

Comparison between the hemodynamic stability of dexmedetomidine and clonidine infusions among patients undergoing laproscopic cholecystectomy- A randomized controlled trial

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Article Info

Received: 26th March, 2019

Accepted: 22nd July, 2019

Published Online: 22nd August, 2019

Keywords: Clonidine, Dexmedetomidine, Cardiovascular stability.

Abstract

Introduction: The anesthesiologist's traditional approach to anesthesia for laproscopic cholecystectomy is to ensure that the patient is hemodynamically stable during the entire procedure. Hemodynamic instability is very common during pneumoperitoneum particularly after CO₂ insufflations.

Aim: To compare the efficacy between dexmedetomidine and clonidine on hemodynamic stability among patients undergoing laproscopic cholecystectomy.

Materials and Methods: A double blinded randomized controlled trial was conducted by the department of anesthesiology of KLES Dr Prabakhar Kore hospital and research centre for a period of 6 months. Patients undergoing laproscopic cholecystectomy under general anesthesia were included as our study subjects. The entire study subjects were randomized into three groups of 20 each, with one group taken as placebo group and the other two were the study groups with patients receiving clonidine and dexmedetomidine. Hemodynamic parameters were measured and compared between the groups.

Results: The heart rate and the mean arterial pressure was significantly high in placebo group than that of the other two groups but the comparison between clonidine or dexmedetomidine group did not show significant difference in the hemodynamic parameters. Similarly the recovery time after extubation and the number of isoflurane dose requirements were also high among the placebo group when compared to the other two groups.

Conclusion: The measurement of hemostability parameters between the clonidine and dexmedetomidine did not show much variation, but considering clonidine being more cost effective than dexmedetomidine, it can be recommended for maintaining cardiovascular stability during laproscopic cholecystectomy.

Introduction

Hemodynamic stability during perioperative period is of paramount importance as there are many patients who have a compromised cardiovascular status and are on medications.¹ The anesthesiologist's traditional approach to anesthesia for laproscopic cholecystectomy is emphasizing on hemodynamic stability of the patients during the entire procedure. Hemodynamic instability is very common during pneumoperitoneum particularly after CO₂ insufflations. Numerous volatile agents like isoflurane and sevoflurane had been used to overcome this problem but it was found to have limited success.²

Laprosopic surgeries require creation of pneumoperitoneum which is produced by the insufflations of carbondioxide in the abdominal cavity. Inflation pressure can be varied from 0 – 30 mm hg with a total gas flow can be set between 1–9.9 L/min. Problems related to hemodynamic stability in laproscopic surgeries occurs due

to pneumoperitoneum and the patient positioning.³ The induction of pneumoperitoneum in laproscopic surgeries leads to rise in the intra-abdominal pressure thereby causing high circulating blood volume followed by raise in the cardiac output and mean arterial pressure with subsequent rise in systemic and pulmonary vascular resistance.^{4,5} To overcome this problem two novel alpha 2 agonist namely clonidine and dexmedetomidine were registered under FDA.⁶

Clonidine is a selective alpha 2 agonist with a short half-life of less than 10 hrs. It is known for its sedation action, maintaining the perioperative hemodynamic stability and there by reduces the dose requirement of anesthesia.^{7,8} Similarly dexmedetomidine is also a alpha 2 agonist with a shorter half life than clonidine and has a similar a hemodynamic response during tracheal intubation and laproscopic insufflations of carbondioxide, as both these

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<http://doi.org/10.18231/ijca.2019.084>

drugs act by inhibiting the release of catecholamines and vasopressin.^{9,10}

Laparoscopic cholecystectomy being a routinely performed surgery maintaining stable hemodynamic mechanism is of utmost important and very few studies as of today had compared clonidine and dexmedetomidine as preferred drug for maintainance of the hemodynamic system and so the current study was undertaken.

Aims

To compare the hemodynamic response between dexmedetomidine and clonidine among patients undergoing laparoscopic cholecystectomy.

Materials and Methods

A double blinded randomized controlled trial was conducted by the department of anesthesiology of KLES Dr. Prabhakar Kore hospital and research centre for a period of 6 months. Institutional ethical clearance approval was obtained before the start of the study. Patients ASA grading was assessed and patients with grade I and II were included for the study. For all the patients the operative procedure was conducted under general anesthesia. Hypertensive patients, patients with ischemic or valvular heart disease, patients with liver or renal dysfunction, pregnant or lactating mothers were excluded from the study. Patients who were willing to sign the informed consent were included for the study. A total of 60 patients were included as our study subjects and the entire study subjects were randomized into three groups of 20 each. Group A was taken as placebo group where only normal saline was given, Group B patients received clonidine in the dosage of 4mcg/kg/hr in 0.9% of normal saline and Group C patients received dexmedetomidine in the dosage of 0.4mcg/kg/hr in 0.9% of normal saline. A complete pre-anesthetic examination was conducted on all patients and all the vital parameters were recorded. Patients were randomized based on computer generated randomization table. The study drug was started 30 minutes before induction using infusion pump at the rate of 0.08ml/kg/hr. Throughout the procedure any 20% rise in MAP above the basal level, Isoflurane concentration was

increased and any fall in MAP of more than 20% Isoflurane was stopped to maintain the MAP in the normal level. MAP was measured at regular interval throughout the procedure.

All data were entered and analysed using SPSS version 22. Mean and standard deviation were derived for all parametric variables ANOVA was used to study the statistical inference of the parametric variables between the groups and similarly and Man-whitney U test was used to study the statistical significance of non-parametric variables.

Results

The mean age, gender distribution, mean bodyweight and the mean duration of the operative procedure did not have any significant variations between the three groups (Table 1). The heart rate before the start of the procedure and the heart rate at the time of induction were almost similar in all the three groups. The heart rate of the placebo group started to increase within minutes after induction and it was maximum during the period of pneumoperitoneum. The mean heart rate of the clonidine group was less than 75 and during pneumoperitoneum it was between 75 and 80 among the patients who received dexmedetomidine, in the placebo group it was between 90 and 95 beats/min. Between the three groups a statistical significant difference was observed between the heart rates but no such difference was observed between the two study groups (Table 2). A similar type of result was observed in the mean arterial pressure measurements among the three groups (Table 3). Usage of isoflurane during the procedure was more among the patients who received normal saline (placebo) and similarly the duration of recovery after extubation in these patients were longer than the other two groups and the difference was found to be statistically significant. But between the study groups (clonidine Vs dexmedetomidine) the recovery time and isoflurane usage did not show significant difference. Atropine was not used in placebo group whereas few patients in clonidine and dexmedetomidine group received atropine to maintain the hemodynamic stability (Table 4).

Table 1: Demographic characteristics of the study subjects

Variable	Group A (placebo)	Group B (clonidine)	Group C (dexmedetomidine)	P value
Age (mean ± SD)	43.2 ± 13.1	44.9 ± 8.1	45.9 ± 11.2	0.800
Gender (M:F)	11:9	13:7	9:11	0.549
Body weight (in kgs) (mean ± SD)	59.4 ± 8.5	59.2 ± 5.9	58.6 ± 7.3	0.716
Duration of surgery (mean ± SD)	68.1 ± 12.3	73.4 ± 27.6	76.5 ± 19.8	0.374

Table 2: Mean and SD of the heart rate of the study subjects measured at various intervals

Heart rate	Group A	Group B	Group C	P value
Pre-operative	88.13±13.8	87.8±13.3	87.7±14.7	0.936
At induction	87.7±14.2	81.0±12.8	84.0±15.1	0.179
After intubation	108.4±15.1	77.4±11.9	87.0±14.4	<.001
Before pneumoperitoneum	93.6±13.6	81.6±14.1	81.07±16.1	0.005
10 mins after pneumoperitoneum	90.8±13.9	73.4±13.6	83.5±15.8	0.004
20 mins after pneumoperitoneum	90.8±14.9	69.7±11.6	73.5±14.9	0.004
30 mins after pneumoperitoneum	94.2±15.3	69.8±12.4	76.9±16.9	0.001
End of pneumoperitoneum	83.0±11.7	67.5±11.6	72.9±16.7	0.006
Postoperative in recovery room	86.4±10.4	67.9±8.6	73.2±15.2	0.001

p value derived by applying ANOVA

Table 3: Mean and SD of the mean arterial pressure (MAP) of the study subjects measured at various intervals

Heart rate	Group A	Group B	Group C	P Value
Pre-operative	95.1±8.9	96.0±10.5	94.9±11.4	0.936
At induction	85.0±9.4	84.2±11.2	86.5±10.5	0.860
After intubation	117.9±11.4	91.6±9.8	90.2±12.3	0.0001
Before pneumoperitoneum	100.2±10.8	90.5±12.2	90.0±8.9	0.081
10 mins after pneumoperitoneum	109.6±12.6	94.6±13.6	99.5±12.2	0.014
20 mins after pneumoperitoneum	103.9±16.5	92.3±8.6	97.6±13.2	0.034
30 mins after pneumoperitoneum	102.7±14.3	90.6±9.4	93.5±11.8	0.007
End of pneumoperitoneum	101.8±8.6	91.6±10.1	95.5±11.6	0.024
Postoperative in recovery room	101.6±6.9	90.0±8.8	91.9±10.6	0.001

Table 4: Various other factors used to assess the efficacy between the three groups

Variable	Group A	Group B	Group C	P value
Recovery time following extubation (mean ± SD)	6.8 ± 2.1	2.6 ± 1.8	3.4 ± 0.9	<.0001
Number of patients requiring >1.5% isoflurane during intraoperative period	20 (100%)	5 (25%)	6 (30%)	<.0001
Number of patients required atropine in the dose of 0.6 mg i.v.	0	4 (20%)	2 (10%)	0.0721

Discussions

Intraoperative tachycardia and hypertension are the most common hemodynamic disturbances among patients undergoing laproscopic cholecystectomy. In addition there is increase in systemic vascular resistance, and is associated with decrease in cardiac index and metabolic changes. Various studies had been conducted with various pharmacological interventions that results in reduced incidence of tachycardia and hypertension and provide a stable hemodynamic state without significant undesirable effects.¹¹⁻¹³ In our study we compared the efficacy of clonidine with dexmedetomidine on hemodynamic stability among patients undergoing laproscopic cholecystectomy. A placebo group was taken as a control. In the present study we found no significant change in the heart rate and blood pressure among both the study groups in comparison with the placebo group. In a study done by Taittonen et al comparing clonidine 4mcg/kg with dexmedetomidine 2.5 mcg/kg had found that the heart rate and MAP was significantly lower in both these group in comparison with the placebo group.¹⁴ A study done by Hall JE et al on comparing between clonidine and placebo group had found an increase in MAP and a decrease in MAP in placebo and clonidine groups respectively in comparison with the baseline values which is in par with our study and an other

conducted by Das M et al in 2007 had also quoted a similar type of results.^{15,16}

A recent study done by Singh S et al had monitored the MAP intaroperatively by giving 150 mcg of oral clonidine before induction and found that the perioperative MAP was lower at all time in the clonidine group compared to the placebo group.¹⁷ Another study done by Tufanogullari et al and Bhattacharjee et al comparing between different doses of dexmedetomidine with the placebo group among the patients undergoing laproscopic cholecystectomy and they found a significant increase in MAP and heart rate in the placebo group whereas in the dexmedetomidine group there was no significant rise and the usage of isoflurane is more in placebo and the results are in par with our study.^{18,19} The use of atropine in the present study was very minimal in the study group as quoted by the previous studies.^{20,21}

In patients suffering from coronary artery disease, the heart rate lowering effect of both the drugs reduced the myocardial oxygen demand of the patient which was very useful. Dexmedetomidine was found to be more effective in this situation and these findings were consistent with study done by Naz Anjum et al.²² Thus, both the study drugs provided hemodynamic stability during laparoscopic surgeries and dexmedetomidine was equally effective as

clonidine for this purpose. A study done by Pravin Ubale et al showed that using oral clonidine as premedication has similar results as found in the present study.²³ In a study done by Pooja Gautham had revealed that both clonidine and dexmedetomidine being an α_2 agonists were found to be effective in attenuating the hemodynamic response to pneumoperitoneum during laparoscopic surgeries and provides reliable postoperative analgesia and sedation when used as a premedication agent.²⁴

Conclusion

Our study had proved the use of alpha 2 agonist namely clonidine and dexmedetomidine in providing hemodynamic stability by reducing the sympathetic response to laryngoscopy, extubation and during the period of pneumoperitoneum in laproscopy surgeries. In addition clonidine being more cost effective than dexmedetomidine, it can be recommended for maintaining cardiovascular stability during laproscopic cholecystectomy.

Conflict of Interest: None.

Source of Funding: None.

References

- Anno H, Takeda A, Tarver SD, Goto H. Stress response in three different anesthetic techniques for carbon dioxide laproscopic cholecystectomy. *J Clin Anesth* 1998;10(7):546-50
- Luchetti M, Palomba R, Sica G, Massa G, Tufano R. Effectiveness and safety of combined epidural and general anesthesia for laproscopic cholecystectomy. *Reg Anesth* 1996;21(5):465-69.
- Glick DB. The Autonomic Nervous system. In – Miller's Anesthesia 7th ed New York: Churchill Livingstone; 2010.
- Kaleman G, Swapp G. Cardiac output and arterial blood gas tension during laproscopy. *Br J Anesth* 1972; 44:1155
- Jorris J, Noriott D, Legrand MJ, Jacquet NJ, Lammy ML. Hemodynamic changes during laproscopic cholecystectomy. *Anesth Analg* 1993;76:1067-72.
- Kamibayashi T, Maze M. Clinical uses of alpha 2 adrenergic agonists: *Anesthesiology* 2000; 93:1345-49.
- Cunningham AJ, Brull SJ. Laproscopic cholecystectomy: Anesthetic implications: *Anesth Analg* 1993;76(110):20-33.
- Kang Ws, Kim SY, Son JC, Kim JD, Muhammad HB, Kim SH et al. The effect of dexmedetomidine on the adjuvant propofol requirement and intraoperative hemodynamics during remifentanyl-based anesthesia. *Korean J Anesth* 2012;62:113-8.
- MD RAjakumaraswamy N, Maze M. Alpha2 adrenoceptor agonists: Shedding light on neuroprotection. *Br Med Bull* 2004;71:77-92.
- Ohtani N, Kida K, Shoji K, Y Asui Y, Masaki E. Recovery profiles from dexmedetomidine as a general anesthetic adjuvant in patients undergoing lower abdominal surgery. *Anesth Analg* 2008;107:1871-74.
- J Amadharkana S, Gopal S. Clonidine in adults as a sedative agent in the intensive care unit. *J Anesth Clin Pharm* 2010;26:439-45.
- Samantaray A, Rao MH, Chandra A. The effect on post-operative pain on intravenous clonidine given before induction of anesthesia. *Indian J Anaesth* 2012;56:359-64.
- Marinangeli F, Ciccozzi A, Donatelli F, Di Pietro A, Lovinelli G, Rawal N, et al. Clonidine for treatment for postoperative pain: A-dose finding study. *Eur J Pain* 2002;6:35-42.
- Taittonen T, Kirvela OA, Aantaa R, Kanto JH. Effect of clonidine and dexmedetomidine premedication on the perioperative oxygen consumption and hemodynamic state. *BJA* 1997;78:400-6.
- Hall Je, Barney JA, Toni D, Uhrich MS, Colinco M. The effects of increasing plasma concentrations of dexmedetomidine in Humans. *Anesth* 2000;93:382-94.
- Das M, Ray M, Mukherjee G. Hemodynamic changes during laproscopic cholecystectomy. Effect of clonidine premedication. *IJA* 2007;51(3):205-10.
- Singh S, Arora K. Effect of oral clonidine premedication on perioperative hemodynamic response and post-operative analgesic requirement of patients undergoing laproscopic cholecystectomy. *IJA* 2011;55(1):26-30.
- Tufanogullari B, White PF, Deixoto MP, Kianpour D, Lacour T, Griffin J et al. Dexmedetomidine infusion during laproscopic bariatric surgery. The effect on recovery outcome variables. *Anesth Analg* 2008;106 (6):1741-8.
- Bhattacharjee DP, Nayak SK, Dawn S, Bandopadhyay G, Gupta K. Effects of dexmedetomidine on hemodynamics in patients undergoing laproscopic cholecystectomy-A Comparative study. *J Anesth Clin Pharm* 2010;26(1):45.
- Etta LV, Burchell H. Severe bradycardia with clonidine *JAMA* 1978;240:2047
- Aho M, Erkola OA, Scheinin H, Lehinerr AM, Kortilla KT. Effect of intravenously administered dexmedetomidine on pain after laproscopic tubal ligation. *Anesth Analg* 1991;73:112-8.
- Anjum N, Tabish H, Debdas S, Bani Choudhuri HP, Dastidar RG, Basu A. Effects of dexmedetomidine and clonidine as propofol adjuvants on intra-operative hemodynamics and recovery profiles in patients undergoing laproscopic cholecystectomy: A prospective randomized comparative study.
- Ubale P, Kumar IH. Effect of intravenous clonidine on hemodynamic changes in laproscopic cholecystectomy: a randomized control study. *Anaesth Pain Intensive Care* 2016;20:182-6.
- Pooja Gautam. Comparative Study of Clonidine Vs Dexmedetomidine for Hemodynamic Stability and Postoperative Analgesia during Laproscopic Surgery. *IJCMR* 2019;6(1):A1-7.

How to cite this article: Rajaprabu T, Kumar V. Comparison between the hemodynamic stability of dexmedetomidine and clonidine infusions among patients undergoing laproscopic cholecystectomy- A randomized controlled trial, *Indian J Clin Anaesth* 2019;6(3):437-40.