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 [1]. Laparoscopic cholecystectomy has revolutionized gall bladder surgeries and became the gold standard for the treatment of cholelithiasis. Since the introduction of diagnostic laparoscopic procedures in early 1970's and the first laparoscopic cholecystectomy procedures in late 1980's, laparoscopy has expanded impressively. Increasing the success of laparoscopic surgery can be attributed to the fact that it results in multiple benefits compared with open procedures such as reduced trauma to the patient, disturbance of homeostasis, morbidity, mortality, recovery time, and hospital stay with a consequent reduction in healthcare costs. Inspite of multiple benefits, all laparoscopic surgeries are challenging for anesthesiologist point of view, mainly due to significant alteration of hemodynamics, resulting from the combined effects of pneumoperitoneum, patient position, and hypercapnia from the absorbed CO2. Pneumoperitoneum creation raises the intra-abdominal pressure (IAP) and is immediately followed by an increased plasma renin activity and increase in plasma norepinephrine and epinephrine levels. There is also an increase in the circulating blood volume, which is due to the shifting of blood from the splanchnic capacitance blood vessels to the systemic circulation. All these changes collectively lead to an elevated arterial pressure, increased systemic and pulmonary vascular resistance, and decreased cardiac output. These hemodynamic responses are well tolerated in otherwise healthy individuals, but in patients with hypertension, coronary heart disease, cerebrovascular disease, and intracranial aneurysm; these transient changes can result in potentially deleterious effects such

as left ventricular failure, pulmonary edema, myocardial ischemia, ventricular dysrhythmias, and cerebral hemorrhage [2,3]. Various agents have been tried alone and in combination in an effort to minimize the hemodynamic instability during this period. Volatile agents such as isoflurane and sevoflurane [3] have been used with limited success in maintaining hemodynamic stability as volatile agents decrease surgical stimulus induced catecholamine secretion. Infusions of nitroglycerine or beta blockers, propofol, opioids to control perioperative stress have been tried. Combined general with epidural anesthesia [4] is yet another strategy employed by anesthesiologists to control perioperative hemodynamic instability with limited success. Still no intravenous agent has been used successfully with significant hemodynamic stability without any side effects, so we designed this study to compare the effects of oral premedication of clonidine and atenolol

Material & Mehtods

After getting ethical committee approval a prospective, randomised, double blind study was conducted at tertiary care hospital on 50 patients of ASA grade I & II of either sex with the age and weight between 15-50 years and 45 to 70 kg respectively, undergoing laparoscopic cholecystectomy surgery. After taking informed written consent, patients were randomly divided into two groups, of 25 patients each using a computer generated randomization schedule. In group C, patients received single dose oral clonidine 5mcg/kg and in group A patients received oral atenolol 1mg/kg, 90 minutes before induction of anaesthesia. Patients with age less than 15 years and more than 50 years, patients preferring local anaesthesia, patients with major systemic diseases like rheumatic heart disease, ischaemic heart disease, hypertension, heart blocks, diabetes mellitus, anaemia, sick sinus syndrome, sinus bradycardia, respiratory diseases like chronic obstructive pulmonary disease, bronchial asthma , renal and hepatic derangements, disease of central nervous system, allergic fungal sinusitis, patients on clonidine or beta blockers, agents influencing autonomic nervous system and blood coagulation were excluded from the study.A detailed case history, clinical examination and all relevant investigations were done for all the patients. Baseline parameters like pulse rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure were noted, 90 min before surgery and all patients received oral premedication clonidine 5mcg/kg or atenolol 1mg/kg on the day of surgery 90 minute before operation with sips of water. On operation table, standard monitoring devices ECG, NIBP, SPO_2 and $ETCO_2$ were applied to the patient. For all the patients standard protocol for induction of general anaesthesia was used, premedication with Inj. Glycopyrrolate 5µg/kg, Inj Pantoprazole 40mg, Inj. Ondensetron 0.08mg/kg, Inj. Midazolam 0.03mg/kg, Inj. Fentanyl 2µg/kg also given before induction of anaesthesia. General anaesthesia was induced with inj. Propofol 2mg/kg followed by injection succinylcholine 2mg/kg body weight and patients were intubated with appropriate sized cuffed portex endotracheal tube & throat packing done. Anaesthesia was maintained with oxygen (33%), nitrous oxide (66%), isoflurane 0.2%-0.8% and vecuronium 0.08 mg/kg as skeletal muscle relaxant. The tidal volume (VT) and the ventilator frequency was adjusted and intermittent positive pressure ventilation was continued by mechanical ventilation to maintain end-tidal carbon dioxide between 35-45 mm Hg. Any intraoperative hypertensive episodes were managed with rescue bolus doses of Propofol (10mg/bolus). At the end of the procedure oropharyngeal suctioning done, throat pack was removed & reversal of neuromuscular blockade was achieved using injection neostigmine 0.04 mg/ kg & injection glycopyrrolate 10 µg

/ kg. When patient started obeying commands, extubation was done and shifted to recovery room. Intraoperative hemodynamic variables i.e, PR, SBP, DBP, and MAP were recorded at the interval of 10 min till the end of surgery. After shifting to the postoperative recovery room, hemodynamic parameters (PR, SBP, DBP, and MAP) were again recorded at 15min interval for 2 hours and then 1 hourly till 8 hours. Also side effects if any were observed such as bradycardia, hypotension, nausea, vomiting, shivering and sedation. The detailed data was entered into the Microsoft excel sheet and subsequently analyzed by using appropriate statistical tests. Graphical display was done for better visual inspection.

Observation and Results

A total of 50 patients who underwent functional endoscopic sinus surgery were enrolled for the study and were randomly allocated to 2 groups of 25 patients each. In Group C, 50% patients were males and 50% patients were females, while in Group A, 54% patients were males and 46% patients were females. Table 1 show that mean age of patients in Group C and Group A was 36.60 ± 7.49 yrs and 37.10 ± 6.40 yrs respectively, mean weight in Group C was 59.40 ± 8.07kg while mean weight in Group A was 60.14 ± 8.47kg, the mean duration of surgery in group C was 77.94 ± 7.50 min and group A was 77.16 ± 7.06 min. Both the groups were comparable with respect to age, weight and duration of surgery,(P> 0.05).

Table 1. Comparison of age(years), weight(kg) & duration of surgery and in group 1 and group 2

Variables	Group 1	Group 2	p-value
Age (years)	36.60 ± 7.49	37.10 ± 6.40	0.721
Weight (kg)	59.40± 8.07	60.14± 8.47	0.656
duration of surgery (min)	77.94 ± 7.50	77.16 ± 7.06	0.593

Figure 1 and figure 2 shows that comparison between PR and SBP, DBP, MAP respectively, we observed that oral premedication 90 minutes before induction with clonidine 5mcg/kg and atenolol 1mg/kg showed reduction in PR, SBP, DBP and MAP in both the groups. But on comparison the reduction in PR, SBP, DBP and MAP in clonidine group was more than that with atenolol group but without any significant bradycardia or hypotension. So, overall due to blunting of stress response & sympatho-adrenal stimulation hemodynamic stability was better in clonidine group compared to that of atenolol group.

Figure 1. Graphical comparison of pulse rate in group 1 and group 2.

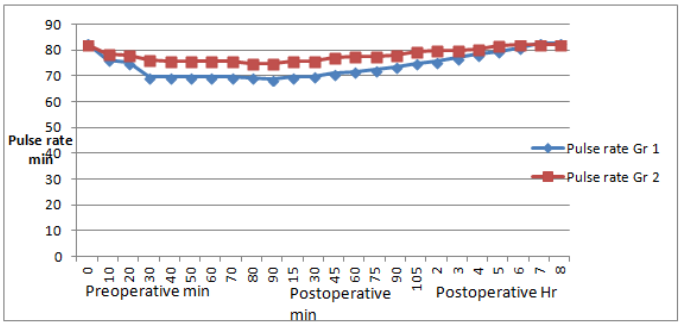
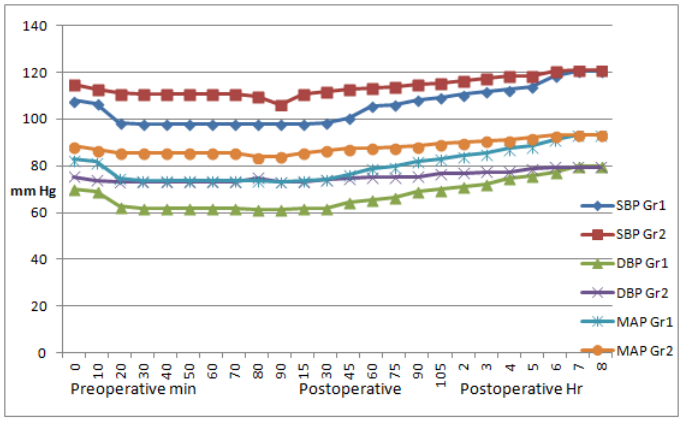


Figure 2. Graphical comparison of SBP, DBP, MAP in group 1 and group 2.



We did not observe the significant sedation which require any additional interventions in preoperative period and

postoperative period in patients of both groups. There were no any serious side effects (like nausea, vomiting, hypotension, bradycardia, or shivering) observed after giving clonidine and atenolol as premedication in either groups.

Discussion

Laparoscopic cholecystectomy with its unique advantages is now the 'gold standard' technique for gall bladder diseases, but pneumoperitoneum required for this surgery has its own disadvantages. The pathophysiological changes are because of the combination of mechanical and neuro-humoral factors. The factors being an increase in intra-abdominal pressure, effect of absorbed CO2 caused by pneumoperitoneum and release of various hormonal factors because of the same [5,6]. More important is the releases of vasopressin and catecholamine's that are potentially deleterious in patients, such as elderly patients, or patients with limited cardio-pulmonary reserve [7]. The pathophysiological effects of pneumoperitoneum on the cardiovascular system may further compromise the cardiac function in such high risk group. To prevent these adverse hemodynamic effects many surgical interventions such as abdominal wall lift method (Laprotensers) providing gasless field for visualization, low intra-abdominal pressure techniques, or use of helium/argon gas instead of CO2 are tried and well-studied [8,9,10]. Clonidine is a centrally acting selective alpha$_2$ adrenergic agonist with alpha$_2$: alpha$_1$ activity 200:1. Clonidine has gained popularity as an adjuvant drug in anesthesia for its sedative and analgesic effects [11], as well as for its favorable effects on the hemodynamic profile of patients [12]. Atenolol is a beta$_1$ selective (cardioselective) beta-adrenergic receptor blocking agent without membrane stabilizing or intrinsic sympathomimetic (partial agonist) activities. Atenolol was primarily used as an antihypertensive agent. All beta-blockers reduce the blood pressure and heart rate by reducing cardiac output through their negative inotropic effect and by reduction of sympathetic activity[13]. Hence we decided to compare oral clonidine and oral atenolol as premedication, as both of them posses nearly similar pharmacokinetic and pharmacodynamic profile. We compare these two drugs as oral premedication, because hypotension and bradycardia are major adverse effects of intravenous administration of clonidine and beta blockers as compared with oral premedication, so oral premedication is considered as safe option [14,15]. Laurito CE et al. [16] studied the effectiveness of oral clonidine as a sedative/ anxiolytic and as a drug to blunt the hemodynamic responses to laryngoscopy. Clonidine has been used in various doses (from 2 to 8 mg/kg) to attenuate haemodynamic responses to PNP in laparoscopic cholecystectomy. Malek et al. [17] used 150 µg of clonidine as IV infusion and intramuscularly while Sung et al. [18] and Yu et al. [19] used 150 µg of oral clonidine as premedication for maintenance of haemodynamic stability during pneumoperitoneum.

Matot et al [20], Singh and Arora [21] and Gupta et al [22] studied the hemodynamic stability after oral clonidine and oral atenolol premedication and reported decrease in pulse rate and blood pressure. In present study, there was a significant decrease in PR, SBP, DBP and MAP in both the groups inspite of surgical stimulus. On comparison the reduction in PR, SBP, DBP, MAP was greater in clonidine group than atenolol group, which shows that hemodynamic stability was better in spite of intraoperative instrumentation in clonidine group. We did not observed the significant sedation in preoperative period and postoperative period in patients of both groups. This findings correlates with the study done by Gupta et al [22] and he observed that postoperative sedation score

were lower in clonidine and atenolol group compared to control group that might be due to reduced introperative anaesthetic drug requirement resulting in rapid and safe awakening. In present study there were no significant effect changes in respiratory rate, Spo_2 and $Etco_2$ in either of the groups. There were no significant ECG abnormalities observed in either groups of patients perioperatively. During our evaluation it was observed that intraoperative anaesthetic agent requirement was less in clonidine group compared to atenolol group but it was no statistically analysed. Sedation may be associated side effect with the clonidine use, but none of the patient was sedated in intraoperative or postoperative period. As well as postoperative nausea and vomiting was less in clonidine group similar to study done by Shukla et al [23].

Conclusion

So in the present study concluded that premedication with oral clonidine 5mcg/kg 90 min before the induction is better than oral atenolol 1mg/kg in terms of hemodynamic stability without any significant side effects. Tablet clonidine is a cheaper drug so when used as preanaesthetic medication in laparoscopic cholecystectomy is cost-effective, also it has anxiolytic property, analgesic property, reduces the anaesthetic agent requirement.

Reference

[1]. Dubois F, Icard P, Berthelot G, Levard H. Coelioscopic cholecystectomy. Preliminary report of 36 cases. Ann Surg 1990;211:60-2.

[2]. Joris JL, Noirot DP, Legrand MJ, Jacquet NJ, Lamy ML. Hemodynamic changes during laparoscopic cholecystectomy. Anesth Analg 1993;76:1067-71.

[3]. Lenz RJ, Thomas TA, Wilkins DG. Cardiovascular changes during laparoscopy. Studies of stroke volume and cardiac output using impedance cardiography. Anaesthesia 1976;31:4-12.

[4]. Luchetti M, Palomba R, Sica G, Massa G, Tufano R. Effectiveness and safety of combined epidural and general anesthesia for laparoscopic cholecystectomy. Reg Anesth 1996;21:465-9.

[5]. Boussofara M, Mtaallah MH, Nefaa MN, KaddourC (2004) Clonidine and anesthesia.Tunis Med 82(3): 249-257.

[6]. O'Leary E, Hubbard K, Tormey W, Cunningham AJ (1997) Laparoscopic cholecystectomy: haemodynamic and neuroendocrine responses after pneumoperitoneum and changes in position. Br J Anaesth 76(5): 640- 644.

[7]. Solis-Herruzo JA, Moreno D, Gonzalez A, et al. (1991) Effect of intra-thoracic pressure on plasma arginine vasopressin levels. Gastroenterology 101(3): 607-617.

[8]. Saunders CJ, Gunther RA, Wolfe BM, Ho HS (1995) Effector of hemodynamics during laparoscopy: CO2 absorption or intra-abdominal pressure? J Surg Res 59(4): 497- 503.

[9]. TidoJunghans, BartholomasBohm, kerstinGrundel, Wolfgang Schwenk (1997) Effects of pneumoperitoneum with carbon dioxide, Argon or Helium on hemodynamic and respiratory function. Arch Surg 132(3): 272-278.

[10]. Menes T, Spivak H (2000) Laparoscopy: searching for the proper insufflation gas. SurgEndosc 14(11): 1050-1056.

[11]. Dahmani S, Brasher C, Stany I, Golmard J, Skhiri A, Bruneau B, Nivoche Y, Constant I, Murat I. Premedication with clonidine is superior to benzodiazepines. A meta analysis of published studies. Acta Anaesthesiol Scand. 2010;54:397–402.

[12]. Sung CS, Lin SH, Chan KH, Chang WK, Chow LH, Lee TY. Effect of oral clonidine premedication on perioperative hemodynamic response and postoperative analgesic requirement for patients undergoing

laparoscopic cholecystectomy. Acta Anaesthesiol Sin. 2000;38:23–29.

[13]. Okopski JV.Recent advances in pharmaceutical chemistry review III, A new wave of beta blockers. J ClinPharm and Ther. 1987; 12:369-388.

[14]. Masood Mohseni, Amin Ebneshahidi, The effect of oral clonidine premedication on blood loss and the quality of the surgical field during endoscopic sinus surgery: a placebo-controlled clinical trial. J Anesth. 2011;25:614–617.

[15]. Engleman E, Lipszyc M, Gilbert E, Van der Linden P, Bellins B, et al. Effect of clonidine on anaesthetic drug requirement and hemodynamic response during aortic surgery. Anesthesiology. 1989;71:178-187.

[16]. Laurito CE, Baughman VL, Becker GL, DeSilva TW, Carranza CJ (1991) The effectiveness of oral clonidine as a sedative/anxiolytic and as a drug to blunt the hemodynamic responses to laryngoscopy. J ClinAnesth 3(3): 186-193.

[17]. Yu HP, Hseu SS, Yien HW, Teng YH, Chan KH (2003) Oral clonidine premedication preserves heart rate variability for patients undergoing laparoscopic cholecystectomy. Acta Anaesthesiol Scand 47(2): 185-190.

[18]. Sung CS, Lin SH, Chan KH, Chang WK, Chow LH, Lee TY (2000) Effect of oral clonidine premedication on perioperative hemodynamic response and postoperative analgesic requirement for patients undergoing laparoscopic cholecystectomy. ActaAnaesthesiol Sin 38(1): 23-29.

[19]. Mutzbauer TS, Obwegeser JA, Gratz KW (2005) Clonidine in oral medicine, literature review and our experience. SchweizMonatsschrZahnmed 115(3): 214-218.

[20]. Matot I, Sichel JY. The Effect of Clonidine Premedication on Hemodynamic Responses to Microlaryngoscopy and Rigid Bronchoscopy. AnesthAnalg. 2000;91:828–833.

[21]. Singh S, Arora K. Effect of oral clonidine premedication on perioperative haemodynamic response and posroperative analgesic requirement for patients undergoing laparoscopic choleystectomy. Ind J anaesth. 2011; 55(1): 26-29.

[22]. Gupta D, Srivastava S, Dubey RK, Prakash PS, Singh PK, Singh U. Comparative evaluation of atenolol and clonidine premedication on cardiovascular response to nasal speculum insertion during trans-sphenoid surgery for resection of pituitary adenoma: A prospective, randomised, double blind, controlled study. Ind JAnaesth. 2011;55(2):135-140.

[23]. Shukla U, MalhotraK, and Prabhakar T. Comparative study of the efffect of clonidine and tramadol in post- spinal anaesthesia shivering. Ind J. Anaesth. 2011; 55(3):242-246.