

A Study to Evaluate Hemodynamic Response in Patients Undergoing Laparoscopic Surgeries Premedicated with Oral Clonidine in a Tertiary Medical Centre of South Bihar

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Abstract

Introduction: Insufflation of CO₂ into the peritoneal cavity, ports from which instruments can be negotiated into the distended abdomen, and various changes in patient position depending on the type of operation are all required during laparoscopic procedures. Increased intraabdominal pressure (IAP), blood pooling in the periphery, and stress hormone responses (cortisol, epinephrine, and nor-epinephrine) all lead to the hemodynamic variations. Furthermore, patient's IAP is elevated, and his or her location is changed, in laparoscopic procedure making ventilation difficult. **Aim:** To observe hemodynamic changes during pneumoperitoneum (without and with) oral clonidine 150 ug in laparoscopic surgery.

Material and Methods: This is a prospective observational study, will be conducted on 60 study subjects at Narayan medical college and Hospital, Rohtas, South Bihar. Study subjects will be selected as per Inclusion and exclusion criteria from general surgery theatre complex of the hospital. Patients will be divided into two groups (30 each) Group A (Clonidine) 150 ug - Patients will be given tab. Clonidine 150 ug orally 60 minutes prior to induction. Group B (Control) - Patients will be given sugar coated placebo tablet 60 minutes prior to induction. Hemodynamic assessment was done in both the groups and compared. **Result:** SBP, DBP, MAP was also measured at the time of induction, 5 min after induction, 5 min after insufflation, 15 min and 30 min after insufflation and it was found that there was statistically significant difference between the two groups, with p value <0.005 each time respectively. **Conclusion:** Prior to laparoscopic surgeries in adults, oral clonidine 150 mg will effectively blunt the hemodynamic response to pneumoperitoneum. Because of this benefit and the low, easily treatable side effect profile, regular use is recommended.

Keywords: SBP, DBP, MAP, Heart rate, clonidine

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Introduction

Previously, gynaecology was the only specialty that performed laparoscopy on a regular basis, usually for brief, basic procedures or tubal ligations. Laparoscopic techniques have advanced as a therapeutic modality with the introduction of newer technologies. In 1987, Phillipe Mouret pioneered laparoscopic cholecystectomy, ushering in a new age of minimally invasive surgery. Laparoscopy, on the other hand, is linked to certain unfavourable haemodynamic shifts[1]. Insufflation of CO₂ into the peritoneal cavity, the making of ports from which instruments can be negotiated into the distended abdomen, and various changes in patient position depending on the type of operation are all required during laparoscopic procedures. Increased intraabdominal pressure (IAP), blood pooling in the periphery, and stress hormone responses (cortisol, epinephrine, and nor-epinephrine) all lead to the hemodynamic variations. Furthermore, patient's IAP is elevated, and his or her location is changed, in laparoscopic procedure making ventilation difficult[2].

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In most studies, a 10% to 30% reduction in cardiac output has also been recorded. Reduced compliance characterises pulmonary function changes without significant changes in arterial oxygen saturation (PaO₂), but tissue oxygenation may be compromised as a result of reduced O₂ delivery[3]. CO₂-stimulated release of various vasoactive substances, such as catecholamines, prostaglandins, vasopressin, angiotensin, cortisol, and adrenocorticotropin hormone, adds to the issue (ACTH)[4]. Several medications, including opioids, β blockers, nitroglycerine, magnesium sulphate, and others, have been attempted to reduce PNP-related haemodynamic instability with mixed results[5]. Clonidine, an agonist of the α_2 adrenergic receptor, has shown promise in reducing these hemodynamic responses. ⁶ Clonidine premedication reduces the amount of narcotic and anaesthetic medications used during laparoscopic surgery by reducing hemodynamic shifts[7]. It effectively suppresses frustration, reaction to the environment, and fear of surgery when used as a premedication. During surgery, the drug lowers myocardial oxygen demand, stabilises haemodynamics, and effectively reduces stress reactions by lowering catecholamine excretion. Clonidine, despite its sedative properties.[8] The G-protein coupled family of transmembrane receptors includes the α_2 adrenoceptors, which are found in both pre- and post-synaptic autonomic ganglia in the central and peripheral nervous systems. Endogenous (norepinephrine) and exogenous (clonidine and dexmedetomidine) agonists bind to G-proteins, inhibiting both adenylyl cyclase and phospholipase C activity and causing downstream impact[9].

With the above background we plan to conduct this study having following aim and objectives

Aim

To observe hemodynamic changes during pneumoperitoneum (without and with) oral clonidine 150 ug in laparoscopic surgery.

Material and Method

This is a prospective observational study, will be conducted on 60 study subjects at Narayan medical college and Hospital, Rohtas , South Bihar. Study subjects will be selected as per Inclusion and exclusion criteria from general surgery theatre complex of the hospital. Institutional ethical committee approval will be obtained and written informed consent will be obtained from all patients

Inclusion criteria

- Patients of both sexes.
- ASA Physical Status 1-2.
- Age 16- 65 years.

Exclusion Criteria

- Diabetics
- Hypertensives
- Patients with Ischaemic Heart Disease
- COPD patients/ Asthmatics
- Patients with known allergy to drugs used in the study.
- Patients with difficult airway.

Patients will be divided into two groups (30 each)

Group A (Clonidine) 150 ug - Patients will be given tab. Clonidine 150 ug orally 60 minutes prior to induction.

Group B (Control) - Patients will be given sugar coated placebo tablet 60 minutes prior to induction.

On arrival in the operating room, pulse rate and blood pressure will be taken. Monitors will be applied (ECG, blood pressure, pulse oximetry) and Inj. Glycopyrrolate 0.004 mg/kg, inj. fentanyl 1.5 ug/kg inj. Midazolam 1 mg, inj. Ondansetron 2 mg. will be given

intravenous before induction. Patients will be preoxygenated with 100% O₂ for 5 min. Induction will be done with inj. thiopentone sodium 2.5%, 5-7 mg/kg i.v. followed by inj. Succinylcholine 2 mg/kg IPPV with 100% O₂ by face mask for a minute. Trachea will be intubated with adequate size or tracheal portex cuffed endotracheal tube. After confirming bilateral air entry equal tube will be fixed. Anesthesia will be maintained with O₂ and N₂O (50:50) mixture along with 0.6% to 1% isoflurane, inj. Atracurium 0.5 mg/kg body weight and then SOS 0.1 mg/kg as supplement. Through the surgery, the study outcome measures (i.e) the haemodynamic variables heart rate, systolic, diastolic, and mean arterial pressures will be noted at these times -

1. On table- before induction.
2. Just after intubation
3. 5 min after intubation
4. 5 min after insufflation
5. 15 min after insufflation
6. 30 min after insufflation
7. After extubation

The incidence of complications in hemodynamic parameters, (hypotension, bradycardia, hypertension), and the need for treatment will also be noted in both groups. They will be defined and treated as follows; A mean arterial pressure of less than 60mmHg will be considered hypotension and will be treated with i.v bolus of 6 mg ephedrine, which will be repeated as needed.

A heart rate of less than 50 beats/ min will be considered as bradycardia and will be treated with 0.6mg i.v bolus of Atropine. A mean arterial pressure of more than 120mmHg lasting more than five minutes will be treated with intravenous infusion of nitroglycerin 5µg/kg/hr.

Result

Table 1: Distribution of study subjects as per Age

Group	Mean(yrs)	Standard deviation	P value
Group –Placebo	30.77	11.67	t, test – 0.49 P =0.62
Group – Clonidine	32.23	11.08	

Table 1 shows distribution of study subjects as per Age. The mean age in the clonidine group were 32.23±11.08 yrs , whereas in the placebo group it was 30.77±11.67, On comparing and applying t test

we found there is no significant difference with p value- 0.62. Age wise they are comparable.

Table 2: Mean of Heart rate in both the groups

Heart rate	Clonidine group	Placebo group	P value
HR BSD	82.90±12.88	83.07±14.31	0.96, NS
HR ASD	73.57±13.71	87.57±15.64	<0.001, Significant
HR-JA1	77.33±9.34	101.30±13.42	<0.001, Significant
HR-5 MIN I	64.73±11.29	82.40±14.75	<0.001, Significant
HR 5 MIN PP	63.47±8.02	78.97±14.29	<0.001, Significant
HR 15 Min PP	63.63±7.61	80.13±15.39	<0.001, Significant
HR 30 Min PP	63.73±7.33	78.80±14.90	<0.001, Significant
HR -AE	74.17±13.70	97.97±15.64	<0.001, Significant

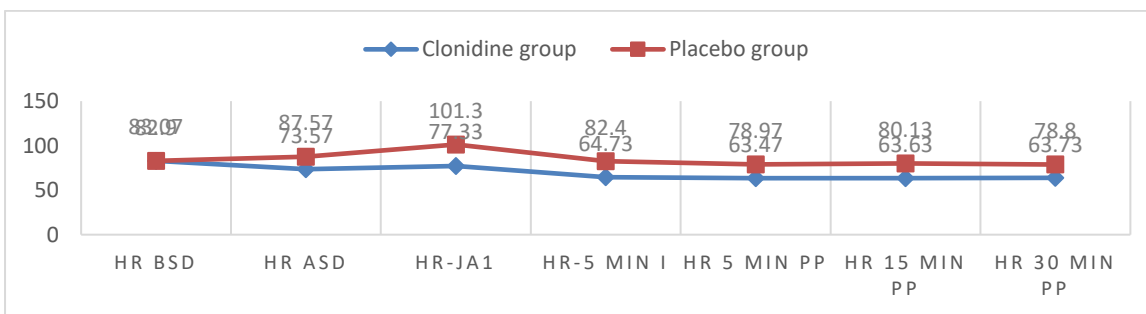


Fig 1: Clonidine group and Placebo group

Table 2 shows Mean of Heart rate in both the groups. At baseline heart rate in clonidine group were 82.90 ± 12.88 whereas in the placebo group it was 83.07 ± 14.31 . There was no statistically significant difference between both the group. Heart rate was also

measured at the time of induction, 5 min after induction, 5 min after insufflation, 15min and 30 min after insufflation and it was found that there was statistically significant difference between the two groups, with p value <0.005 each time respectively.

Table 3: Mean of SBP in both the groups

SBP	Clonidine group	Placebo group	P value
SBP BSD	119.53 ± 10.55	118.51 ± 11.76	0.72
SBP ASD	114.20 ± 14.72	126.87 ± 11.13	<0.001 , Significant
SBP-JA1	115.0 ± 17.81	138.80 ± 19.53	<0.001 , Significant
SBP-5 MIN I	102.13 ± 11.95	115.40 ± 20.08	<0.001 , Significant
SBP 5 MIN PP	121.73 ± 16.98	137.67 ± 12.14	<0.001 , Significant
SBP 15 Min PP	122.57 ± 16.87	138.60 ± 10.49	<0.001 , Significant
SBP 30 Min PP	122.23 ± 15.64	135.67 ± 13.05	<0.001 , Significant
SBP -AE	120.33 ± 11.39	140.03 ± 13.49	<0.001 , Significant

Table 3 shows Mean of SBP in both the groups. At baseline SBP in clonidine group were 119.53 ± 10.55 whereas in the placebo group it was 118.51 ± 11.76 . There was no statistically significant difference between both the group. SBP was also measured at the time of

induction, 5 min after induction, 5 min after insufflation, 15min and 30 min after insufflation and it was found that there was statistically significant difference between the two groups, with p value <0.005 each time respectively.

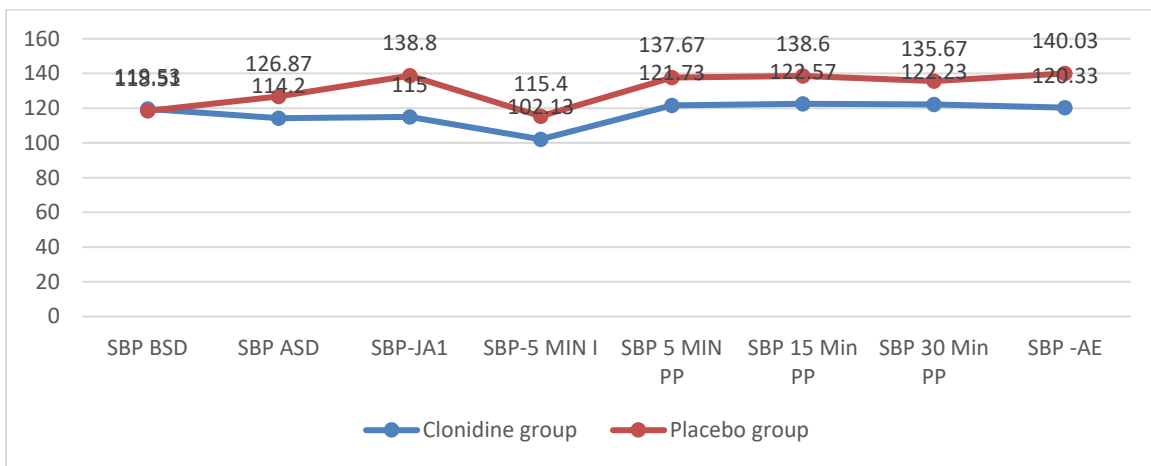


Fig 2: Clonidine group and Placebo group

Table 4: Mean of DBP in both the groups

DBP	Clonidine group	Placebo group	P value
DBP BSD	77.57 ± 7.93	79.27 ± 7.21	0.39, non-significant
DBP ASD	72.37 ± 9.82	83.57 ± 7.75	<0.001 , significant
DBP-JA1	73.73 ± 15.44	95.33 ± 18.32	<0.001 , Significant
DBP-5 MIN I	66.10 ± 10.27	77.87 ± 14.25	<0.001 , Significant
DBP 5 MIN PP	79.27 ± 17.69	98.10 ± 9.65	<0.001 , Significant
DBP 15 Min PP	81.60 ± 11.15	96.30 ± 8.23	<0.001 , Significant
DBP 30 Min PP	82.37 ± 10.64	93.83 ± 8.65	<0.001 , Significant
DBP -AE	79.00 ± 8.15	93.03 ± 8.42	<0.001 , Significant

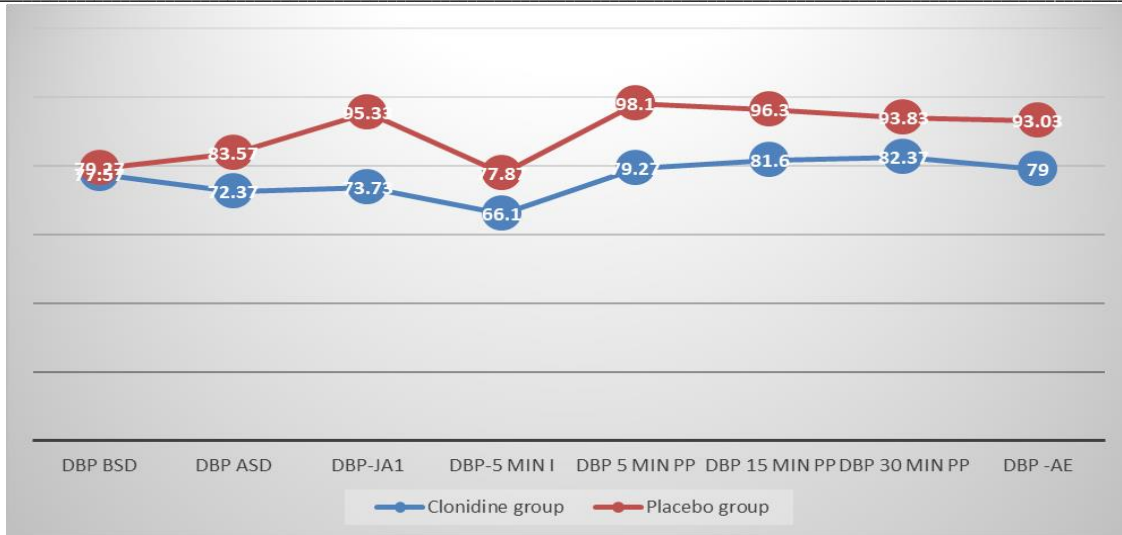


Fig 3:DBP in clonidine group and placebo group

Table 4 shows Mean of DBP in both the groups. At baseline DBP in clonidine group were 77.57 ± 7.93 whereas in the placebo group it was 79.27 ± 7.21 . There was no statistically significant difference between both the group. DBP was also measured at the time of induction, 5

min after induction, 5 min after insufflation, 15min and 30 min after insufflation and it was found that there was statistically significant difference between the two groups, with p value <0.005 each time respectively.

Table 5:Mean of MAP in both the groups

MAP	Clonidine group	Placebo group	P value
MAP BSD	91.83 ± 7.92	92.27 ± 7.06	0.82, non-significant
MAP ASD	87.07 ± 11.07	97.53 ± 8.01	<0.001 , significant
MAP-JA1	87.77 ± 15.71	109.47 ± 17.31	<0.001 , significant
MAP-5 MIN I	78.00 ± 10.41	90.40 ± 15.11	<0.001 , significant
MAP 5 MIN PP	95.83 ± 13.82	110.97 ± 9.73	<0.001 , significant
MAP 15 Min PP	95.30 ± 12.57	109.93 ± 7.64	<0.001 , significant
MAP 30 Min PP	94.97 ± 11.91	107.43 ± 9.06	<0.001 , significant
MAP -AE	92.63 ± 8.78	108.53 ± 9.53	<0.001 , significant

Table 5 shows Mean of DBP in both the groups. At baseline DBP in clonidine group were 91.83 ± 7.92 whereas in the placebo group it was 92.27 ± 7.06 . There was no statistically significant difference between both the group. DBP was also measured at the time of induction, 5

min after induction, 5 min after insufflation, 15min and 30 min after insufflation and it was found that there was statistically significant difference between the two groups, with p value <0.005 each time respectively.

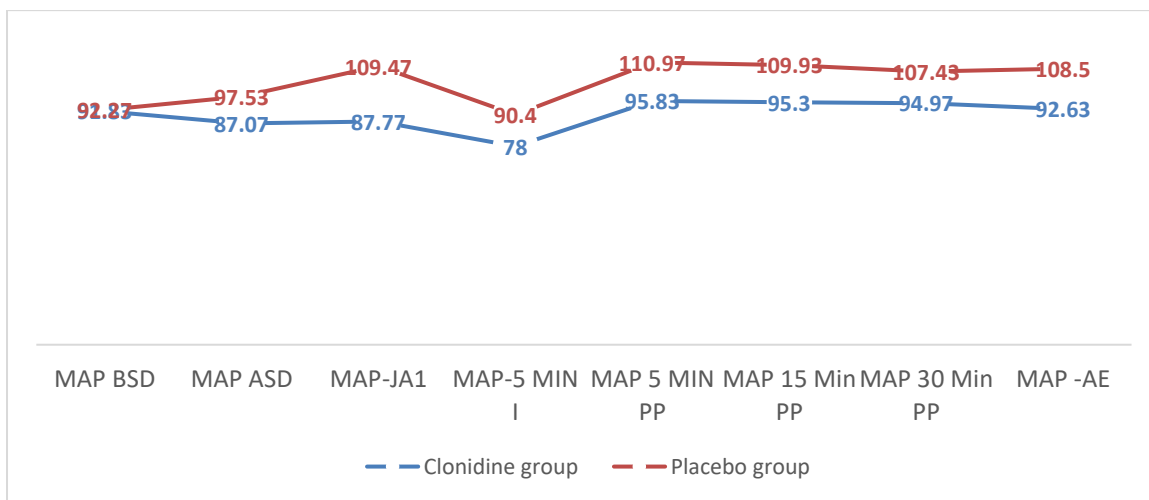


Fig 4:MAP in clonidine group and Placebo group

Table 5: Distribution of study subjects as per Incidence of Adverse effect

Event	Clonidine group	Placebo group	
No Adverse effect	25	27	Mid P exact test applied, P value- 0.48
Hypertension	0	3	
Bradycardia	4	0	
Hypotension	1	0	
Total	30	30	

Table 5 Shows distribution of study subjects as per Incidence of Adverse effect. In clonidine group 25 out of 30 subjects do not have any adverse effect, 4 subjects had bradycardia, 1 had hypotension whereas in placebo group 27 of 30 were having no adverse effect, and rest 3 had hypertension. On applying Mid P exact test we found no significant difference with p value- 0.48.

Discussion

Pneumoperitoneum during laparoscopy produces significant haemodynamic changes, which can be detrimental especially in elderly and haemodynamically compromised patients. Various techniques and pharmacological agents have been used to counteract these detrimental effects of pneumoperitoneum. This observational study was carried out in 60 adult patients, to evaluate the effect of clonidine premedication in attenuating haemodynamic stress response associated with pneumoperitoneum. General Anaesthesia with muscle paralysis, tracheal intubation, and occasional positive pressure ventilation is the recommended anaesthetic technique for laparoscopic surgery. While regional Anaesthesia is possible, there are drawbacks such as the need for a high degree of blockade, a high incidence of post-operative shoulder pain, increased patient discomfort and anxiety, and the need for high minute ventilation to maintain normocarbida during spontaneous ventilation. In our study, all of the patients were given general Anaesthesia with controlled ventilation. The sympatholytic action of Clonidine and therapeutic effect starts after 30 to 60 minutes of ingestion. Clonidine was given 60 to 90 minutes prior to surgery in almost all of the reference studies, and it was given at the same time in our research. Preoperative volume loading is a scientifically proven intervention for avoiding laparoscopy-related cardiovascular complications. The baseline hemodynamic variables (before ingestion of study drug-BSD) were comparable between the groups. 30 min after the study drug(ASD), heart rate(HR), systolic, diastolic and mean arterial pressures (SBP, DBP & MAP) were lower than the baseline in Group C, whereas it was higher in Group P. HR(bpm) SBP (mmHg) DBP(mmHg) MAP(mmHg)

Effect on Heart Rate

At all times during the surgery, Group C had a slightly lower mean heart rate. The mean heart rate was observed to be lower than baseline in both groups after insufflation, which may be due to propofol Anaesthesia. However, the drop in Group C was 31.4 percent, compared to 7.27 percent in Group P, demonstrating the importance of Clonidine premedication. In the study by S.Goel[9] major decreases in mean pulse rate were observed after 5 and 10 minutes of insufflation. In Group P, heart rates ranged from 78.80±14.90 to 101.30±13.42 beats per minute (bpm), while in Group C, heart rates ranged from 63.47±8.02 to 82.90±12.88 beats per minute (bpm). In their placebo-controlled trials, Y. Passi et al[10] and M. Das et al[11] found that mean pulse rate was significantly lower in clonidine-premedicated patients in all cases. A. Islam et al[12] found that the Clonidine group had a lower pulse rate than the Atenolol and placebo groups. At all stages during the surgery, Norimasa S et al[13] found a substantially lower heart rate in patients premedicated with Clonidine than in those premedicated with Atropine Hydroxyzine.

Effect on Systolic Blood Pressure

The mean systolic blood pressure in Group C was substantially lower than in Group P from pre-induction to post-extubation. Both groups' mean systolic pressure levels were found to be higher than baseline

after pneumoperitoneum induction. In group P, the mean systolic blood pressure ranged from 115.40±20.08 to 140.03±13.49 mmHg, while in group C, it ranged from 102.13±11.95 to 122.57±16.87 mmHg. In their trials, M. Das et al[11] and Y. Passi et al[10] found a substantial reduction in systolic blood pressure in Clonidine-premedicated patients relative to the placebo group. Clonidine patients had substantially lower systolic pressure at 5, 10 minutes after insufflations, as found by M. Sinha and S.Goel[9]. These observations correlate well with our study.

Effect on Diastolic Blood Pressure

In Group C, diastolic pressure remained reliably low during the surgery. In Group P, the mean diastolic pressure ranged from 77.87±14.25 to 98.10±9.65 (mmHg), while in Group C, it ranged from 66.10±10.27 to 82.37±10.64 (mmHg). Clonidine, Atenolol, and Placebo were compared for premedication in laparoscopic cholecystectomy by A.Islam et al[12], They found that the Clonidine group had a greater decrease in diastolic blood pressure from baseline, and that the mean diastolic blood pressure remained lower than the other groups, though this was not statistically important. M.Das et al[11], M. Sinha & S. Goel[9] obtained results that matched our findings.

Effect on Mean Arterial Pressure

The hemodynamic changes during laparoscopy were studied by Joriset al[14] who assessed mean arterial pressure, heart rate, cardiac output, and systemic vascular resistance. On peritoneal insufflations, a 39.8 percent increase in MAP was observed, with a major blunting of this response when Clonidine was administered. The average mean arterial pressure in Group P ranged from 90.40±15.11 to 109.93±7.64, while in Group C it ranged from 78.00±10.41 to 95.83±13.82. M. Das et al[11] observed a more than 20% rise in mean arterial pressure in the placebo group after pneumoperitoneum induction, but it never crossed the baseline value in the Clonidine group. His findings back up the proof that clonidine reduces the increase in MAP. Patients premedicated with Clonidine had a steeper decline in MAP than those premedicated with Atenolol or Placebo, according to A. Islam et al[12]. At all points during the surgery, Y. Passi et al[10] found that mean arterial pressure was consistently lower in the clonidine group than in the placebo group. Joris et al[14] investigated the endocrine correlates of hemodynamic changes during laparoscopy and pneumoperitoneum in order to better understand these changes. They discovered that laparoscopy resulted in a progressive and substantial increase in cortisol, epinephrine, norepinephrine, rennin, and vasopressin plasma concentrations. Prior to surgery, an intravenous injection of 8g/kg clonidine greatly decreased catecholamine levels while having little effect on vasopressin or cortisol levels. Both of these findings are in line with the findings of this study. As previously mentioned, neurohumoral responses are the primary mediators of cardiovascular changes during laparoscopy. Sung et al[15] used 150g oral clonidine as a premedicant for laparoscopic cholecystectomy and found that it maintains hemodynamic stability. This hypothesis is supported by the findings of our research.

Adverse effect

In Group P, three patients (10%) experienced hypertension. In studies by M.Das et al[11] and Y. Passi et al[10], 33 percent of patients in the treatment group and 36 percent of patients in the placebo group need nitroglycerine for hypertension treatment. The lower incidence in our research may be due to Propofol Anaesthesia,

while in the previous studies, Isoflourane was used for Anaesthesia maintenance. Bradycardia was found in four patients in Group C (13.33 percent) and none in Group P. In studies by Y. Passi et al[10] and M. Sinha & S. Goel[9], the incidence was 4 percent and 6 percent, respectively. Bradycardia was intermittent and quickly treated with a single bolus dose of 0.6 mg Inj. Atropine, with no need for repeat boluses. In Group C, one patient (3.33 percent) had hypotension. Y. Passi et al[10] found a similar rate of hypotension in the clonidine population (one out of every 25 patients). In studies by M. Das et al[11] and M. Sinha & S. Goel[9], none of the patients had hypotension. A single bolus of inj. Ephedrine 6 mg i.v. was needed for treatment, and no more than that was allowed.

Conclusion

Prior to laproscopic surgeries in adults, oral clonidine 150 mg will effectively blunt the hemodynamic response to pneumoperitoneum. Because of this benefit and the low, easily treatable side effect profile, regular use is recommended. More research is required to determine if this drug can be used as a premedication for laproscopic surgeries in patients with reduced cardiac reserve.

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