A STUDY OF EFFECTS OF ORAL CLONIDINE ON PREMEDICATION AND HAEMODYNAMIC CHANGES DURING LAPAROSCOPIC SURGERY

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ABSTRACT

BACKGROUND

Use of Clonidine as a premedicant started incidentally. Clonidine is a potent antihypertensive drug that suppresses RAAS. Clonidine may be beneficial during laparoscopy in patients with hypertension, cardiovascular and/or renal diseases.

AIM OF STUDY

To determine the effects of Oral Clonidine on premedication and haemodynamic changes during Laparoscopic surgery.

MATERIAL AND METHODS

Study was conducted on 60 adult patients belonging to ASA physical status I & II. They were randomly assigned to 2 groups of 30 each. Group C received oral clonidine 150 mcg 90 minutes before surgery and group P received oral ranitidine 150 mg 90 minutes before surgery. Sedation score was noted on arrival to operation theatre. All vital parameters were recorded at regular intervals intra-operatively.

RESULTS

Clonidine premedication was able to achieve haemodynamic stability during pneumoperitoneum.

CONCLUSION

Premedication with 150mcg oral Clonidine has been found to be relatively safe as well as effective method that provides stable haemodynamics and protection against stress response triggered by pneumoperitoneum in patients undergoing laparoscopic surgeries.

KEYWORDS

Premedication, Clonidine, Laparoscopic surgery, Antihypertensives.

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INTRODUCTION: Laparoscopic surgery has revolutionized General surgeries by less invasive, small incision and early discharge of patients. Laparoscopic surgeries are cosmetically acceptable because of No scars, No sutures. Patients can be sent home early compared to conventional surgeries.

However, these procedures are not without risk. In fact, it produces significant haemodynamic changes especially in elderly and haemodynamically compromised patients.

Pneumoperitoneum effects several haemostatic mechanisms leading to alteration in acid base balance, cardiovascular, pulmonary physiology and stress response. The extent of cardiovascular changes associated with pneumoperitoneum include a decrease in cardiac output and an increase in systemic vascular resistance, increase in mean arterial pressure which in turn compromise tissue perfusion. Various pharmacological agents were chosen to prevent haemodynamic changes associated with pneumoperitoneum.

Nitroglycerine was used to correct the reduction of cardiac output associated with increased pulmonary occlusion pressure and systemic vascular resistance in a study conducted by Feig BW et al[(1)] (1994). Aho et al[(2)] used α_2 adrenergic receptor agonist for prevention of haemodynamic responses associated with laparoscopic surgery. They found that Dexmedetomidine effectively reduces the maximum heart rate response after intubation and pneumoperitoneum. Clonidine inhibits the release of catecholamine and vasopressin and thus modulates the haemodynamic changes induced by pneumoperitoneum.

Considering all these observations the present study was designed to evaluate the type and extent of haemodynamic changes associated with Laparoscopic surgery and also to find out the efficacy of Clonidine in prevention of such haemodynamic changes.

AIM OF STUDY: The present study is undertaken to determine the effects of Oral Clonidine on premedication and haemodynamic changes during Laparoscopic surgery.

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MATERIALS AND METHODS: This randomized prospective study was carried out in 60 adult patients of ASA physical status I & II, scheduled for Laparoscopic surgery.

The study was approved by the Institutional Ethical Committee and written informed consent was obtained from all the patients before being included in the study.

Patients with history of hypertension, ischemic heart disease, aortic stenosis, left ventricular failure and atrioventricular conduction block were excluded from the study. Patients taking clonidine, methyldopa, beta blocking drugs, benzodiazepines and MAO inhibitors were also excluded from the study.

All patients received Diazepam 5mg orally on the night before surgery. They were randomly assigned to one of the two groups to receive either Clonidine 150mcg (Group C) or Ranitidine 150mcg (Group P) orally 90 minutes before induction of anaesthesia. The observer was totally blind about the groups or medications received by the patients. Group sizes of 30 were determined by power analysis based on standard deviation data from previously published reports.

On arrival in the operation theatre, monitors were attached and baseline parameters such as heart rate, systemic blood pressure and peripheral oxygen saturation were noted, level of sedation (sedation score) was assessed by sedation scale - (1) Awake and agitated (2) Awake and comfortable (3) Asleep but arousal (4) Asleep with sluggish response to persistent call or touch and (5) No response to call or touch.

After intravenous cannulation, glycopyrrolate 0.2mg was administered intravenously. Patients were induced with sleep dose of Thiopentone sodium. Endotracheal intubation was facilitated by succinylcholine 1.5mg/kg of body weight.

Anaesthesia was maintained with 33% Oxygen in Nitrous oxide. 0.4% Halothane and Vecuronium bromide. Pre-operative analgesia was provided by Fentanyl citrate 1.5mcg/kg body weight. The tidal volume (VT) and the ventilator frequency was adjusted and intermittent positive pressure ventilation (IPPV) was continued by mechanical ventilation to maintain end-tidal carbon dioxide between 35-45 mm Hg.

Pneumoperitoneum was created by insufflation of carbon dioxide. Intra-abdominal pressure (IAP) was not allowed to exceed 14mm Hg throughout the surgical procedure. After pneumoperitoneum, necessary changes in ventilator setting (tidal volume, respiratory rate) were made to maintain normocapnia.

Throughout the procedure any rise in mean arterial pressure more than 20% from the baseline was treated with nitroglycerine drip.

The following Parameters were noted: Systemic blood pressure including the systolic, diastolic and mean arterial pressure, heart rate, SpO_2, $ETCO_2$ and electrocardiography (ECG) with ST segment analysis were recorded at the following points of time: (1) Prior to induction (2) 3 minutes after tracheal intubation (3) before pneumoperitoneum (4) 15 minutes after pneumoperitoneum (5) 30 minutes after pneumoperitoneum (6) 10 minutes after release of carbon dioxide and (7) 10 minutes after extubation.

At the end of surgery, residual neuromuscular block was reversed by appropriate dose of Neostigmine and Glycopyrrolate intravenously. Patients were extubated and transferred to recovery room in the post-anaesthesia care unit (PACU), where they were monitored for any evidence of complications or adverse events. Degree of sedation and intensity of pain were also assessed by using 10 point Visual Analogue Scale.

VISUAL ANALOGUE SCALE		
0	-	No pain
1, 2, 3	-	Mild pain
4, 5, 6	-	Moderate pain
7, 8, 9	-	Severe pain
10	-	Worst ever felt pain

The results obtained in the study are presented in tabulated manner. Statistical analysis was done by students 't' test. Chi square test was performed for non-parametric values and corresponding P was computed. P value <0.05 was considered statistically significant.

OBSERVATIONS AND RESULTS: Demographic profile and preoperative vital parameters were compared among the two groups and no significant difference were found (Table 1 & 2). Mean intra-abdominal pressure was 13.2±1.48 mm Hg in group P and 12.6±1.14 mm Hg in group C. Normocapnia was maintained throughout the procedure. $ETCO_2$ varied from 31.12±3.44 to 35.45±5.35 mmHg in group P and 30.65±2.35 to 34.05±3.15 mm Hg in group C.

Demographic Profile	Group C	Group P	P value	Significance
Age (years)	37.12±8.45	34.12±8.25	0.186	NS
Weight (kg)	56.05±5.86	58.82±6.98	0.107	NS
Sex (M:F)	11:19	12:18		
ASA grade	I-25/II-5	I-24/II-6		

Table 1: Demographic profile (Mean±SD)

Vitals	Group C	Group P	p value	Significance
PR (bpm)	78.18±7.72	83.38±11.12	0.346	NS
MAP (mmHg)	93.76±6.98	90.68±8.98	0.149	NS

SpO2 (%)	96.48±1.24	96.98±1.18	0.12	NS
Sedation score	1.24±0.45	1.34±0.50	0.064	NS

Table 2: Preoperative vital parameters (Mean±SD)

NS- Not significant, PR- pulse rate.

Mean pulse rate varied from 80.46±11.42 to 112.78±12.84 bpm in group P, and in group C it varied from 74.12±8.46 to 92.64±7.84 bpm. Upon statistical comparison in two groups of patients, significant variation was observed throughout the intra-operative period except for the baseline value when no significant difference was observed (Table 3).

PR (bpm)	Group P (mean± SD)	Group C (mean± SD)	p value	Significance
Before premedication	80.47±11.20	78.78±7.62	0.0354	NS
Before induction	87.88±13.92	74.12±9.84	0.086	S
After intubation	106.88±14.02	86.72±10.84	0.0070	HS
Before pneumoperitoneum	84.86±15.84	75.86±9.34	0.052	S
15min after pneumoperitoneum	95.08±20.86	74.87±10.08	0.008	HS
30 min after pneumoperitoneum	93.78±18.98	74.54±10.15	0.0045	HS
After release of CO2	83.78±14.65	73.76±8.45	0.0027	HS
After extubation	112.04±12.84	92.76±7.84	0.0049	HS

Table 3: Changes in pulse rate in two groups

NS- Not significant; S – Significant; HS – Highly significant.

Changes in blood pressure when compared in the two groups of patients was found to be statistically highly significant excepting the baseline values where no significant difference was found (Table 4).

	SBP(mmHg)				DBP(mmHg)				MAP(mmHg)			
	Gr-P	Gr-c	p	Sig	Gr-P	Gr-C	p	Sig	Gr-P	Gr-C	p	Sig
Before premedication	117.8±12.07	120.84±7.89	0.376	NS	78.84±7.89	80.84±7.14	0.018	NS	90.78±9.88	94.54±6.78	0.0884	NS
Before induction	120.78±10.94	110.45±8.75	0.00018	HS	82.45±9.98	72.76±9.78	0.00076	HS	94.76±10.54	84.76±9.45	0.00059	HS
After intubation	142.07±20.84	119.78±6.95	0.0062	HS	97.84±12.86	79.78±8.45	0.0006	HS	112.76±15.54	92.85±7.46	0.00018	HS
Before pneumoperitoneum	122.78±13.76	112.6±8.76	0.0019	HS	82.76±12.04	78.76±9.45	0.074	NS	98.45±13.75	90.3±9.84	0.0128	S
15min after pneumoperitoneum	142.68±18.72	118.78±10.04	0.00016	HS	98.76±13.04	80.78±8.45	0.0016	HS	113.75±15.87	92.88±8.12	0.00183	HS
30min after pneumoperitoneum	138.98±18.57	118.44±7.98	0.0028	HS	93.74±13.85	80.46±9.45	0.00016	HS	106.98±15.45	92.76±8.45	0.033	S
After release of CO2	124.68±12.88	114.98±9.48	0.0033	HS	82.74±11.84	76.97±9.87	0.094	NS	96.74±10.84	90.84±7.96	0.0163	S
After extubation	138.74±9.54	123.14±8.4	0.018	S	91.84±8.76	82.85±8.46	0.00139	HS	107.48±7.84	96.86±7.76	0.042	S

Table 4: Changes in systolic, diastolic and mean pressures in both groups

NS- Not significant; S – Significant; HS – Highly significant.

SBP-Systolic blood pressure, DBP-Diastolic blood pressure, MAP-Mean arterial pressure, Gr P-Group P, Gr C-Group C, p-p value, Sig-Significance.

10 patients in group P received nitroglycerine infusion (0.5mcg/kg/min) for treatment of intra-operative hypertension. It was not required in group C patient because they remained haemodynamically stable.

Intensity of pain was less in group C as compared to group P (VAS 1.91±1.68 vs 5.214±2.114) during early postoperative period.

Incidence of nausea & vomiting, hypertension, shivering and shoulder pain was 35.1%, 35.1%, 10.01% and 14% respectively in group P while only 6.8 % patients suffered from nausea and vomiting in group C. Sedation was common in group C (33%) while other complications were not observed in group C. None of the patients showed any evidence of ischemia or arrhythmia intraoperatively.

DISCUSSION AND SUMMARY: This study was undertaken to determine the effect of oral Clonidine as a premedicant on haemodynamic changes during laparoscopic surgery.

Sixty patients of ASA grade – I and II were selected at random for this double blind prospective study to evaluate the effect of oral Clonidine premedication in attenuating haemodynamic stress response associated with pneumoperitoneum.

Clonidine, an imidazole derivative is a selective α_2 adrenergic agonist. It is a potent anti-hypertensive drug. It produces a fall in the heart rate and blood pressure associated with decreased systemic vascular resistance and cardiac output. 150 mcg (2.7 mcg/kg) Clonidine was administered orally, 90 minutes before surgery in this series.

Dose of Clonidine varied from 2 -5 mcg/kg in different studies. Higher dose of Clonidine (5mcg/kg) is usually required for potentiation of post-operative analgesia by intrathecal Morphine.

Aho et al[2] used 3 mcg/kg and 4.5 mcg/kg Clonidine for suppression of haemodynamic response to pneumoperitoneum. Rise in blood pressure and heart rate was less in both the groups but, 4.5mcg/kg Clonidine produced greater fall in mean arterial pressure before induction.

Joris et al[3] used very high dose of Clonidine (8mcg/kg) for reducing the level of catecholamine and vasopressin following pneumoperitoneum.

Malek et al[4] used 150 mcg of Clonidine as intravenous infusion, while Sung et al[5] and Yu et al,[6] Mrinmoy Das[7] used 150mcg oral Clonidine as premedication for maintenance of haemodynamic stability during pneumoperitoneum.

Following pneumoperitoneum with Carbon dioxide, patients were hyperventilated to maintain normocapnia. Every effort was made to maintain intra-abdominal pressure (IAP) below 14mm Hg, Mean intra-abdominal pressure was 13.12±1.48mmHg in group P and 12.8±1.6mm Hg in group C. Haemodynamic changes associated with pneumoperitoneum was first recognized in 1947. Diamant[8] et al reported 35% decrease in cardiac output in dog with raised intraabdominal pressure of 40mm Hg.

Ishizaki et al[9] observed that no significant changes in haemodynamics occurred at an IAP between 8 and 12 mmHg.

Cunningham et al[10] and Dorsay et al[11] assessed the ejection fraction (EF) of left ventricle by trans oesophageal echocardiography during pneumoperitoneum. No significant change in ejection fraction was reported upto 15mmHg intra-abdominal pressure. Considering all these facts intra-abdominal pressure was kept below 14mm Hg in this study. Inspite of maintaining normocapnia and keeping intra-abdominal pressure below 14mmHg, significant rise in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure was noticed in group 'P' which was more than 20% from the baseline. Slight fall in systolic, diastolic and mean arterial blood pressure was noticed following premedication with Clonidine. Following intubation and pneumoperitoneum, increase in arterial pressure was noticed but it never crossed the baseline value. Hence, Clonidine premedication was able to achieve haemodynamic stability during pneumoperitoneum.

Similar findings were reported by Aho et al,[2] Joris et al,[3] Malek et al,[4] Sung et al,[5] Yu et al[6] and Laisalmi et al.[12]

Aho et al [2] observed that 4.5mcg/kg of Clonidine significantly decreased the mean arterial pressure before induction of anaesthesia. So they recommended 3mcg/kg of Clonidine for peri-operative haemodynamic stability. Joris et al[3] used higher dose of Clonidine for reduction of catecholamine and vasopressin associated with pneumoperitoneum. Clonidine significantly reduced the concentration of catecholamine but not vasopressin and cortisol concentration. Similarly, Sung et al[5] observed haemodynamic stability during pneumoperitoneum with 150mcg oral Clonidine. Requirement of Isoflurane was also less by 30% in the Clonidine group. Esmolol, Labetalol, Nifedipine, NTG were used to control hypertension in control group. Yu et al[6] recommended the routine use of Clonidine premedication in laparoscopic surgery.

There was incidence of shivering in 10.01% patients in the placebo group compared to none in the Clonidine group. Nicolaou et al[13] concluded that Clonidine inhibits cold thermo regulatory response due to an effect on central integration control and output from the thermoregulatory centres.

35.1% of patients of the group P suffered from nausea ± vomiting, while only 6.8% of patients receiving Clonidine had such episodes. Many workers have reported the antiemetic property of Clonidine, the mechanism of which is not known.

CONCLUSION: Premedication with 150mcg oral Clonidine has been found to be relatively safe as well as effective method that provides stable haemodynamics and protection against stress response triggered by pneumoperitoneum in patients undergoing laparoscopic surgeries. Clonidine also affords an added advantage of reduction in post-operative complications such as nausea, vomiting and shivering.

Hence 150 mcg oral Clonidine can reasonably be recommended as premedicant for all laparoscopic procedures in otherwise healthy patients. However, further study is required to find out its efficacy in patients with compromised cardiovascular system.

REFERENCES:

1. Feig BW, Berger DH, Doughtery TB, et al. Pharmacologic interventions cane re-establish baseline haemodynamic parameters during laparoscopy. Surgeryn 1994;116(4):733 -7.
2. Aho M, Scheinin M, Lehtinen AM, et al. Intramuscularly administered dexmedetomidine attenuates haemodynamic and stress responses to gynaecologic laparoscopy. Anesth Analg 1992;75(6): 932-9.
3. Joris J, Chiche JD, Lamy M. Clonidine reduced haemodynamic changes induced by pneumoperitoneum during laparoscopic cholecystectomy. Br. Anaesth 1995;74(Suppl):A124.
4. Malek KJ, Knor J, Kurzova A, et al. Adverse haemodynamic changes during laparoscopic cholecystectomy and their possible suppression with clonidine premedication comparison with intravenous and intramuscular premedication. Rozhl Chir 1997; 78:286-91.
5. Sung CS, Lin SH, Chan KH, et al. Effect of oral clonidine premedication on perioperative haemodynamic response and postoperative analgesic requirement for patients undergoing laparoscopic cholecystectomy. Acta Anaesthesiol Scand 2000; 38(1):23-9.
6. Yu HP, Hseu SS, Yien HW, et al. Oral clonidine premedication preserves heart rate variability for patients undergoing laparoscopic cholecystectomy. Acta Anaesthesiol Scand 2003;47(2):185-90.

7. Mrinmoy Das, Manjushree Ray, Gauri Mukherjee. Haemodynamic changes during laproscopic cholecystectomy: Effects of clonidine premedication. Indian Journal of Anaesthesia 2007;51(3):205-210.
8. Diamant M, Benumot JL, Saidman LJ. Haemodynamics of increased intra-abdominal pressure: interaction with hypovolemia and halothane anaesthesia. Anesthesiology 1978;48(1):23-7.
9. Ishizaki Y, Bandae Y, Shimomura K, et al. Safe intra abdominal pressure of carbon dioxide pneumoperitoneum during laparoscopic surgery. Durgery 1993;114(3):549-54.
10. Cunningham AJ, Turner J, Rosenbaum S, et al. Transoesophageal echocardiographic assessment of haemodynamic function during laparoscopic cholecystectomy. Br.J Anaesth 1993;70(6):621-625.
11. Dorsay GA, Greene FL, Baysinger CL. Haemodynamic changes during laparoscopic cholecystectomy-monitored with trans oesophageal echocardiography. Surg Endosc 1995;9(2):128-133.
12. Laisalmi M, Koivusalo AM, Valta P, et al. Clonidine provides opioid-sparing effects, stable haemodynamics and renal integrity during laparoscopic cholecystectomy. Surg Endosc 2001; 15(11):1331-5.
13. Nicolaou G, Jonston CE, Bristow GK. Clonidine decreases vasoconstriction and shivering threshold, without effecting the sweating threshold. Can J Anaesth 1997;44(6):636-44.