IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 11 Ver. VI (Nov. 2015), PP 19-23
www.iosrjournals.org

Hemodynamic Stress Response of Carbon-Di-Oxide Pneumoperitoneum during Laparoscopic Surgery: Effect of Oral and Intravenous Clonidine Premedication

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Abstract : *Hemodynamic response to carboperitoneum can be avoided by use of several pharmacological agents. Clonidine is an α 2 adrenoreceptor agonist having sympatholytic effects. Clonidine has been shown to reduce perioperative hemodynamic instability. The aim of this study was to investigate the clinical efficacy of oral versus intravenous clonidine premedication in prevention of hemodynamic response associated with carboperitoneum .*

Sixty adult patients of ASA grade I and II, scheduled for elective laparoscopic cholecystectomy were recruited for a prospective randomized double blinded comparative study. They were randomly allocated to one of the two groups to receive either intravenous clonidine 0.8micrograms/kg (Group A) in 20ml dilution 30 minutes before or oral clonidine 150 µg (Group B) 90 minutes before induction of anaesthesia. In our study following carboperitoneum the trend of heart rate showed that Group B has a better effect on heart rate at the end of 30minutes with the heart rate for Group A being 75.73/min,. compared to Group B which was 74.2/min, this was statistically insignificant. The trend of mean arterial pressure(MAP) showed that Group A has a better effect on MAP at the end of 30 minutes with the MAP for 77.73±5.9mmhg in Group A being compared to Group B which was 91.8±8.75mmhg. Hence we found a significantly decrease in MAP in response to carboperitoneum with intravenous clonidine.

To conclude intravenous clonidine at a dose of 0.8 micrograms/kg is a useful premedication drug to alleviate the hemodynamic response to carboperitoneum.

Keywords: *Clonidine oral/IV, Hemodynamic response, Laproscopic cholecystectomy, Pneumoperitoneum.*

I. Introduction

Laparoscopic surgeries have revolutionized surgical procedures mainly due to the important advantages it offers. It takes lesser time in experienced hands, decreased post-operative pain, shorter duration of hospital stay, minimal scar, minimal post operative morbidity and mortality. Hans Christian Jacobaeus in 1910 coined this term. It refers to a minimal access procedure allowing endoscopic access to peritoneal cavity after insufflations of gases to create space between anterior abdominal wall and viscera for safe manipulation of instruments and organs.

Pneumoperitoneum is created by insufflations of gas into the peritoneal cavity. Various gases including CO_2, N_2O, Helium has been used. Currently CO_2 is most commonly used. Pneumoperitoneum is known to cause various hemodynamic changes.

Several drugs including Nitroglycerin, Dexmeditomedine have been used for attenuating these effects. Clonidine, an α-2 selective adrenergic receptor agonist has been associated with attenuation of these responses. Our study deals with usage of clonidine in oral and intravenous route to attenuate the hemodynamic changes during pneumoperitoneum in laparoscopic cholecystectomy surgeries.

II. Aims And Objectives

1.1 Primary: To record the Heart Rate, Non-Invasive Blood Pressure, SPO2, End Tidal CO_2 values in both groups at basal, at carboperitoneum and every 3 minutes for 30 minutes.

1.2 Secondary: To determine the significance of patient positioning with Mean Arterial Pressure.

III. Methods And Methodology

Ours was a prospective study conducted in a tertiary health centre. We included a total of 60 participants who were scheduled to undergo laparoscopic cholecystectomy.

Pre-anaesthetic evaluation was done for all the patients and they were optimized for laparoscopic surgery. Institutional ethics committee approval and informed written consent from all participants was taken. The inclusion criteria were ASA grade I and II Patients; aged between 18-50yrs; scheduled for elective laparoscopic cholecystectomy. The exclusion criteria were patient refusal to participate in study; ASA grade

III/IV/V; hypertensive patients; patients with renal dysfunction; hepatic diseases including Child Pugh score B, C; patients with preexisting history of IHD, valvular heart disease and congenital heart disease; conduction abnormalities; heart rate less than 60/min; patient with history of allergic drug reactions; BMI<30; patients receiving tricyclic antidepressants, beta blockers, diltiazem, verapamil.

60 consecutive patients were selected based on inclusion and exclusion criteria and were randomly assigned to receive oral or IV clonidine.

Oral clonidine group: Received 150micrograms of clonidine 90 min prior to surgery.

IV clonidine group: Received 0.8 microgram/kg body weight of clonidine diluted in 20 ml of NS given over 10 minutes, 30 minutes prior to surgery.

Patients were shifted to Operating room and SPO2, NIBP, ECG, ETCO2 monitors connected. Premedication with Inj.Glycopyrolate 0.2mg was given IV. Patients were preoxygenated with 100% oxygen for 3 min. The basal readings were recorded at time prior to intubation. Patients were induced with Inj propofol 2mg/kg body weight and intubated with appropriate size tube with Suxamethonium 1.5mg/kg body weight. Pneumoperitoneum with CO2 was created with IAP not exceeding 15mmhg.

A blinded observer was then allowed to enter into the OR to take the values of Heart rate, SBP, DBP, MAP, ETCO2, SPO2 readings. The readings were taken at carboperitoneum and subsequently every 3 minutes till the end of 30 minutes. The patient position was also noted during the surgical procedure.

A 15 º Tilt of reverse Trendelenberg was given in most patients. Patient was maintained with mechanical ventilation O_2:N_2O with Isoflurane and Vecuronium for muscular relaxation. Any change in hemodynamic variables on either side of the base value by 20% was taken to be significant. Intraoperative fluid management was optimal. At the end of surgery neuromuscular blockade was reversed with Neostigmine 0.05 mg/kg body weight and glycopyrollate at 0.01 mg/ kg body weight. The patient after surgery was extubated and shifted to PACU for further follow-up.

The results obtained were analysed using statistical analysis, average with standard deviations were calculated between the two groups. Unpaired student t-test was used to assess statistical significance.

IV. Results

All the participants chosen for the study completed it (n=60). The demographic pattern for the participants were similar in both groups (Table 1).

	Group A (IV)	**Group B (Oral)**
Age (yrs)	28.96 ± 7.01	33.5 ± 7.24
Weight (kg)	60.93 ± 7.38	60.8 ± 5.73
Height (cms)	165.26 ± 7.38	164.46 ± 5.76
Sex (M:F)	1:2	3:7
BMI(kg/m^2)	22.35 ± 2.62	22.54 ± 2.14

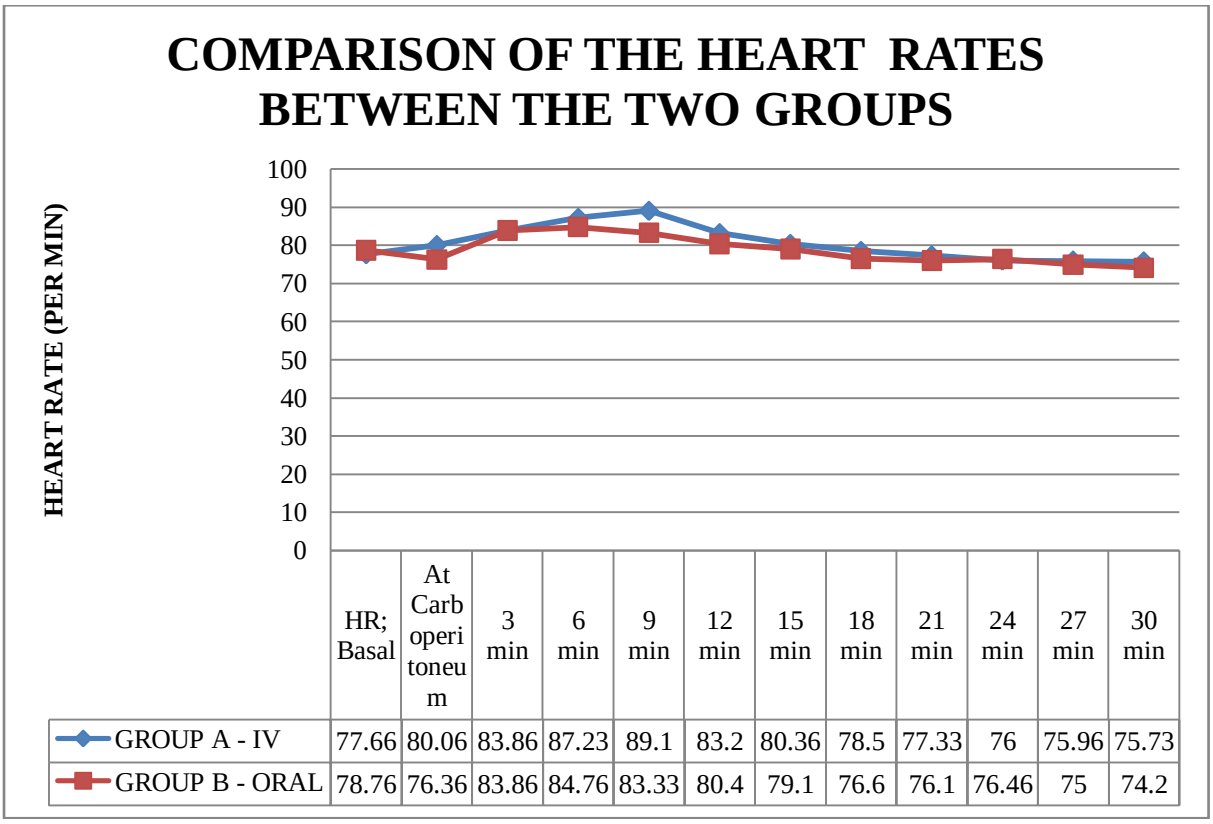
Table 1: Depicting the demographic profile of the two groups

The hemodynamic parameters were measured at various intervals to achieve a trend. They were measured at : 1. Basal value prior to the start of surgery and intubation; 2. At the start of carboperitoneum; 3. Every 3 minutes subsequently after carboperitoneum till 30 minutes.

The Heart Rate, Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure were all noted by a blinded observer. The overall duration of carboperitoneum was 90 – 120 minutes. The patients were given 15 º tilt in reverse Trendelenburg position for the surgery.

4.1 Heart rate:

The basal heart rates records were 77.66 ± 7.46/minute for group A (IV) whereas they were 78.76 ± 5.63/minute for group B (Oral). The recording of the heart rates between the two groups depicted as a line graph is shown in the figure below (Figure 1). The trend of the heart rate showed that oral clonidine has a better effect on the heart rate at the end of 30 minutes with the heart rate for IV group being 75.73/minute compared to oral group which was 74.2/minute; however compared to IV clonidine but it was statistically insignificant.

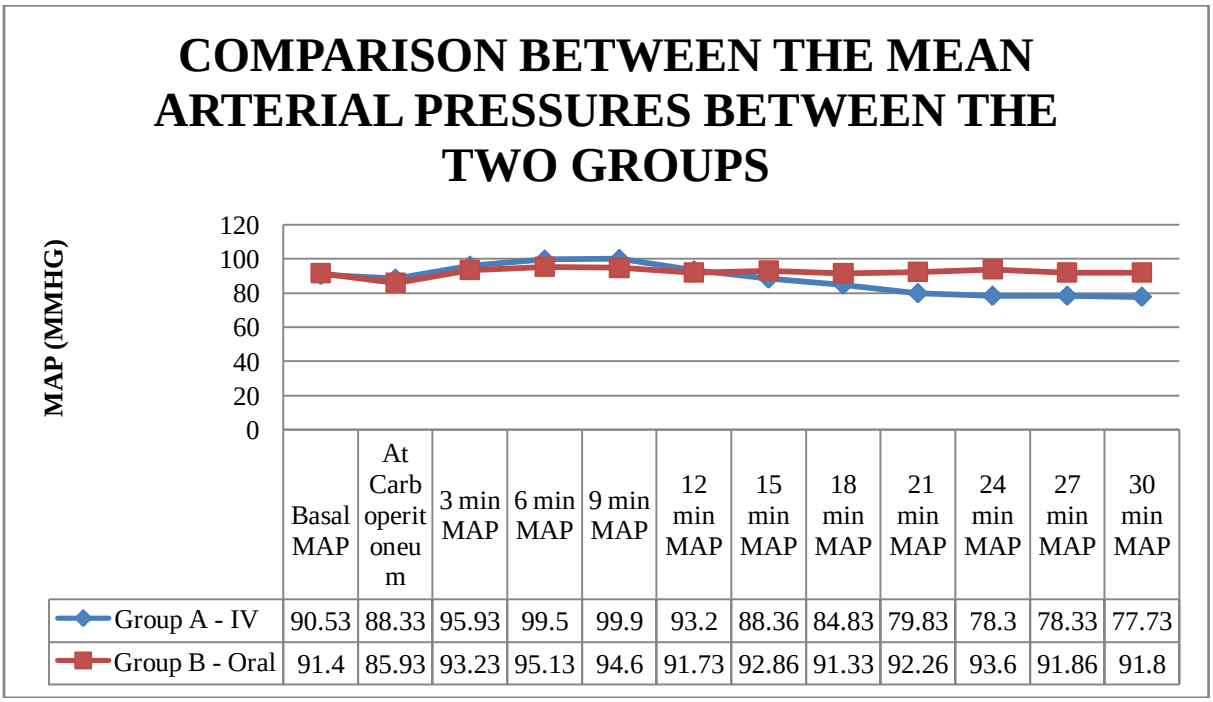


	HR; Basal	At Carb operitoneum	3 min	6 min	9 min	12 min	15 min	18 min	21 min	24 min	27 min	30 min
GROUP A - IV	77.66	80.06	83.86	87.23	89.1	83.2	80.36	78.5	77.33	76	75.96	75.73
GROUP B - ORAL	78.76	76.36	83.86	84.76	83.33	80.4	79.1	76.6	76.1	76.46	75	74.2

Figure 1: Depicting the difference between the heart rates between the two groups

4.2 Mean arterial Pressure:

The basal mean arterial pressures recorded were 90.53 ± 6.45 mmHg for group A (IV) whereas they were 91.4 ± 6.16 mmHg for group B (Oral). The recording of the MAP between the two groups depicted as a line graph is shown in the figure below (Figure 2). The trend of the MAP showed that IV clonidine has a better effect on the MAP at the end of 30 minutes with the MAP for 77.73 ± 5.9 mmHg in IV group being compared to oral group which was 91.8 ± 8.75mmHg.



	Basal MAP	At Carb operitoneum	3 min MAP	6 min MAP	9 min MAP	12 min MAP	15 min MAP	18 min MAP	21 min MAP	24 min MAP	27 min MAP	30 min MAP
Group A - IV	90.53	88.33	95.93	99.5	99.9	93.2	88.36	84.83	79.83	78.3	78.33	77.73
Group B - Oral	91.4	85.93	93.23	95.13	94.6	91.73	92.86	91.33	92.26	93.6	91.86	91.8

Figure 2: Depicting the difference between the mean arterial pressures between the two groups.

V. Discussion

Laparoscopy is a very well established procedure since more than two decades. Almost all procedures are now being performed laparoscopically including oesophagectomy, intestinal resection and donor nephrectomy. However experience with understanding of the effects of CO2 pneumoperitoneum are far from nascent [1]. Insufflation of about 2.5 to 5 litres of CO2 are more appropriately called as carboperitoneum routinely used to give the region in interest a good exposure.[2] Carboperitoneum along with resultant increase in the intra-abdominal pressure affects all the systems of the body, affecting hemostasis and leads to alterations in cardiovascular, pulmonary physiology and stress response. Cardiovascular changes includes increase in the MAP with no significant changes in heart rate[3-5], decrease in cardiac output and increase in Systemic vascular resistance. These pressor responses are consequent to hypercarbia induced release of catecholamines[6-8] vasopressin or both. [3,9,10]

The physiological changes that occur in pneumoperitoneum are related to patient factors such as patient position, the insufflations of gas and the effect of insufflations on intraabdominal pressure. Also the BMI of the patient is significant as in obese to morbidly obese patients the intraabdominal pressures are 2 to 3 times that of non-obese patients.[11] Also systemic absorption of carbon-di-oxide in obese patients and increased need to eliminate the carbon-di-oxide in these patients is also a challenge. CO2 is used for insufflations at the rate of 4-6 L/min[12] and intra-abdominal pressure of 10-15 mmHg is maintained. Intra-abdominal pressure refers to the pressure in the peritoneal cavity. It is maintained between 12- 15 mmHg in pneumoperitoneum to prevent adverse effects.

On the cardiovascular system, a raised Intra-abdominal pressure can lead to a decreased venous return due to the compression of Inferior vena cava and thereby a fall in the cardiac output and also there is increased systemic vascular resistance[13]. This increase in Systemic vascular resistance is a consequence of activation of neurohumoral mechanisms including sympathetic activation, ADH and Renin- Angiotensin – Aldosterone system stimulation. The heart rate and MAP are seen to increase with intra-abdominal pressure [14]. The central venous pressure may also increase due to increased intrathoracic pressure. Hence due to an increased myocardial overload even myocardial ischemia may occur. Also Giaquinto et al published a case of acute congestive heart failure after laparoscopic cholecystectomy in a 59 year old lady with morbid obesity[15]. Adequate preoperative hydration is also said to be helpful in alleviating acid base changes to hypercarbia[16] . Patient positioning is also important as it has a lot of influence on hemodynamics of the patient.

ETCO2 changes also occur due to the use of CO2 as insufflating agent and also as CO2 can be absorbed by the body and hence ventilation control becomes an important factor in preventing hypercarbia[17].

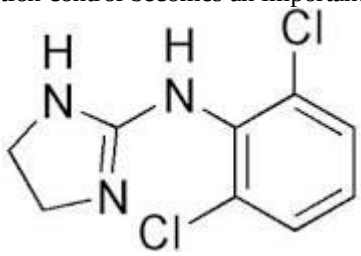


Figure 3: Structure of clonidine hydrochloride

Clonidine hydrochloride is a centrally acting α 2 adrenergic receptor agonist which has been used in various routes including oral, intravenous, intrathecal, epidural, sublingual forms. The adult dosage is between 2 to 7 micrograms per kilogram body weight. Studies have shown that 2.4 mg is the maximum effective dosage[18]. The major use of clonidine is to alleviate the rise in blood pressure. There are various studies that have demonstrated the use of clonidine in varying doses intravenously.

In our study similar to the other authors we found a significant decrease in MAP in response to the carboperitoneum with intravenous clonidine. It has to be used with caution due to its interactions with tricyclic antidepressants, beta-blockers, diltiazem, verapamil to name a few.

VI. Conclusion

Intravenous clonidine at a dosage of 0.8 micrograms/kg is a useful premedication to alleviate the hemodynamic stress response to CO2 pneumoperitoneum.

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