

Comparative Assessment of the Hemodynamic Parameters with Low Dose Oral Clonidine (100mcg) and Placebo Group in Laparoscopic Surgeries

Venu Gopal¹, Ganesh Kumar²

¹Assistant Professor, Department of Anesthesia, JNKTCH, Madhepura, Bihar, India

²Assistant Professor, Department of Surgery, JNKTCH, Madhepura, Bihar, India

Received: 10-02-2022 / Revised: 22-03-2022 / Accepted: 25-04-2022

Corresponding author: Dr. Ganesh Kumar

Conflict of interest: Nil

Abstract

Aim: This study aims at comparing the hemodynamic variation with low dose oral clonidine (100mcg) and placebo group in laparoscopic surgeries.

Material & Methods: 80 consecutive patients undergoing laparoscopic procedures of 90 to 180 minutes were enrolled into the study.

Results: Of the 80 cases, 70 were laparoscopic cholecystectomies and 10 were laparoscopic hernia repair, which was comparable between the two groups. However, at 90 minutes the diastolic blood pressure was lower in the test group, but at 120 mts there was no statistically significance between the two groups (p=0.762).

Conclusion: Low dose oral clonidine is a very efficient, easy to administer and cost-effective premedication drug during laparoscopic procedures.

Keywords: Low dose clonidine, Pneumoperitoneum, Laparoscopic surgery, Heart rate, Blood pressure

This is an Open Access article that uses a fund-ing model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

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

The hallmark of laparoscopy is creation of carbon dioxide (CO₂) pneumoperitoneum and change in the patient's position from Trendelenberg to reverse Trendelenberg. It also results in stress hormone responses (cortisol, epinephrine and nor-epinephrine) especially when CO₂ pneumoperitoneum is used concomitantly. [3]

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

Oral clonidine premedication reduces peripheral sympathetic discharge, induces sedation by inhibiting pontine locus cerulleus, attenuates hemodynamic response to noxious stimuli such as

tracheal intubation [6-7] and reduces postoperative pain and analgesic requirement in neuraxial block. [8] It also increases cardiac baroreflex sensitivity in hypertensive individuals and stabilize blood pressure. [9] Furthermore clonidine increases perioperative hemodynamic stability in patients undergoing laparoscopic cholecystectomy with enhancement of parasympathetic control of heart rate. [10-11]

The effectiveness of clonidine in preventing postoperative adverse effects of pneumoperitoneum (pain, nausea and vomiting) and general anesthesia (shivering and postoperative oxygen requirement) were also taken into consideration. Thus, this study aims at comparing the hemodynamic variation between low dose oral clonidine (100mcg) and placebo group in laparoscopic surgeries.

Material & Methods:

A Comparative Study in Department of Anesthesiology, JNKTCH, Madhepura, Bihar, India For 1 year.

80 consecutive patients undergoing laparoscopic procedures of 90 to 180 minutes were enrolled into the study. Inclusion criteria was ASA (American Society of Anesthesia) I and II in the age group of 18 and 70 years. Exclusion criteria were patients of ASA III and IV, patients on antihypertensive medications and patients with known cardiac disease.

Methodology

Rapidly after 60 seconds of succinylcholine administration to avoid distention of the stomach. Inj ondansetron 4mg IV was given to all patients to reduce postoperative nausea and vomiting. Anesthesia was maintained with 33% of oxygen & 66% nitrous oxide, 1% isoflurane and vecuronium. Pneumoperitoneum was created with insufflation of carbon-dioxide. Patient was adequately ventilated to maintain the end

tidal carbon dioxide between 30 and 35. Intra-abdominal pressure was maintained within 15 mmhg throughout the surgical procedure. Intraoperative heart rate and blood pressure (systolic, diastolic and mean) were recorded prior to intubation, prior to pneumoperitoneum, 15, 30, 60, 90 and 120 minutes of pneumoperitoneum, after carbon-dioxide release and after extubation.

An increase in heart rate by 15 beats or mean arterial pressure by 15% from baseline was managed with additional bolus of 20 mcg of inj fentanyl iv and increase of isoflurane by 1% to 1.5% alternatively. Fall in heart rate below 50 bpm with the drop in BP was given inj atropine 0.6mg IV. Intraoperative requirement of opioids(fentanyl) and inhalational agents (isoflurane) were recorded. Patient was reversed with inj neostigmine 2.5mg and inj glycopyrrolate 0.2 mg intravenously and extubated. Postoperative sedation was score by 5 point sedation score, pain by 10 point visual analog scale and presence of nausea, vomiting and shivering were recorded. Postoperative requirement of oxygen was also recorded.

Statistical analysis

The data was entered and analyzed using "SPSS for windows (Version 17)" statistical software. All the continuous variables were described using descriptive statistics and dichotomous variables using proportions. Student's t test and Pearson's Chi square test was the statistical test of significance. P value lesser than 0.05 was considered as significant.

Results:

The mean age was 40.38 and 45.71 in the clonidine and placebo groups respectively. Sex ratio and BMI were comparable between both groups. Of the 80 cases, 70 were laparoscopic cholecystectomies and 10 were laparoscopic hernia repair, which was comparable between the two groups.

Total number of ASA I patients were 40 of which 20 were in clonidine group and 20 were in the placebo group. Total number of ASA II patients were 40, of which 20 were in the clonidine group and 20 in the placebo group.

These parameters were comparable between both the two groups and were not statistically significant.

Table 1 shows there is statistically significant difference and reduction in heart rate in clonidine group compared to placebo group at various interval.

Table 2 shows a significantly lower arterial blood pressure (systolic, diastolic and mean) immediately after pneumoperitoneum, various intervals during surgery and after extubation between the clonidine and placebo group. At 90 and 120 minutes, systolic and mean arterial blood pressure were similar between the clonidine and placebo group. However, at 90 minutes the diastolic blood pressure was lower in the test group, but at 120 mts there was no statistically significance between the two groups ($p=0.762$).

Table 1: Heart rate (in Bpm)

Heart rate	Test		Control	
	Mean	std	Mean	Std
Prior to intubation	82.4	10.6	82.7	13.71
Prior to Pneumoperitoneum	76.2	13.71	84.5	19.63
15 mts of pneumoperitoneum	77.1	11.49	88.9	16.44
30 mts of pneumoperitoneum	79.0	10.84	85.3	10.83
60 mts of pneumoperitoneum	72.6	18.03	84.8	13.81
After CO ₂ release	74.4	9.66	80.6	10.70
After extubation	81.7	12.52	91.7	9.41

Table 2: Blood pressure (in mm of Hg)

	Mean Systolic blood pressure		Mean Diastolic Blood pressure		Mean arterial pressure	
	Test	Control	Test	Control	Test	Control
Prior to intubation	114.28	125.83	71.40	76.23	87.29	92.59
Prior to Pneumoperitoneum	106.73	118.37	63.72	72.12	76.47	84.72
5 mts of Pneumoperitoneum	122.81	135.26	81.87	84.73	93.74	104.38
30 mts of pneumoperitoneum	128.53	133.84	77.39	81.73	94.42	102.94
60 mts of Pneumoperitoneum	120.92	127.92	78.37	80.20	95.99	96.30
After CO ₂ release	120.02	130.04	75.19	80.01	94.48	97.66
After extubation	133.88	141.73	78.39	82.63	95.80	103.52

Discussion:

Pneumoperitoneum created during laparoscopic surgery induces certain drastic changes in the patients' hemodynamics. These include an increase in MAP, decrease in CO and increase in SVR which manifest as hypertension,

tachycardia and may also compromise tissue perfusion and affect the acid-base homeostasis. This necessitates the use of anesthetic interventions for maintaining hemodynamic parameters in acceptable range in order to maintain blood supply to vital organs. Techniques like use of low

intra-abdominal pressure and gasless laparoscopies using abdominal elevators have been used with limited success. [12-13]

The first stimulus for sympathoadrenal response i.e. laryngoscopy and intubation was associated with a steep rise in HR, SBP, DBP and MAP in the placebo group. This rise in HR and BP did not occur in clonidine group patients. Our findings matched the findings of Rawal, et al who used a dose of 4 µg/kg clonidine for attenuation of hemodynamic response to laryngoscopy and intubation. [14]

Looking at oral clonidine dose wise, the rate of propofol reduction was more in study done by Imai et al [15]. The difference in the findings could be due to the fact that they conducted their study in minor surgery and the mean duration of anesthesia in their study was longer than our study. Further, they also used nitrous oxide during maintenance of anesthesia along with propofol infusion. Richards and coworkers [16] reported oral clonidine 600 mg to reduce the minimum anesthetic concentration of propofol with prolonged recovery from anesthesia.

In laparoscopic surgeries a greater sympathetic tone and catecholamine release may trigger nausea and vomiting. [17] Clonidine increases gastrointestinal motility by decreasing sympathetic outflow and increasing parasympathetic outflow from the central nervous system and reduces the postoperative nausea and vomiting. In our study, clonidine group did not have nausea and vomiting but the placebo group had significant patients with nausea and vomiting. Similar observation was seen in studies done by B Ghrab et al [18] and Javaher Froosch et al. [19,20]

Conclusion:

Low dose oral clonidine is a very efficient, easy to administer and cost-effective premedication drug during laparoscopic procedures. It has an added advantage of

lesser postoperative complications like shivering, pain, nausea and vomiting.

References:

1. Vecchio R, MacFayden BV, Palazzo F. History of laparoscopic surgery. *Panminerva Med* 2000; 42:87-90.
2. Joris JL. Anesthesia for laparoscopic surgery. In: Miller RD, editor. *Miller's Anesthesia*. 7th ed. Elsevier: Churchill livingstone; 2010. p. 2185-6.
3. Naude GP, Ryan MK, Pianim NA, Klein SR, Lippmann M, Bongard FS. Comparative stress hormone changes during helium versus carbon dioxide laparoscopic cholecystectomy. *J Laparoendosc Surg* 1996; 6:93-8.
4. Hayashi Y, Maze M. Alpha 2 adrenoceptor agonists and anesthesia. *Br J Anaesth* 1993; 71:108-18.
5. Harron DW, Riddell JG, Shanks RG. Effects of azepexole and clonidine on baroreceptor mediated reflex bradycardia and physiological tremor in man. *Br J Clin Pharmacol* 1985;20: 431-6.
6. Laurito CE, Baughman VL, Becker GL, DeSilva TW, Carranza CJ. The effectiveness of oral clonidine as a sedative/anxiolytic and as a drug to blunt the hemodynamic responses to laryngoscopy. *J Clin Anesth* 1991; 3:186-93.
7. Ghignone M, Quintin L, Duke PC, Kehler CH, Calvillo O. Effects of clonidine on narcotic requirements and hemodynamic response during induction of fentanyl anesthesia and endotracheal intubation. *Anesthesiology* 1986; 64:36-42.
8. Goyagi T, Nishikawa T. Oral clonidine premedication enhances the quality of Postoperative analgesia by intrathecal morphine. *Anesth Analg* 1996; 82:1192-6.
9. Parlow JL, Begou G, Sagnard P, Cottetr Emard JM, Levron JC, Annat G. Cardiac baroreflex during the postoperative period in patients with

- hypertension: Effect of clonidine. *Anesthesiology* 1999; 90:681-92.
10. Ndiaye AL, Guyon F, Knorr M, Huch V, Veith M, Anorg Z. Adverse hemodynamic changes during LC and their possible suppression with clonidine premedication. comparison with intravenous intravascular premedication *Rozal chir* 1999;78(6):286- 91.
 11. DeBoer RW, Karemaker JM, Strackee J. Hemodynamic fluctuations and baroreflex sensitivity in humans: a beat-to-beat model. *Am J Physiol* 1987; 253: 608—609.
 12. Dexter SPL, Vucevic M, Gibson J, McMahon MJ. Hemodynamic consequences of high- and low-pressure capnoperitoneum during laparoscopic cholecystectomy *Surg Endosc.* 1999;13(4):376-81.
 13. Gurusamy KS, Samraj K, Davidson BR. Abdominal lift for laparoscopic cholecystectomy. *Cochrane database Syst Rev.* 2008;16(2):CD006574.
 14. Raval DL, Mehta MK. Oral clonidine premedication for attenuation of hemodynamic response to laryngoscopy and intubation. *IJA.* 2002;46(2):124-9.
 15. Imai Y, Muammoto T, Murakami K, Sakai T, Kirita T, Sugimura M et al. The effects of preanesthetic oral clonidine on total requirement of propofol for general anesthesia. *J. clin anesthesia* 1998; 10:660- 665.
 16. Richards MJ, Skues MA, Jarvis AP, Prys- Roberts C. Total i.v. anesthesia with propofol and alfentanil: dose requirements for propofol and the effect of premedication with clonidine. *Br J Anaesth* 1990; 65:157– 63.
 17. Arman Taheri, Mohammad Ali Javadi manesh and Haleh Ashraf, “The effect of oral clonidine premedication on nausea and vomiting after ear surgery” *Middle east journal of anesthesia* 2010, 5 (20), 691-694.
 18. Ghrab. B, Khemakhem. K, Chaari. M, Kolsi. K, Karoui. A, “Clonidine improves postoperative analgesia and reduces nausea and vomiting after laparoscopic cholecystectomy: 14AP58” *European Journal of Anaesthesiology* (2007 June), 24,181.
 19. Javaher Froosch F, M Raza Pipelzadeh, Namazi M, “Clonidine reduces postoperative nausea and vomiting in laparoscopic Gynaecological surgery” *Pakistan journal of medical science* 2009: 25(5), 782- 785.
 17. Sussan Soltani Mohammadi, Mirsadegh Seyedi, “Effect of oral clonidine in preventing postoperative shivering after general anesthesia” *International journal of pharmacology* 2007, 3 (5), 441–443.
 20. Tomasi, D., & Webb, S. Human Gastrointestinal Microbiota and Neural Activity: Effects of Probiotics on Mental and GI Health. *Journal of Medical Research and Health Sciences*, 2020;3(9), 1070–1077.