e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(9); 09-15

Original Research Article

A study on Attenuation of Cardiovascular Responses to Pneumoperitoneum and Reduction of Perioperative Haemodynamic Instability During Laparoscopic Surgery with Oral Clonidine Premedication.

Monali Patil Baviskar[1], R Gehdoo[2]

[1]Associate Professor, Department of Anaesthesia, PGIMS, Nerul, Maharashtra, India.
[2]Professor & Head, Department of Anaesthesia, PGIMS, Nerul, Maharashtra, India.

Received: 10-07-2026 / Revised: 02-08-2026 / Accepted: 01-09-2026
Corresponding Author: Dr. Monalee Patil Baviskar
Conflict of interest: Nil

Abstract:

Objectives: The present study was to evaluate the attenuation of cardiovascular responses to pneumoperitoneum and reduction of perioperative haemodynamic instability during laparoscopic surgery with oral clonidine premedication at tertiary care hospital.

Methods: Detailed preanaesthetic evaluation was carried out with history, general examination and systemic examination including airway assessment. Vital parameters including pulse rate, respiratory rate, blood pressure, oxygen saturation was noted. They were randomly assigned to two groups to receive either clonidine 3 ug /kg (group C) and placebo-vitamin C (group P) orally with sips of water 90 min before estimated time of induction of anaesthesia. Premedication given to all patients in each group with IV Midazolam 0.03 mg /kg, IV Fentanyl 2 mcg /kg, IV Ondansetron 0.05 - 0.15 mg/kg, IV Glycopyrolate 0.004 mg/kg if required (HR<45).

Results: A total of 50 patients were enrolled. Dose of Clonidine- 3mcg/kg of both group patients was not significant differenced (P=0.647). While, duration of surgery of both group patients (clonidine and non-clonidine group) was statistically significant differenced (p=0.016). Sedation score at one hour post operative (p<0.0001) and time of first analgesia requirement (Opioids/NSAIDS) (p<0.0001) of both group patients were highly significant difference.

Conclusion: Oral low dose clonidine premedication provides stable perioperative hemodynamics as revealed by less acute cardiovascular events that needed rescue drugs and protection against stress response triggered by pneumoperitoneum in patients undergoing laparoscopic surgery. Hence, low dose oral clonidine 3mcg/kg can be prescribed as a routine premedication for all laparoscopic procedure.

Keywords: Laparoscopic surgery, Premedication, Clonodine, Vitamin C, Haemodynamic Instability.

DOI: 10.25258/ijcpr.18.9.1

Introduction

The Laparoscopic surgery also called as minimally invasive surgery (MIS), band aid surgery, keyhole surgery or pinhole surgery is a modern surgical technique in which operations in the abdomen are performed through small incisions (usually 0.5-1.5cm) as compared to larger incisions needed in traditional surgical procedures. In the last few years, laparoscopic surgery has got tremendous popularity because of its several advantages over the conventional laparotomy technique. These include shorter hospital stay, more rapid return to normal activities, less pain, smaller incisions and less postoperative ileus. The prerequisite for laparoscopic surgery is a working space allowing endoscopic access to the peritoneal cavity after insufflation of a gas to create space between the anterior abdominal wall and the viscera. This space is necessary for the safe manipulation of instruments and organs [1].

Carbon dioxide pneumoperitoneum (PNP), the hallmark of laparoscopic surgery and patient positioning lead to significant haemodynamic changes in laparoscopic surgeries. Postoperative nausea and vomiting is also a major drawback of laparoscopic surgery [2].

Various drugs like opioids, ß blockers, nitroglycerine, magnesium sulphate etc have been tried to attenuate the PNP-associated haemodynamic instability but with limited success [3,4].

Pneumoperitoneum along with changes in position of the patients during the procedure affects multi-organ systems leading to release of stress hormones

(cortisol, epinephrine, norepinephrine, etc.), alternation in acid-base balance, cardiovascular, pulmonary, renal physiology [5].

During laparoscopic cholecystectomy, there is reduction of venous return, left ventricular and diastolic pressure, increase of intrathoracic pressure, right atrial and pulmonary artery occlusion pressure during insufflations. There is also increase in mean arterial pressure, heart rate and systemic and pulmonary vascular resistance [6]. Objective of the present study was to evaluate the attenuation of cardiovascular responses to pneumoperitoneum and reduction of perioperative haemodynamic instability during laparoscopic surgery with oral clonidine premedication at tertiary care hospital.

Material & Methods

The present study was conducted in the Department of Anaesthesia, PGIMS, Nerul, Maharashtra, India during a period from March 2026 to June 2026.

A total of 50 adult patients with age group 18-75 years and who belonged to ASA class I and II scheduled for elective laparoscopic surgeries of duration > 1 hour were enrolled in the present study.

Methods: Patients with known allergy to Clonidine and NSAIDS, Patients taking clonidine, methyl-dopa, b-blocking drugs, mono-amine oxidase inhibitors were excluded.

Detailed pre-anaesthetic evaluation was carried out with history, general examination and systemic examination including airway assessment. Vital parameters including pulse rate, respiratory rate, blood pressure, oxygen saturation was noted.

They were randomly assigned to two groups to receive either clonidine 3 ug /kg (group C) and placebo-vitamin C (group P) orally with sips of water 90 min before estimated time of induction of anaesthesia.

(GROUP C) with Tablet Vit C (ascorbic acid) as placebo (GROUP P) with sips of water confirming that the heart rate >45 min and systolic blood pressure > 100 mmHg (baseline reading).

Premedication: Premedication-Given to all patients in each group with IV Midazolam 0.03 mg /kg, IV Fentanyl 2 mcg /kg, IV Ondansetron 0.05 - 0.15 mg/kg, IV Glycopyrolate 0.004 mg/kg if required (HR<45).

Induction: In both groups, adequate preoxygenation was achieved by giving 100% oxygen for 3 min Induced was done with IV Pentothal sodium 5-7 mg/kg was given slowly and incremental doses of 25 mg. Endotracheal intubation was facilitated by IV succinylcholine 1.5 mg/kg. Direct laryngoscopy was done and an appropriate sized cuffed endotracheal tube was passed beyond the vocal cords. Air entry was checked by auscultation of chest and after confirming equal air entry, the cuff was inflated with air till there was no paratracheal leak palpated on either side of trachea.

Maintenance: Maintenance with oxygen-nitrous oxide mixture (50:50) with adequate isoflurane. To facilitate IPPV neuromuscular blockade was achieved with Vecuronium bromide 0.08 mg/kg was given as a loading dose and 1/5 of the loading dose was repeated as and when neuromuscular blockade with the previous dose starts wearing off.

Adequate depth of anaesthesia and optimum hemodynamic and surgical conditions were maintained with 02 + N20 (50:50) + Isoflurane.

Intraabdominal pressure (IAP) was kept between 12-15 mmg throughout the surgical procedure.

After pneumoperitoneum necessary changes in ventilator settings (Tidal volume-decreased, Respiratory frequency-increased, PEEP was added-5 cm H2O) were made to maintain normocapnia. Air entry was again checked after 10 min to confirm bilateral equality and adequacy at bases.

The tidal volume (Vt) and the ventilatory frequency (RR) was adjusted and intermittent positive pressure ventilation (IPPV) was continued by mechanical ventilator to maintain End Tidal CO2 between 30-35 mmHg and Peak Airway Pressures kept within normal limits between 18-22 cm of H2O.

Rescue Drugs Used Were:

- MAP >110 OR 30% ABOVE BASELINE - Esmolol (500microgram/kg bolus -followed by 50 microgram/kg iv infusion), NTG-nitroglycerine (1-2.5 mg/kg iv infusion),
- MAP <60 OR 30% BELOW BASELINE - Ephedrine 3-6 mg IV bolus doses.
- HR <40
- Glycopyrrolate(0.2 mg) or atropine (0.5 mg)

After release of pneumoperitoneum and once the closure (peritoneal and abdominal wall) was started, the ventilator settings and patient position again changed to normal.

Post Operative Pain Relief: It Was provided with 0.25% preservative and dextrose free Bupivacaine at port and drainage site as local infiltration (2cc at each port) just before closure of incision.

Reversal: At the end of surgery when spontaneous breathing pattern was established, neuromuscular blockade was reversed with IV neostigmine 0.05 mg/kg and IV glycopyrrolate 0.008 mg/kg. Patients were extubated after doing an oral suction and return of oropharyngeal reflexes and shifted to recovery.

In The Recovery Room (Post Anaesthesia Care Unit)

Modified Ramsay Sedation Scale:

1. Agitated, restless, irritable, anxious
2. Calm, tranquil, co-operative, oriented
3. Responds to oral commands.
4. Responds to light, glabellar tap, loud noise
5. Sluggish response to light, glabellar tap, loud noise.
6. No response

Heart Rate, Blood pressure, SpO2, End tidal CO2, End tidal Isoflurane, Dial concentration of Isoflurane vaporizer and Intraabdominal pressure were recorded at the following points of time:

- Prior to administration of clonidine (Baseline Reading)
- On arrival in operation (preinduction)
- Post intubation
- Before pneumoperitoneum
- After pneumoperitoneum
- After release of pneumoperitoneum
- After extubation
- Post op in recovery room for 2 hours

Statistical Analysis: Data was analysed with the help of IBM SPSS software version 26. Mean and standard deviations were observed. Chi-squared test was applied. P-value was taken less than or equal to 0.05 ($p \leq 0.05$) for significant differences.

Results

The heart rate and blood pressure were noted before giving the medication (clonidine or placebo) and was recorded as baseline reading. The heart rate and blood pressure were monitored preinduction, postintubation, just before creation of pneumoperitoneum (insufflation of CO2 gas), during pneumoperitoneum, after release of pneumoperitoneum (exsufflation), post-extubation and 2 hrs postoperatively and compared with baseline value.

Following CO2 insufflation, normocapnia (End Tidal CO2 in a range of 35-40 mmHg) was maintained. Mean intraabdominal pressure was kept constant between 12-14 mmHg.

The anaesthetic management in our study was to maintain the perioperative hemodynamic parameters (HR and MAP) within 30% of the baseline values.

The mean heart rate (HR) and mean arterial pressure (MAP) in both the groups was compared. The End Tidal-Isoflurane was recorded in both the groups and was compared. The side effects in both groups C and P were noted and compared during intraoperative and postoperative period.

The perioperative HR which was variable at each time interval was slower in the Clonidine group in comparison with the placebo group. The clonidine group had statistically significant low systolic and diastolic and mean blood pressure pre induction, post intubation, during pneumoperitoneum, post extubation and during their immediate postoperative period in PACU (post anaesthesia care unit) compared to the non-clonidine group.

None of the patients showed any evidence of ischaemia or arrhythmia intraoperatively. On the contrary there were episodes of bradycardia that needed acute drug intervention in some patients of clonidine group. 2 patients had to be given IV glycopyrrolate 0.2 mg.

Adverse events during postoperative period were nausea, vomiting, shivering and restlessness. These were less in group C in comparison with placebo premedication.

Both groups had mild somnolence, which was comparable. No side effects other than bradycardia was observed in clonidine group, but no treatment was required as no patient had HR less than <45/min.

Intensity of pain was less (as assessed by the time of first analgesic requirement in immediate postoperative period was prolonged) in patients of clonidine group in comparison with the placebo group.

Table 1: Comparison of clonidine and control group patients

Variables	Group		P-value
	Clonidine	Control	
	Mean ± SD	Mean ± SD	
ASA	1.34 ± 0.52	1.34 ± 0.49	1.00
Dose of Clonidine- 3mcg/kg	157.09 ± 40.13	160.24 ± 27.42	0.647
Duration of surgery	2.10 ± 0.52	2.34 ± 0.46	0.016

Table 2: Comparison of Heart Rate at Various Time Intervals Between Clonidine and Control Groups

Heart rate at-	Group		P-value
	Clonidine	Control	
	Mean ± SD	Mean ± SD	
Baseline	78.86 ± 8.10	77.54 ± 8.42	0.426
Pre induction	73.47 ± 9.21	79.24 ± 8.10	0.001
Post intubation	81.46 ± 9.72	92.45 ± 8.23	<0.0001
Pre insufflations	72.32 ± 9.34	76.41 ± 7.72	0.018
Post insufflation- 15 min	70.91 ± 9.15	78.45 ± 7.78	<0.0001
Post insufflations- 30 min	68.24 ± 8.72	78.45 ± 7.62	<0.0001
Post insufflations- 45 min	68.45 ± 8.68	78.84 ± 7.12	<0.0001
Post insufflations-60 min	67.34 ± 8.48	79.63 ± 7.63	<0.0001
Post insufflation-75 Min	66.32 ± 9.24	80.34 ± 8.12	<0.0001
Post insufflations- 90 min	65.42 ± 10.52	80.72 ± 7.12	<0.0001
Post insufflation-105 min	63.54 ± 9.34	79.62 ± 6.64	<0.0001
Post insufflation-120 min	65.32 ± 10.42	79.53 ± 7.09	<0.0001
Exsufflation	68.34 ± 8.62	74.42 ± 6.65	<0.0001
Post- extubation	80.85 ± 7.76	93.12 ± 5.07	<0.0001
Post–op-30 min	72.79 ± 6.94	79.48 ± 7.62	<0.0001
Post-op-60 min	70.84 ± 7.46	81.42 ± 6.82	<0.0001
Post-op-90 min	69.26 ± 7.83	79.24 ± 5.63	<0.0001
Post-op-120 min	69.48 ± 5.72	76.62 ± 4.92	<0.0001

Table 3: Comparison of Mean Arterial Pressure at various time intervals between Clonidine and Control groups.

Mean arterial pressure at-	Group		P-value
	Clonidine	Control	
	Mean± SD	Mean±SD	
Baseline	95.71±8.24	95.00±7.12	0.645
Pre induction	91.21±7.14	95.82±8.43	0.004
Post intubation	92.74±8.46	112.49±8.87	<0.0001
Pre insufflations	85.84±7.12	92.74±5.34	<0.0001
Post insufflation- 15 min	97.58±6.47	114.24±9.22	<0.0001
Post insufflations-30 min	93.25 ± 6.23	115.85 ± 12.32	<0.0001
Post insufflations-45 min	91.26 ± 7.86	111.92 ± 8.87	<0.0001
Post insufflations-60 min	89.32 ± 5.42	112.78 ± 11.52	<0.0001
Post insufflation-75 min	86.54 ± 4.76	109.86 ± 8.94	<0.0001
Post insufflations-90 min	87.86 ± 5.76	109.48 ± 8.37	<0.0001
Post insufflation-105 min	88.74 ± 6.62	109.32 ± 9.68	<0.0001
Post insufflation-120 min	87.62 ± 5.34	108.79 ± 10.21	<0.0001
Exsufflation	85.56 ± 7.34	98.64 ± 6.27	<0.0001
Post-extubation	96.85 ± 5.83	113.14 ± 8.34	<0.0001
Post –op-30 min	90.42 ± 6.36	99.24 ± 6.21	<0.0001
Post-op-60 min	88.25 ± 5.28	100.15 ± 6.18	<0.0001
Post-op-90 min	86.11 ± 6.24	97.76 ± 4.67	<0.0001
Post-op-120 min	86.74 ± 5.81	94.48 ± 5.24	<0.0001

Table 4: Comparison of clonidine and control group patients

Variables	Group		P-value
	Clonidine	Control	
	Mean ± SD	Mean ± SD	
Sedation Score- 1 Hour Post OP	1.68 ± 0.64	1.93 ± 0.62	<0.0001
Time of First Analgesia Requirement (Opioids/NSAIDS)	2.44 ± 0.72	1.54 ± 0.87	<0.0001

Table 5: Comparison of clonidine and control group patients

	Clonidine			Control Group
Pre Induction	HR: 73.44+/-7.8			79.14+/-6.27
	MAP: 90.45+/-5.86			93.56+/-8.12
Post Intubation	HR: 79.94+/-9.43			90.45+/-8.01
	MAP: 90.99+/-8.31			110.89+/-8.58
Post Insufflation	HR	30 MIN	68.56+/-7.78	77.46+/-6.46
		60 MIN	65.96+/-7.72	77.88+/-6.60
		90 MIN	64.82+/-8.48	78.72+/-6.64
	MAP	30 MIN	93.13+/-6.24	115.21+/10.45
		60 MIN	89.14+/-5.64	110.94+/9.98
		90 MIN	86.68+/-5.12	107.23+/-8.23
Post Extubation	HR: 78.89+/-7.43			91.00+/-5.12
	MAP: 96.24+/-5.12			111.42+/-6.42
Post Operative	HR	30 MIN	72.12+/-4.64	77.21+/-7.12
		60 MIN	68.97+/-5.64	79.86+/-6.24
	MAP	30 MIN	88.87+/-4.86	98.65+/-4.98
		60 MIN	86.67+/-4.23	95.54+/-3.978

Discussion

The hallmark of laparoscopy is creation of carbon dioxide (CO2) pneumoperitoneum and change in the patients 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 [7].

Clonidine is an α–2 adrenoreceptor agonist. It exerts central sympatholytic effect and has a half life of 9-12 h [8]. Premedication with clonidine blunts the stress response to surgical stimuli and the narcotic and anaesthetic doses are also reduced. In addition, clonidine increases cardiac baroreceptor reflex sensitivity to increase in systolic blood pressure, and thus stablises, blood pressure [9].

Pneumoperitoneum during laparoscopic surgery, especially carbon dioxide gas insufflation, produces significant hemodynamic changes in healthy patients. Hypertension and tachycardia accompanied by increased sympathetic nervous system activity may lead to an imbalance between myocardial oxygen demand and supply. The cardiovascular changes associated with laparoscopy is an increase in systemic vascular resistance (SVR), mean blood pressure(MAP) and myocardial filling pressures, accompanied by a fall in the cardiac index (CI). Heart rate does not change or increases only slightly [10].

The increase in SVR is not only related to mechanical factors but also neurohumoral factors as it outlasts the end of pneumoperitoneum. The neurohumoral factors like catecholamines (norepinephrine and epinephrine), prostaglandins, the renin angiotensin system especially vasopressin are potential mediators. These surges are reasonably expected to cause an increase in systemic vascular resistance and mean arterial pressure. These changes can be detrimental especially in elderly patients.

Clonidine premedication has been proved to prevent perioperative myocardial ischemia by improving myocardial oxygen balance [11].

The increase in SVR is not only related to mechanical factors but also neurohumoral factors as it outlasts the end of pneumoperitoneum. The neurohumoral factors like catecholamines (norepinephrine and epinephrine), prostaglandins, the renin angiotensin system especially vasopressin are potential mediators. These surges are reasonably expected to cause an increase in systemic vascular resistance and mean arterial pressure. These changes can be detrimental especially in elderly patients. Clonidine premedication has been proved to prevent perioperative myocardial ischemia by improving myocardial oxygen balance [11].

It causes a reduction of tonic sympathetic outflow (documented to decrease plasma catecholamine levels) and prevents activation of RAAS (renin angiotensin aldosterone system) seen as decreased plasma renin activity. Oral clonidine premedication decreases the release of pro inflammatory cytokines interleukin (IL)-6, IL-1b and tumour necrosis factor and stress hormones cortisol and adrenocorticotropic hormone (ACTH).

The drug has been recently used for anaesthetic premedication, providing sedative, anxiolytic and analgesic effects that reduce the requirement for IV and volatile anaesthetics and narcotics. Clonidine smoothed the changes in arterial pressure, HR, SVR and cardiac output during laparoscopic surgery (as seen in many studies), which are caused by CO2 PP. These benefits are mediated by a reduction of neurohumoral secretion secondary to stress induced sympatho-adrenal hyperactivation. Clonidine premedication prevents sympathetic hyperactivity

but does not suppress hypothalamopituatary adrenocortical responses in patients undergoing laparoscopy. Clonidine effects are not only limited to the pre and intra-operative period but also extend to postoperative period. The only limitation is that it cannot be applied to patients presenting for emergency surgery. Joris et al used very high dose of clonidine - 8 mcg/kg for reducing the level of catecholamine and vasopressin following PNO. Malek et al used 150 mcg/kg of clonidine as IV infusion and intramuscularly while Sung et al and Yu et al used 150 ug/kg of oral clonidine as premedication for maintenance of hemodynamic stability during PNO.

Mean Hemodynamic Values Were as Follows: Thus, clonidine premedication was able to effectively blunt the cardiovascular response to surgical stress especially pneumoperitoneum and achieve hemodynamic stability. Similar findings were reported by Sung et al, Yu et al.

Thus, clonidine premedication was able to effectively blunt the cardio vascular response to surgical stress especially pneumoperitoneum and achieve hemodynamic stability. Similar findings were reported by Joris et al, [12] Sung et al. [13] Yu et al [14].

In our study the depth of anaesthesia was viewed by the reflection of cardiovascular variables (HR, MAP) at an inspired isoflurane concentration greater than 0.6-0.8%. Electroencephalography was not applied to monitor the neurophysiologically defined depth of anaesthesia.

No any patients with Clonidine premedication suffered from respiratory depression in our study, which coincided with Sung cs et al [13].

The number of analgesics required in the placebo group was also higher than in the clonidine group. Only 3 patients of the clonidine group had to be given tramadol within 2 hours postop as an additional analgesic in contrast to 20 patients in the non-clonidine group who received the same. This postoperative anaigesic effect of clonidine in our study was in agreement with reports by Mikawa et al, [15] Segal et al [16]. Despite the fact that clonidine was not a pure analgesic and 150 ug oral Clonidine premedication without another postoperative supplement could not completely relieve postoperative pain, clonidine premedication provided additional postoperative analgesia. The decrease in patient demand analgesia could also improve post-operative care.

Thus, clonidine, an alpha agonist, has been shown to decrease peripheral sympathetic outflow without increasing the baroreceptor reflex and decreases the anaesthetic requirement. Thus, it appears to be an appropriate drug for premedication in laparoscopic surgery to fulfil the anaesthetic aims of reducing stress response and subsequent adverse events.

Attenuation of perioperative hemodynamic responses may reduce myocardial oxygen demand and overall cardiovascular stress during laparoscopic surgery, a factor that is particularly vital in optimizing outcomes for patients with subclinical cardiovascular vulnerabilities. Furthermore, intravenous clonidine is highly inexpensive, widely available globally, straightforward to prepare and administer, and associated with a very favorable safety profile.

Conclusion

The present study concluded that the oral low dose clonidine premedication provides stable perioperative hemodynamic as revealed by less acute cardiovascular events that needed rescue drugs and protection against stress response triggered by pneumoperitoneum in patients undergoing laparoscopic surgery. Hence, low dose oral clonidine 3mcg/kg can be prescribed as a routine premedication for all laparoscopic procedure.

References

1. Mali A, Asthana U, Prakash J, Londhe N, Bandey S, Arya G. Effect of oral clonidine premedication on hemodynamic responses during laparoscopic cholecystectomy. Int J Res Med Sci 2017; 5:2982-8.
2. Thune A, Appalgren L, Haglind E. Prevention of post-operative nausea and vomiting after laparoscopic cholecystectomy. Eur J Surg. 1995; 161:265-8.
3. Koivusalo AM, Scheinin M, Tikkanen I, Yli-Suomu T, Ristkari S, Laakso J et al. Effects of esmolol on hemodynamic responses to CO2 pneumoperitoneum for laparoscopic surgery. Acta Anaesthesiol Scand. 2008:510-7.
4. Jee D, Lee D, Yun S, Lee C. Magnesium sulphate attenuates arterial pressure increases during laparoscopic cholecystectomy. Br J Anaesth. 2009;103(4):484-9.
5. Jeong-Yeon Hong, KeumHee Chung, Young-Ju Lee. The changes of ventilator parameters in laparoscopic cholecystectomy. Yonsei Medical Journal 1999;40(4):307-312.
6. Ahmed ALM, Hirok R. Effect of oral clonidine premedication on haemodynamic changes during laparoscopic cholecystectomy - a clinical study. J. Evid. Based Med. Healthc. 2016; 3(34), 1608-1614.
7. 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.

8. Hayashi Y, Maze M. Alpha 2 adrenoceptor agonists and anaesthesia. Br J Anaesth 1993;71:108-18.
9. 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.
10. Kabakchiev C, Valverde A, Singh A, Beaufrère H. Cardiovascular and respiratory effects of carbon dioxide pneumoperitoneum in the domestic rabbit (Oryctolagus cuniculus). Can J Vet Res. 2020 Apr;84(2):108-114.
11. Wahba RW, Béïque F, Kleiman SJ. Cardiopulmonary function and laparoscopic cholecystectomy. Can J Anaesth. 1995 Jan;42(1):51-63.
12. Joris JL, Noirot DP, Legrand MJ, Jacquet NJ, Lamy ML. Hemodynamic changes during laparoscopic cholecystectomy. Anesth Analg. 1993 May;76(5):1067-71.
13. 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;38:23-9.
14. Yu HP, Hseu SS, Yien HW, Teng YH, Chan KH. Oral clonidine premedication preserves heart rate variability for patients undergoing larparoscopic cholecystectomy. Acta Anaesthesiol Scand 2003;47:185-90.
15. Mikawa K, Nishina K, Maekawa N, Obara H. Oral clonidine premedication reduces postoperative pain in children. Anesth Analg 1996;82:225-30.
16. Segal IS, Jarvis DJ, Duncan SR, White PF, Maze M. Clinical efficacy of oral-transdermal clonidine combinations during the perioperative period. Anesthesiology 1991;74:220-5.