Scholars Journal of Applied Medical Sciences (SJAMS)
Abbreviated Key Title: Sch. J. App. Med. Sci.
ISSN 2320-6691 (Online)
ISSN 2347-954X (Print)

A Unit of Scholars Academic and Scientific Society, India
www.saspublishers.com

Anaesthesiology

A Comparative Evaluation of Intravenous Clonidine on Haemodynamic Stress Response during Pneumoperitoneum in Laparoscopic Abdominal Surgeries

Sandeep Kothiya, Nidhi Sharma*
Department of Anaesthesiology, G.R. Medical College, Gwalior, M.P., India

Original Research Article

***Corresponding author**
Nidhi Sharma

Article History
Received: 19.07.2018
Accepted: 24.07.2018
Published: 01.08.2018

DOI:
10.36347/sjams.2018.v06i08.022

Abstract: Laparoscopic surgeries are gaining importance nowadays because of their benefits and less complication rate when compared with open surgical procedures. But laparoscopic procedures are not free from complications too. Pneumoperitoneum created during laparoscopic procedure leads to hemodynamic instability. So many pharmacological agents are used to subside effect of pneumoperitoneum. Clonidine is one such agent which is an α- 2 agonist. This randomized control study was conducted on 60 patients of ASA grade 1 and 2 after taking ethics committee approval. Group CL (n=30) clonidine is infused during the surgery and in group C (n=30) normal saline is infused. Diastolic and systolic blood pressure, mean arterial blood pressure and heart rate were measured throughout the procedure till 30 minutes after the procedure. Sedation score was also measured after the surgery. Effect of intubation and laryngoscopy induced stress response, creation of pneumoperitoneum, reversal of pneumoperitoneum and extubation was seen over heart rate, SBP, DBP and MAP in both the groups but was significantly less in the clonidine(CL) group compared to the control(C) group showing better stability of the hemodynamic vitals in the patients given cloidine intraoperatively ($P<0.05$). Clonidine suppresses pneumoperitoneum induced hemodynamic instabilities in patients undergoing laparoscopic cholecystectomy under general anaesthesia.

Keywords: Blood pressure, Clonidine, General anaesthesia, Heart rate, Sedation.

INTRODUCTION

Laparoscopic approach is safe and reliable technique with several advantages over the standard open procedure[1,2]. Laparoscopic abdominal surgeries are quite common with complication rate being less than 1.5% and mortality rate less than 0.1%[3]. Because of its less cosmetic scar, less postoperative pain, decreased hospital stay and obviously less mortality, it has become the gold standard for treatment of gall bladder diseases[4].

For laparoscopic abdominal surgeries, anesthesiologists mainly emphasized on maintaining haemodynamic stability by avoiding hypertension, hypotension or tachycardia but the problem has been more complex and most of the haemodynamic instability is persistent during the duration of pneumoperitoneum (PNP) [5, 6] namely carbon dioxide (CO2) insufflations and patient positioning[7, 8].

CO2 is the main gas used for insufflations in laparoscopic procedure although gases like helium and air can also be used[9,10]. The cardiopulmonary changes occur during laparoscopy.Insufflation of CO_2 and increased IAP (>10 torr) produces significant alterations in haemodynamic parameters characterised by decreased cardiac output, increased arterial pressures, increased systemic vascular resistance (SVR) and pulmonary vascular resistance (PVR)[11, 12].Pneumoperitoneum decreases thoracopulmonary compliance by 30-50%[13].

Reduction in FRC[14] and atelectasis due to elevation of diaphragm and changes in ventilation and perfusion results from increased airway pressure[15]. Many pharmacological agents like adrenoreceptorblockers[16], beta blockers[17], Ca channel blocker, lidocaine[18], opioids[19], pregabalin[20], magnesium sulfate[21], vasodilators[22], remifentanil[23] have been used to attenuate these responses with varying success.

Clonidine a centrally acting selective partial α-2 agonist is known to induce sedation, decrease anaesthetic drug requirement and improvement in perioperative haemodynamic stability by altering blood pressure and heart rate responses to surgical

stimulation, and protection against perioperative myocardial ischemia [24,25].

MATERIALS & METHODS

After obtaining approval from the ethics committee and well written informed consent from the patients, study was carried out on 90 patients of ASA grade I and II, aged 20-50 years, undergoing laparoscopic cholecystectomy lasting 1-3 hours requiring general anesthesia with endotracheal intubation at J.A Group of Hospitals of G.R. Medical College, Gwalior (M.P), India. Patients were allocated randomly using envelope technique in two groups of 30 each. In group C, normal saline is infused and it is a control group while in group CL, clonidine is infused during the surgery.

Exclusion Criteria were**:** ASA grade III and above, BMI >30,patients undergoing laparoscopic to open surgery conversion intraoperatively, pneumoperitoneum duration >90 minutes, known history of allergy or sensitivity or any other reaction to study drugs, patients with cardiopulmonary and respiratory disorders, patients with hypertension on treatment with beta-Blocker, Methyl-dopa, MAO inhibitors, tricyclic antidepressant, patients with psychiatric illness, patients with renal and hepatic dysfunction, pregnant and lactating females.

Consent

Details of procedure were explained to all the patients during preanaesthetic assessment and an informed and written consent was obtained.

Patients' grouping

90 patients of ASA grade I & II of either sex scheduled for abdominal surgeries under general anaesthesia were divided into 2 groups (n=30 each) randomly using envelope technique as below:

Group C (n=30)	50 ml normal saline over a period of 10 minutes after induction and before pneumoperitoneum (PNP), followed by a continuous slow infusion at the rate of 0.5 ml/kg/hr.
Group CL (n=30)	Clonidine 1.5µg/kg in 50ml normal saline over a period of 10 minutes after induction and before PNP, followed by a continuous infusion at the rate of 2 µg/kg/hr.

Preparation of the patient

Upon arrival of the patient in the operation room, intravenous access with 18G cannula was established and 500 mL of crystalloid infusion was started. All the baseline vital parameters (HR, SBP, DBP, MAP), electrocardiography using three lead ECG were monitored. Oxygen saturation (SPO2) was monitored by using pulse oximeter. End tidal Carbon dioxide was monitored intraoperatively and kept between 25 and 30 mmHg.

Anaesthesia procedure and recording

All the drugs were administered by a person who was not involved in the study to avoid bias. Patients were preoxygenated with 100% oxygen at appropriate flow for 3 minutes by facemask. After premedication with i.v.InjPentazocine0.5mg/kg, general anesthesia was induced with i.v.Inj Thiopentone Sodium 5 mg/kg body weight. Endotracheal intubation was facilitated with i.v. Inj. Succinylcholine 1.5 mg/kg body weight and IPPV was done for 60 seconds with 100% oxygen.

Laryngoscopy was done with laryngoscope having Macintosh blade and tracheal intubation done with appropriate size of cuffed endotracheal tube. Cuff was inflated and bilateral equal air entry was checked and then tube was fixed.

General anaesthesia was maintained with nitrous oxide & oxygen (67:33) and Isoflurane (0.5-1%) with Bain's anaesthetic circuit. Loading and intermittent dosage of non-depolarizing muscle relaxant, IV AtracuriumBesylate0.5mg/kg body weight initially followed by increment doses at 0.1mg/kg was used to maintain general anaesthesia under controlled ventilation throughout the surgical procedure. After intubation, the infusion of Clonidine (1.5µg/kg) in 50 mL normal saline or 50 mL normal saline was started 10 min before induction of pneumoperitoneum. This was followed by a continuous infusion clonidine at a rate of 2 µg/kg/hr and NS at a rate of 0.5 ml/kg/hr according to the study group.

During study period haemodynamic parameters such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were recorded at 0 minute (B), D_0, D_{10}, BPN, APN, APN_{10}, APN_{20}, APN_{30}, APN_{40}, APN_{50}, APN_{60}, APN_{90},RPN, AR, AR_{15}, AR_{30}, intervals. PNP- Pneumoperitoneum, B- Basal value (0 minute), D_0- Before study drug, D_{10}- After study drug, BPN-Before pneumoperitoneum, APN- After pneumoperitoneum, RPN- Release of pneumoperitoneum, AR- After reversal.

All the study drugs were stopped once surgical procedure was done and pneumoperitoneum was released.

After surgery, patients were reversed with Inj. Glycopyrrolate0.005mg/kg and Neostigmine 0.08mg /kg intravenously. After extubation patients were

observed for recovery time defined as time to vocalize after extubation.

Side effects and complications

Patients were closely observed for bradycardia / tachycardia (± 20% of basal value), hypotension / hypertension (± 20% of basal value), bradyarrythmia& desaturation (<85%) during intra and postoperative period. During postoperative period along with above, nausea, vomiting, respiratory depression, sedation and shivering were also recorded if occurred. Any complication if occurred was treated with appropriate medications.

Statistical analysis

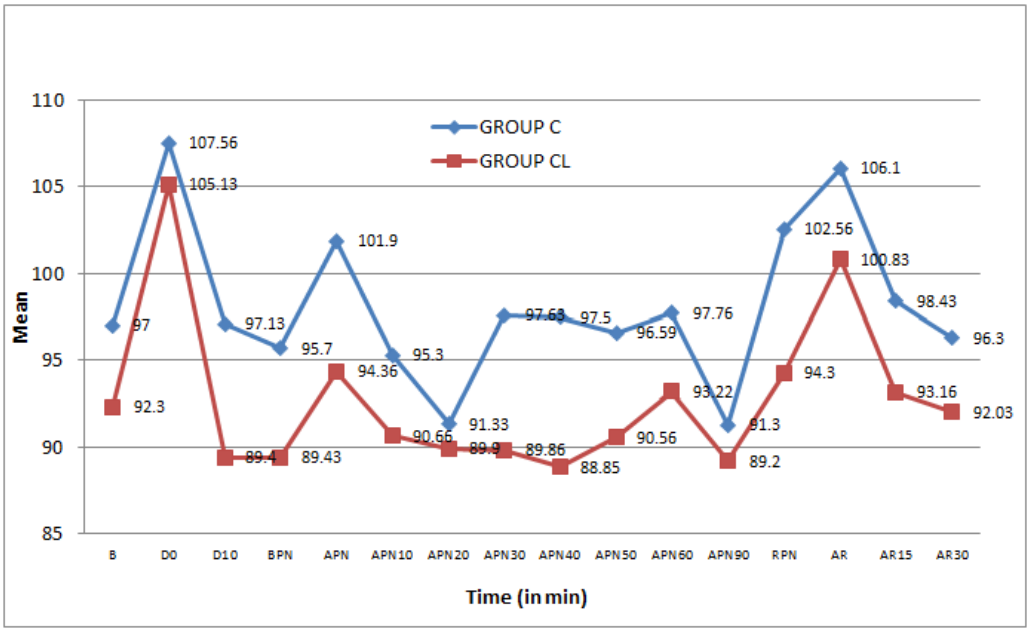
The observations were recorded and subjected to statistical analysis using students "t" test by statistics calculator SPSS 17. Student 't'-test for inter group comparison was used. p-value>0.05 was taken to be statistically insignificant & p-value <0.05 was taken statistically significant and p-value <0.01 taken to be statistically highly significant.

RESULTS

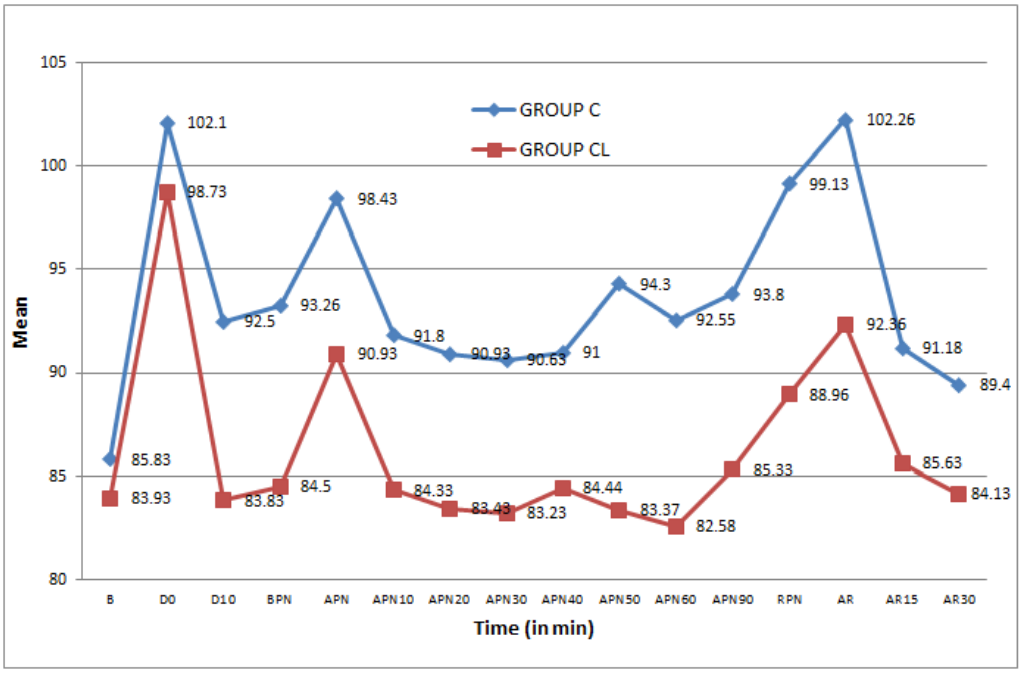
Data obtained from the patients involved in the study were analyzed. The mean age, weight, sex, type of surgery, duration of pneumoperitoneum, duration of anaesthesia, type of surgery and Ramsay sedation scoreafter extubationwere comparable in all the three study groups as shown in table. Preoperative heart rate, systolic, diastolic and mean blood pressure and blood sugar level were comparable in all the two groups.

Table- 1: Showing demographic variables of two groups

DEMOGRAPHIC DATA	Group A	Group B
Age	34.43±8.75	35.16±8.49
Weight (Kg)	53.23±7.20	53±6.45
Sex (Female)	73.33%	86.67%
Duration Of Pneumoperitoneum (Min)	62.96±18.14	58.4±17.78
Duration Of Anaesthesia (Min)	89.16±19.47	85±9.73
Type Of Surgery Laparoscopic Cholecystectomy	93.33	93.33
2. Laparascopic Hernia	6.67	6.67
Ramsay Sedation Score After Extubation(Mean+SD)	1.43±0.56	1.73±0.69



Graph-1: Statistical analysis of mean (± SD) mean arterial pressure (mmHg)



Graph-2: Statistical analysis of mean pulse rate (bpm)

DISCUSSION

Pneumoperitoneum used for laparoscopic procedure is a complex patho-physiologic phase with significant haemodynamic variation. Pneumoperitoneum (PNP) is produced by administration of carbon dioxide (CO_2) during laparoscopic surgical procedure [9, 10]. Both pneumoperitoneum and CO_2 cause adverse cardiovascular effects due to increase of plasma levels of epinephrine, nor-epinephrine, vasopressin, neurophysin and plasma renin activity increase [26]. All these changes contribute to increase in heart rate, arterial pressure, systemic and pulmonary vascular resistance and reduced cardiac output. In addition trendelenburg position causes diminished venous return and reduction in cardiac output [7].

Various studies have been done over the years for attenuating these unwanted detrimental effects which occur during pneumoperitoneum and intraoperative period. Drugs like beta blockers, magnesium sulphate, opioids, nitroglycerine, lidocaine, pregabalin, calcium channel blockers and gasless approach [27] to negate the haemodynamic variations. In modern anesthesia practice α-2agonist due to their beneficial effects like sedation, analgesia, attenuation of stress response and reduction of anesthesia requirement has been studied to attenuation of these responses. Clonidine is one such drug of alpha-2 agonist category that significantly reduces the release of catecholamines, predominantly having an effect on systemic vascular resistance and improves intra and postoperative haemodynamic stability by stabilizing the changes in heart rate, arterial pressure and cardiac output.

The present studywas conducted to evaluate and compare the effects and efficacies of clonidine on HR, SBP, DBP and MAP during pneumoperitoneum. This study was also aimed to observe any untoward effects of study drugs and effect on sedation after extubation.

Selected groups were comparable for the demographic variables like age and weight parameters, type of surgery, sex, duration of pneumopeitoneum and duration of anaesthesia with P>0.05. Effect of intubation and laryngoscopy induced stress response, creation of pneumoperitoneum, reversal of pneumoperitoneum and extubation was seen over heart rate, SBP, DBP and MAP in both the groups but was significantly less in the clonidine(CL) group compared to the control(C) group showing better stability of the hemodynamic vitals in the patients given cloidineintraoperatively.

Joris JL *et al.* conducted a study in which clonidine (8µg/kg) was given before pneumoperitoneum reduced the release of catecholamines and thus significantly attenuated the increase in MAP and heart rate in comparison to placebo.

Singh S *et al.* [28] observed significant rise in MAP in placebo group compared to oral clonidine group (150µg) after pneumoperitoneum.

Passi Y *et al.* [29] observed that with oral clonidine (150µg) premedication 60-90 minutes before laparoscopy, change in MAP was significantly lower and MAP varied between 88±9 to 95±9 mmHg as

compared to control group (vit B comlpex tablets) in which MAP varied between 97±14 to106±5 mmHg.

Sung CS *et al*. [30] also found that isoflurane requirements were less by 30% in patients who received clonidine premedication. Ahoetal. [31] used 4.5µg/kg and 3µg/kg iv clonidine 15 minute prior to induction. They observed significant reduction in MAP in the 4.5µg/kg group before induction of anaesthesia. They recommended 3 µg/kg of clonidine for perioperative haemodynamic stability.

Similar findings were observed by Altan *et al*. [32], where they used 3µg/kg of clonidine IV over a period of 15 minutes before induction and followed by 2µg/kg/hr as continuous infusion. Ray *et al*. [33] also used 3µg/kg clonidine as IV bolus followed by 1µg/kg/hr infusion intraoperatively and found significant reduction in blood pressure compared to the control group.

Roy S *et al.* [34] used clonidine as 2.25µg/kg iv 15 minutes before induction followed by 0.9µg/kg/hr infusion intraoperatively while comparing iv clonidine with iv lignocaine. Arterial pressure was better controlled in clonidine group, with no episode of hypotension and bradycardia.

Our findings were also supported byKumkum G *et al*. [35], Kalra *et al*. [36] and Malek *et al.* [37]. Tripathi DC *et al*. [38] who studied two different doses of clonidine (1µg/kg and 2µg/kg).

According to previously done studies, clonidine has better and positive effect over the haemodynamic stability of heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure.

CONCLUSION

Study conducted can be concluded as the creation of pneumoperitoneum in laparoscopic abdominal surgeries produces significant increase of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) and clonidine decreases and thus stabilizes all haemodynamic parameters (HR, SBP, DBP and MAP) during pneumoperitoneum in laparoscopic abdominal surgeries.

REFERENCES

1. Matovic E, Hasukic S, Ljuca F, Halilovic H. Quality of life in patients after laparoscopic and open cholecystectomy. Med Arch 2012; 66(2):97-100.
2. Leonard IE, Cunningham AJ. Anesthetic considerations for laparoscopic cholecystectomy. Best Pract Res ClinAnaesthesiol. 2002;16(1):1-20.
3. Osborne DA, Alexander G, Boe B, Zervos EE. Laparoscopic cholecystectomy: past, present and future. Surg Technol Int. 2006; 15:81-5.
4. NIH Consensus conference. Gall stones and laparoscopic cholecystectomy. JAMA 1993; 269(8):1018-24.
5. Hodgeson G, MC Clelland RMA, Newton JR. Some effects of the peritoneal insufflation of carbon-dioxide. Anaesthesia. 1970; 25:382-389.
6. Blobner M, Felber AR, Gögler S, Feussner H, Weigl EM, Jelen G, Jelen-Esselborn S. The resorption of carbon dioxide from the pneumoperitoneum in laparoscopic cholecystectomy. Der Anaesthesist. 1993 May;42(5):288-94.
7. Richardson JD, Trinkle JK. Hemodynamic and respiratory alterations with increased intra-abdominal pressure. Journal of surgical research. 1976 May 1;20(5):401-4.
8. JorisJL, Noirot DP, LegrandMJ, Jacquet NJ, Lamy ML. Hemodynamic changes during laparoscopic cholecystectomy. AnesthAnalg 1993;76(5):1067-71.
9. Safran DB, Orlando R. Physiological effects of pneumoperitoneum. Am J Surg 1994; 167(2):281-6.
10. Lacy A, Blanch XS, Visa J. Alternative gases in laparoscopic surgery. InThe pathophysiology of pneumoperitoneum 1998 (pp. 7-17). Springer, Berlin, Heidelberg.
11. Ivankovich AD, Miletich DJ, Albrecht RF, Heyman HJ, Bonnet RF. Cardiovascular effects of intraperitoneal insufflation with carbon dioxide and nitrous oxide in the dog. Anesthesiology. 1975 Mar;42(3):281-7.
12. Struthers AD, Cuschieri A. Cardiovascular consequences of laparoscopic surgery. The Lancet. 1998 Aug 15;352(9127):568-70.
13. Bardoczky GI, Engelman E, Levarlet M, Simon P. Ventilatory effects of pneumoperitoneum monitored with continuous spirometry. Anaesthesia. 1993 Apr;48(4):309-11.
14. Fahy BG, Barnas GM, Flowers JL, Nagle SE, NjokeMJ. The effects of increased abdominal pressure on lung and chest wall mechanics during laparoscopic surgery. AnesthAnalg 1995;81(4):744-50.
15. Anderson LE, Baath M, Thorne A, Aspelin P, odenberg-Wernermans S. Effect of carbon dioxide pneumoperitoneum on development of atelectasis during anesthesia, examined by spiral computed tomography. Anesthesiology 2005;102(2):293-9.
16. JorisJL, Chiche JD, CanivetJL, Jacquet NJ, LegrosJJ, Lamy ML. Hemodynamic changes induced by laparoscopy and their endocrine correlates: Effects of clonidine. J Am CollCardiol 1998; 32(5):1389-96.
17. Koivusalo AM, Scheinin M, Tikkanen I, Yli-Suomu T, Ristkari S, Laakso J, Lindgren L. Effects of esmolol on haemodynamic response to

CO2 pneumoperitoneum for laparoscopic surgery. Acta anaesthesiologica scandinavica. 1998 May;42(5):510-7.
18. De Oliveira GSJr, Fitzgerald P, Streicher LF, Marcus RJ, McCarthy RJ. Systemic lidocaine to improve postoperative quality of recovery after ambulatory laparoscopic surgery. AnesthAnalg 2012; 115(2):262-7.
19. Lentschener C, Axler O, Fernandez H, Megarbane B, Billard V, Fouqueray B, Landault C, Benhamou D. Haemodynamic changes and vasopressin release are not consistently associated with carbon dioxide pneumoperitoneum in humans. Acta anaesthesiologica scandinavica. 2001 May;45(5):527-35.
20. Gupta K, Sharma D, Gupta PK. Oral premedication with pregabalin or clonidine for hemodynamic stability during laryngoscopy and laparoscopic cholecystectomy: A comparative evaluation. Saudi J Anaesth 2011; 5(2):179-84.
21. Jee D, Lee D, Yun S, Lee C. Magnesium sulphate attenuates arterial pressure increase during laparoscopic cholecystectomy. Br J Anaesth 2009;103(4):484-9.
22. Feig BW, Berger DH, Dougherty TB, Dupuis JF, Hsi B, Hickey RC, Ota DM. Pharmacologic intervention can reestablish baseline hemodynamic parameters during laparoscopy. Surgery. 1994 Oct;116(4):733-9.
23. Mase M, Tranquilli W. Alpha-2 adrenoceptor agonists: defining the role in clinical anaesthesia. Anaesthesiology. 1991;74:581-605.
24. Malek J, Knor J, Kurzova A, Lopourova M. Adverse hemodynamic changes during laparoscopic cholecystectomy and their possible suppression with clonidine premedication. Comparison with intravenous and intramuscular premedication. Rozhledy v chirurgii: mesicnik Ceskoslovenske chirurgicke spolecnosti. 1999 Jun;78(6):286-91.
25. Sharma KC, Brandstetter RD, Brensilver JM, Jung LD. Cardiopulmonary physiology and pathophysiology as a consequence of laparoscopic surgery. Chest. 1996 Sep 1;110(3):810-5.
26. Baratz RA, karisJH. Blood gas studies during laparoscopic under general anesthesia. Anesthesiology 1969;30(4):463-64.
27. HarronDW, Riddell JG, Shanks RG. Effects of azepexole and clonidine on baroreceptor mediated reflex bradycardia and physiological tremor in man. Br J ClinPharmacol 1985;20(2):431-6.
28. Myre K, Rostrup M, Buanes T, Stokland O. plasma catecholamines and haemodynamic changes during pneumoperitoneum, ActaAnaesthesiol Scand. 1998;42(3):343-7.
29. Singh S, Arora K. Effect of Oral clonidine premedication on perioperative hemodynamic response and postoperative analgesic requirement for patients undergoing laparoscopic cholecystectomy. Indian J Anaesth. 2011; 55(1):26-30.
30. Passi Y, Raval B, Rupakar VB, Chadha IA. Effect of oral clonidine premedication on haemodynamic response during laparoscopic cholecystectomy. J AnaesthClinPharmacol 2009;25(3):329-332.
31. 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 patient undergoing laparoscopic cholecystectomy. ActaAnaesthesiol Sin 2003;38(1):23-9.
32. Aho M, Scheinin M, Lehtinen AM, Erkola O, Vuorinen J, Korttila K. Intramuscularly administered dexmedetomidine attenuates hemodynamic and stress hormone responses to gynecologic laparoscopy. AnesthAnalg 1992;75(6):932-9.
33. Altan A, Turgut N, Yildiz F, Turkmen A, Ustun H. Effect of magnesium sulphate and clonidine on propofol consumption, haemodynamics and postoperative recovery. Br J Anaesth 2005;94(2):438-41.
34. Ray M, Bhattacharjee DP, Hajra B, Pal R, Chatarjee N. Effect of clonidine and magnesium sulphate on anaesthetic consumption, haemodynamics and postoperative recovery: A comparative study. Indian J Anaesth 2010;54(2):137-41.
35. Roy S, Chaudhary A, Saha D, MaulikSG, Bandopadhyay AK. Comparative study of clonidine versus lignocaine for attenuation of haemodynamic responses during laparoscopic hysterectomy. J Basic ClinReprodSci 2014;3(1):38-43.
36. Gupta K, Lakhanpal M, Gupta PK, Krishan A, Rastogi B, Tiwari V. Premedication with clonidine versus fentanyl for intraoperative hemodynamic stability and recovery outcome during laparoscopic cholecystectomy under general anesthesia. Anesthesia, essays and researches. 2013 Jan;7(1):29.
37. KalraNK, Verma A, Agrawal A, Pandey H. Comparative study of intravenously administered clonidine and magnesium sulphate on hemodynamic responses during laparoscopic cholecystectomy. J AnaesthClinPharmacol 2011;27(3):344-8.
38. Tripathi DC, Shah KS, Dubey SR, Doshi SM, Raval PV. Hemodynamic stress response during Laparoscopic cholecystectomy: Effect of two different doses of intravenous clonidine premedication. J AnaesthClinPharmacol 2011;27(4):475-80.