International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2020): 7.803

Comparative Study of the Intravenously Administered Dexmedetomidine and Clonidine on Attenuation of Haemodynamic Responses to Pneumoperitoneum during Laparoscopic Cholecystectomy

Ashima Gupta[1], Arpit Singhal[2], C.K.Vyas[3]

[1]PG student department of AnaesthesiaSMS Medical College, Jaipur, India

[2]PG student department of Anaesthesia Jhalawar Medical College, Jhalawar, India

[3]Senior professor department of Anaesthesia SMS Medical College, Jaipur, India

Abstract: ***Background: Now a day's laparoscopy has become the standard technique for cholecystectomy over open surgery because of reduced postoperative pain and instabilities.Clonidine and dexmedetomidine both are alpha 2 adrenoreceptor agonist, but as compare to clonidine dexmedetomidine is more selective. This study compares the effect of intravenously administered clonidine and dexmedetomidine in attenuating the haemodynamic responses to pneumoperitoneum during laproscopic cholecystectomy. Methodology: 60 adult consented patients of ASA physical status I and II, aged between 18 to 60 years, of either sex scheduled for elective laparoscopic cholecystectomy were randomized into 2 groups (Group C, D) in a double-blind fashion, to receive either clonidine 1 µg/kg or dexmedetomidine 1 µg/kg both diluted with normal saline to make total volume 50 ml and administered over a period of 15 minutes before induction. Result: Group D showed better control in attenuation of increase heart rate and blood pressure due to pneumoperitoneum creation than Group C. Conclusion: Both clonidine and dexmedetomidine attenuate thehaemodynamic responses to pneumoperitoneum but dexmedetomidine showed better attenuation.***

Keywords: clonidine, dexmedetomidine, laparoscopic cholecystectomy, haemodynamic responses, pneumoperitoneum

1. Introduction

Now a days laparoscopy has become the standard technique for cholecystectomy over open surgery because of reduced postoperative pain and instabilities.In laparoscopy pneumoperitoneum is created with carbon dioxide (CO_2). This peritoneal insufflation leads to alteration in haemodynamic parameters like increase in arterial pressure and systemic and pulmonary vascular resistance and decrease in cardiac output.[1-3] Theses changes may prove fatal in high risk patients like with pre-existing essential hypertensionand limited cardiopulmonary reserve.[4]

Pneumoperitoneum created during laparoscopic cholecystectomy cause stimulation of the sympathetic nervous system which leads to release of catecholamine and vasopressin.[5]Different pharmacological agents like α_2 adrenergic agonists[1]- clonidine, dexmedetomidine, beta-blockers[6], opioids[7],vasodilatorsare often used to attenuate circulatory response due to pneumoperitoneum.

The present study was designed in a prospective, randomized, double-blind fashion to compare the efficacy of intravenously administered clonidine versus dexmedetomidine in attenuation of hemodynamic responses during laparoscopic cholecystectomy.

2. Methodology

After getting approval from the institutional ethical committee and written informed consent from patients, this study was conducted in a tertiary care SMS medical college hospital, Jaipur from Aug 2017 to Feb 2019. 60 patients of ASA physical status I and II, aged between 18 to 60 years, of either sex scheduled for elective laparoscopic cholecystectomy (pneumoperitoneum with CO2) patients were randomized into 2 groups (Group C, D) in a double-blind fashion, to receive either clonidine 1 µg/kg or dexmedetomidine 1 µg/kg both diluted with normal saline to make total volume 50 ml and administered over a period of 15 minutes before induction. Patients in whom surgery could not be completed laparoscopically were excluded from the study

On arrival in the operating room, monitors were attached and baseline parameters, e.g. heart rate, NIBP, oxygen saturation and ECG, were recorded. Patients were premedicated with glycopyrrolate 0.02 mg/kg,Inj fentanyl 2mcg/kg, Inj midazolam0.04mg/kg.

Patients of group C were given Inj Clonidine 1 mcg /kg iv in 50 ml saline over15 minutes before induction.

Patients of group D were given Inj Dexmedetomidine 1 mcg/kg in 50 ml saline over 15 minutes before induction.

After preoxygenation anesthesia was induced with intravenous Thiopentone sodium 5 mg/kg followed by Inj. Succinylcholine 2 mg/kg to facilitate endotracheal intubation.Formaintenance O2 and N2O mixture with Isoflurane and Inj.Vecuronium bromide were used. CO2 was used to create pneumoperitoneum and intra-abdominal pressure was maintained at 14 mm Hgand etco2 was maintained between 25-45 mm Hg. Intraoperatively patients were monitored with continuous ECG, SBP, DBP, MAP, SPO2, EtCO2 at;

Baseline
After study drug given
After intubation
Before pneumoperitoneum
2 min after pneumoperitoneum
5 min after pneumoperitoneum
10 min after pneumoperitoneum
20 min after pneumoperitoneum
30 min after pneumoperitoneum
40 min after pneumoperitoneum Then every 30 min till end of surgery
End of Pneumoperitoneum
After extubation

After completion of surgery oropharyngeal suction was doneand patient is reversed with neostigmine 0.07mg/kg and glycopyrolate0.01mg/kg.Extubation was done when patient had established protective reflexes with adequate tidal volume and then patient was observed for side effects like sedation in recoveryroom.

Statistical Analysis

Data was expressed as mean and standard deviation (SD). The homogeneity in two groups of mean and SD was analysed using student's t-test.Tables of mean and standard deviation were prepared for meaningful comparison of the two groups. A p value of less than or equal to 0.05 was considered as significant.

3. Result

There were no significant differences between the two groups with regard to demographic data such as age, sex, weight, ASA grade and duration of surgery (Table 1). Preoperative vital parameters were compared among the two groups of patients and no significant difference was found (Base line values of table 2, 3, 4 and 5). Mean intra-abdominal pressure was maintained at 14 mm Hg throughout the laparoscopic surgery. No patient was excluded from study. NTG drip for control of hypertension was not required in group C or D patients, because they remained hemodynamically stable.

Table 1: Demographic profile (Mean ± SD)

Demographic profile	Group D	Group C	P Value	Significance
Age(years)	35.1±9.6	35.4±8.5	0.921	NS
Sex(F:M)	23:7	22:8	0.766	NS
ASA(I:II)	21:9	23:7	0.559	NS
Weight(Kg)	48±6.5	59.7±7.5	0.875	NS
Duration of surgery(Minutes)	48±6.5	48.5±6.3	0.779	NS

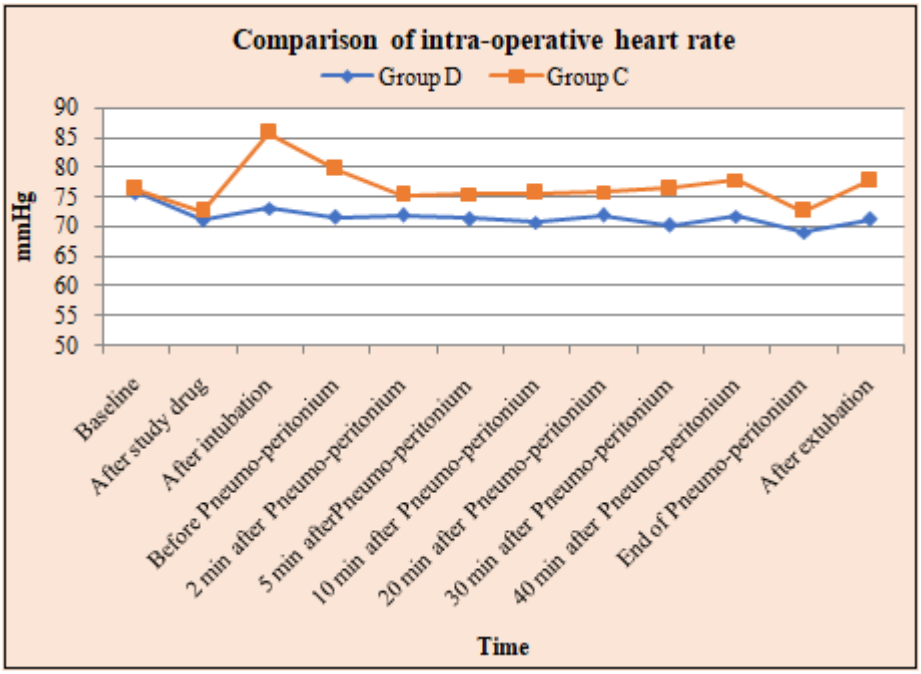

Figure 1: Changes in heart rate (per minute) in two groups

Table 2: Comparison of intra-operative heart rate (per minute) among study groups

Time	Group D	Group C	P value	Significance
Baseline	75.8 ± 6.6	76.3 ± 6.6	0.786	NS
After study drug	67.1 ± 5.8	71.6 ± 4	0.019	S
After intubation	73.2 ± 3.6	85.8 ± 3.6	<0.001	HS
Before Pneumo-peritonium	71.7 ± 5.4	79.7 ± 4.4	<0.001	HS
2 min after Pneumo-peritonium	71.9 ± 4.8	75.3 ± 4.6	0.008	HS
5 min after Pneumo-peritonium	71.4 ± 6.4	75.5 ± 6.4	0.018	HS
10 min after Pneumo-peritonium	70.8 ± 7	75.7 ± 6	0.005	HS
20 min after Pneumo-peritonium	71.9 ± 4.8	75.9 ± 4.1	0.001	HS
30 min after Pneumo-peritonium	70.2 ± 4.9	76.5 ± 5	<0.001	HS
40 min after Pneumo-peritonium	71.8 ± 7	77.9 ± 5.6	<0.001	HS
End of Pneumo-peritonium	69.1 ± 5.7	72.7 ± 6.6	0.029	HS
After extubation	71.3 ± 5.6	77.8 ± 5.7	<0.001	HS

Upon statistical comparison of heart rate in two groups of patients, significant variation was observed throughout the intraoperative period except for the baseline where no significant difference was observed (Figure 1, table 2). Mean heart rate was lowest for group D. 3 out of 30 patients in group D required intravenous atropine due to bradycardia

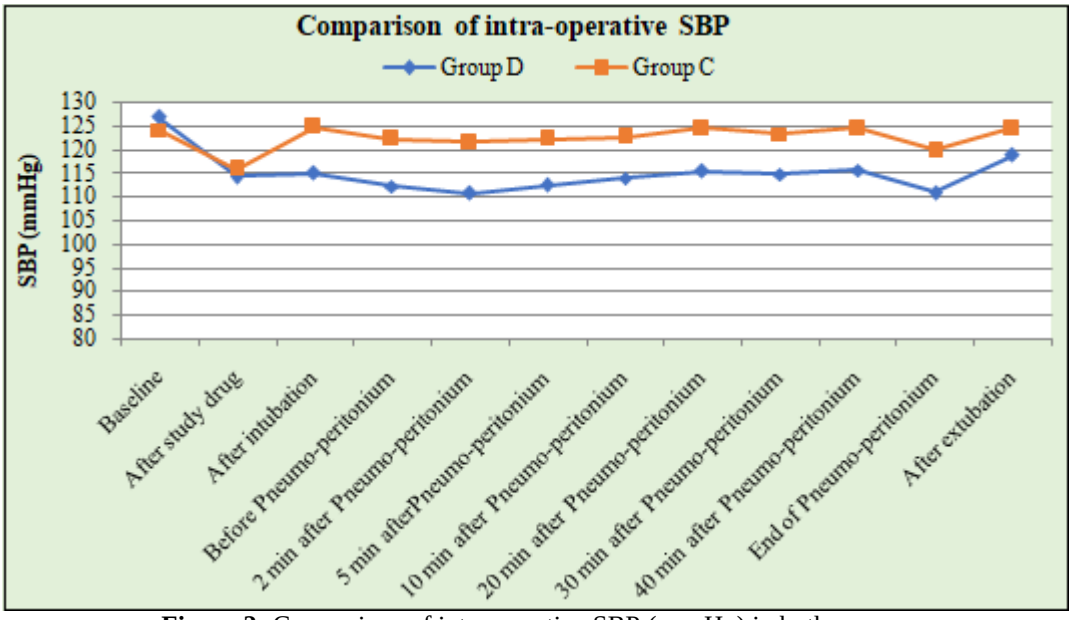

Figure 2: Comparison of intraoperative SBP (mm Hg) in both groups

Table 3: Comparison of intra-operative SBP (mmHg) among study groups

Time	Group D	Group C	P value	
Baseline	126.8 ± 9	124.2 ± 9	0.262	NS
After study drug	111.3 ± 8.9	115.8 ± 9.1	<0.001	HS
After intubation	114.9 ± 9.1	124.8 ± 9.4	<0.001	HS
Before Pneumo-peritonium	112.3 ± 8.9	122.2 ± 9.3	<0.001	HS
2 min after Pneumo-peritonium	110.8 ± 8.9	121.5 ± 9.3	<0.001	HS
5 min after Pneumo-peritonium	112.4 ± 8.9	122.1 ± 10.1	<0.001	HS
10 min after Pneumo-peritonium	114 ± 8.9	122.7 ± 10.1	0.001	HS
20 min after Pneumo-peritonium	115.4 ± 8.9	124.5 ± 10.2	0.001	HS
30 min after Pneumo-peritonium	114.8 ± 9	123.3 ± 9.9	0.001	HS
40 min after Pneumo-peritonium	115.7 ± 8.7	124.5 ± 10.2	0.001	HS
End of Pneumo-peritonium	110.9 ± 8.5	119.8 ± 10.2	<0.001	HS
After extubation	118.8 ± 8.4	124.5 ± 10.2	0.021	HS

Table 3 shows fall in systolic arterial pressure was more in group D compare to group C which was statistically significant at each interval except at baseline.

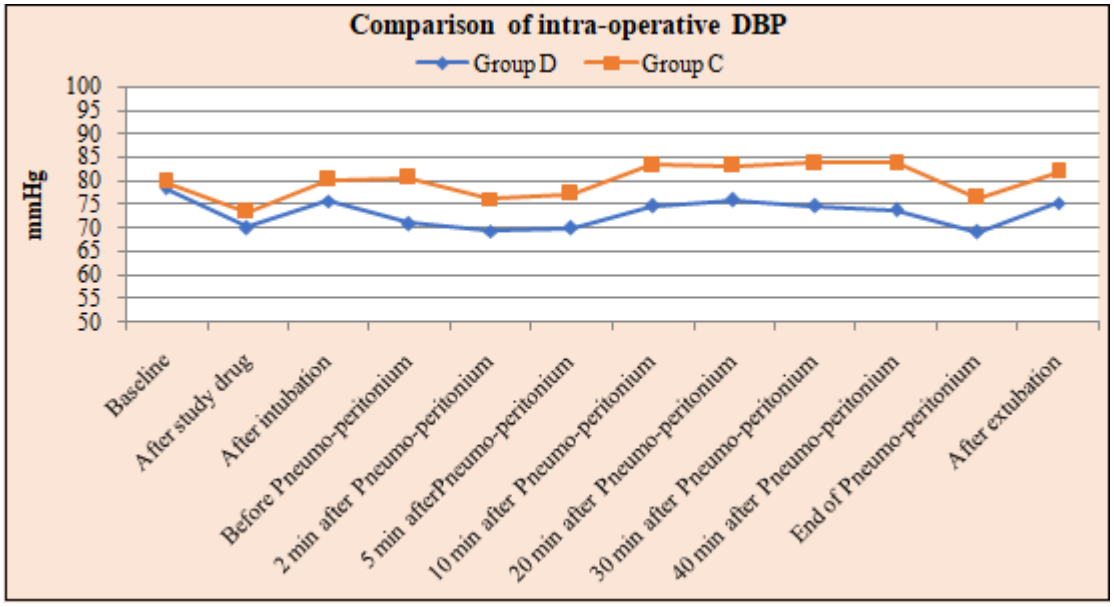

Figure 3: Comparison of intraoperative DBP (mm Hg) in two study groups

Table 4: Comparison of intra-operative DBP (mmHg) among study groups

Time	Group D	Group C	P value	
Baseline	78.6 ± 7	79.9 ± 6.4	0.468	NS
After study drug	69.2 ± 7.3	73.4 ± 6.5	0.021	S
After intubation	75.8 ± 7.4	80.3 ± 6.6	0.017	S
Before Pneumo-peritonium	71 ± 6.7	80.7 ± 6.5	<0.001	HS
2 min after Pneumo-peritonium	69.4 ± 6.5	76.2 ± 6.6	<0.001	HS
5 min after Pneumo-peritonium	70 ± 6.7	77.2 ± 6.6	<0.001	HS
10 min after Pneumo-peritonium	74.7 ± 6.9	83.4 ± 6.8	<0.001	HS
20 min after Pneumo-peritonium	76 ± 6.6	83.2 ± 7.2	<0.001	HS
30 min after Pneumo-peritonium	74.8 ± 6.8	83.8 ± 7.3	<0.001	HS
40 min after Pneumo-peritonium	73.9 ± 6.3	83.8 ± 8.3	<0.001	HS
End of Pneumo-peritonium	69.2 ± 6.3	76.4 ± 8.9	0.001	HS
After extubation	75.4 ± 6.3	81.9 ± 9.1	0.002	HS

Figure 3 and table 4 shows diastolic blood pressure was significantly lower in group D compare to group Cat each time interval except at baseline.

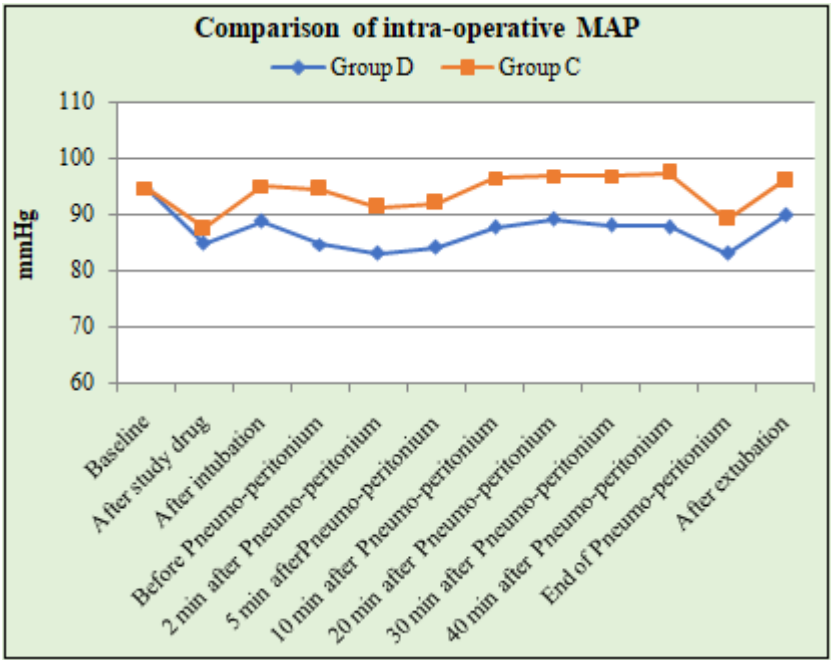

Figure 4: Comparison of intraoperative MAP in both the study groups

Table 5: Comparison of intra-operative MAP (mmHg) among study groups

Time	Group D	Group C	P value	
Baseline	94.7 ± 6.6	94.7 ± 5.5	0.983	NS
After study drug	83.4 ± 6.7	87.5 ± 5.5	0.042	S
After intubation	88.8 ± 6.5	95.1 ± 5.6	<0.001	HS
Before Pneumo-peritonium	84.8 ± 6.4	94.5 ± 5.5	<0.001	HS
2 min after Pneumo-peritonium	83.2 ± 6.3	91.3 ± 5.6	<0.001	HS
5 min after Pneumo-peritonium	84.1 ± 6.4	92.1 ± 6.2	<0.001	HS
10 min after Pneumo-peritonium	87.8 ± 6.5	96.5 ± 6.3	<0.001	HS
20 min after Pneumo-peritonium	89.1 ± 6.4	96.9 ± 6.7	<0.001	HS
30 min after Pneumo-peritonium	88.1 ± 6.6	96.9 ± 6.6	<0.001	HS
40 min after Pneumo-peritonium	87.9 ± 6.2	97.4 ± 7.4	<0.001	HS
End of Pneumo-peritonium	83.1 ± 6.1	89.2 ± 7.9	0.002	HS
After extubation	89.9 ± 6	96.1 ± 8.1	0.001	HS

Mean arterial pressure was significantly lower in group D compare to group C (Figure 4and table5) at each time interval except at baseline.

4. Discussion

Pneumoperitoneum during laparoscopy produces significant haemodynamic changes, which can be detrimental especially in elderly and haemodynamically compromised patients[8]. In our study the demographic parameters (age, sex, weight, ASA grade) & duration of surgery was comparable i.e. no statistically significant difference. Dexmedetomidine is highly selective and specific alpha 2 receptor, attenuates haemodynamic responses to tracheal intubation and decrease plasma catecholamine level during anaesthesia. Clonidine, an imidazoline derivative is a selective alpha 2 adrenergic agonist. In our study dexmedetomidine showed better attenuation in HR than clonidine which was statistically significant ($p < 0.05$).At the end of pneumoperitoneum the HR in dexmedetomidine group was significantly lower than clonidine group.Our observations were similar to study done by **Kholi A et al [9]** , **Ahmed ALM et al [10]**, **Sharma A et al (2014)[11]** . **Kumar S et al (2014)[12]** used2 µg/kg of clonidine and 1 µg/kg of dexmedetomidine diluted in normal saline, given slow intravenous infusion over 10 min found that dexmedetomidine and clonidine both were equally efficacious in attenuation of increase in hear rate while in our study we use 1mcg/kg dexmedetomidine and 1 mcg/kg and observed thatdexmedetomidine was better as compared to clonidine. The decrease in heart rate in dexmedetomidine was more in our study and can also be explained by **Thomas C et al[13].**

The heart rate lowering effect of both study drugs reduces the myocardial oxygen demand of the patient which was very useful in patient suffering from coronary artery disease and dexmedetomidine is more effective in this regard and our finding was consistent with previous study by **Frederic et al [14]**.Dexmedetomidine as a pre-anaesthetic medication and intraoperative infusion significantly attenuates sympathoadrenal response to tracheal intubation compared to clonidine and it was also seen in previous study by **Panda Bijoy et al[15]**.Ghodki et al[16] used dexmedetomidine 1 µg/kg intravenously over 15 minutes before induction followed by maintenance infusion of 0.2 µg/kg/h and observed favorable vasopressor response during laryngoscopy, with minimal change in BP with pneumoperitoneum. In the present study, a single dexmedetomidine bolus of 1 µg/kg was used before induction and similar hemodynamic control in terms of heart rate, mean arterial pressure systolic blood pressure,diastolic blood pressure was noted. **Ishizaki et al[17]** tried to determine the safe range of intra-abdominal pressures during laparoscopic surgery. At 16 mm Hg of intra-abdominal pressure, significant fall in cardiac output was observed. However, at 12 mm Hg of intra-abdominal pressure, hemodynamic alterations were not observed. During laparoscopy, the current recommendation is to monitor intra-abdominal pressure and to keep it as low as possible. In this present study, mean intra-abdominal pressure was maintained at 14 mm Hg throughout the duration of surgery.**Joris et al[18]** used higher dose of clonidine (8mcg/kg) for reduction of catecholamine and vasopressin associated with pneumoperitoneum. **Chiruvella et al[19]** studied IV 1 mcg/kg of dexmedetomidine and clonidine for attenuation of stress responses during laparoscopic cholecystectomy and found dexmedetomidine more effective than clonidine however chances of hypotension and bradycardia were more with dexmedetomidine as similar to our study.Our study is also supported by **Yazbek[20]**who concluded that dexmedetomidine has many desirable clinical benefits that encourage its use perioperatively

5. Conclusion

Administration of clonidine or dexmedetomidine before commencement of pneumoperitoneum effectively attenuates hemodynamic response to pneumoperitoneum. However, dexmedetomidine blunts the hemodynamic response to pneumoperitoneum more effectively with a greater chance of developing hypotension and bradycardia.

References

[1] Joris J. Anesthetic management of laparoscopy. In – Miller's Anesthesia 5th ed. New York: Churchill Livingstone; 1994. p. 2011–2029.
[2] Wabha RW, Beique F, Kleiman SJ. Cardiopulmonary function and laparoscopic cholecystectomy. Can J Anaesth1995;42:51-63. [PubMed]
[3] Sharma KC, Brandstetter RD, Brensilver JM, Jung LD. Cardiopulmonary physiology and pathophysiology as a consequence of laparoscopic surgery. Chest 1996;110:810-5. [PubMed]
[4] Joris JL, Noirot DP, Legrand MJ, Jacquet NJ, Lamy ML. Hemodynamic changes during laparoscopic

cholecystectomy. Anesth Analg1993;75:1067–1071. [PubMed]
[5] O' leary E, Hubbard K, Tormey W et al. Laparoscopic cholecystectomy: haemodynamic and neuroendocrine responses after pneumoperitonium and changes in position. Br J Anaesth1996;76:640-644. [PubMed] [Free Full Text]
[6] Koivusalo AM, Scheinin M, Tikkanen I, et al. Effects of esmolol on haemodynamic response to CO_2 pneumoperitoneum for laparoscopic surgery. Acta AnaesthesiolScand1998;42:510-7. [PubMed]
[7] Lentschener C, Axler O, Fernandez H, et al. Haemodynamic changes and vasopressn release are not consistently associated with carbon dioxide pneumoperitoneum in humans. Acta AnaesthesiolScand2001;45:527-35. [PubMed]
[8] Dhoste K, Lacoste L, Karayan J, et al. Haemodynamic and ventilatory changes during laparoscopic cholecystectomy in elderly ASA III patients. Can J Anaesth 1996;
[9] Kholi AV, Ishaq S, BhadralN, Gulati S, ManhasR Comparison of Efficacy of Clonidine Vs Dexmedetomidine on Hemodynamic Changes in Laproscopic Cholecystectomy.Vol. 19 No. 2, April.-June 2017.
[10] Ahmed ALM, Bora J. A clinical study of intravenous dexmedetomidine and intravenous Clonidine for attenuation of haemodynamic responses to laryngoscopy & intubation. J. Evid. Based Med. Healthc. 2016; 3(33), 1558-1564. DOI: 10.18410/jebmh/2016/351
[11] Sharma A ,Shankaranarayana P P .Pre-medication with I.V. dexmedetomidine Vs I.V. clonidine in attenuating the pressor response during laryngoscopy & endotracheal intubation.IJBR (2014) 05 (07) Journal DOI:10.7439/ijbr
[12] S Kumar, B B Kushwaha, R Prakash, S Jafa, A Malik, R Wahal, J Aggarwal, R Kapoor. Comparative Study Of Effects Of Dexmedetomidine And Clonidine Premedication In Perioperative Hemodynamic Stability And Postoperative Analgesia In Laparoscopic Cholecystectomy . The Internet Journal of Anesthesiology. 2014 Volume 33 Number 1.
[13] Thomas C, Westfall, David P. Westfall, Adrenergic agonists and antagonists, Goodman & Gilman's ThePharmacological Basis of Therapeutics : 12th edition, Pages 277-288.
[14] Frederic J. Gerges, Ghassan E. Kanazi, Samar I. Jabbour-khoury, Anesthesia for laparoscopy: a review. Journal of Clinical Anesthesia. 2006; 18: 67 – 78.
[15] Panda Bijoy Kumar, Singh Priyanka, Marne Sourabh, PawarAtmaram, KeniyaVarshali, Ladi Sushma, Swami Sarita. Comparison study of Dexmedetomidine vs. Clonidine for sympathoadrenal response, perioperative drug requirements and cost analysis. Asian Pacific Journal of Tropical Disease (2012)1-6.
[16] Ghodki PS, Thombre SK, Sardesai SP, Harnagle KD. Dexmedetomidine as an anesthetic adjuvant in laparoscopic surgery: An observational study using entropy monitoring. J Anaesthesiol Clin Pharmacol2012;28:334-8. [PubMed] [Free Full Text]
[17] IshizakiY, Bandae Y, Shimomura K,Abe H, Ohtomo Y, Idezuki Y. Safe intra abdominal pressure of carbon dioxide pneumoperitoneum during laparoscopic surgery. Surgery 1993; 114: 54954.
[18] Joris J, Chiche JD, Lamy M. Clonidine reduced haemodynamic changes induced by pneumoperitoneum during laparoscopic cholecystectomy. Br J Anaesth 1995; 74 (suppl) : A124.
[19] Sunil Ch, Balaji D, Venkata S, Dorababu (2014) Comparative Study of Clonidine versus Dexmedetomidine for Hemodynamic Stability during Laparoscopic Cholecystectomy
[20] Yazbek-Karam VG, Aouad MM. Peri-operative uses of dexmedetomidine. MEJ Anesth 2006; 18: 1043-58.