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Attenuation of Intra-Operative Pressure Response to Pneumoperitoneum in Patients Undergoing Laparoscopic Cholecystectomy – A Comparative Study between Dexmedetomidine and Esmolol

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Abstract :

Background*: Dexmedetomidine is a selective α2-adrenergic receptor agonist which is known to produce sedation, analgesia, and also has sympatholytic, anaesthetic sparing and haemodynamic stabilising properties without significant respiratory depression.Its sympatholytic effect decreases mean arterial pressure and heart rate by reducing norepinephrine release and hence improves haemodynamic stability during laparoscopy Esmolol is an ultra-short-acting β1-adrenoceptor antagonist without any partial agonistic action or local anaesthetic action which is known to produce haemodynamic stability during laryngoscopy, intubation and pneumoperitoneum .In view of the above context., the present study was undertaken for comparison of dexmedetomidine and esmolol to determine their clinical efficacy in case of laparoscopic cholecystectomies.*

Materials and Methods*: We conducted this study as an open label observer blind prospective randomized controlled study of 100 cases. Cases were divided into 2 groups of 50 each. A total of 100 adult patients were randomly selected who fulfilled the inclusion criteria. They were divided into groups and study was conducted.*

Results*: In this study, we measured the results of each drug by its attenuation of pressure response and recovery profile.*

Conclusion*: From our study we conclude that both dexmedetomeidine and esmolol promote satisfactory attenuation of pressure response and help in recovery profile of the patient but Esmolol is found to be superior.*

Keywords: *dexmedetomidine, esmolol, pressure response, recovery profile and laparoscopic cholecystectomy*

I. Introduction

The word '*Laparoscopy*' is derived from Ancient Greek *lapara*, meaning '*flank, side'*, and *skopeó*, meaning '*to see*'. Laparoscopy is an operation performed in the abdomen or pelvis through small incisions with the aid of a camera. It can either be used to inspect and diagnose a condition or to perform surgery. Surgery involving laparoscope is also called minimally invasive surgery because operations are performed using multiple small incisions (0.5 to 1.5 cm) in contrast to traditional methods which use large incisions.

Operative laparoscopy has become the standard approach for most common surgeries, including tubal ligation, cholecystectomy, appendectomy, and ovarian cystectomy. [Goldberg JM. Indications and contraindications for laparoscopy. In: Falcone T, Goldberg JM. Basic, Advanced and Robotic Laparoscopic Surgery. Saunders; 2010:Chap 2]

Currently, technology is so advanced that almost all surgical procedures can be performed laparoscopically. The laparoscopic approach has been gaining popularity for several reasons:

- Usually can be performed in the outpatient setting
- Shorter hospitalization when admission is necessary
- Better cosmetics
- Faster recovery and earlier return to normal activity
- Less risk of postoperative adhesion formation

The higher cost of the procedure may be outweighed by social benefits, including lack of or shorter hospitalization and earlier return to work. [Bardwil T. Operative laparoscopy. [online] [cited 2014 Apr 03] Available from: URL: http://emedicine.medscape.com/article/1848486-overview]

No other operation has been so profoundly affected by the advent of laparoscopy as cholecystectomy. Laparoscopic cholecystectomy has rapidly become the procedure of choice for routine gallbladder removal and has become the most common major abdominal procedure performed in western countries. [Litwin DE, Cahan MA. Laparoscopic cholecystectomy.SurgClin North Am. Dec 2008;88(6):1295-313]

Laparoscopic cholecystectomy has been gaining popularity over open cholecystectomy for the following reasons: [Calland JF, Tanaka K, Foley E, Bovbjerg VE, Markey DW, Blome S, et al. Outpatient laparoscopic cholecystectomy: patient outcomes after implementation of a clinical pathway. Ann Surg. May 2001;233(5):704-15.], [Shea JA, Berlin JA, Bachwich DR, Staroscik RN, Malet PF, McGuckin M. Indications for and outcomes of cholecystectomy: a comparison of the pre and postlaparoscopic eras. Ann Surg. Mar 1998;227(3):343-50]

- Lesser postoperative pain
- Lesser need for postoperative analgesia
- Shorter hospital stay from 1 week to less than 24 hours
- Earlier return to full activity within 1 week compared to 1 month after open cholecystectomy
- Better cosmetics
- Improved patient satisfaction

Although the direct operating room and recovery room costs are higher for LC, the shortened length of hospital stay leads to a net savings. More rapid return to normal activity may lead to indirect cost savings. [Nealon WH, Bawduniak J, Walser EM. Appropriate timing of cholecystectomy in patients who present with moderate to severe gallstone-associated acute pancreatitis with peripancreatic fluid collections. Ann Surg. Jun 2004;239(6):741-9; discussion 749-51]

The procedure of laparoscopy essentially involves creating an artificial pneumoperitoneum, usually using carbon dioxide (CO_2) gas. This elevates the abdominal wall above the internal organs like a dome to create a working and viewing space. CO_2 is used because it is common to the human body and can be absorbed by tissue and removed by the respiratory system. It is also non-flammable, which is important because electrosurgical devices are commonly used in laparoscopic procedures.

However, abdominal insufflation using CO_2 is also associated with various pathophysiological changes, especially involving cardiovascular and respiratory systems. There is an increase in arterial pressures, systemic vascular resistance and heart rate and decrease in cardiac output and urine output. Also, laparoscopic cholecystectomy is performed in the reverse trendelenburg position which leads to diminished venous return and hence further reduces cardiac output. [Junghans T, Neudecker J, Dörner F, Raue W, Haase O, Schwenk W. Effect of increasing cardiac preload, sympathetic antagonism, or vasodilation on visceral blood flow during pneumoperitoneum. Langenbecks Arch Surg. 2005 Nov; 390(6):538-43.]

These changes are usually well tolerated by healthy adults but can be detrimental in elderly and in patients with cardiorespiratory compromise. Hence, it is essential for the anaesthesiologist to have proper understanding of various pathophysiologic changes that occur during laparoscopy so that one can evaluate and optimize the patient in the preoperative period and also manage the haemodynamic changes that occur during the perioperative period.

To overcome these changes various pharmacological agents such as β-adrenergic antagonists [Koivusalo AM, Scheinin M, Tikkanen I, Yli-Suomu T, Ristkari S, Laakso J, et al. Effects of Esmolol on Haemodynamic response to Carbondioxide pneumoperitoneum for laparoscopic surgery. ActaAnaesthesiologica Scandinavia, May 1998;42(5):510-7], clonidine [Laisalmi M, Koivusalo AM, Valta P, Tikkanen I, Lindgren L. Clonidine provides opioid sparing effect, stable haemodynamics and renal integrity during laparoscopic surgery. SurgEndosc 2001;15:1331-5], nicardipine [Hea JO Yoon, Young Suck JE. Haemodynamic effects of intravenous bolus dosing of nicardipine on pneumoperitoneum during laparoscopically assisted vaginal hysterectomy. Korean j anaesthesiol 2006;50:43-7], and propofol boluses [Marana E, Colicci S, Meo F, Ricardo MR. Poeirotti. Neuroendocrine stress response in gynaecological laparoscopy: TIVA with propofol versus sevoflurane anaesthesia. Journal of clinical anaesthesia 2007;22(4):250-255] have been used to control haemodynamic changes that occur during laparoscopy.

Dexmedetomidine [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 Dec; 75(6):932-9] is a selective α2-adrenergic receptor agonist which is known to produce sedation, analgesia [Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions.AnesthAnalg. 2000 Mar; 90(3):699-705.], and also has sympatholytic, anaesthetic sparing and haemodynamic stabilising properties without significant respiratory depression. [Keniya VM, Ladi S, Naphade R. Dexmedetomidine attenuates sympathoadrenal response to tracheal intubation and reduces perioperative anaesthetic requirement. Indian J Anaesth. 2011 Jul-Aug; 55(4): 352-7] Its sympatholytic effect decreases mean arterial pressure and heart rate by reducing norepinephrine release and hence improves haemodynamic stability during laparoscopy. [Málek J, Marecek F, Hess L, Kurzová A, Ocadlík M, Votava M. A combination of dexmedetomidine with ketamine and opioids results in significant inhibition of hemodynamic changes associated with laparoscopic cholecystectomy and in prolongation of postoperative analgesia. RozhlChir. 2010 May; 89(5):275-81.] [Bajwa SS, Kaur J, Singh A, Parmar SS, Singh G, Kulshrestha A, et al. Attenuation of pressor response and dose sparing of opioids and anaesthetics with pre-operative dexmedetomidine. Indian J Anaesth 2012;56:123-8] It has also been documented to decrease post-operative nausea and vomiting after laparoscopic surgery. [Massad IM, Mohsen WA, Basha AS, Al-Zaben KR, Al-Mustafa MM, Alghanem SM. A balanced anesthesia with dexmedetomidine decreases postoperative nausea and vomiting after laparoscopic surgery. Saudi Med J. 2009 Dec; 30(12):1537-41]

. [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. ActaAnaesthesiol Scand. 1998 May; 42(5):510-7.] It selectively blocks β1 adrenoceptors and competitively reduces receptor occupancy by catecholamines and other β-adrenergic agonists. It has been shown to blunt haemodynamic responses to perioperative noxious stimuli. [Ozturk T, Kaya H, Aran G, Aksun M, Savaci S. Postoperative beneficial effects of esmolol in treated hypertensive patients undergoing laparoscopic cholecystectomy. Br J Anaesth. 2008 Feb;100(2):211-4.] It also decreases the need for opioids during surgery and recovery. [Ozturk T, Kaya H, Aran G, Aksun M, Savaci S. Postoperative beneficial effects of esmolol in treated hypertensive patients undergoing laparoscopic cholecystectomy. Br J Anaesth. 2008 Feb; 100(2):211-4.]

The present study evaluates the comparative effect of dexmedetomidine and esmolol on the intra-operative pressure response to pneumoperitoneum in patients undergoing laparoscopic cholecystectomy.

II. Aims And Objectives

1. To compare the effects of intravenous dexmedetomidine and intravenous esmolol in attenuating pressure response to pneumoperitoneum with CO2 in patients undergoing laparoscopic cholecystectomy, in relation to:
   - Heart rate
   - Systolic blood pressure, diastolic blood pressure and mean arterial pressure
2. To compare the recovery profile between the dexmedetomidine and esmolol groups in relation to time required for :
   - Response to commands
   - Extubation
   - To become fully awake
3. Perioperative requirement of anaesthetic agents.
4. To study the complications if any.

III. Material And Methods

Sample size and duration: Out of 100 patients, 50 received intravenous dexmedetomidine and the other 50 received intravenous esmolol. Duration of the study was one year.

Materials and method:

Study Design: The study was an open label observer blind prospective randomized controlled study of 100 cases. Cases were divided into 2 groups of 50 each:

Group 'D': In this group, patients received an intravenous bolus of 0.5µg/kg dexmedetomidine and 0.4µg/kg/hr infusion by infusion pump starting 5 minutes before induction, continued till the end of surgery.

Group 'E': In this group, patients received an intravenous bolus of 0.5mg/kg esmolol and 50µg/kg/min infusion by infusion pump starting 2 minutes after intubation, continued till the end of surgery.

The drug was given to the patient by the investigator according to random number table but the observer taking the readings was blind about the drug given.

Inclusion Criteria:

1. Patient undergoing laparoscopic cholecystectomy.
2. ASA grade I and II patients.
3. Age between 18 to 60 years.

Exclusion Criteria:

1. Patient's refusal.
2. ASA grade III patients and above.
3. Patients on beta-blockers.
4. Patients with uncontrolled asthma and COPD despite treatment.
5. Pregnant women and lactating mothers.
6. Morbid obesity.
7. Patients with acute cholecystitis.
8. Patients having severe hepatic and renal disease and those taking medications for it.

Study Procedure: The study was started after ethics committee approval. Preoperatively, the patients were kept nil by mouth for the last 10-12 hours prior to surgery. On the day of surgery, patient's pre-operative investigations like Hb, PCV, TLC, DLC and platelet count were checked for. Urine routine and microscopy were checked. For patients older than 40 years, ECG and blood sugar levels were done. Patients were examined thoroughly and allocated randomly into two predetermined groups. Well informed written consents were taken. Preoperative vitals were recorded in the form of baseline pulse, ECG, SPO2 and blood pressure. Venous cannulation was done. All patients were premedicated with midazolam 0.03mg/kg iv, fentanyl 2µg/kg iv 10 minutes before induction. Inj. Ondansetron 4mg iv was also given before induction.

Preparation of study medication and administration:
Group 'D': Study medication was prepared in a 20 ml syringe. Inj. Dexmedetomidine 100µg (1ml) was added to 19 ml normal saline making a total volume of 20 ml resulting in a concentration of 5 µg/ml. A bolus of 0.5µg/kg was given over 10mins 5 minutes before induction and the drug was infused at a rate of 0.4µg/kg/hr.
Group 'E': Study medication was prepared in a 20 ml syringe. Inj. Esmolol 100mg (10ml) was added to 10 ml normal saline making a total volume of 20 ml resulting in a concentration of 5mg/ml. A bolus of 0.5mg/kg was given over 30seconds 2minutes after intubation and the drug will be infused at a rate of 50µg/kg/min.

All patients received 500ml of lactated Ringer's solution prior to induction. Induction agent used was Inj. Propofol 2mg/kg iv and the muscle relaxant used was Inj. Vecuronium 0.1mg/kg iv. Patients were intubated with appropriate sized PVC endotracheal tubes. Anaesthesia was maintained by nitrous oxide in oxygen 50:50 and 1% isoflurane. Intra abdominal pressure was maintained at 10-15 mm Hg and CO2 insufflation rate at 6L/min. Patient's heart rate was maintained at a rate of 60-90 beats/min and systolic blood pressure at 110-140 mm Hg and diastolic blood pressure at 70-100 mm Hg. Any increasing BP, heart rate were treated with propofol boluses and heart rate <40 was treated with Inj. Glycopyrrolate 0.004mg/kg. Anaesthesia was reversed with Inj. Neostigmine 0.05 mg/kg and Inj. Glycopyrrolate 0.008 mg/kg.

Monitoring was done by cardioscope (HR), pulse oximetry (SPO2), non-invasive blood pressure (NIBP) and end tidal CO2 (EtCO2). Heart rate, systolic and diastolic BP, respiratory rate and SPO2 were recorded preoperatively (baseline), at the time of dexmedetomidine bolus f/b infusion in group D (5minutes before induction), at induction and at intubation. Heart rate, systolic and diastolic BP, SPO2, EtCO2 were recorded at the time of esmolol bolus f/b infusion in group E (2minutes after intubation), at gas insufflation, at every 5 minutes after gas insufflation, at the end of gas insufflation, at the time of reversal and at extubation.
Patient recovery profile was observed in the form of extubation time, response to verbal command and time for orientation. Vitals were recorded post-operatively before shifting the patient to the ward.
Statistical analysis: Categorical data will be analysed using 'Chi-Square test.' Numerical data will be tested for normality using 'Kolmogorov-Smirnov test'. If they follow normal distribution, 'Repeated measures ANNOVA test' will be applied for intra-group comparison; if they don't follow normal distribution, 'Freidman's test' will be applied for intra-group comparison.

To compare between the two groups 'D' and 'E,' data will be tested for normality. If they follow normal distribution, 'Unpaired "t" tests' will be applied and if they don't follow normal distribution, 'Mann-Whitney "U" test' will be applied.

IV. Results And Analysis

Statistical Methods[3]: Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance.

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups, inter group analysis and on metric parameters. Chi-square test has been used to find the significance of study parameters on categorical scale between two or more groups.

Significant figures

+ Suggestive significance (P value: $0.05<P<0.10$)

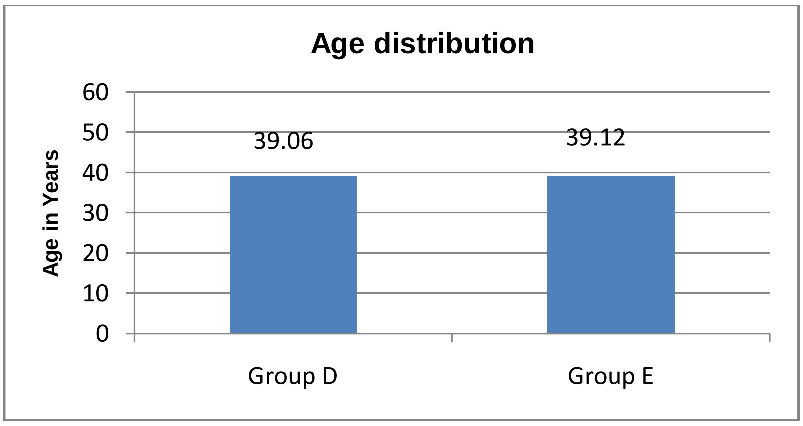
* Moderately significant (P value: $0.01<P \leq 0.05$)

** Strongly significant (P value: $P\leq0.01$)

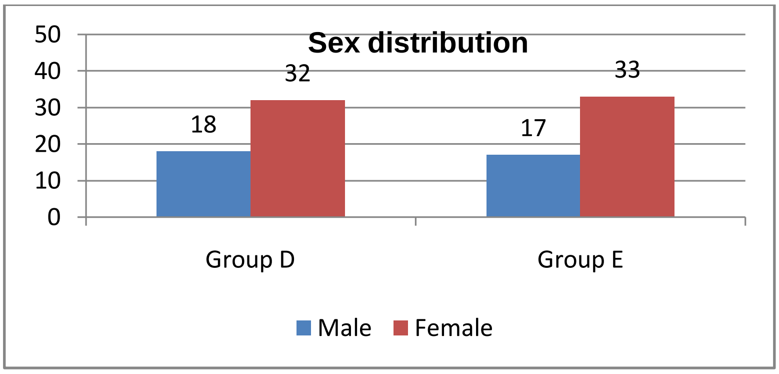
Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

Demographic Data

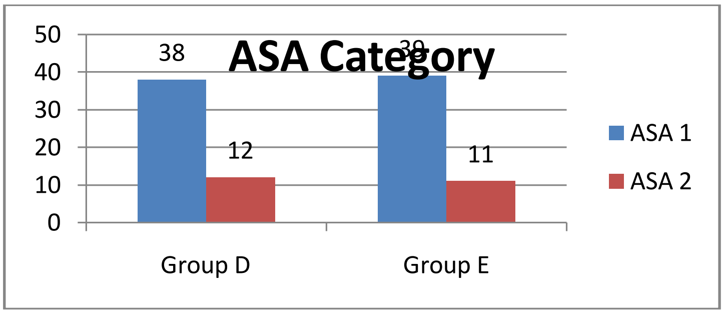
In the above study,age of the patients ranged from 19-60 years with an average of 39.06yrs in Group D and 39.12 yrs in Group E with p value of 0.488, showing no stastical significance.



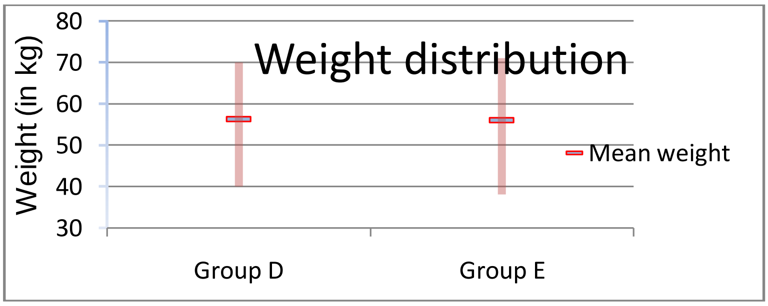
In our study Group D has 32(64%) female subjects and 18(36%) male subjects, Group E has33(66%) female and 17(34%) male subjects.



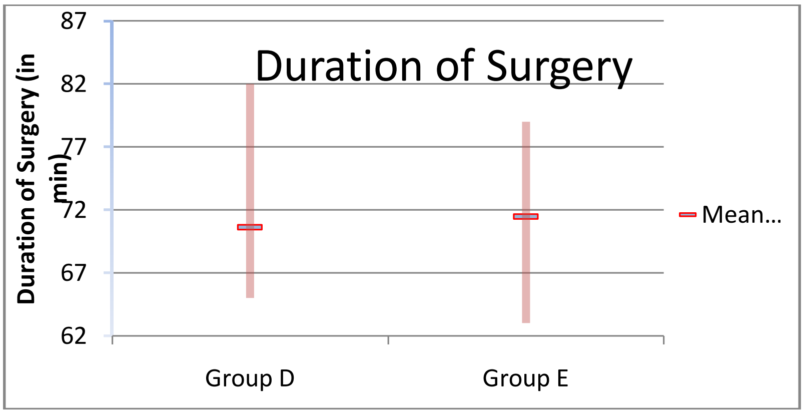
In our study Group D has 38 subjects belonging to ASA 1 and 12 subjects who belong to ASA 2 and Group E has 39 subjects who belong to ASA 1 and 11 subjects who belong to ASA 2 respectively.

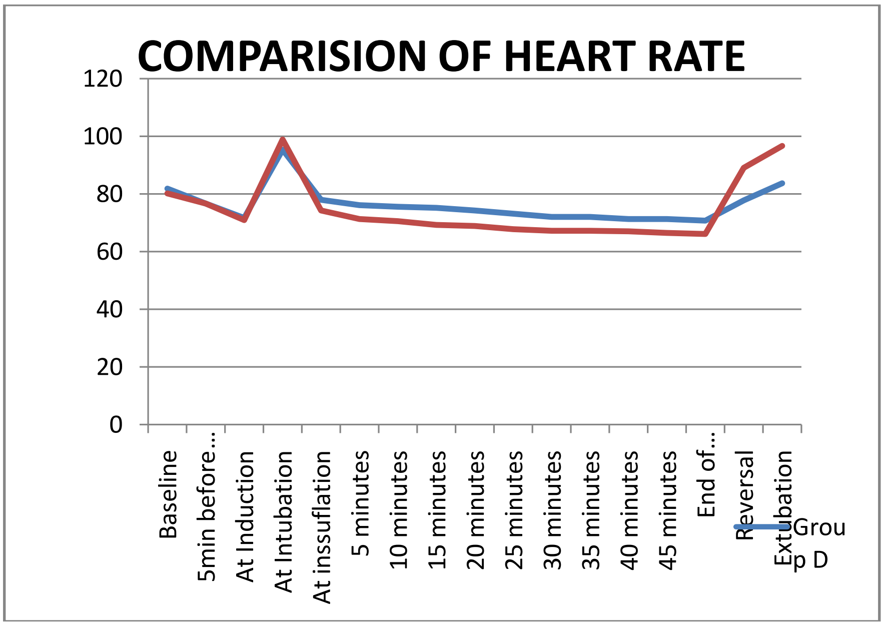


In our study mean weight of the patients in Group D was56.22kg and Group E was 55.9 with p value of 0.82 and both the groups were comparable.



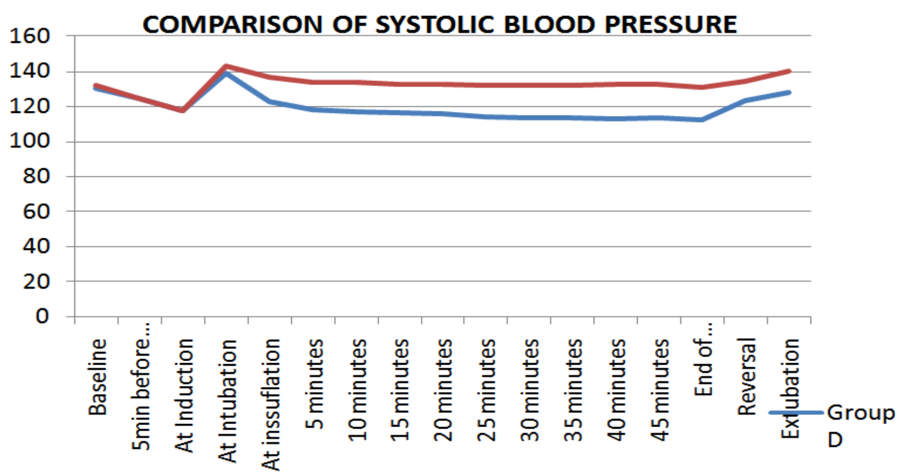
Mean duration of surgery in Group D was 70.58 min and in Group E it was 71.44 min with p value of 0.292613, hence both the groups were similar statistically.



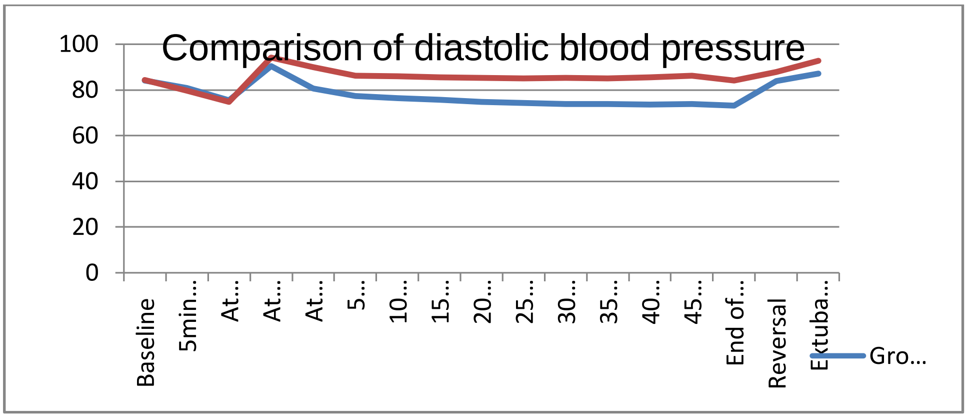


Observation

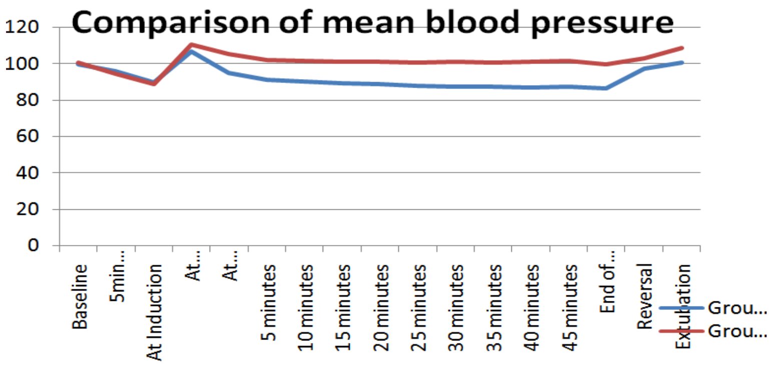
Baseline heart was comparable in both the groups,Group D(81.8±11.8) and Group NS(80.1±9.583681) and there is no statistical significance. There is increase in heart rate in both the groups during intubation. Group E also showed significantly lower heart rates compared to Group D. At the time of reversal and extubation there is significantly higher heart rates in Group E compared to Group D.



Observation
Baseline systolic blood pressure was similar in bothGroup D and Group E. There was fall in systolic blood pressure after bolus dose in group D and showed an increase during intubation and insufflation which was within the 20% of the baseline and remained stable till extubation showing less hemodynamic instability. However in Group E there was statistically significant increase in systolic blood pressure starting from intubation which remained high till extubation compared to Group D.

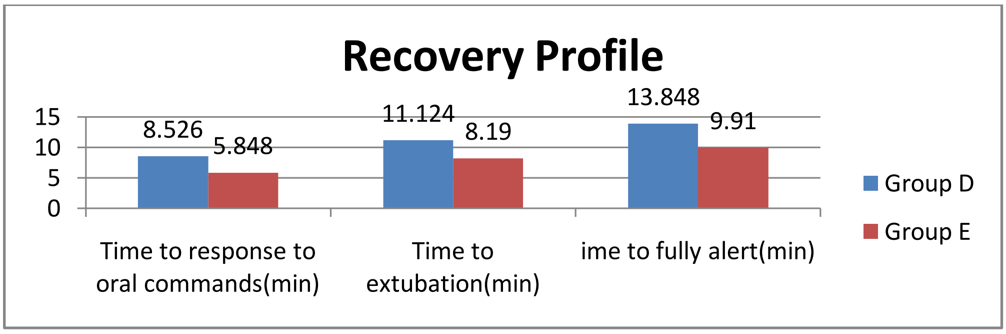


Observation:
Baseline systolic blood pressure was similar in both Group D and Group E. There was fall in diastolic blood pressure after bolus dose in group D and showed an increase during intubation and insufflation which was within the 20% of the baseline and remained stable till extubation showing less hemodynamic instability. However in Group E there was statistically significant increase in diastolic blood pressure starting from intubation which remained high till extubation compared to Group D.

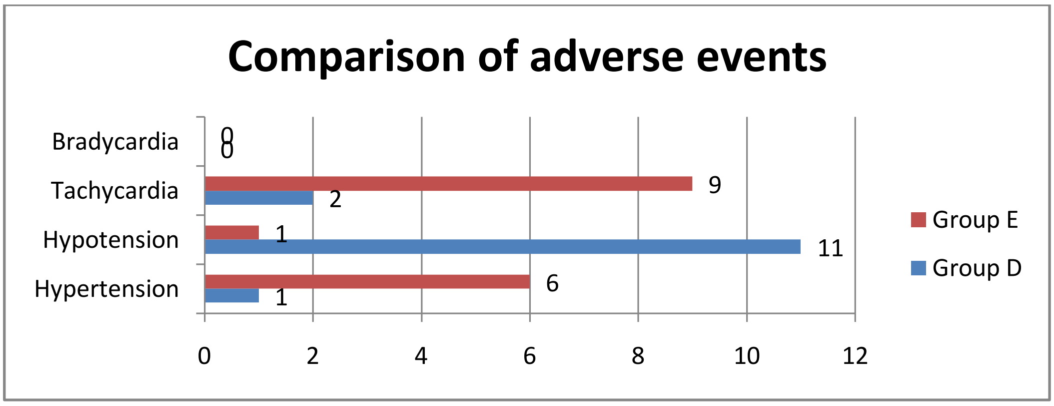


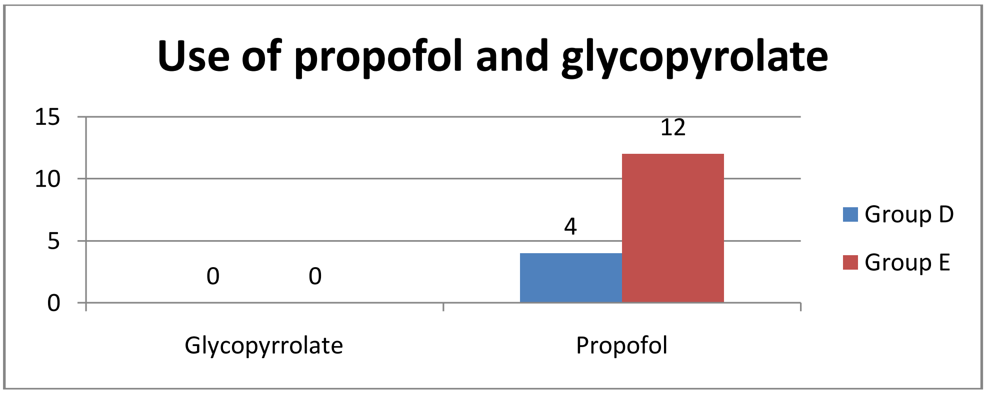
Observation
Baseline systolic blood pressure was similar in both Group D and Group E. There was fall in mean blood pressure after bolus dose in group D and showed an increase during intubation and insufflation which was within the 20% of the baseline and remained stable till extubation showing less hemodynamic instability. However in Group E there was statistically significant increase in mean blood pressure starting from intubation which remained high till extubation compared to Group D.

Obeservation
As shown here dexmedetomidine prolongs the time to response, to verbal commands, extubation and to become fully alert which is indicated by the P value which is significant.



Bradycardia was defined as sustained heart rate less than 45 bpm. In this study none of the patients had bradycardia in both the groups. Hence glycopyrrolate was also not used. Tachycardia (defined as sustained heart rate > 20% of basal heart rate) was seen in 2(4%) patients in Group D and 9(18%) patients in Group E with a P value <0.05.Hypotension (defined as < 20% of basal MAP sustained for 2 or more readings) was found in 11(22%) patients in Group D and 1(2%) patients in Group E with a P value <0.05.Hypertension (defined as > 20% of basal MAP sustained for 2 or more readings) was found in 1(2%) patients in Group D and 6(12%) patients in Group E with a P value <0.05.The use of propofol was required in 4(8%) patients in Group D and 12(24%) patients in group E with a P value <0.05.





V. Discussion

Significant hemodynamic fluctuations can occur during pneumoperitoneum at laparoscopy which can be especially detrimental in patients with reduced cardiopulmonary reserve. Various techniques and pharmacological agents have been studied to counteract these adverse hemodynamic changes during pneumoperitoneum.

In our study "Attenuation of intra-operative pressure response to pneumoperitoneum in patients undergoing laparoscopic cholecystectomy – A comparative study between dexmedetomidine and esmolol" we compared 50 patients who underwent laparoscopic cholecystectomy and received dexmedetomidine, with 50 patients who underwent laparoscopic cholecystectomy and received esmolol.

All the patients were ASA grade I/II. The Group D received injection dexmedetomidine 0.5mcg/kg by intravenous infusion over 10min (starting 5 min prior to induction) and 0.4mcg/kg/hr continuous intravenous infusion throughout the intraoperative period till the end of pneumoperitoneum. The Group E received injection esmolol 0.5mg/kg bolus over 2 min (starting 2 min after intubation) and 50mcg/kg/min continuous intravenous infusion throughout the intraoperative period till the end of pneumoperitoneum. Intraoperative monitoring of HR, ECG, MAP, EtCO2and saturation was done. In the perioperative period, we observed patients for occurrence of complications like bradycardia, tachycardia, hypotension, hypertension, excess sedation, nausea, vomiting and complications of laparoscopy like pneumothorax,endobronchial displacement of ET tube,air embolismetc.

Demographic Parameters

All the patients were comparable with respect to the demographic parameters: age, sex and weight. In the dexmedetomidine group the mean age was 39.06 years and in the esmolol group it was 39.12 years. In our study Group D has 32(64%) female subjects and 18(36%) male subjects; Group E has33(66%) female and 17(34%) male subjects. In our study mean weight of the patients in Group D was 56.26kg and Group E was 55.9 with p value of 0.82 and both the groups were comparable.

Hemodynamic Parameters

Baseline heart rate in Group D(81.8±11.8) and Group E (80.1±9.583681) are comparable and there is no statistical significance. The baseline systolic blood pressure in group D was 129.72±12.08818mmHg and group E was 131.72±12.20244 mmHg; baseline diastolic blood pressure was 84.2±9.149551mmHg and 85.12±8.227976 mmHg in study and control groups respectively. These baseline characteristics are comparable and there is no statistical significance.

Ishizaki et al tried to evaluate the safe intra-abdominal pressure during laparoscopic surgery. They observed a significant fall in cardiac output at 16 mm Hg of intra-abdominal pressure.

Berg et al observed hemodynamic parameters, i.e. heart rate, central venous pressure, and arterial blood pressure during CO2 insufflation. They felt increased vasopressin concentration more than likely contributes to these changes. In spite of the observed changes no cardiopulmonary complications occurred in their patient group. Therefore they felt that it is possible to omit invasive monitoring in cardiopulmonary healthy patients. In patients with concomitant history of cardiopulmonary disease, however, they felt that further studies were required to study the hemodynamic changes during laparoscopy.

Cunningham et al (10) and Dorsay et al assessed the ejection fraction (EF) of left ventricle by trans-oesophageal echocardiography during pneumoperitoneum. No significant change in ejection fraction was reported up to 15 mm Hg of intra-abdominal pressure. Considering all these facts intra abdominal pressure was kept below 12 mm Hg.

In our study end tidal carbon-dioxide level was maintained between 30-40 mmHg and intra-abdominal pressure below 12 mmHg.

In both the groups, there was a significant increase during intubation and insufflation which was within the 20% of the baseline and remained stable till extubation.however, in Group E the mean, systolic and diastolic blood pressure was higher, which was statistically significant.

Dexmedetomidine, an imidazoline derivative is a selective α-2 adrenergic agonist with sedative,anxiolytic,analgesic,sympatholytic and antihypertensive effects. It produces a fall in the heart rate and blood pressure associated with decreased systemic vascular resistance by activating presynaptic alpha-2 adrenergic receptors.

Various studies report using dexmedetomidine infusion rates ranging from 0.1 to 10 micrograms/kg/hr. Higher infusion rates had higher incidence of adverse events like hypotension and bradycardia. In our study we used dexmedetomidine at rate of 0.5mcg/kg bolus dose followed by infusion at rate of 0.4mcg/kg/hr without any incidence of adverse effects.

Esmolol is an ultra-short-acting selective $beta_1$ blocker. The structure of esmolol contains an ester linkage; esterases in red blood cells rapidly metabolize esmolol to a metabolite that has a low affinity for beta receptors. Esmolol has a short half-life of about 10 minutes. During continuous infusions of esmolol steady-state concentrations are achieved quickly and the therapeutic actions of the drug are terminated rapidly when its infusion is discontinued. In our study we used esmolol at rate of 500mcg/kg bolus dose followed by infusion at rate of 50mcg/kg/min without any incidence of adverse effects.

We observed that:

1. The control of heart rate was significantly better in the dexmedetomidine group than the esmolol group.

In the present study, inGroup D baseline HR was 81.8±11.8 bpm v/s 80.1±9.583681 bpm Group E, showing no statistical significance. The HR after intubation in Group D was 95.32±10.1 bpm v/s 98.82±10.31086 bpm in the Group E. There is a statistically significant increase heart rate in the esmolol group compared to dexmedetomidine after intubation; however, it was not clinically significant. From insufflation to the end of pneumoperitoneum, heart rate was lower in esmolol group than in the dexmedetomidine group, which was statistically significant, as shown below. During reversal and extubation heart rates were higher in the esmolol group than in the dexmedetomidine group, which was statistically significant, as shown below.

Yildiz M, Tavlan A, Tuncer S, Reisli R, Yosunkaya A, Otelcioglu S,(50)studied the effect of dexmedetomidine on haemodynamic responses to laryngoscopy and intubation : perioperative haemodynamics and anaesthetic requirements and found that preoperative administration of a single dose of dexmedetomidine resulted in progressive increases in sedation, blunted the haemodynamic responses during laryngoscopy, and reduced opioid and anaesthetic requirements. Furthermore, dexmedetomidine decreased blood pressure and heart rate as well as the recovery time after the operation.

2. The control of the systolic blood pressure was significantly better in dexmedetomidine group compared to esmolol group. In the present study baseline SBP in Group D was 129.72±12.08818 mmHg v/s 131.72±12.20244 mmHg in Group E, which is statistically not significant (P>0.05).

There was statistically significant increase in systolic blood pressure in group E 143.06±10.30at the time of intubation in comparison to Group D 138.6±11.46 (P<0.001) and remained elevated till extubation. The statistical difference in SBP between two groups was significant after CO_2insufflation at various time intervals
Uysal et al. studied the effects of dexmedetomidine, esmolol and sufentanylon hemodynamic responses to trachealintubation in hypertensive patients. They demonstrated that administration of asingle dose of dexmedetomidine before anaesthesiainduction was an effective method forattenuating the hemodynamic response to trachealintubation in hypertensive patients. They found that"baseline" and "immediately after intubation"values showed greater percentage variation in systolic blood pressure inthe esmolol group compared to the dexmedetomidinegroup. They concluded thatas far as hypertensivepatients are concerned dexmedetomidinecan safely be used as an adjunct toanaesthesia induction.

3. The control of diastolic blood pressure was better in the dexmedetomidine group than the esmolol group during intubation and throughout the period of pneumoperitoneum.

The Baseline diastolic pressure was comparable between both the groups Group D 84.2±9.149551 mmHg v/s Group E 84.2±8.22 mmHg (p value 0.598225). From the period following intubation the diastolic pressure was higher in group E compared to group D till extubationand the difference between two groups remained statistically significantThe control mean blood pressure was better in the dexmedetomidine group than the esmolol group during intubation and throughout the period of pneumoperitoneum.

The Baseline diastolic pressure was comparable between both the groups Group D 99.37333±9.619906 mmHg v/s Group E 100.6533±8.705814 mmHg (p value 0.487076). From the period following intubation the mean pressure was higher in group E compared to group D till the end of pneumoperitoneum and the difference between two groups remained statistically significant

Koivusalo et al.studied the effects of esmolol on haemodynamic response to CO_2 pneumoperitoneum for laparoscopic surgery. They found that mean blood pressure could maintatined at baseline levels with esmolol.Esmolol effectively reduced the amount of opioid needed during laparoscopic surgery and ensuredstable intraoperative haemodynamics.

Aho et al. studied effect of intramuscularly administered dexmedetomidine on hemodynamic and stress hormone responses to gynecologic laparoscopy. They found a dose dependant attenuation of the mean blood pressure. Also they found that the increase in heart rate due to intubation and laparoscopy was substantially bluntedby dexmedetomidine.

4. Esmolol group had significantly faster recovery profile compared to dexmedetomidine group in the form of time response to oral commands,extubation timeand time for full orientation.

In our study, it was noticed that mean time to response to oral commands was 8.526±0.665417 min in dexmedetomidine group and 5.84±0.48 min in esmolol group, which is statistically significant (P<0.01). Mean time to extubation was 11.124±0.926384 min in dexmedetomidine group and 8.19±0.51min in esmolol group, which is statistically significant (P<0.01). Mean time to become fully alert was 13.848±0.666774 min in dexmedetomidine group and 9.91±0.51 min in esmolol group, which is statistically significant (P<0.01).

Hall et al. studied the sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions in healthy volunteers. They concluded that small doses ofdexmedetomidine provided sedation that could be easilyreversed with verbal or physical stimuli while also caused some analgesia and immediate(not retrograde) memory impairment.

Kol et al. Studied controlled hypotension with desflurane combined with esmolol or dexmedetomidine duringtympanoplasty in adults. They concluded that esmolol and dexmedetomidine, combined with desflurane, provided an effective and well tolerated method of achieving controlled hypotension. However, esmolol was associated with significantly shorter extubation and recovery times and significantly less postoperative sedation compared with dexmedetomidine.

5. In the present study, none of the patients had bradycardia (HR <45bpm) in both the groups.Tachycardia (defined as sustained heart rate > 20% of basal heart rate) was seen in 2(4%) patients in Group D and 9(18%) patients in Group E with a P value <0.05 which is statistically significant. Hypotension (defined as

< 20% of basal MAP sustained for 2 or more readings) was found in 11(22%) patients in Group D and 1(2%) patients in Group E with a P value <0.05which is statistically significant. However, none of the patients required treatment for hypotension. Hypertension (defined as > 20% of basal MAP sustained for 2 or more readings) was found in 1(2%) patients in Group D and 6(12%) patients in Group E with a P value <0.05 which is statistically significant.The use of propofol was required in 4(8%) patients in Group D and 12(24%) patients in group E with a P value <0.05which is statistically significant.

Our findings were similar to the study conducted by FerdiMenda et al, they showed that none of the patients experienced bradycardia requiring treatment even though patients have been premedicated with beta blockers. They showed that the incidence of hypotension was not any higher than that observed in placebo group patients.

Bekkeret al. studied the effect of dexmedetomidine on perioperative hemodynamics in patients undergoing craniotomy and determined that intraoperative dexmedetomidine infusion was effective for blunting the increases in SBP perioperatively. The use of dexmedetomidine did not increase the incidence of hypotension or bradycardia, excessive sedation, nausea, vomiting common side effects of the drug.

Wiest studied the therapeutic efficacy and pharmacokinetic characteristics of esmolol.The principal adverse effect of esmolol was noted to be hypotension (incidence of 0 to 50%), which was frequently accompanied with diaphoresis. The incidence of hypotension appeared to increase with doses exceeding 150 micrograms/kg/min and in patients with low baseline blood pressure. Hypotension infrequently required any intervention other than decreasing the dose or discontinuing the infusion. Symptoms generally resolved within 30 minutes after discontinuing the drug. They concluded that in surgical and critical care settings the pharmacokinetic profile of esmolol allows the drug to provide rapid pharmacological control and minimises the potential for serious adverse effects.

VI. Conclusion

Reflex Adrenergic response during intubation and pneumoperitoneum causes tachycardia and hypertension. Various pharmacological agents like clonidine, beta-blockers and opioids have been tried to attenuate this adverse response.

In this study, we compared the use of dexmedetomidine and esmolol in attenuation of pressure response during pneumoperitoneum during laparoscopic cholecystectomy. 100 patients belonging to ASA physical status I and II were randomly divided into two groups. Group D had 50 patients who received dexmedetomidine 0.5mcg/kg IV bolus over 10min and followed by 0.4mcg/kg/hr infusion till the end of surgery. Group E had 50 patients who received esmolol 500mcg/kg bolus followed by 50mcg/kg/min infusion till the end of surgery. Intraoperative HR, MAP, SpO_2, ETCO2were recorded after bolus administration, 1min after induction, 1min after intubation, and after pneumoperitoneum at 5min interval till discontinuation of study drug and extubation. Patients were observed for any adverse events .Timing of following events were recorded-time from stopping isoflurane to response to oral commands, to tracheal extubation, and to become fully alert

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