

## 4 STUDY OF ORAL CLONIDINE PREMEDICATION IN LAPAROSCOPIC SURGERIES

Dr. Shruti M. Shah Asso. Prof. Dr. Mauli Kinnar Gandhi Asst. Prof Anaesthesia Dr. Dimple K. Pandya Asst. Prof. Dr. Jigar R. Patel 2 nd Year Resident, Dr. Hetavi U. Contractor  
3rd Year Resident Anaesthesia dept. V.S.Hospital N.H.L.Medical college Elisbridge Ahmedabad pin 380008

### ABSTRACT

Clonidine has anti-hypertensive properties and augments the effects of anaesthesia, so it is considered to be an ideal agent to reduce the stress response to pneumoperitoneum in laparoscopic surgeries. The aim of the study was to investigate the clinical efficiency of oral clonidine premedication in prevention of haemodynamic response associated with pneumoperitoneum. Clonidine premedication provides perioperative haemodynamic stability, hence it can be recommended as a routine premedication for laparoscopic procedure.

**KEY WORDS** :Laparoscopic surgeries; Pneumoperitoneum, Haemodynamic response; Clonidine premedication.

### INTRODUCTION

Laparoscopic surgeries has now become the “gold standard”. It offers many benefits than conventional surgeries and promoted as a “gentle surgery”.<sup>[1]</sup> However, it is not risk free. It produces significant haemodynamic changes specially in elderly and haemodynamically compromised patients.<sup>[2]</sup>

The hallmark of laparoscopy is creation of carbon dioxide (CO<sub>2</sub>) pneumoperitoneum and change in the patient's position from Trendelenberg to reverse Trendelenberg. Pneumoperitoneum(Pnp) affects several homeostatic systems leading to alteration in acid-base balance, cardiovascular, pulmonary physiology and stress response.<sup>[3]</sup> The extent of cardiovascular changes associated with pneumoperitoneum include an increase in mean arterial pressure, decrease in cardiac output and increase in systemic vascular resistance which in turn compromise tissue perfusion.<sup>[4]</sup>

Various pharmacological agents like nitroglycerine, adrenergic receptor agonist, dexmedetomidine, clonidine were chosen to prevent haemodynamic changes associated with pneumoperitoneum.<sup>[2,4]</sup>

Clonidine is an  $\alpha$ -2 adrenoreceptor agonist.<sup>[5]</sup> It exerts central sympatholytic effect and has a half life of 9-12 h. Premedication with clonidine blunts the stress response to surgical stimuli and intubation. The narcotic and anaesthetic doses are also reduced.<sup>[6]</sup> In addition, clonidine increases cardiac baroreceptor reflex sensitivity to increase in systolic blood pressure, and thus stabilises blood pressure. Clonidine inhibits the

release of catecholamine<sup>[7]</sup> 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.

## **METHOD**

50 adult patients of ASA physical status I & II, scheduled for elective laparoscopic surgeries were recruited for a prospective randomized, single-blinded comparative study. 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. They were randomly allocated to one of the two groups to receive either with oral clonidine 150 µg (Group A) or without oral clonidine (Group B), 60 minutes before induction of anaesthesia.

On arrival in the operation theatre, monitors were attached and baseline parameters such as heart rate, blood pressure and peripheral oxygen saturation were noted down. Level of sedation (sedation score) was assessed by sedation scale : (1) awake and agitated (2) awake and comfortable (3) asleep but arousable (4) asleep with sluggish response to persistent call or touch and (5) no response to call or touch.

After intravenous cannulation, glycopyrrolate 0.2 mg and fentanyl citrate 1 µg/kg i.v. given. Patients were induced with thiopentone sodium 5-7-mg/kg and succinylcholine 2mg/kg and endotracheal intubation was done. Anaesthesia was maintained with oxygen, nitrous oxide, sevoflourane and vecuronium bromide 0.1 mg/kg.

Pneumoperitoneum was created by insufflation of Carbon dioxide. Intra abdominal pressure (IAP) was not allowed to exceed 15 mm Hg throughout the surgical procedure. Ventilation was done to maintain end tidal carbon dioxide between 35-45 mm Hg. Systemic arterial pressure including the systolic, diastolic and mean arterial pressure, heart rate, SpO<sub>2</sub>, EtCO<sub>2</sub> were recorded at the following points of time : (1) prior to induction (2) during intubation (3) 3 minutes after endotracheal intubation (4) before pneumoperitoneum (5) five minutes after pneumoperitoneum (6) ten minutes after pneumoperitoneum (7) fifteen minutes after pneumoperitoneum (8) thirty minutes after pneumoperitoneum (9) five minutes after exsufflation of gas and (10) ten minutes after extubation.

Significant rise in heart rate was observed following pneumoperitoneum in Group B as compared to Group A ( $98\pm 9.1$  Vs  $84.44\pm 5.7$  bpm). Similarly, rise in systolic arterial pressure ( $124.96\pm 7.0$  Vs  $150.6\pm 3.8$  mm Hg), diastolic arterial pressure ( $94.04\pm 3.8$  Vs  $79.1\pm 3.6$  mm Hg) and mean arterial pressure ( $112.7\pm 3.2$  Vs  $94.2\pm 4.1$  mm Hg) was more in Group B following pneumoperitoneum.

At the end of surgery residual neuromuscular block was assessed and reversed by appropriate dose of glycopyrrolate and Neostigmine intravenously. Patients were extubated and transferred to recovery room, where they were monitored for complications or adverse events.

## **Results**

Demographic profile and preoperative vital parameters were compared among the two groups of patients and no significant difference was found (Table 1 & 2).

**Table 1 Demographic profile (Mean ± SD)**

	<b>Gr A</b>	<b>Gr B</b>	<b>P Value</b>
<b>Age</b>	39.84±13.60	42.4±10.65	0.27
<b>Sex(M:F)</b>	9:16	8:17	

**Table 2 Preoperative vital parameters (Mean ± SD)**

<b>Parameters</b>	<b>Gr A</b>	<b>Gr B</b>	<b>P value</b>
Pulse	85.48±8.4	84.08±9.0	0.5736
SBP	125.8±10.4	124.6±11.1	0.7055
DBP	79.2±6.6	82.2±6.5	0.1153
MAP	94.5±7.3	96.2±7.3	0.4375

Sedation

**Table 3 Changes in pulse rate in two groups**

**Changes in Pulse Rate(bpm)**

	<b>HR of gr A (Mean±SD)</b>	<b>HR of gr B (Mean±SD)</b>	<b>p value</b>
1 hr prior to sx	85.48±8.4	84.08±9.0	0.5736
before intubation	81.84±6.2	85.76±9.5	0.094
during intubation	92.88±6.6	101.16±9.7	<0.005
3 min after intubation	86.04±6.5	95.16±9.2	<0.005

10 min after intubation	83.56±7.8	94.4±10.3	<0.005
before pneumopertonium	83.16±6.9	93.68±8.9	<0.005
5 min after pneumoperitonium	84.04±5.8	97.96±10.1	<0.005
10 min after pneumoperitonium	84.44±5.7	98±9.1	<0.005
15 min after pneumoperitonium	83.4±6.6	96.24±9.5	<0.005
30 min after pneumoperitonium	82.76±7.0	98.04±5.9	<0.005
5 min after exsufflation	83.48±5.7	92.72±9.0	<0.005
During Extubation	90.88±5.9	99.6±8.1	<0.005
5 min After Extubation	83.36±5.7	93.48±8.1	<0.005

**Table 4 Changes in systolic blood pressure in two groups**

**Changes in SBP(mm Hg)**

	<b>SBP of gr A (Mean±SD)</b>	<b>SBP of gr B (Mean±SD)</b>	<b>p value</b>
1 hr prior to sx	125.8±10.4	124.6±11.1	0.7055
before intubation	122.72±10.8	125.2±10.6	0.4106
during intubation	134.56±10.0	144.8±8.9	<0.005
3 min after intubation	126.76±9.3	140.8±10.6	<0.005
10 min after intubation	123.08±9.7	137.04±9.9	<0.005
before pneumopertonium	122.92±8.2	136.44±9.4	<0.005
5 min after pneumoperitonium	126.48±10.6	141.6±11.2	<0.005
10 min after pneumoperitonium	124.96±7.0	150.6±3.8	<0.005

15 min after pneumoperitonium	123.56±8.3	155.6±4.8	<0.005
30 min after pneumoperitonium	122.92±7.5	152.7±3.2	<0.005
5 min after exsufflation	123.72±7.6	130.7±8.0	<0.005
During Extubation	132.64±7.4	140.68±7.4	<0.005
5 min After Extubation	123.32±7.8	133.08±7.1	<0.005

**Table 5 Changes in mean arterial pressure in two groups**

**Changes in MAP(mm Hg)**

	<b>MAP of gr A (Mean±SD)</b>	<b>MAP of gr B (Mean±SD)</b>	<b>p value</b>
1 hr prior to sx	94.5±7.3	96.2±7.3	0.4375
before intubation	92.4±7.6	96.7±7.0	0.0426
during intubation	102.0±6.9	110.7±5.9	<0.005
3 min after intubation	95.5±6.0	107.3±6.9	<0.005
10 min after intubation	93.3±6.3	104.9±7.3	<0.005
before pneumopertonium	93.6±4.9	104.2±6.7	<0.005
5 min after pneumoperitonium	95.0±5.6	107.6±8.1	<0.005
10 min after pneumoperitonium	94.2±4.1	112.7±3.2	<0.005
15 min after pneumoperitonium	93.3±4.5	116.2±4.7	<0.005
30 min after pneumoperitonium	93.1±4.3	114±4.2	<0.005
5 min after exsufflation	93.4±4.3	99.8±5.8	<0.005
During Extubation	100.6±4.9	107.2068±5.4	<0.005
5 min After Extubation	92.9±5.3	101.1±5.0	<0.005

**Table 6 Changes in diastolic blood pressure in two groups**

<b>Changes in DBP(mm Hg)</b>	<b>DBP of gr A (Mean±SD)</b>	<b>DBP of gr B (Mean±SD)</b>	<b>p value</b>
1 hr prior to sx	79.2±6.6	82.2±6.5	0.1153
before intubation	77.4±6.5	82.6±6.2	0.0061
during intubation	86.0±6.1	93.8±5.4	<0.005
3 min after intubation	80.1±4.9	90.8±6.2	<0.005
10 min after intubation	78.6±5.2	89.2±7.1	<0.005
before pneumoperitonium	79.1±3.6	88.2±6.9	<0.005
5 min after pneumoperitonium	79.5±4.2	91.04±8.5	<0.005
10 min after pneumoperitonium	79.1±3.6	94.04±3.8	<0.005
15 min after pneumoperitonium	78.4±4.1	98±3.1	<0.005
30 min after pneumoperitonium	78.4±3.8	96.04±3.1	<0.005
5 min after exsufflation	78.5±3.6	84.68±6.2	<0.005
During Extubation	84.8±4.2	90.7±5.6	<0.005
5 min After Extubation	77.92±4.4	85.32±5.4	<0.005

**Table 7 Changes in etco2 in twogroups**

**6) Changes in etco2**

<b>Mean Etco2of cases</b>	<b>Mean Etco2of control</b>	<b>p value</b>
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1 hr prior to sx	-	-	-
before intubation	-	-	-
during intubation	-	-	-
3 min after intubation	29.4±0.9	29.6±1.8	0.36
10 min after intubation	30.6±1.4	30.9±1.2	0.4
before pneumopertonium	30.3±1.1	30.5±0.8	0.49
5 min after pneumoperitonium	31.1±1.3	31.6±1	0.2
10 min after pneumoperitonium	31±1.6	31.7±0.9	0.07
15 min after pneumoperitonium	30.7±1.6	31.3±1.2	0.14
30 min after pneumoperitonium	31.6±1.7	31.8±1.1	0.56
5 min after exsufflation	29.8±1	29.9±0.7	0.54
During Extubation	-	-	-
5 min After Extubation	-	-	-

**Table 8 Post operative monitoring**

	<b>Gr A</b>	<b>Gr B</b>
Nausea- Vomiting	4	2
Sedation (sedation score)	8	27
1	20	3
2		
3	2	

## Discussion

Pneumoperitoneum during laparoscopy produces significant haemodynamic changes, which can be detrimental especially in elderly and in haemodynamically compromised patients. Various techniques and pharmacological agents have been used to counteract these detrimental effects of pneumoperitoneum.

This single blinded prospective study was carried out in 50 adult patients, to evaluate the effect of clonidine premedication in attenuating haemodynamic stress response associated with intubation and pneumoperitoneum.<sup>[3]</sup>

Clonidine, an imidazoline derivative is a selective  $\alpha$ -2 adrenergic agonist. It produces a fall in the heart rate and blood pressure associated with decreased SVR and cardiac output.<sup>[8]</sup> 100  $\mu$ g clonidine was administered orally, 60 minutes before surgery. In operation theater standard monitoring devices were applied. Inj. glycopyrrolate and Inj. Fentanyl 1  $\mu$ g/kg were given and patients were induced with pentothal sodium and Succinyl choline and maintained with oxygen, nitrous oxide, sevoflourane and vecuronium bromide 0.1 mg/kg. all throughout surgeries haemodynamic parameters were monitored. Following pneumoperitoneum with carbon dioxide, patients were hyperventilated to maintain normocapnia. Intra abdominal pressure (IAP) was maintained below 14 mm Hg.

Following intubation and pneumoperitoneum, increase in arterial pressure was noticed but it never crossed more than 30% of baseline value in group A. Hence clonidine premedication was able to achieve haemodynamic stability during pneumoperitoneum.<sup>[9,10,11]</sup>

The adverse effects in the postoperative period were less in the patients who had clonidine premedication in comparison with placebo premedication.

In conclusion, premedication with 150  $\mu$ g 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 postoperative complications such as nausea-vomiting. Hence 150  $\mu$ g oral clonidine can reasonably be recommended as premedication for all laparoscopic procedures in otherwise healthy patients.

## SUMMARY

To conclude, the administration of oral clonidine 150  $\mu$ g as a simple and cost effective form of premedication in patients undergoing laparoscopic surgeries. It has good perioperative haemodynamic stability.

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