COMPARATIVE EVALUATION OF EFFECT OF ORAL CLONIDINE AND ORAL GABAPENTIN PREMEDICATION ON INTRAOPERATIVE HAEMODYNAMIC CHANGES IN LAPAROSCOPIC CHOLECYSTECTOMY- A PROSPECTIVE, RANDOMIZED, DOUBLE- BLIND, PLACEBO-CONTROLLED STUDY

Ravi Prakash[1], Rajesh Tope[2], Chitra Chatterji[3], Ashish Malik[4]

[1]Senior Resident, Department of Anaesthesiology, Indraprastha Apollo Hospital, New Delhi.
[2]Senior Consultant, Department of Anaesthesiology, Indraprastha Apollo Hospital, New Delhi.
[3]Senior Consultant, Department of Anaesthesiology, Indraprastha Apollo Hospital, New Delhi.
[4]Senior Consultant, Department of Anaesthesiology, Indraprastha Apollo Hospital, New Delhi.

ABSTRACT

BACKGROUND

Laparoscopic surgeries form an essence of today's surgical practice. It has been adapted as standard procedure for cholecystectomy at most centres. Haemodynamic perturbations associated with pneumoperitoneum during laparoscopic cholecystectomy may cause serious health hazard to the patient. The aim of the study is to compare the effect of oral clonidine and gabapentin premedication on intraoperative haemodynamic stability with a placebo.

MATERIALS AND METHODS

A prospective, randomized, double-blind, placebo-controlled study was conducted on 90 patients with ASA physical status I and II aged between 20-60 years undergoing elective laparoscopic cholecystectomy. They were randomly allocated to one of the three groups containing 30 patients each. Group C (n=30) received 150? g clonidine, group G (n=30) received 600 mg gabapentin and group P (n=30) received a multivitamin tablet 2 hrs. prior to the surgical procedure. We then assessed haemodynamics of the patients with parameters HR, SBP, DBP, MAP at different points of time and any postoperative adverse events.

RESULTS

Demographically all the three groups were statistically comparable. Following data interpretation, it was observed that both clonidine and gabapentin group had significantly lower HR and BP changes than placebo group ($P<0.05$) during pneumoperitoneum. The incidence of adverse events was also comparable and not significant between the groups.

CONCLUSION

Clonidine 150 mcg and gabapentin 600 mg are better in maintaining haemodynamic stability than placebo during pneumoperitoneum with minor adverse events which were easily controllable.

KEYWORDS

Laparoscopic Cholecystectomy, Pneumoperitoneum, Haemodynamic Stability Clonidine, Gabapentin, Premedication.

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BACKGROUND

Laparoscopic cholecystectomy (LC) is one the most commonly performed minimally invasive surgery for the removal of gall bladder. German surgeon, Dr. Med Erich Muhe is credited for performing first laparoscopic cholecystectomy on 12 September 1985.[1] Pneumoperitoneum (PNP) an integral component of LC, means creation of space inside abdominal cavity by insufflating it with carbon dioxide. The creation of PNP is associated with sympathetic stimulation causing haemodynamic perturbations such as wide swings in blood pressure and heart rate. These changes may prove to be detrimental in patients with limited cardiac reserve.

Premedication refers to the drug treatment given to a patient before a surgical or invasive medical procedure. A wide variety of drugs have been used to prevent this stimulation such as alpha-2 agonist, beta blockers, vasodilators, opioids, anticonvulsants gabapentin, pregabalin and benzodiazepines etc.

Clonidine is an alpha-2 agonist. It has central sympatholytic effect with a half-life ($t_{½}$) of 9-12 hours.[2] Clonidine premedication prevents the stress response to surgical stimuli. It also increases cardiac baroreceptor reflex

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Corresponding Author:
Dr. Ravi Prakash,
Village and Post, Jawa District,
Rewa- 486223, Madhya Pradesh.
E-mail: dr.ravi0610@gmail.com
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sensitivity to increased blood pressure and thus stabilizes B.P.[3] Clonidine may lower HR due to reduction of presynaptic noradrenaline release or a direct vagomimetic action.[4] The adverse effects associated with the use of clonidine include rebound hypertension[5] hypotension, bradycardia[6] sedation, headache, dryness of mouth[7] dizziness.

Gabapentin is an anticonvulsant used in the treatment of seizures, chronic pain syndromes and neuropathic pain. The $\alpha_2\delta$ subunit of the voltage-dependent calcium channel is a binding site for gabapentin.[8] The elimination half-life of gabapentin is between 4.8 and 8.7 hrs.[9] The most frequent side effects reported with use of gabapentin are somnolence, headache dizziness, ataxia, fatigue, unsteadiness, nystagmus and tremors.

The present study was conducted to compare the effect of oral clonidine and gabapentin premedication on intraoperative haemodynamic stability with a placebo.

MATERIALS AND METHODS

This prospective, randomized, double-blind study was conducted in the Department of Anaesthesiology at Indraprastha Apollo Hospital, New Delhi over a period of one year. After obtaining approval from Institutional Ethical Committee 90 patients were enrolled in the study undergoing laparoscopic cholecystectomy. Then following thorough preanaesthetic check-up well informed written consent was taken from the patients.

The inclusion criteria were patients with ASA Grade 1 and 2, between age of 20 to 60 yrs. either sex, elective cases undergoing LC for cholelithiasis. The exclusion criteria were patient's refusal, ASA Grade 2 patients with hypertension, planned other concomitant surgery, patients with alcohol abuse, pregnant women, obese patients with BMI >35.0 kg/m^2, patients concomitantly using MAO-Inhibitors, tricyclic antidepressants or opioids.

Patients were randomly allocated between the three groups of 30 each-

- Group C: Patients in this group received 150 µg of clonidine 2 hrs prior to surgery
- Group G: Patients in this group received 600 mg of gabapentin 2 hrs prior to surgery
- Group P: Patients in this group received placebo multivitamin tablets 2 hrs prior to surgery.

After overnight fasting, patients were given premedicant drug 2 hours prior to surgery. Patients were transferred to preoperative holding area 30 min prior to start of surgery, where their HR, SBP, DBP and MAP were recorded. After transferring the patient to operation theatre monitors including ECG, pulse oximeter, and non-invasive B.P. cuff were attached and an 18/20 G intravenous catheter was secured for administering intravenous fluid and drugs. Again, vital parameters HR, SBP, DBP, MAP were noted.

Following pre-oxygenation with 100% oxygen for 3 min, anaesthesia was induced with a standard anaesthetic protocol using fentanyl 2 µg/kg, propofol 2-3 mg/kg and tracheal intubation with appropriate sized cuffed endotracheal tube was facilitated by atracurium 0.5 mg/kg. Inj. ondansetron 4 mg I.V. was given after induction. Lungs were mechanically ventilated (using either Volume controlled ventilation or Pressure controlled ventilation) with FiO_2 of approximately 0.35 and anaesthesia was maintained with sevoflurane MAC 1.0 -1.3 and atracurium 0.1 mg/kg.

Minute ventilation was adjusted to maintain normocapnia (end-tidal carbon dioxide (EtCO2) 30-40 mmHg) throughout the operation. The respiratory rate was increased to maintain normocapnia during pneumoperitoneum. All patients received antibiotic prophylaxis with cefuroxime 1.5 g I.V. prior to surgical incision and paracetamol 1% 1 gm infusion and diclofenac 1.5 mg/kg for pain.

PNP was created by insufflation of CO_2 and the patient was in supine position with 15° left lateral tilt and 30^o head elevation (Reverse Trendelenburg position). Intra-abdominal pressure was not allowed to exceed 14 mmHg.

Intraoperatively HR, SBP, DBP, MAP were recorded at following points of time: prior to induction, 3 minutes after intubation, before PNP, 5, 10, 15, 20, 25, 30 minutes after PNP, 5 minutes after the release of CO_2 and 5 minutes after extubation. In case of acute and severe haemodynamic fluctuations, following medical interventions were instituted: for bradycardia (HR <50 beats/min), bolus dose of atropine 0.3 mg; for hypotension (MAP <60 mm Hg) increased rate of infusion of I.V. fluid and/or bolus dose of ephedrine 6 mg; for hypertension (MAP >110 mm Hg), bolus dose of metoprolol 1 mg or labetalol 5 mg. At the end of surgery, residual neuromuscular block was reversed by using neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg intravenously and patients were extubated when respiration was sufficient, and were awake to be able to follow commands. Postoperatively patients were transferred to the post anaesthesia care unit (PACU) for observation.

The quantitative variables in all the groups are expressed as Mean ± SD and compared using unpaired t-test between groups and paired t-test within each group at various follow-ups. A p-value <0.05 was considered statistically significant. Statistical Package for Social sciences (SPSS) version 16.0 was used for statistical analysis.

RESULTS

The demographic characteristics of the patient were comparable in all the three groups (Table 1).

Demographic Profile	Group C	Group G	Group P	Significance
Number (n)	30	30	30	NS
Age (mean ± SD) in years	44.30 ± 10.43	44.20 ± 9.73	45.47 ± 9.28	NS
Sex (M:F)	14:16	14:16	13:17	NS
BMI (kg/m^2)	25.03 ± 1.13	25.19 ± 1.16	25.03 ± 1.78	NS

Table 1. Demographic Profile

NS- Not significant.

The mean HR varied from 68.50 ± 7.87 to 77.80 ± 3.42 beats/min in group C; from 74.10 ± 7.95 to 84.10 ± 3.42 beats/min in group P and from 71.87 ± 4.62 to 80 ± 4.01 beats/min in group G, without any statistical difference between the groups in baseline values. In groups C and G statistically, significant difference was noted compared to baseline and group P values. During the period of PNP, mean HR was significantly lower in groups C and G than group P till 15 minutes of PNP. Thereafter the difference between mean HR in group G and group P became insignificant, whereas the group C continued to have significantly lower (all p values <0.05) mean HR than groups P and G till 5 minutes after extubation. (Table 2; Figure 1)

Heart Rate	C		P	G			p-values		
	Mean ± SD	p-value vs BSLN	Mean ± SD	p-value vs BSLN	Mean ± SD	p-value vs BSLN	C vs. P	C vs. G	P vs. G
Baseline value	76.37 ± 2.74	-	76.60 ± 3.7	-	75.87 ± 2	-	0.782	0.422	0.343
Preop holding area	72.57 ± 2.4	<0.001	77.47 ± 3.6	0.149	72.67 ± 2.37	<0.001	<0.001	0.872	<0.001
Prior to induction	74.67 ± 2.34	0.001	78.90 ± 3.25	<0.001	73.57 ± 2.5	<0.001	<0.001	0.084	<0.001
3 min after intubation	77.80 ± 3.42	0.047	84.10 ± 5.29	<0.001	77.97 ± 3.01	0.002	<0.001	0.842	<0.001
Before PNP	70.97 ± 5.79	<0.001	75.17 ± 6.55	0.340	72.27 ± 4.73	<0.001	0.011	0.345	0.054
5 min after PNP	70.83 ± 8.16	<0.001	74.70 ± 6.15	0.187	71.87 ± 4.62	<0.001	0.043	0.548	0.048
10 min after PNP	70.83 ± 8.63	0.001	76.77 ± 5	0.886	72.33 ± 5.43	0.004	0.002	0.424	0.002
15 min after PNP	69.50 ± 8.62	<0.001	74.93 ± 5.67	0.225	73.70 ± 5.2	0.030	0.005	0.026	0.383
20 min after PNP	69.00 ± 9.62	<0.001	74.33 ± 7.48	0.150	74.63 ± 5.77	0.262	0.020	0.008	0.862
25 min after PNP	68.50 ± 7.87	<0.001	74.10 ± 7.95	0.135	74.00 ± 5.74	0.120	0.008	0.003	0.956
30 min after PNP	69.30 ± 8.11	<0.001	74.13 ± 5.87	0.070	73.73 ± 6.08	0.089	0.011	0.020	0.796
5 min after release of CO2	70.50 ± 6.9	<0.001	74.80 ± 5.14	0.144	73.90 ± 4.74	0.051	0.008	0.030	0.484
5 min after extubation	76.90 ± 4.53	0.579	81.07 ± 6.26	<0.001	80.00 ± 4.01	<0.001	0.005	0.007	0.435

Table 2. Comparison of Mean Heart Rate between the Groups

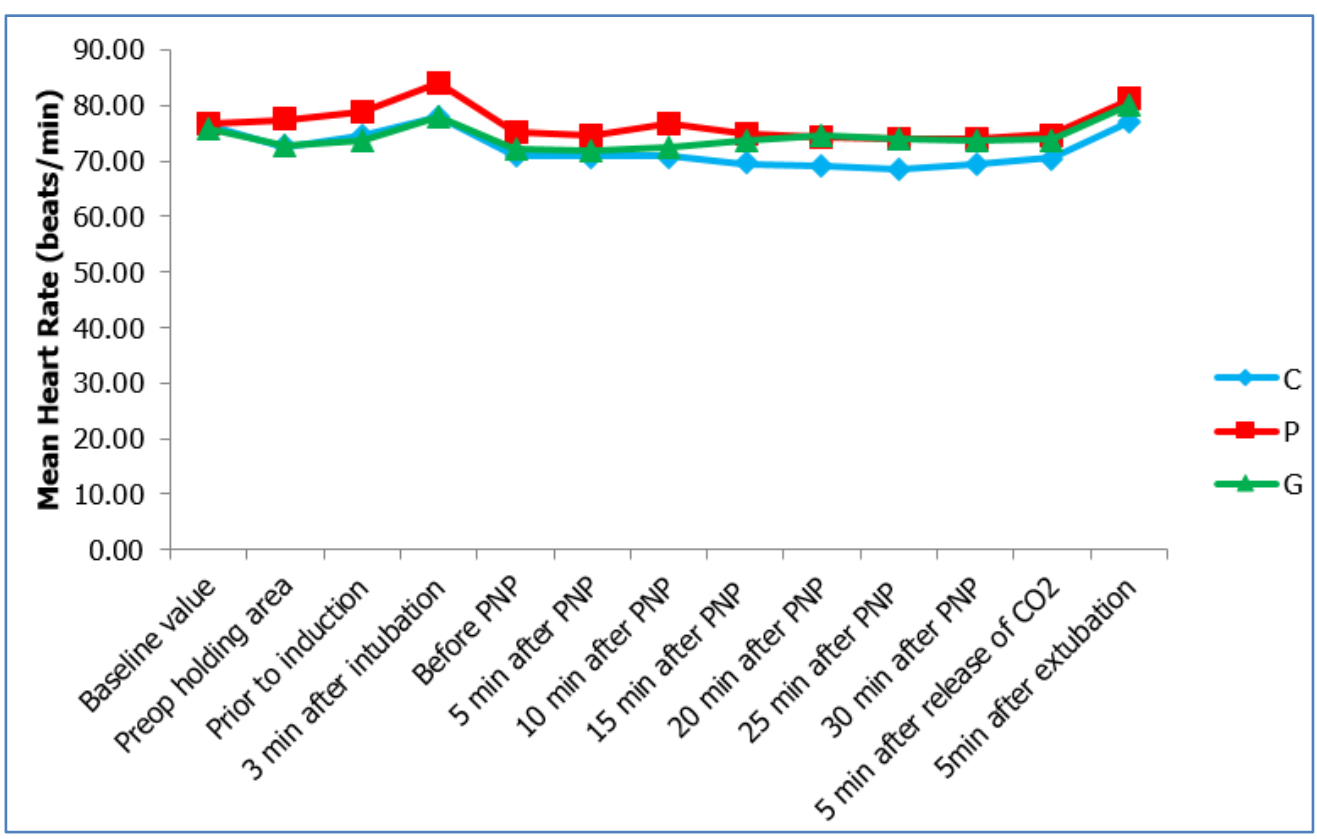

Figure 1. Comparison of Mean Heart Rate between the Groups

The mean SBP varied from 102.53 ± 7.49 to 122.27 ± 8.72 mmHg in group C; from 113.30 ± 11.38 to 139.70 ± 11.76 mmHg in group P and from 109.67 ± 7.11 to 123.6 ± 2.61 mmHg in group G without any statistically significant (p value <0.05) difference between the groups in baseline values. The change in SBP within the group at different points of time compared to baseline was statistically significant in groups C and P but not in group G. The mean SBP in placebo and gabapentin group were significantly higher in comparison to clonidine, p<0.05. (Table 3; Figure 2)

BP (Systolic)	C		P		G		p-values		
	Mean ± SD	p-value vs. BSLN	Mean ± SD	p-value vs. BSLN	Mean ± SD	p-value vs. BSLN	C vs. P	C vs. G	P vs. G
Baseline value	119.40 ± 7.95	-	121.40 ± 6.69	-	119.00 ± 4.35	-	0.296	0.810	0.105
Preop holding area	111.03 ± 6.24	<0.001	124.80 ± 4.66	0.006	115.70 ± 4.75	0.002	<0.001	0.002	<0.001
Prior to induction	120.67 ± 7.6	0.425	125.30 ± 5.87	<0.001	118.07 ± 3.93	0.359	0.011	0.102	<0.001
3 min-post intubation	117.07 ± 10.44	0.213	129.50 ± 9.05	<0.001	119.30 ± 5.88	0.802	<0.001	0.311	<0.001
Before PNP	102.53 ± 7.49	<0.001	113.30 ± 11.38	<0.001	109.67 ± 7.11	<0.001	<0.001	<0.001	0.144
5 min after PNP	107.17 ± 14.67	<0.001	125.53 ± 7.53	0.006	116.17 ± 7.84	0.029	<0.001	0.004	<0.001
10 min after PNP	109.23 ± 13.44	<0.001	135.53 ± 11.33	<0.001	118.47 ± 8.33	0.700	<0.001	0.002	<0.001
15 min after PNP	110.57 ± 13.94	0.001	139.70 ± 11.76	<0.001	118.60 ± 8.41	0.781	<0.001	0.009	<0.001
20 min after PNP	109.37 ± 11.16	<0.001	137.43 ± 11.54	<0.001	116.47 ± 6.06	0.024	<0.001	0.003	<0.001
25 min after PNP	108.10 ± 11.71	<0.001	137.30 ± 11.82	<0.001	115.40 ± 5.86	0.001	<0.001	0.003	<0.001
30 min after PNP	108.10 ± 10.62	<0.001	131.30 ± 8.17	<0.001	114.67 ± 5	<0.001	<0.001	0.003	<0.001
5 min after release of CO2	110.57 ± 8.78	<0.001	126.40 ± 3.49	<0.001	117.83 ± 5.58	0.253	<0.001	<0.001	<0.001
5 min after extubation	122.27 ± 8.72	0.167	133.83 ± 4.56	<0.001	123.60 ± 2.61	<0.001	<0.001	0.425	<0.001

Table 3. Comparison of Mean Systolic Blood Pressure between the Groups

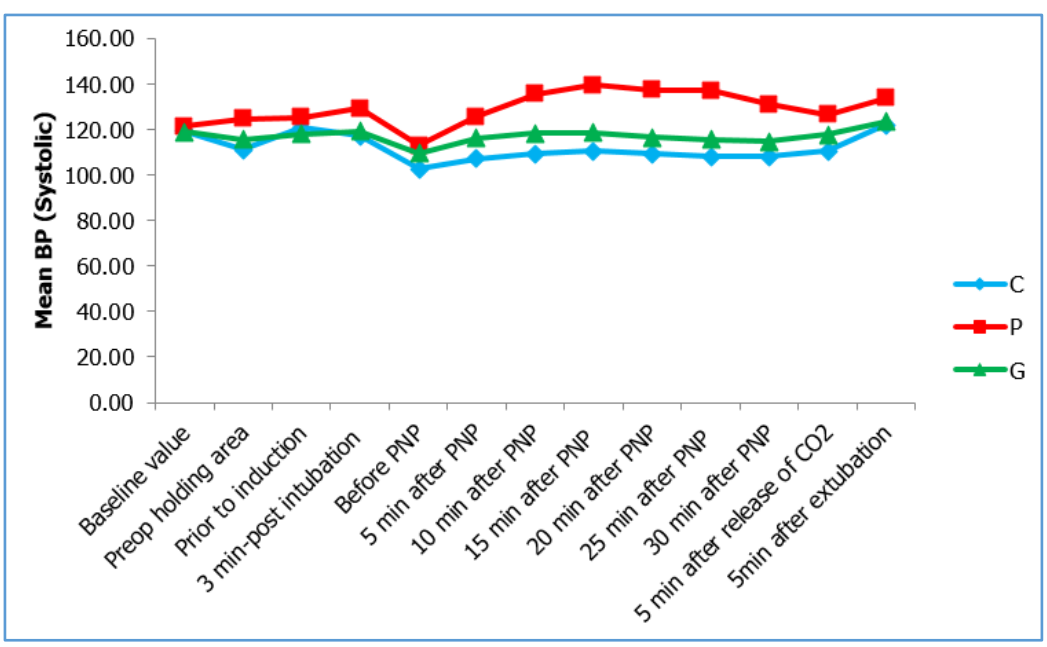

Figure 2. Comparison of Mean Systolic Blood Pressure between the Groups

The mean DBP varied from 62.77 ± 8.82 to 78.60 ± 5.9 mmHg in group C; from 71.40 ± 9.45 to 89.63 ± 13.48 mmHg in group P and from 66.57 ± 7.64 to 81.23 ± 5.69 mmHg in group G, without any statistical difference between the groups in baseline values. During the entire period of PNP and till 5 min after extubation, the mean DBP remained significantly low (p value <0.001) in group C than in groups G and P. Similarly, in between the groups G and P, group G had significantly lower (p value <0.001) mean DBP than in group P (Table- 4; Figure- 3).

BP (Diastolic)	C		P		G		p-values		
	Mean± SD	p-value vs. BSLN	Mean ± SD	p-value vs. BSLN	Mean ± SD	p-value vs. BSLN	C vs. P	C vs. G	P vs. G
Baseline value	78.60 ± 5.9	-	79.13 ± 5.58	-	79.07 ± 4.72	-	0.720	0.736	0.960
Preop holding area	70.97 ± 7.54	<0.001	79.70 ± 4.29	0.656	75.00 ± 7.71	0.016	<0.001	0.045	0.005
Prior to induction	74.87 ± 6.5	0.008	81.47 ± 5.91	0.106	75.10 ± 5.14	0.004	<0.001	0.878	<0.001
3 min-post intubation	71.73 ± 8.63	<0.001	82.07 ± 8.26	0.071	75.33 ± 6.27	0.013	<0.001	0.070	<0.001
Before PNP	62.77 ± 8.82	<0.001	71.40 ± 9.45	<0.001	66.57 ± 7.64	<0.001	<0.001	0.080	0.033
5 min after PNP	63.67 ± 10.02	<0.001	81.83 ± 6.82	0.108	72.23 ± 7.36	<0.001	<0.001	<0.001	<0.001
10 min after PNP	65.87 ± 8.89	<0.001	88.30 ± 10.4	<0.001	72.27 ± 7.92	<0.001	<0.001	0.005	<0.001
15 min after PNP	66.93 ± 11.08	<0.001	88.80 ± 11.93	<0.001	73.17 ± 9.62	0.002	<0.001	0.023	<0.001
20 min after PNP	65.80 ± 9.76	<0.001	87.83 ± 14.12	0.004	71.73 ± 8.09	<0.001	<0.001	0.013	<0.001
25 min after PNP	65.03 ± 8.59	<0.001	89.63 ± 13.48	<0.001	71.57 ± 7.41	<0.001	<0.001	0.003	<0.001
30 min after PNP	65.00 ± 7.81	<0.001	85.60 ± 9.87	0.004	72.10 ± 7.03	<0.001	<0.001	<0.001	<0.001
5 min after release of CO2	66.60 ± 6.93	<0.001	82.67 ± 8.5	0.057	75.23 ± 6.84	0.006	<0.001	<0.001	<0.001
5 min after extubation	74.30 ± 7.28	0.030	86.97 ± 6.88	<0.001	81.23 ± 5.69	0.056	<0.001	<0.001	<0.001

Table 4. Comparison of mean Diastolic Blood Pressure between the Groups

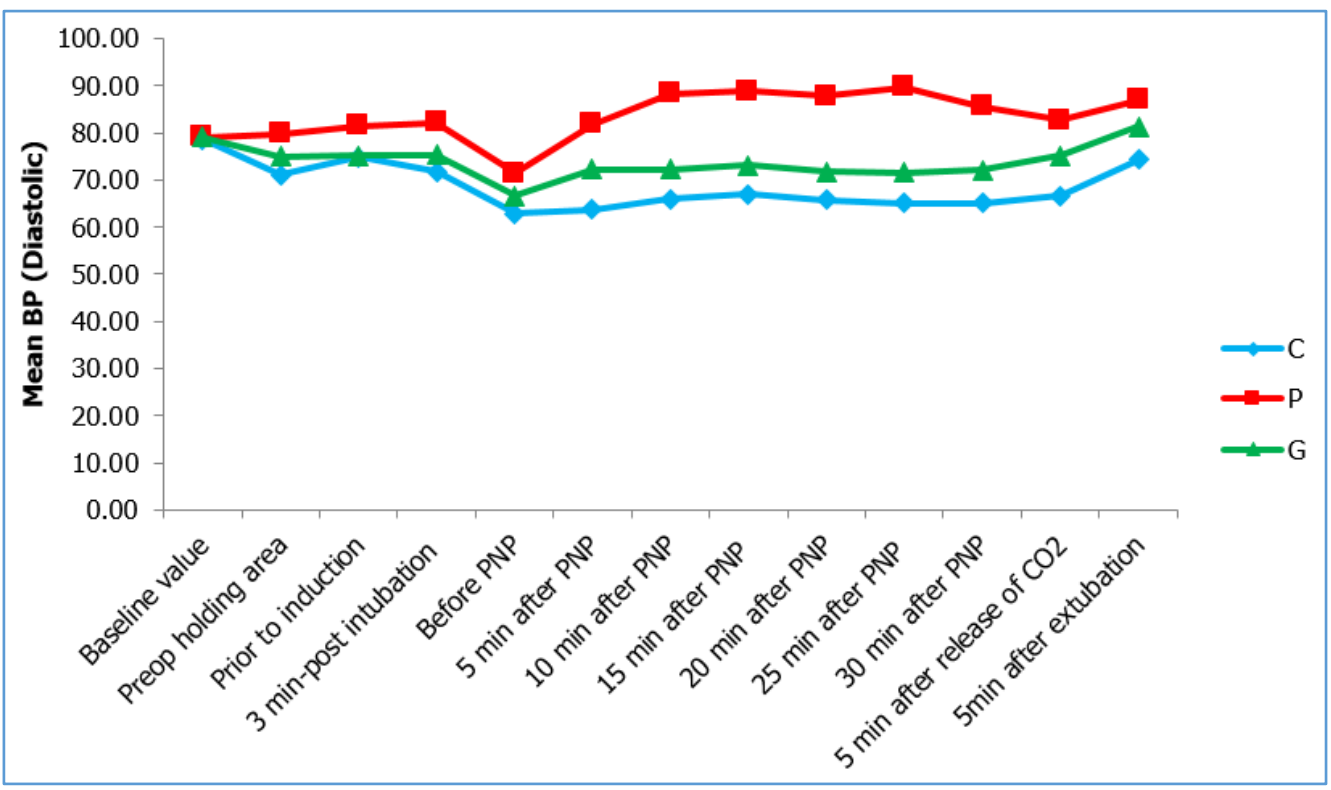

Figure 3. Comparison of Mean Diastolic Blood Pressure between the Groups

The mean MAP varied from 77.30 ± 7.88 to 92.70 ± 6.13 mmHg in group C; from 86.90 ± 9.72 to 105.33 ± 10.84 mmHg in group P and from 82.07 ± 7.41 to 95.73 ± 3.86 mmHg in group G, without any statistical difference between the groups in baseline values. During the entire period of PNP and till 5 min after extubation, the mean MAP remained significantly low (p value <0.001) in group C than in groups G and P. Similarly, in between the groups G and P, group G had significantly lower (p value <0.001) mean MAP than in group P (Table-5; Figure 4).

Mean Arterial Pressure	C		P		G		p-values		
	Mean ± SD	p-value vs BSLN	Mean ± SD	p-value vs BSLN	Mean ± SD	p-value vs BSLN	C vs. P	C vs. G	P vs. G
Baseline value	92.70 ± 6.13	-	93.73 ± 5.48	-	92.87 ± 4.4	-	0.494	0.904	0.502
Preop holding area	84.90 ± 6.45	<0.001	95.20 ± 3.9	0.211	88.43 ± 5.98	0.001	<0.001	0.032	<0.001
Prior to induction	91.57 ± 5.93	0.276	96.43 ± 5.6	0.024	90.33 ± 4.54	0.021	0.002	0.370	<0.001
3 min after intubation	87.63 ± 8.53	<0.001	98.33 ± 8.56	0.007	91.10 ± 5.56	0.128	<0.001	0.067	<0.001
Before PNP	77.30 ± 7.88	<0.001	86.90 ± 9.72	<0.001	82.07 ± 7.41	<0.001	<0.001	0.019	0.034
5 min after PNP	79.43 ± 10.91	<0.001	96.73 ± 6.17	0.026	87.70 ± 7.32	<0.001	<0.001	0.001	<0.001
10 min after PNP	81.83 ± 9.66	<0.001	104.80 ± 10.07	<0.001	88.93 ± 7.39	0.005	<0.001	0.002	<0.001
15 min after PNP	83.23 ± 11.55	<0.001	105.17 ± 11.56	<0.001	89.30 ± 8.34	0.025	<0.001	0.023	<0.001
20 min after PNP	81.47 ± 9.42	<0.001	104.67 ± 12.04	<0.001	87.80 ± 6.6	<0.001	<0.001	0.004	<0.001
25 min after PNP	80.97 ± 9.31	<0.001	105.33 ± 10.84	<0.001	87.30 ± 6.09	<0.001	<0.001	0.003	<0.001
30 min after PNP	80.70 ± 8.2	<0.001	101.53 ± 8.51	<0.001	87.17 ± 6.02	<0.001	<0.001	<0.001	<0.001
5 min after release of CO2	82.33 ± 7.74	<0.001	98.07 ± 6.75	0.012	90.33 ± 6.17	0.016	<0.001	<0.001	<0.001
5min after extubation	90.40 ± 6.8	0.173	101.77 ± 6.17	<0.001	95.73 ± 3.86	0.004	<0.001	<0.001	<0.001

Table 5. Comparison of Mean Arterial Pressure between the Groups

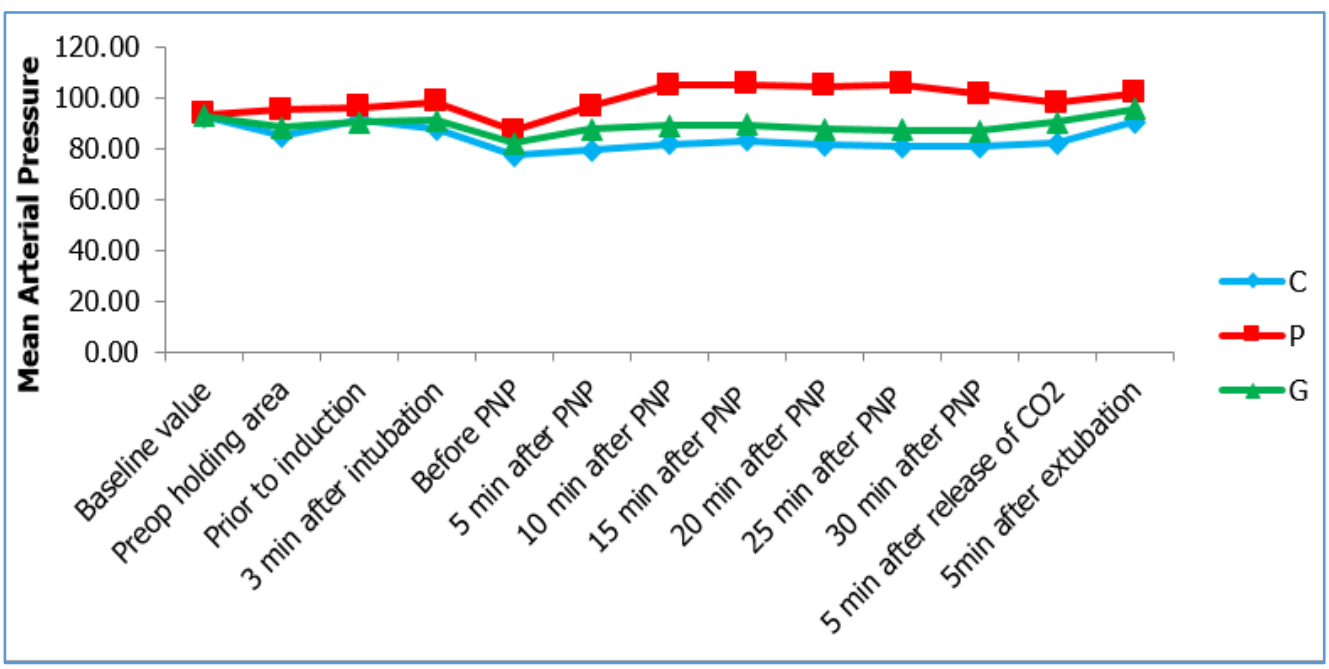

Figure 4. Comparison of Mean Arterial Pressure between the Groups

The incidence of nausea was more in group P (13.33%) as compared to group C (6.67%) and group G (3.33%). Vomiting was seen in 1 case (3.33%) in group P. The dryness of mouth (10%) and bradycardia (10%) was seen in group C. The incidence of dizziness was 6.67% in both groups C and G and 3.33% in group P.

There was no statistically significant (p value =0.065) distribution of adverse events among the groups.

Adverse Events	C		P		G	
	n	%	n	%	n	%
None	20	66.67%	24	80.00%	27	90.00%
Nausea	2	6.67%	4	13.33%	1	3.33%
Vomiting	0	0.00%	1	3.33%	0	0.00%
Dizziness	2	6.67%	1	3.33%	2	6.67%
Dryness of mouth	3	10.00%	0	0.00%	0	0.00%
Bradycardia	3	10.00%	0	0.00%	0	0.00%
Total	**30**	**100%**	**30**	**100%**	**30**	**100%**

Table 6. Comparison of distribution of adverse events between the groups

DISCUSSION

The pneumoperitoneum created during laparoscopic cholecystectomy produces significant stress response in the form of haemodynamic changes, which can be prejudicial to elderly and patient with poor cardiac continence. These haemodynamic alterations were first recognized in 1947 by Booker et al.[10] The rapid and immediate increase in plasma catecholamines and vasopressin[11] was noted following CO_2 insufflation conceivably due to an increase in intraperitoneal pressure and peritoneum stimulation by CO_2[12] Joris et al[13] found a 35% increase in mean arterial pressure, a 65% increase in systemic vascular resistance, and a 90% increase in pulmonary vascular resistance, while there was a 20% decrease in cardiac output. The changes in these haemodynamic variables significantly increase the incidence of myocardial ischemia, infarction and other complications.

In this study 150 µg clonidine tablet was administered orally, 2hrs before surgery. Dose of clonidine varied from 2-5 µg/kg in different studies. Mrinmoy Das et al[14] used 150 µg clonidine orally 90 min before induction. Aho et al[15] used 3 µg/kg and 4.5 µg/kg clonidine for suppression of haemodynamic response to pneumoperitoneum. Similarly, gabapentin most recently has been used perioperatively for reducing stress responses in different clinical scenario. Role of Gabapentin in obtunding haemodynamic response has been exhibited by Fassoulaki et al[16], Memis et al[17] Mausumi Neogi et al[18] used oral gabapentin 900 mg 2h before induction of anaesthesia and showed that gabapentin premedication provided perioperative haemodynamic stability during laparoscopic surgery.

We evaluated and compared oral clonidine and gabapentin in abolishing the haemodynamic response to pneumoperitoneum. In our study, clonidine or gabapentin was given 2 hours before scheduled laparoscopic cholecystectomy.

In preoperative holding area, patients who received clonidine (Group C) or gabapentin (Group G) had significant decrease (p value <0.001) in HR and BP as compared to baseline values. These patients also had significantly lower HR and BP than placebo (Group P). There was statistically no significant difference between patients receiving clonidine or gabapentin. These effects may be due to antihypertensive and antianxiety[19,20] effects of clonidine. Gabapentin provides preoperative anxiolysis, prevent chronic postsurgical pain, attenuate stress responses to noxious perioperative stimuli and prevent postoperative delirium, nausea and vomiting.[21]

Laryngoscopic stimulation of oropharyngeal structures may be an important factor in haemodynamic stress response associated with tracheal intubation.[22] Following laryngoscopy and endotracheal intubation slight increase in heart rate was observed in groups C and G than their baseline values. But this increase is statistically insignificant between the groups C and G. However, in group P the rise in HR following intubation was highly significant (p value <0.001). The systolic, diastolic and mean arterial pressure remained fairly low in groups that received clonidine and gabapentin premedication as compared to placebo group. These findings complement the result of studies of Kumkum Gupta et al,[23] Suzan M Faheim et al[24] and Ali AR et al.[25]

Following pneumoperitoneum with carbondioxide, patients were hyperventilated to maintain normocapnia. The intraabdominal pressure (IAP) was maintained below 14 mmHg. During the period of pneumoperitoneum, the heart rate values remained significantly low compared to baseline value in group C. Moreover, the mean heart rate was lower in group C compared to groups G and P throughout the procedure and it was statistically significant as was shown by Rashmi Patil et al.[26] and HP Yu et al.[27] in their studies. In patient receiving gabapentin and placebo the HR during PNP did not changed significantly as compared to their baseline values.

Inspite of maintaining normocapnia and keeping intraabdominal pressure below 14 mmHg significant rise in systolic, diastolic and mean arterial pressure was noticed in Group P. Patients who received clonidine or gabapentin had significantly reduced systolic, diastolic and mean arterial pressure as compared to placebo. Moreover, the patients receiving clonidine premedication maintained lower systolic, diastolic and mean arterial pressure than gabapentin group for the entire duration of pneumoperitoneum. This was in concordance with the study of Shrestha BR et al,[28] which showed that oral premedication with 600 mg of gabapentin or clonidine 150 µg an hour prior to routine laparoscopic cholecystectomy offers stable haemodynamic profile.

The adverse events like bradycardia (10%) and dryness of mouth (10%) in the postoperative period were more in patient who received clonidine as compared to gabapentin or placebo group, but these were minor and easily controllable. About 16.67% patients who received placebo had PONV (postoperative nausea vomiting) while only 6.67% patient who received clonidine had PONV and 3.33% patients who received gabapentin had such episode. These observations were found consistent with studies of Rita Singh et al,[29] Mrinmoy Das et al.[14] When the adverse effects nausea, vomiting, dizziness, dryness of mouth, bradycardia put together there was no significant difference in between the groups. No incidence of hypotension or hypertension was seen in any of the group in the recovery room.

There are Few Limitations of this Study

1. This was a single centre study. A multicentre larger study may be more informative.
2. The power of study can be increased by increasing the sample size.
3. There was no measurement of stress mediators, i.e. endogenous plasma catecholamines or cortisol values perioperatively.
4. Elderly and poor cardiac reserve patients where it would be useful were not studied due to ethical reasons.

CONCLUSION

We conclude that during routine laparoscopic cholecystectomy both clonidine and gabapentin are effective premedicants, both being superior to placebo. Oral premedication with 150 µg clonidine is better in controlling

haemodynamic response to pneumoperitoneum than 600 mg gabapentin.

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