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Efficacy of different doses of Dexmedetomidine on hemodynamic response during laparoscopic cholecystectomy under general anaesthesia: A prospective analytical study

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Abstract

Background

Laparoscopy or keyhole surgery became the gold standard since the introduction of laparoscopic cholecystectomy in mid-eighties, in managing the symptomatic gall stone diseases. Early mobilization, reduced hospital stay and decreased analgesic requirement besides improved cosmesis are its major benefits. However, the problems are primarily because of insufflation of carbon dioxide and positioning during surgery causing sympathetic over-stimulation. Increased systemic vascular resistance due to Pneumo-peritoneum induced hypercarbia causes tachycardia, hypertension and reduction in cardiac output[1,2]. Hemodynamics are further compromised by anaesthetic procedures like laryngoscopy, intubation and extubation [3].

Severely altered hemodynamics during laparoscopy pose spectrum of management challenges to the anaesthesiologist. Several modifications viz. pharmacological agents (nitroglycerine[4], beta blockers[5], opioids[6], gabapentin[7], pregabalin[8], magnesium sulphate[9], clonidine[9] and dexmedetomidine[10]) and regional anaesthesia [11] have been used to attenuate these changes[11]with variable success.

Dexmedetomidine, a selective α2-adrenoreceptor agonist and an analogue of clonidine utilizes receptors distinct from γ-amino butyric acid (GABA) receptor used by benzodiazepines and propofol[12]. Being a selective α2 receptor agonist with sedative and analgesic effects but minimal respiratory depression, it has been widely used for sedation during mechanical ventilation, short procedures and postoperative anxiolysis to prevent emergence agitation and treatment of substance withdrawal[10].

Dexmedetomidine has properties of analgesia, sympatholysis and titratable sedation without major side effects[12]. It also reduces stress response to surgery ensuring a stable hemodynamic state and also lessens the

opioid requirement and their side effects. It has a very short distribution half-life of approximately 6 min, so can be used successfully even for attenuating the stress response of laryngoscopy[13].

The present study was aimed to evaluate the effective dose of Dexmedetomidine and compare its two different regimes in attenuating the hemodynamic changes taking place during laparoscopic cholecystectomy under general anaesthesia.

Keywords: Dexmedetomidine, Laproscopic Cholecystectomy, Anaesthetic Adjuvant, Pneumoperitoneum, Haemodynamic Changes

Materials And Methods

After the approval from Institutional Ethics Committee, written informed consent was taken from all patients who satisfied the inclusion criteria. 120 patients undergoing laparoscopic cholecystectomy under general anaesthesia were distributed among three different groups (A, B and C) randomly using a computer-generated randomization software.

Inclusion Criteria

1. Age groups between 18 and 65 years of either sex.
2. American Society of Anaesthesiologists physical status Grade I or II
3. Patients undergoing laparoscopic Cholecystectomy Under General Anaesthesia.

Exclusion Criteria

1. Patients with autonomic dysfunction such as the elderly and diabetic patients.
2. Patients with ASA grade III or IV.
3. Patients with controlled hypertension on drugs / uncontrolled hypertension.
4. Pregnant or lactating women.
5. Patients unwilling to participate in the study.
6. Alcohol dependant patients or patients with history of drug abuse.
7. Patients with history of regular use of sedatives including anti psychotics and analgesics including Pregablin.

Study was a double blind study conducted on 03 groups of patients, **Group A** (NS) received normal saline as bolus and infusion during procedure; **Group B** (B&I) received bolus dose of dexmedetomidine at 0.5 mcg/kg over 10 minutes preoperatively followed by continuous infusion at a rate of 0.5 mcg/kg/hr and **Group C** (B only) received dexmedetomidine at 1.0 mcg/kg over 10 minutes as a preoperative bolus and subsequently normal saline as continuous infusion. All three groups received the infusion dose till the closure of surgical wounds.

Infusion solutions were prepared separately for each group in 50 ml syringe, each for bolus and infusion and were administered through infusion pump. In Group A both syringes (bolus and infusion) were of Normal Saline. In Group B both syringes (bolus and infusion) were of Dexmedetomidine. Both were prepared with 0.5 ml Dexmedetomidine containing 50 mcg drug in 50 ml NS giving the concentration of 1 mcg/ml. Group C had bolus dose syringe of Dexmedetomidine and infusion dose syringe of Normal Saline. For bolus syringe, 1 ml Dexmedetomidine containing 100 mcg was diluted up to 50 ml with NS resulting in final concentration of 2mcg/ml. All three groups received the study group specific desired drug as continuous infusion @ 0.5ml/Kg/hr to maintain similarity and effective blinding.

All patients underwent pre-anaesthetic evaluation. Six hours of conventional overnight fasting orders were followed. On arrival to operation theatre, intravenous access was established and basic non-invasive monitoring (NIBP, ECG and SpO_2) was applied. All patients received Inj Midazolam 1mg IV, Inj Ondansetron 4 mg IV and Inj fentanyl 2mcg/kg IV as premedication. Thereafter, all patients received bolus drug infusion over next 10 minutes as per the group allotted. After 5 minutes of bolus administration, patients were induced using Inj Propofol 02mg/Kg and intubated using Inj Succinylcholine 02mg/Kg. Anaesthesia was maintained with Oxygen, Nitrous Oxide and Sevoflurane (01 MAC). Muscle paralysis was obtained using Inj vecuronium 0.1 mg/kg initially followed by intermittent bolus of 1mg IV. Patients were kept on controlled ventilation to maintain ETCO2 between 35 and 45 mm Hg. Subsequently after completing the bolus drug, infusion dose of drugs was started as per the study group and was continued till the closure of the surgical wound. CO_2insufflation was done to create pneumo-peritoneum (@ 01L/min) and intra-abdominal pressure was maintained at 12 mmHg throughout the procedure. After completion of surgery, neuromuscular blockade was reversed with appropriate dose of Inj Neostigmine and Inj Glycopyrrolate and patients were extubated. All the patients were monitored for heart rate and blood pressure (Systolic, Diastolic, Mean arterial) at regular intervals including before and after starting the infusion, after intubation, before and after CO_2 insufflation, 10 and 20 mins after CO_2 insufflation and finally before and after extubation. Any episode of bradycardia, tachycardia, hypotension and hypertension beyond 20% of baseline were recorded and managed appropriately.

Statistical Analysis

The data pertaining to patients' socio demographic and other clinical variables was entered in the form of a data matrix in Microsoft Excel® and analyzed using IBM® SPSS® ver 20.0.0.The descriptive analysis was analyzed in the form of frequencies and percentages for categorical variables and means and standard deviations for continuous variables.

The intra group analysis was accomplished using the parametric, one-way repeated measures analysis of variance or non-parametric, Friedman analysis based upon the data meeting the assumptions for application of the tests. Similarly, the intergroup analysis was accomplished using the one-way analysis of variance and Independent samples Krusal Wallis test. A ***p*** value of <0.05 was considered statistically significant for the purpose of the study.

Results

After obtaining written informed consent, a total of 120 patients were included in the study and were randomly distributed into three study groups of 40 each using computer software. In Group C one patient could not complete this study as he developed severe bradycardia and hypotension requiring the use of Inj Atropine and Inj Mephenteramine and inhalational gases were stopped till the hemodynamics recovered to the baseline value. So 119 patients completed the study and their data was included in the demographic profile. There was no statistically significant difference amongst the groups regarding demographic variables (***p***>0.05) [Table 1]. All groups were comparable in duration of surgery as well.

All the three groups were comparable to each other with respect to the baseline mean arterial pressure (MAP) and heart rate. In Group A, after completing the bolus of NS there was no significant change in value of MAP but it increased significantly after intubation, creation of pneumo-peritoneum and extubation. In other two groups with Dexmedetomidine (Group B&C), MAP fell significantly after finishing the bolus dose of Dexmedetomidine. The fall was more pronounced and prolonged in Group C in comparison to Group B which stabilized fast. After intubation and pneumo-peritoneum, MAP continued to be stable around the post bolus values below the initial baseline values. After extubation there was increase in MAP in both groups as compared to post bolus values but the increase was significantly less than

Group A. It remained below baseline values in Group B but increased above the initial values in Group C which was significant. [Table 2 and Fig 1]In group A, after finishing the NS bolus there was no significant change in heart rate but it increased significantly above preoperative value after intubation, pneumo-peritoneum and extubation. In both the Dexmedetomidine groups, after finishing the bolus dose, the heart rate decreased significantly below the preoperative value but stabilized early in group B as compared to Group C. In both groups after intubation and pneumo-peritoneum, the heart rate continued at a stable level achieved after the bolus dose. After extubation, the heart rate continued to be stable around the preoperative value in group B as compared to group C in which there was increase in the value as compared to the baseline. [Table 3 and Fig 2]

Discussion

This study was aimed to critically analyze the hemodynamic effects of two different regimens of administering Dexmedetomidine in patients undergoing laparoscopic cholecystectomy during various stressful conditions such as intubation, creation of pneumo-peritoneum and extubation.

Laparoscopic procedures are by and large considered to be minimally invasive and have proven benefits like reduced tissue damage, decreased hospital stay, early ambulation, and decreased analgesic requirements. However, carbon dioxide pneumo-peritoneum and patient positioning produces complex physiological changes and hemodynamic variations due to hypercarbia and increased intra-abdominal pressure[14,15].On top of it, anaesthetic procedures like laryngoscopy, intubation and extubation also contribute to sympathetic stimulation leading to undesirable hemodynamic changes like hypertension and tachycardia[3]. These adverse effects can be attenuated to great extent by using various drugs and improvisations in surgical and anaesthetic techniques[16,17].

Dexmedetomidine is one of the leading pharmacological agents being studied for providing stable hemodynamics. It is a highly selective α2 adrenergic agonist providing excellent sedation, analgesia, and anxiolysis besides antihypertensive effects. It has favorable profile in comparison to other pharmacological agents because of minimal respiratory depression. In a study by Amrita Gupta et al Dexmedetomidine provided better hemodynamic control as compared to fentanyl with better cerebral relaxation and faster recovery[6].

Dexmedetomidine also has an edge as an adjunct to general anaesthesia due to its added advantages such as sparing of anaesthetic agents, hemodynamic stability and reduction of emergence agitation. Its pharmacological actions are due to stimulation of α2A receptors in locus coeruleus and spinal cord. It also prevents release of norepinephrine thereby reducing the sympathetic outflow. Therefore, it is highly effective in blunting the hemodynamic response to stressful conditions[18,19]. Dexmedetomidine in past has been studied in various infusion rates ranging from 0.2 to 10mcg/kg/hour. Higher doses have been associated with increased adverse effects like hypotension and bradycardia[12,20].

In our study, we compared and critically analyzed the effect of Dexmedetomidine given through two different regimens. In one regimen, a loading dose of 0.5mcg/kg was given followed by infusion of 0.5mcg/kg/hour (Group B) and in second one only single preoperative bolus dose of 01mcg/kg (Group C) was given. Thus, it was confirmed that there was significant increase in heart rate and mean arterial pressure in control group (Group A) in all stressful conditions like intubation, pneumo-peritoneum and extubation. These results are in consistency with the study conducted by authors Bhattacharjee et al[21] and Keniya et al[13].

Dexmedetomidine in both regimens (Group B & C) was successful to varying degrees in attenuating the hemodynamic surges at all stages as compared to the control group (Group A). This finding was consistent with previous studies. Manne et al concluded that dexmedetomidine infusion in the dose of 0.4mcg/kg/hr effectively reduces hemodynamic stress response during laparoscopic surgery with reduction in post operative analgesic requirements[22]. In 2016, Acharya et al compared doses of 0.3mcg/kg/hr and 0.6mcg/kg/hr infusion after 0.5 mcg/kg of loading bolus in patients undergoing laproscopic cholecystectomy and concluded that there was attenuation of hemodynamic response with use of dexmedetomidine but was more effective at the rate of 0.6mcg/kg/hr[23].

In our study there was decrease in mean HR and MAP which was statistically significant but more stable vital parameters were achieved in group B as compared to group C. In group C, the decrease was not continuous and heart rate and MAP increased above the preoperative value after extubation which was not the case with Group B in which the parameters remained stable and below preoperative values throughout the procedure. Also in group C, the initial fall in heart rate and MAP was more as compared to group B and in one case in group C the study was abandoned due to severe bradycardia and hypotension. So there was an effective and better attenuation of hemodynamic responses with minimal side effects with the use of low dose of bolus Dexmedetomidine followed by continuous infusion (Group B) as compared to single large preoperative bolus dose (Group C). However, as there is no previous study that has compared Dexmedetomidine bolus with Dexmedetomidine bolus and infusion during general anaesthesia, we propose further larger population studies to validate our findings.

Conclusion

Dexmedetomidine effectively attenuates the hemodynamic stress response at all times during laparoscopic cholecystectomy, though in a dose dependent manner. Use of Dexmedetomidine infusion @ 0.5mcg/kg/hr after a loading dose of 0.5mcg/kg serves as a better adjuvant for anaesthesia with minimal side effects and effectively controls hemodynamic stress response during laparoscopic surgery as compared to single large bolus dose of 1mcg/Kg.

References

1. Veekash G, Wei LX, Su M. Carbon dioxide pneumoperitoneum, physiologic changes and anesthetic concerns. Ambul Surg. 2010; 16:41–46

2. Atkinson TM, Giraud GD, Togioka BM, Jones DB, Cigarroa JE. Cardiovascular and Ventilatory Consequences of Laparoscopic Surgery. Circulation. 2017;135(7):700–710

3. Tabari M, Alipour M, Ahmadi M. Hemodynamic changes occurring with tracheal intubation by direct laryngoscopy compared with intubating laryngeal mask airway in adults: A randomized comparison trial. Egypt J Anaesth. 2013;29(2):103–107

4. Omar P, Katiyar S, Gupta V. Comparative Study Of Intravenous Nitroglycerine And Clonidine on Haemodynamic Stability in Laproscopic Cholecystectomy. J Evol Med Dent Sci. 2013;2(19):3239–3248

5. Dhir R, Singh MR, Kaul TK, Tewari A, Oberoi R. Effect of intravenous esmolol on analgesic requirements in laparoscopic cholecystectomy. J Anaesthesiol Clin Pharmacol. 2015;31(3):375–379

6. Gupta A, Dwivedi Y, Saxena S. A randomized control study of dexmedetomidine versus fentanyl as an anesthetic

adjuvant in supratentorial craniotomies. INTENSIVE CARE. 2017;21:306–311

7. Hassani V, Pazouki A, Nikoubakht N, Chaichian S, Sayarifard A, Shakib khankandi A. The Effect of Gabapentin on Reducing Pain After Laparoscopic Gastric Bypass Surgery in Patients With Morbid Obesity; A Randomized Clinical Trial. Anesthesiol Pain Med [Internet]. 2015;5(1):1-5

8. Peng PWH, Li C, Farcas E, Haley A, Wong W, Bender J, et al. Use of low-dose pregabalin in patients undergoing laparoscopic cholecystectomy. Br J Anaesth. 2010;105(2):155–161

9. Kamble SP, Bevinaguddaiah Y, Nagaraja DC, Pujar VS, Anandaswamy TC. Effect of Magnesium Sulfate and Clonidine in Attenuating Hemodynamic Response to Pneumoperitoneum in Laparoscopic Cholecystectomy. Anesth Essays Res. 2017;11(1):67–71

10. Waindeskar V, Khan M, Agarwal S, Gaikwad MR. Role of Dexmedetomidine as an Anesthetic Adjuvant in Laparoscopic Surgery. Peoples J Sci Res. 2015;8(2):46–50

11. Singh RK, Saini AM, Goel N, Bisht D, Seth A. Major laparoscopic surgery under regional anesthesia: A prospective feasibility study. Med J Armed Forces India. 2015;71(2):126–131

12. Gerlach AT, Dasta JF. Dexmedetomidine: An Updated Review. Ann Pharmacother. 2007;41(2):245–254

13. Keniya V, Naphade R, Ladi S. Dexmedetomidine attenuates sympathoadrenal response to tracheal intubation and reduces perioperative anaesthetic requirement. Indian J Anaesth. 2011;55(4):352-357

14.O'Leary E, Hubbard K, Tormey W, Cunningham AJ. Laparoscopic cholecystectomy: haemodynamic and neuroendocrine responses after pneumoperitoneum and changes in position. Br J Anaesth. 1996;76:640–644

15. Mann C, Boccara G, Pouzeratte Y, Eliet J, Gal CS-L, Vergnes C, et al. The Relationship Among Carbon Dioxide Pneumoperitoneum, Vasopressin Release, and Hemodynamic Changes. Anesth Analg. 1999;89:278–283

16. Panchgar V, Shetti A, Sunitha H, Dhulkhed V, Nadkarni A. The effectiveness of intravenous dexmedetomidine on perioperative hemodynamics, analgesic requirement, and side effects profile in patients undergoing laparoscopic surgery under general anesthesia. Anesth Essays Res. 2017;11(1):72-77

17. Madhusudan, Lavakumar A, Rao, Samantaray A, Charupalli K. Effect of intravenous dexmedetomidine on haemodynamic responses to laryngoscopy, tracheal intubation and anaesthetic and analgesic requirements: a randomized double-blind clinical efficacy study. J Clin Sci Res. 2016;5(4):205–213

18. Wijeysundera DN, Naik JS, Beattie S. Alpha-2 adrenergic agonists to prevent perioperative cardiovascular complications: a meta-analysis. ACC Curr J Rev. 2003;114:742-752

19. Chalikonda SA. α2-Adrenergic Agonists and Their Role in the prevention of perioperative adverse cardiac events. AANA J. 2009;77(2):103-108

20. Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colinco MD. The Effects of Increasing Plasma Concentrations of Dexmedetomidine in Humans: Anesthesiology. 2000;93(2):382–394

21.Bhattacharjee DP, Nayek SK, Dawn S, Bandopadhyay G, Gupta K. Effects of Dexmedetomidine on Haemodynamics in Patients Undergoing Laparoscopic Cholecystectomy- A Comparative Study. J Anaesth Clin Pharmacol. 2010;26(1):45–48

22. Manne G, Upadhyay M, Swadia V. Effects of low dose dexmedetomidine infusion on haemodynamic stress response, sedation and post-operative analgesia requirement in patients undergoing laparoscopic cholecystectomy. Indian J Anaesth. 2014;58(6):726-731

23. Acharya G, Gokharu S, Arora KK, Kumar D. Effect of Two Different Doses of Dexmedetomidine on Hemodynamics in Patients undergoing Laparoscopic Surgeries under General Anesthesia - A Comparative Study. Int J Healthcare Edu Med Inform. 2016;3(1):12–18

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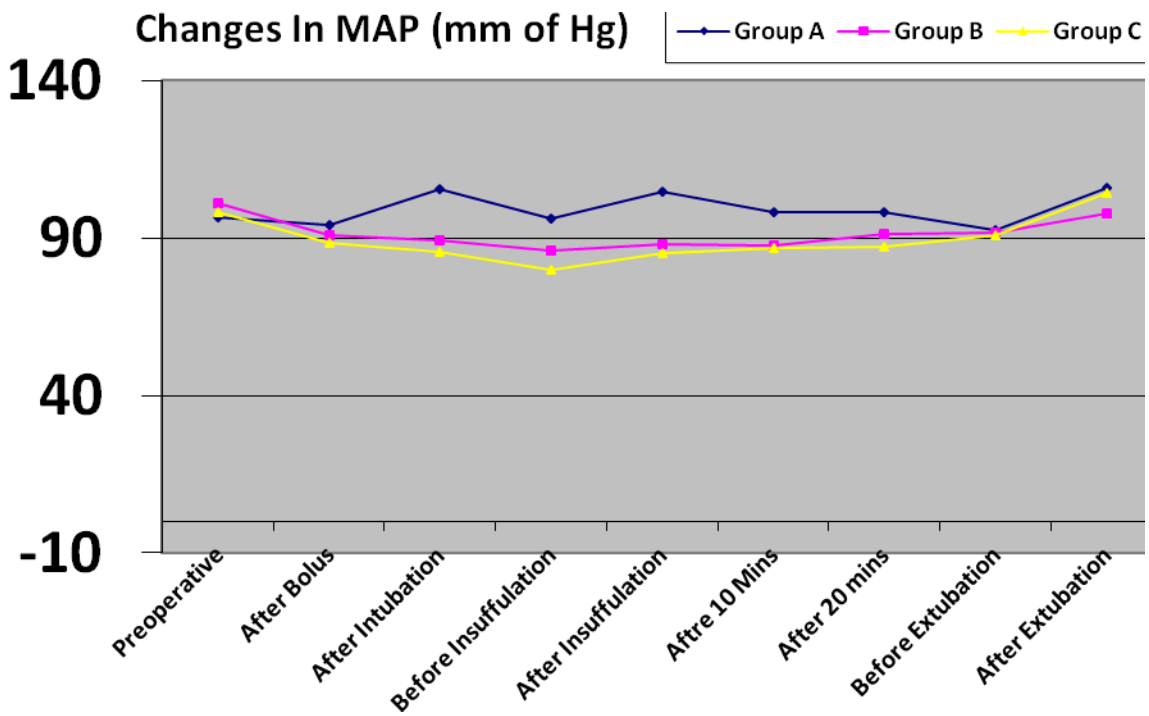

Fig 1: Changes in MAP (mm of Hg)

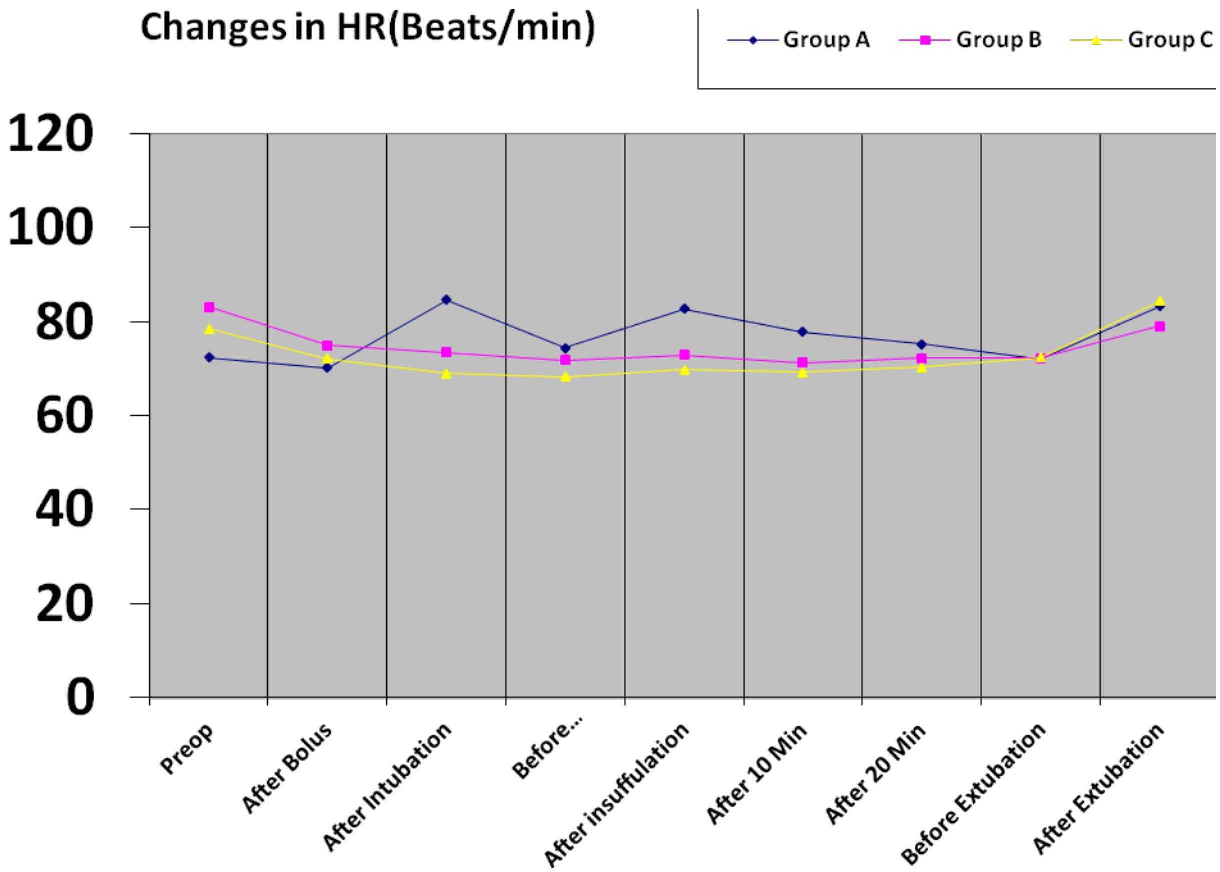

Fig 2: Changes in Pulse (Beats/Min)

Variables	GROUP A (NS)	GROUP B(B&I)	GROUP C (B ONLY)
Age(yr)	42.37±14.36	44.75±15.55	44.95±13.87
Gender (M/F)	7/33	5/35	6/33
Weight (Kg)	59.77±9.35	59.58±7.66	62.64±8.87
Duration (min)	80.92±4.47	81.20±5.09	81.25±4.58

Table 1: Demographic Characteristics and Duration of Surgery

Time	GROUP A (NS) (Mean ± SD)	GROUP B (B&I) (Mean ± SD)	GROUP C (B ONLY) (Mean ± SD)	*p* value	POST HOC TESTS		
					GROUP A (NS) VS GROUP B(B&I)	GROUP B(B&I) VS GROUP C (B ONLY)	GROUP C (B ONLY) VS GROUP A (NS)
Preoperative	96.52±8.68	100.95±7.62	98.02±8.15	0.108	--------	-------	-------
After bolus	94.00±8.37^{NS}	91.05±8.15**	88.61±8.78**	0.016	0.202	0.932	0.014
After Intubation	105.32±7.75**	89.40±6.95**	85.77±7.20**	‹0.001	‹0.001	0.411	‹0.001
Before CO_2 Insufflation	96.32±7.23^{NS}	86.17±6.72**	80.07±9.05**	‹0.001	‹0.001	0.055	‹0.001
After CO_2Insufflation	104.67±6.33**	88.17±6.80**	84.97±10.56**	‹0.001	‹0.001	0.930	‹0.001

After 10 min	98.075±6.34^{NS}	87.65±6.23**	86.82±5.18**	‹0.001	‹0.001	1.0	‹0.001
After 20 min	98.00±6.16^{NS}	91.10±7.14*	87.05±6.80**	‹0.001	‹0.001	0.075	‹0.001
Before Extubation	92.32±4.60^{NS}	91.62±6.54**	91.05±6.89*	0.644	--------	--------	--------
After Extubation	105.92±4.58**	97.57±5.60^{NS}	104.13±6.71**	‹0.001	‹0.001	‹0.001	0.354

P < 0.05-(*) - significant ***p***<0.001- (**) - highly significant

Table 2: Changes in MAP (mm of Hg)

Time	Group A (Mean ±SD)	GROUP B (Mean±SD)	GROUP C (Mean±SD)	***p***value	POST HOC TESTS		
					GROUP A (NS) VS GROUP B(B&I)	GROUP B(B&I) VS GROUP C (B ONLY)	GROUP C (B ONLY) VS GROUP A (NS)
Preoperative	76.75±8.03	79.80±5.97	80.10±8.39	0.280	-------	-------	-------
After bolus	70.15±5.19*	74.87±7.22**	72.05±9.66*	0.005	0.004	0.312	0.527
After Intubation	84.55±7.17**	73.50±6.90*	68.97±9.71**	‹0.001	‹0.001	0.033	‹0.001
Before Insufflation	74.40±6.36^{NS}	71.85±5.48**	68.30±7.22**	‹0.001	0.324	0.056	‹0.001
After Insufflation	82.75±6.20*	72.85±6.58**	69.77±7.13**	‹0.001	‹0.001	0.425	‹0.001
After 10 min	77.80±5.49^{NS}	71.20±6.57**	69.23±7.63**	‹0.001	‹0.001	0.975	‹0.001
After 20 min	75.20±5.87^{NS}	72.15±7.99**	70.35±6.88**	0.019	0.181	1.0	0.018
Before Extubation	72.10±5.34*	72.15±6.49**	72.30±8.35*	0.990	----------	---------	---------
After Extubation	83.25±6.05*	79.00±5.30^{NS}	84.31±6.82^{NS}	‹0.001	1.0	0.007	‹0.001

P < 0.05-(*) - significant ***p***<0.001- (**) - highly significant

Table 3: Changes in Pulse (Beats/Min)