EFFECT OF ORAL CLONIDINE PREMEDICATION ON HAEMODYNAMIC CHANGES DURING LAPAROSCOPIC CHOLECYSTECTOMY - A CLINICAL STUDY

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ABSTRACT

BACKGROUND

Laparoscopic surgeries are the recent advances in the field of surgery and are the essence of today's surgical practice. Laparoscopic cholecystectomy has revolutionised gall bladder surgeries and has become the treatment of choice for cholelithiasis. This procedure has minimised the numbers of open cholecystectomy performed these days.

AIMS AND OBJECTIVES

To study the effect of oral clonidine premedication on haemodynamic changes during laparoscopic cholecystectomy**.**

MATERIALS & METHODS

The present study was conducted in the Department of Anaesthesiology of Assam Medical College, Dibrugarh for a period of one year from July 2012 to June 2013 on patients undergoing laparoscopic cholecystectomy at operation theatre of Department of General Surgery of Assam Medical College and Hospital, Dibrugarh. A total of 150 adult patients of either sex between the age group of 18 to 40 years of ASA-1 and ASA-2 undergoing elective laparoscopic cholecystectomy were divided randomly into two groups of 75 patients each.

RESULTS

With the present study that oral premedication with Tab. Clonidine 150 mcg administered 90 minutes before surgery was able to prevent adverse haemodynamic changes during elective laparoscopic cholecystectomy under general anaesthesia.

CONCLUSION

Hence, from the findings of this study, we can reasonably recommend oral premedication with Tab. Clonidine 150 mcg in otherwise healthy patients undergoing laparoscopic cholecystectomy.

KEYWORDS

Clonidine, Premedication, Laparoscopic, Cholecystectomy, Haemodynamic.

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INTRODUCTION: Laparoscopic cholecystectomy was first performed by Phillipe Mouret in 1987. Laparoscopy confers many benefits to the patients over conventional cholecystectomy. Despite the potential advantages like small incision, less pain, early ambulation and early discharge of the patients with resumption of normal life, it has some disadvantages especially due to pneumoperitoneum by carbon dioxide insufflation. This induces serious physiological changes on cardiovascular and respiratory system, which are not usually encountered with traditional open procedures which poses great challenges to an anaesthesiologist. In fact, it produces significant haemodynamic changes[1] especially in elderly and in haemodynamically compromised patients. It is of paramount importance for an anaesthesiologist to maintain haemodynamic stability during perioperative period. Critical events during perioperative period like induction, intubation and surgical stimulus initiative metabolic response to trauma that also need to be considered and attended.

Laparoscopic surgeries require creation of pneumoperitoneum which is produced by insufflations of carbon dioxide in the abdominal cavity by using automated flow controlled carbon dioxide insufflator which supplies gas till the required intra-abdominal pressure is reached. Inflation pressure can be varied from 0-30 mmHg whereas the total gas flow volume can be set from 0-9.9 L/min. Intra-abdominal pressure (IAP) should be maintained at 6 to 12 mmHg which should not be allowed to exceed 15 mmHg. After pneumoperitoneum, necessary changes are required in ventilator settings like tidal volume and respiratory rate to maintain normocapnia.

Pneumoperitoneum along with changes in position of the patients during the procedure affects multi-organ systems leading to release of stress hormones (cortisol,

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epinephrine, norepinephrine, etc.), alternation in acid-base balance, cardiovascular, pulmonary, renal physiology.[2]

During laparoscopic cholecystectomy, there is reduction of venous return, left ventricular and diastolic pressure, increase of intrathoracic pressure, right atrial and pulmonary artery occlusion pressure during insufflations. There is also increase in mean arterial pressure, heart rate and systemic and pulmonary vascular resistance.

AIMS & OBJECTIVES: The main aim of an anaesthesiologist for laparoscopic cholecystectomy is to maintain haemodynamic stability. The problem is more complex and most of the haemodynamic instability is observed during the period of pneumoperitoneum created by carbon dioxide[3] insufflations. Various agents and its combination have been used in an effort to minimise the haemodynamic instability during this period. Volatile agents like isoflurane and sevoflurane[1] have been used with limited success in maintaining haemodynamic stability as volatile agents decreases the surgical stimulus induced catecholamine secretion. Opioids have been used for blunting the perioperative stress response during general anaesthesia. Although, general anaesthesia prevents haemodynamic instability by rendering patients insensate to pain of surgery and discomfort, it is unable to completely abolish the perioperative stress response.

General anaesthesia has been supplemented on occasions with intraoperative infusions of propofol due to its intrinsic ability to inhibit catecholamine secretion, infusions of nitroglycerin[4] or beta blockers, to control perioperative stress. Again, a procedure of general anaesthesia combined with epidural anaesthesia[5] is another strategy employed by anaesthesiologist to control perioperative haemodynamic instability, but with limited success. But the search for the ideal agent to control this instability in haemodynamics is still on.

Premedication plays an integral part of anaesthetic management and some form of premedication is universally administered before any anaesthesia.

The premedication is given with the following objectives:

1. Should be effective and pleasant to be taken orally.
2. Should produce sedation and facilitate smooth induction of anaesthesia.
3. Should have antisialogogue effect.
4. Should not impair cardiovascular stability.
5. Should not depress respiration.
6. Should have analgesia and antiemetic properties.
7. Should reduce the requirement of anaesthetic drugs.

Clonidine, a centrally acting selective partial alpha-2 agonist (a2:a1-200:1). Clonidine acts by stimulating alpha-2 adrenoceptors, thereby decreasing non-adrenergic release from sympathetic nerve terminal and consequently decreasing sympathetic over activity. The drug acts by reducing responsiveness of peripheral vessels to vasoactive substances and to sympathetic stimulation. The analgesic effects are mediated by activating of alpha-2 adrenoceptors in dorsal horn of spinal cord. Clonidine has a half-life around 6 to 12 hours, has been shown to reduce peripheral sympathetic discharge, reduces intra-operative anaesthetic requirement, reduces postoperative pain and analgesic requirement in clinical use.

These characteristics suggest that Clonidine may be useful as a premedicant in the anaesthetic management of patient undergoing laparoscopic cholecystectomy.

The only clinically available oral alpha-2 adrenergic agonists in our country is clonidine, which is mainly used as an antihypertensive agent, but has many properties of an ideal premedicant and also has beneficial effects on haemodynamics during stressful conditions like laryngoscopy and pneumoperitoneum.

In this study, oral clonidine is used as a premedicant to evaluate its effectiveness in attenuation of the haemodynamic response associated with pneumoperitoneum during laparoscopic cholecystectomy.

MATERIALS & METHODS: The present study was conducted in the Department of Anaesthesiology of Assam Medical College, Dibrugarh for a period of one year from July 2012 to June 2013. Randomised double blind clinical trial. A total of 150 adult patients of either sex between the age group of 18 to 40 years of ASA-1 and ASA-2 undergoing elective laparoscopic cholecystectomy were divided randomly into two groups of 75 patients each.

Approval and Consent: This study was conducted after the approval from the Institutional Ethical Committee and with written informed consent from each patient after explaining the study procedure to them in their own language.

Inclusion criteria:

- Patients aged between 18-40 years of both sexes
- Patients with ASA Grade 1 or 2
- Patients undergoing elective laparoscopic cholecystectomy under general anaesthesia

Exclusion Criteria:

- Unwilling patients or patient's refusal
- Emergency surgeries
- Patients with ASA Grade 3 or higher
- Patients with neurological and endocrine abnormalities
- Patients with hypertension, ischaemic heart disease, valvular heart disease, diabetes mellitus
- Patients on concomitant use of monoamine oxidases inhibitors, other psychotropic drugs or history of drug allergies.

Randomisation: Patients were randomly allocated into one of the two - group P and group C each having 75 patients by an anaesthesiologist not associated with the study.

Group P – Placebo group: Patients receiving Tab. Ranitidine 10 mg orally 90 minutes before surgery.

Group C – Clonidine group: Patients receiving Tab. Clonidine 150 mcg orally 90 minutes before surgery.

Preparation and administration of drugs was made by an anaesthesiologist not involved in study.

Statistical analysis: Demographic data, parametric variables like heart rate (HR), systolic BP, diastolic BP and mean arterial pressure (MAP) were tabulated as Mean ±SD and analysed by unpaired 't' test. Fisher's exact test was used to determine p value of frequency of complications and number of patients in ASA category, p value of less than 0.05 was considered significant.

RESULTS AND OBSERVATIONS: In this present randomised double blind controlled trial of 150 patients aged between 18 to 40 years of ASA 1 and 2 undergoing laparoscopic cholecystectomy were studied to evaluate the intraoperative haemodynamic changes. Patients were divided into two groups of 75 each namely Group P (Tab. Ranitidine 150 mg) and Group C (Tab Clonidine 150 mcg).

The data recorded on predesigned and pretested proforma was tabulated and master chart was prepared. The analysis was done as below.

Age (years)	Group P		Group C	
	Number	% in Group	Number	% in Group
18-30	44	58.67	48	64.00
31-40	31	41.33	27	36.00

Table 1: Age distribution

Group	Age (Mean±SD)	P value
Group P	29.43±0.7365	0.5436
Group C	28.79±0.7503	

Table 2: Age comparison

The mean age of patients in group P was 29.43±0.7365 years and in group C was 28.79±0.7503 years with a p value more than 0.05 and hence both the groups were comparable.

Weight (Kg)	Group P		Group C	
	Number	% in Group	Number	% in Group
40-50	29	38.67	27	36.00
51-60	39	52.00	45	60.00
61-70	7	9.33	3	4.00

Table 3: Weight distribution

Group	Weight in Kg (Mean±SD)	P value
Group P	53.080±5.402	0.4059
Group C	52.427±4.111	

Table 4: Weight comparison

The mean weight of patients in group P was 53.080±5.402 kg and in group C was 52.427±4.111 kg with p value of more than 0.05 which is not significant and hence both the groups are comparable.

Sex	Group P		Group C	
	Number	% in Group	Number	% in Group
Male	17	22.67	17	22.67
Female	58	77.33	58	77.33

Table 5: Sex distribution

In this study, 22.67% were males and 77.33% were females in group P; and 22.67% were males and 77.33% were females in group C. Hence, both the groups had compatible sex distribution.

Group	ASA 1	%	ASA 2	%	P value
Group P	65	86.67	10	13.33	0.802
Group C	67	89.33	8	10.67	
Total	132	88.00	18	12.00	

Table 6: ASA physical status of patients

In the whole study, 88% belonged to ASA 1 and 12% were having ASA 2 physical status. In group P 86.67% were of ASA 1 as compared to 89.33% in group C. Patients having ASA 2 comprised 13.33% in group P and 10.67% in group C. The p value is 0.802 and hence, both the groups were comparable with respect of ASA physical status.

Group	Sedation Score (Mean±SD)	P value
Group P	1.507±0.05812	0.0696
Group C	1.653±0.05532	

Table 7: Sedation score

The mean sedation score before induction was assessed by Ramsay Sedation Score and was 1.507 for group P which was less as compared to group C with a mean score of 1.653. However, this was not statistically significant.

Group	SpO_2 (Mean±SD)	P value
Group P	99.53±0.1112	>0.9999
Group C	99.53±0.09741	

Table 8: Pre-operative oxygen saturation

The preoperative oxygen saturation was statistically comparable in both the groups.

Abbreviations:

T1 (Before Premedication)
T2 (Before Intubation)
T3 (3 minutes after endotracheal intubation)
T4 (Before pneumoperitoneum)
T5 (15 minutes after pneumoperitoneum)
T6 (30 minutes after pneumoperitoneum)
T7 (5 minutes after release of carbon dioxide)
T8 (10 minutes after extubation)

Time Interval	SBP (Mean± SD)	DBP (Mean± SD)	MAP (Mean± SD)	HR (Mean± SD)
Group P				
T1	120.53±5.91	78.48±4.80	92.53±3.96	88.89±12.39
T2	123.28±5.89	81.24±4.97	95.32±4.39	102.55±13.89
T3	143.21±4.98	101.37±5.15	115.29±4.59	115.29±4.59
T4	129.99±4.60	90.44±3.99	103.65±3.49	98.57±10.71
T5	139.53±4.08	97.35±2.85	111.41±2.59	124.74±11.30
T6	143.32±5.55	101.73±3.83	115.67±3.99	128.49±9.19
T7	132.95±4.64	92.99±3.65	106.28±3.34	111.19±9.76
T8	126.27±5.72	86.37±3.97	99.64±3.90	85.79±9.37
Group C				
T1	122.28±7.15	79.88±6.09	94.03±6.13	86.33±9.24
T2	113.97±4.96	73.92±3.83	86.23±9.78	80.23±6.47
T3	115.69±5.42	76.19±4.43	89.35±4.29	84.83±6.56
T4	110.63±4.65	72.39±3.33	85.12±3.25	72.29±4.19
T5	110.39±5.57	70.32±5.95	83.72±5.52	74.08±4.60
T6	111.24±6.21	71.63±6.70	84.88±6.26	76.84±5.3
T7	108.29±4.53	69.6±4.21	82.39±3.74	75.44±5.01
T8	109.35±5.29	71.85±4.43	84.39±4.26	77.64±5.08

Table 9: Haemodynamic parameters

Systolic Blood Pressure (mm Hg)	Group P (Mean±SD)	Group C (Mean±SD)	p Value	Significance
T1	120.53±5.91	122.28±7.15	0.1050	NS
T2	123.28±5.89	113.97±4.96	<0.001	HS
T3	143.21±4.98	115.69±5.42	<0.001	HS
T4	129.99±4.60	110.63±4.65	<0.001	HS
T5	139.53±4.08	110.39±5.57	<0.001	HS
T6	143.32±5.55	111.24±6.21	<0.001	HS
T7	132.95±4.64	108.29±4.53	<0.001	HS
T8	126.27±5.72	109.35±5.29	<0.001	HS

Table 10: Comparison between intraoperative systolic blood pressure changes in group P and group C

NS – Not Significant. HS – Highly Significant

The table shows intraoperative systolic blood pressure changes of Clonidine group of patients are at lower level as compared to placebo group at various periods of the procedure.

Diastolic Blood Pressure (mm Hg)	Group P (Mean±SD)	Group C (Mean±SD)	p Value	Significance
T1	78.48±4.80	79.88±6.09	0.1203	NS
T2	81.24±4.97	73.92±3.83	<0.001	HS
T3	101.37±5.15	76.19±4.43	<0.001	HS
T4	90.44±3.99	72.39±3.33	<0.001	HS
T5	97.35±2.85	70.32±5.95	<0.001	HS
T6	101.73±3.83	71.63±6.70	<0.001	HS
T7	92.99±3.65	69.6±4.21	<0.001	HS
T8	86.37±3.97	71.85±4.43	<0.001	HS

Table 11: Comparison between diastolic blood pressure changes in group P and group C

NS – Not Significant. HS – Highly Significant

The figure shows intraoperative diastolic blood pressure changes of Clonidine group of patients are at significantly lower level as compared to placebo group at various intraoperative periods of the procedure.

Mean Arterial Pressure (mm Hg)	Group P (Mean±SD)	Group C (Mean±SD)	p Value	Significance
T1	92.53±3.96	94.03±6.13	0.0785	NS
T2	95.32±4.39	86.23±9.78	<0.001	HS
T3	115.29±4.59	89.35±4.29	<0.001	HS
T4	103.65±3.49	85.12±3.25	<0.001	HS
T5	111.41±2.59	83.72±5.52	<0.001	HS
T6	115.67±3.99	84.88±6.26	<0.001	HS
T7	106.28±3.34	82.39±3.74	<0.001	HS
T8	99.64±3.90	84.39±4.26	<0.001	HS

Table 12: Comparison between mean arterial blood pressure changes in group P and group C

NS – Not Significant. HS – Highly Significant

The table indicates that intraoperative mean arterial blood pressure changes of Clonidine group of patients are at significantly lower level as compared to placebo group at various intraoperative periods of the procedure.

Heart Rate (/min)	Group P (Mean±SD)	Group C (Mean±SD)	p Value	Significance
T1	88.89±12.39	80.23±9.24	0.1536	NS
T2	102.55±13.89	80.23±6.47	<0.001	HS
T3	115.29±4.59	84.83±6.56	<0.001	HS
T4	98.57±10.71	72.29±4.19	<0.001	HS
T5	124.74±11.30	74.08±4.60	<0.001	HS
T6	128.49±9.19	76.84±5.30	<0.001	HS
T7	111.19±9.76	75.44±5.01	<0.001	HS
T8	85.79±9.37	77.64±5.08	<0.001	HS

Table 13: Comparison between heart rate changes in group P and group C

NS – Not Significant. HS – Highly Significant

The table indicates that intra-operative changes in heart rate of clonidine groups of patients are at significantly lower level as compared to placebo group at various intraoperative periods of the procedure.

Adverse effect	Group P	Group C	p Value	Significance
Nausea	3	16	0.0024	S
Vomiting	1	8	0.0335	S
Bradycardia	1	0	1.0000	NS
Hypotension	0	0		
Bradypnoea	0	0		
Shivering	0	7	0.0135	NS

Table 14: Comparison of adverse effects in group P and group C

The above statistics indicates that there were significantly less incidences of post-operative nausea and vomiting in patients receiving clonidine than placebo group. There was 1 case of bradycardia in clonidine group but it was not statistically significant. The incidence of shivering was more in case of placebo group.

DISCUSSION: Laparoscopic cholecystectomy has become the operation of choice for routine gallbladder removal. It is one of the most common major abdominal procedure performed in Western countries and is gaining rapid popularity in our country. Now a day, patients demand for laparoscopic removal of gall bladder and is gaining popularity ever since its induction.

Laparoscopic cholecystectomy decreases morbidity and shortens hospital stay from 1 week to less than 24 hours, and patient can perform full activity within 1 week compared to 1 month after open cholecystectomy.

However, this great achievement carries some disadvantages mainly in the form of intraoperative haemodynamic instability.

Laparoscopic cholecystectomy is performed by the production of carbon dioxide (CO_2) pneumoperitoneum and change in the patient position from Trendelenburg to reverse Trendelenburg which results in release of stress hormones (cortisol, epinephrine and norepinephrine) especially when CO_2 pneumoperitoneum is used concomitantly. This stress hormonal responses results in intraoperative hypertension and tachycardia. There is also increase in systemic vascular resistance, and is associated with a decrease in cardiac index and metabolic changes.

Many studies have been conducted with various pharmacological agents that resulted in reduced incidence of tachycardia, hypertension during laparoscopic cholecystectomy and provide a stable haemodynamic state without significant undesirable effects.

Clonidine, an alpha-2 adrenoceptor agonist drug which exerts central sympatholytic effect and has a half-life of 6-12 hrs. it decreases peripheral norepinephrine release by stimulation of prejunctional inhibitory alpha-2 adrenoceptors and by inhibition of neural transmission in different brainstem areas, such as the nucleus tractus solitarius and lateral reticular nucleus in the ventrolateral medulla. Clonidine has also agonism on the 11-receptor (imidazoline receptor), which mediates the sympathoinhibitory actions of imidazoline to lower blood pressure.

The above-mentioned properties suggest that Clonidine may be useful in the anaesthetic management of patients undergoing laparoscopic surgeries. Hence, this study was undertaken to evaluate the effects of oral clonidine premedication in maintaining haemodynamic stability by reduction of perioperative stress response in 150 patients undergoing laparoscopic cholecystectomy at Assam Medical College & Hospital which were divided into two groups viz. group P receiving Tab. Ranitidine 150 mg and group C receiving Tab. Clonidine 150 mcg.

In this study, 22.67% were males and 77.33% were females in both the groups with male to female ratio of 1:29.31. Most of the patients in both the groups (Group P 58.67% and group C 64.00%) were aged between 18-30 ears. The mean age in group P was 29.43±0.7365 years and in group C it was 29.79±0.7503 years suggesting that both the groups had comparable demographic characteristics. The mean weight in group P was 53.080 ± 5.402 Kg and in group C it was 52.427 ± 4.111 Kg suggesting mean weights were also comparable in both the groups. About the ASA grading, 86.67% of patients had ASA status 1 and 13.33% had ASA 2 status in group P and 89.33% and 10.67% patients belonged to ASA 1 and ASA 2 respectively in group C which was statistically comparable.

In the present study, results clearly showed intraoperative SBP changes were significantly lower in clonidine group. The reading of SBP found at different time intervals were – {T2 (113.97±4.96) mmHg, T3 (115.69±5.42) mmHg, T4 (110.63±4.65) mmHg and T5 (110.39±5.57) mmHg and at T6 (111.24±6.21) mmHg, T7 (108.29±4.53) mmHg, T8 (109.35±5.29) mmHg} with a p value <0.001 as compared to control group at all intervals. Thus, SBP remained under satisfactory control throughout the procedure.

Study of results clearly showed that intraoperative DBP changes were significantly lower in Clonidine group, that is {T2(73.92±3.83) mmHg, T3(76.19±4.43) mmHg, T4(72.39±3.33) mmHg, and T5(70.32±5.95)mmHg, T6(71.63±6.70)mmHg, T7(69.6±4.21) mmHg, T8(71.85±4.43) mm Hg} with a p value <0.001 as compared to control group at all intervals. This finding clearly shows that DBP remained under satisfactory control throughout the procedure in group C.

The study also shows that the intraoperative MAP changes were significantly lower in Clonidine group that is {T2 (86.23±9.78) mm Hg, T3 (89.35±4.29) mmHg, T4 (85.12±3.25) mmHg and T5 (83.72±5.52) mmHg and at T6 (84.88±6.26) mmHg, T7 (82.39±3.74) mmHg, T8 (84.39±4.26) mmHg} with a p value <0.001 as compared to control group at all-time intervals. These findings show that MAP remained under satisfactory control throughout the procedure in group C.

Intra-operative HR changes in this study were significantly lower in Clonidine group, that is T2 (80.23±6.47) mmHg, T3 (76.19±4.43) mmHg, T4 (72.29±4.19) mmHg and T5 (74.08±4.60) mmHg and T6 ((76.84±5.30) mmHg, T7 (75.44±5.01) mmHg, T8 (77.64±5.08) mmHg) with P value <0.001 as compared to control group at all-time intervals. This finding show that HR changes remained under satisfactory control throughout the procedure in group C.

In this study, the haemodynamic parameters after laryngoscopy and intubation i.e. at T3 and T4 clearly showed that Clonidine significantly ($p < 0.001$) blunted the pressor response caused by laryngoscopy and endotracheal intubation as compared to placebo group.

In the Clonidine group, the mean sedation score before induction was 1.653±0.05532 which was more than the placebo group showing more patients were sedated and were less anxious. However, these findings were not statistically significant.

Similar findings of Clonidine were reported in various other studies.

Manjushree Ray et al.[6] (2007) in a study reported significant rise in MAP in Group P (placebo) as compared to Group C (Clonidine 150 mcg) after intubation (113.56±16.33 mmHg vs 93.70±7.33; $p<0.001$), after pneumoperitoneum at 15 minutes as (114.13±16.57 mmHg vs 93.83±8.10 mmHg; $p=0.001$), at 30 minutes (108.60±15.11 mmHg vs 93.64±8.40 mmHg; $p=0.033$). Significant rise in heart rate was noted following pneumoperitoneum in Group P as compared to Group C (99.23±14.02 vs 81.26±8.40 bpm). Similar findings were noted for SBP and DBP. When we compare the results of the study, similar significant rise in MAP was noted in group P at T5 (111.41±2.59 mmHg vs. 83.72±5.52 mmHg) and T6 (115.67±3.99 mmHg vs 84.88±6.26 mmHg). Increase in heart rate during pneumoperitoneum was significantly more in placebo group T5 (124.74±11.30/min. vs 74.08±4.60/min.), T6(128.49±9.19/min. vs 76.84±5.30/min.). Same was the increase in SBP and DBP in this study in group P when compared to group C.

In another study, Shivinder Singh et al.[7] (2011) found that there was significant rise in MAP in placebo group as compared to Clonidine group (Clonidine 150 mcg) at T2 (1 min. after laryngoscopy; 114.8±14.08 mmHg vs 101.92±10.45; $p<0.001$), at T3 (5 minutes after laryngoscopy; 96.99±6.37 mmHg vs 87.61±8.36; $p<0.001$), T6 (at 15 minutes after PNO; 107.65±8.37 mmHg vs 100.75±6.59; $p=0.002$), T7 (at 30 minutes after PNO; 106.16±7.76 mmHg vs 97.17±6.19; $p=0.001$). These results were comparable with the present study that is at T3 (3 min. after laryngoscopy; 115.29±4.59 mmHg vs. 89.35±4.29; $p<0.001$), T5 (at 15 minutes after pneumoperitoneum; 111.41±2.59 mmHg vs 83.72±5.52; $p=0.002$), T6 (at 30 minutes after pneumoperitoneum; 115.67±3.99 mmHg vs. 84.88±6.26; $p<0.001$).

The study is also comparable with study of Mrinmoy Das et al[6.] (2007), who used 150μg of oral Clonidine as premedication in laparoscopic cholecystectomy and observed very less incidence of postoperative shivering.

Attenuation of sympathetic response to laryngoscopy and intubation was observed by Pouttu et al.[8] Clonidine showed a better to attenuate rise in systolic blood pressure comparing it to placebo ($p<0.001$). The aforementioned finding of the study is in agreement with the finding of our study. Here, we found that the mean SBP was 115.69±5.42 mmHg in Clonidine group which was quite less than the mean SBP of 143.21±4.98 mmHg in placebo group at after 3 mins. of laryngoscopy and intubation.

Eva Oddby Muhrbeck et al.[9] (2002) Used 2 mcg/kg of Clonidine intravenously in breast cancer surgery and observed significant reduction in the incidence of nausea and vomiting when compared to control group.

Yuesh Passi et al.[10] (2009) used 150 mcg of oral Clonidine in laparoscopic cholecystectomy and observed less incidence of nausea and vomiting in study group.

The incidence of postoperative shivering was 9.33% in placebo group and none in Clonidine group. There was significantly less incidences of shivering in Clonidine group. This result is in agreement with the findings of Nicolaou et al[11] (1997) where they opined that Clonidine inhibits cold thermoregulatory response due to an effect on central integration control and output from the thermoregulatory centre.

Limitations of our study: This study was done in a small group of 75 patients in each of the groups, all patients belonging to ASA 1 and 2. Most patients were in the young group. Patients with comorbidities like hypertension and diabetes, etc. were all excluded from the study. Hence the advantage of using Clonidine in patients having comorbid diseases could not be appreciated.

SUMMARY: Laparoscopic surgeries have been reported to be associated with intraoperative haemodynamic instability and laparoscopic cholecystectomy is no exception. These adverse haemodynamic changes are mainly caused by pneumoperitoneum by carbon dioxide insufflations as well as due to stress response following laryngoscopy and endotracheal intubation. Alpha-2 receptor agonist Clonidine has been reported to have suppressed these adverse changes in various studies.

All patients received Tab. Alprazolam 0.5 mg orally night before surgery. Preoperative baseline parameters were recorded. Intravenous line was secured with 18G IV cannula and 500 mL crystalloid Ringers Lactate infusion was started. Patients received either Tab. Ranitidine or Tab. Clonidine according to the group they were allotted to, 90 minutes prior to surgery. Level of sedation was assessed before induction by Ramsay sedation scale. They were induced and intubated with appropriate endotracheal tube and maintained on oxygen, nitrous oxide and isoflurane. Systolic blood pressure, Diastolic blood pressure, Mean arterial pressure, Heart rate were recorded at regular predetermined intervals. Any intra-operative or postoperative complications were noted and were managed accordingly.

With the present study, we summarise that oral premedication with Tab. Clonidine 150 mcg administered 90 minutes before surgery was able to prevent adverse haemodynamic changes during elective laparoscopic cholecystectomy under general anaesthesia.

CONCLUSION: From this study, we observed that oral premedication with 150 mcg of Tab. Clonidine 90 minutes before undergoing laparoscopic cholecystectomy had been

found to provide a stable intra-operative haemodynamics especially during the stress response triggered by pneumoperitoneum and also during laryngoscopy and endotracheal intubation in patients. The changes in heart rate were well controlled during pneumoperitoneum, but we should be watchful for bradycardia. Mean arterial blood pressure is well preserved with Clonidine as it provides more haemodynamic stability. So were the changes in systolic blood pressure as well as diastolic blood pressure which were maintained within normal limits. Patients were sedated and less anxious during the preoperative period, thus, maintaining stable haemodynamic parameters. Oral premedication with Tab. Clonidine 150 mcg also provides an added advantage of reducing the incidence of postoperative complications such as nausea, vomiting and shivering.

Hence, from the findings of this study, we can reasonably recommend oral premedication with Tab. Clonidine 150 mcg in otherwise healthy patients undergoing laparoscopic cholecystectomy.

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