
COMPARATIVE EVALUATION OF THREE DIFFERENT DOSES OF INTRAVENOUS CLONIDINE 1mcg/kg, 2mcg/kg, 3mcg/kg FOR HEMODYNAMIC STUDY IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMYSurendra Raikwar¹, Rajni Thakur², Aditya Agarwal³, Radhika Pathak⁴**HOW TO CITE THIS ARTICLE:**

Surendra Raikwar, Rajni Thakur, Aditya Agarwal, Radhika Pathak. "Comparative Evaluation of three different doses of Intravenously Clonidine 1mcg/kg, 2mcg/kg, 3mcg/kg for Hemodynamic study in patients undergoing Laparoscopic Cholecystectomy". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 03, January 20; Page: 530-537, DOI:10.14260/jemds/2014/1861

ABSTRACT: CLONIDINE, an imidazoline derivative and alpha-2 agonist causes sedation, anxiolysis, antisalivation, analgesia and provides hemodynamic stability. The aim of our study was to compare the three different doses of intravenous clonidine 1 microgram per kilogram, 2 microgram per kilogram, 3 microgram per kilogram in patients undergoing laparoscopic surgeries. Forty five patients were grouped equally in Group C1, C2, and C3, who received intravenous clonidine 1 microgram per kilogram, 2 microgram per kilogram and 3 microgram per kilogram respectively. Hemodynamic variables, associated complications and side-effects were recorded. It was found that intravenous clonidine 2 microgram per kilogram is the most appropriate dose for attenuating hemodynamic response to pneumoperitonium without any associated significant side-effects/complications.

KEYWORDS: Laparoscopic Cholecystectomy, Clonidine, Hemodynamic Response.

INTRODUCTION: Laparoscopic Cholecystectomy has revolutionized gall bladder surgeries and has now become "Gold Standard" operation for cholelithiasis. However, this procedure is not risk free, infact it produces hemodynamic changes. A major goal of anaesthesia in these patients is the attenuation of hemodynamic and autonomic functions while preserving mainly circulatory function. Clonidine causes sedation, anxiolysis, antisalivation, analgesia, reduction in dose requirement of anaesthetic agents, provides hemodynamic stability, and reduces tachycardia and hypertensive episodes for smooth anaesthesia.

The aim of our study was to compare the three doses of clonidine for their efficacy in hemodynamic stability for patients undergoing laparoscopic surgeries.

METHOD: After obtaining informed consent from all the patients, Forty five patients of ASA I and II of age 20 to 50 years weighing 50 to 70 kg of either sex were included in our study. These patients were divided equally into 3 Groups, 15 each. Group C1, C2 and C3 received intravenous clonidine 1microgram per kilogram, 2 microgram per kilogram and 3 microgram per kilogram respectively. Patients with significant systemic diseases, those on certain drugs like psychotropic medication, Monoamine Oxidase Inhibitors, Tricyclic antidepressant, alpha-2 adrenergic agonist, methyl dopa and those who were allergic to clonidine were excluded from our study.

All patients were kept nil orally for at least 6 hours prior to starting the procedure. Heart Rate, Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure, Oxygen Saturation and Electrocardiogram were noted. After intravenous cannulation, injection glycopyrollate 0.2

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milligram, Ondansetron 4milligram, ranitidine 50 milligram were given. Particular dose of intravenous clonidine was given 15 min before induction.

General Anaesthesia was induced with intravenous thiopentone 4-6 milligram/kilogram and injection fentanyl 2 microgram/kg for intraoperative analgesia, then endotracheal intubation was facilitated by succinyl choline 1.5 milligram/kilogram, anaesthesia was maintained with 50% Nitrous Oxide + 50% Oxygen, 0.2-1% Halothane and vecuronium loading dose 0.1 milligram/kilogram and maintenance dose 0.01 milligram/kilogram. Intermittent Positive Pressure Ventilation was continued to maintain End tidal Carbon dioxide 35 to 45 mm Hg. Pneumoperitonium was created by Carbon dioxide insufflations and intraabdominal pressure was asked not to be raised beyond 15 mmHg, 15 degree reverse trendelenberg position was given.

Heart Rate and Mean Arterial Pressure was maintained within normal limits by adjusting halothane and intravenously medications.

Expected complications during study and their measures are

1. For Bradycardia (Heart Rate<60 beats per minute) intravenously Atropine 0.6 was administered.
2. Hypotension (Mean arterial blood pressure <20% of baseline values) was managed with fluid and intravenously mephentermine 6 milligram bolus.
3. Hypertension (Mean arterial blood pressure >20% of baseline values) was treated with injection Nitro-glycerine 0.5-5 microgram/kilogram/minute intravenously.

At the end residual neuromuscular blockade was reversed by glycopyrollate 0.01 milligram/kilogram and neostigmine 0.05 milligram/kilogram and extubation done.

Hemodynamic variables were recorded:

- Prior to intravenously clonidine
- 15 mins after intravenously clonidine
- Start of Pneumoperitonium
- 5 min after institution of Carbon dioxide Pneumoperitonium
- 15 min after institution of Carbon dioxide Pneumoperitonium
- 30 min after institution of Carbon dioxide Pneumoperitonium
- 40 min after institution of Carbon dioxide Pneumoperitonium
- Release of Pneumoperitonium
- After extubation

Postoperative Observation: Occurrence of any adverse events like nausea, vomiting and sedation were recorded. Hemodynamic parameters were statistically analyzed using Unpaired T-Test. Nausea and vomiting was analyzed using Chi-square test. A p-value of less than 0.05 was considered significant.

RESULTS: However, in our study we did not observe any major complication/side effects. P-value was found to be insignificant regarding age, sex and weight.

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AGE(YRS)	GROUP C1	GROUP C2	GROUP C3
20-30	8	6	8
31-40	4	4	3
41-50	3	3	4
TOTAL	15	15	15

TABLE NO.1: AGE DISTRIBUTION

SEX	GROUP C1		GROUP C2		GROUP C3	
	N	%	N	%	N	%
Male	8	53	7	46	6	40
Female	7	46	8	53	9	60
Total	15	100	15	100	15	100

TABLE NO. 2: SEX DISTRIBUTION

Weight (in kgs)	GROUP C1		GROUP C2		GROUP C3	
	N	%	N	%	N	%
50-60	6	40	5	33	7	46
61-70	9	60	10	66	8	53
Total	15	100	15	100	15	100

TABLE NO.3: DISTRIBUTION OF CASE ACCORDING TO WEIGHT

Comparison of Heart Rates: C1 had significantly higher heart rate as compared to C2 and C3, C2 had significantly higher heart rate as compared to C3 at start of pneumoperitonium and at all points of observations thereafter. However 15 min later of giving the dose, the difference between C1 and C2, C2 and C3 was found insignificant.

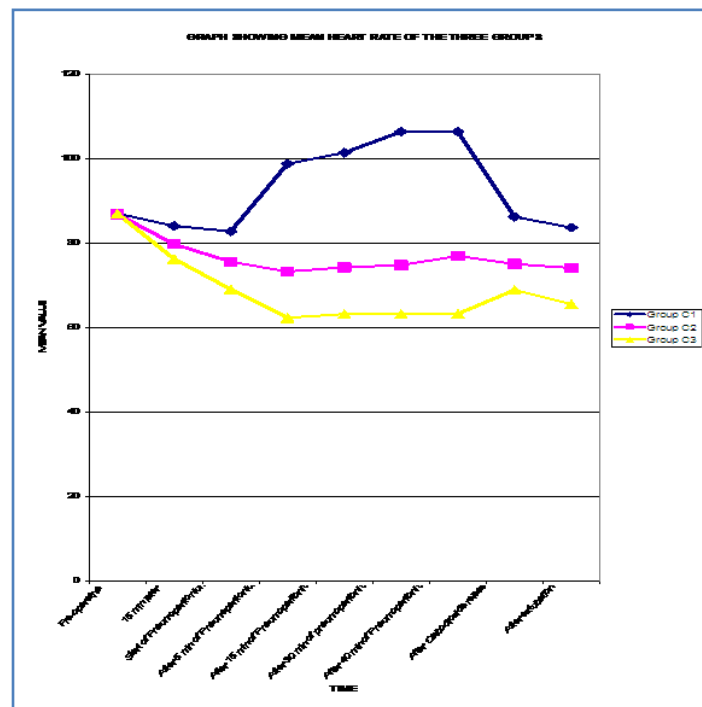


TABLE NO.4: Comparison of Heart Rates

Comparison of Systolic Blood Pressure: C1 had significantly higher SBP as compared to both C2 and C3 at all points of observation except the preoperative values. C2 had significantly higher SBP at all points of observation as compared to C3 from the start to 40 mins of pneumoperitonium. There

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was no significant difference in C2 to C3 15min later of giving the dose, 10 min after release of Carbon dioxide insufflation and 10 min after extubation.

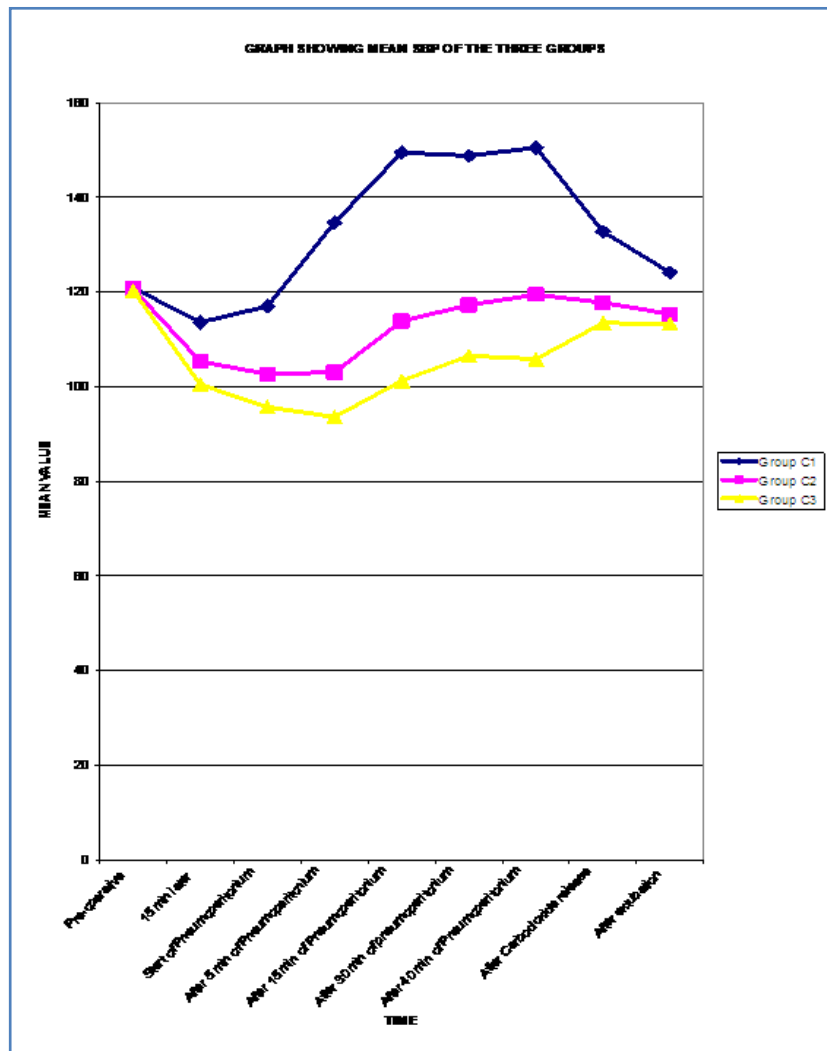


TABLE NO. 5: Comparison of Systolic Blood Pressure

Comparison of Diastolic Blood Pressure: C1 had significantly higher diastolic blood pressure compared to C2 and C3 at all point of observation from start of pneumoperitonium. However 15 min after giving the dose, C1 readings were significant compared to C3 but insignificant to C2. Group C2 had significant observation recorded 15 min after pneumoperitonium however the difference was significant as compared to C3, 15 min later of giving the dose, start of pneumoperitonium and 15 min after start of pneumoperitonium.

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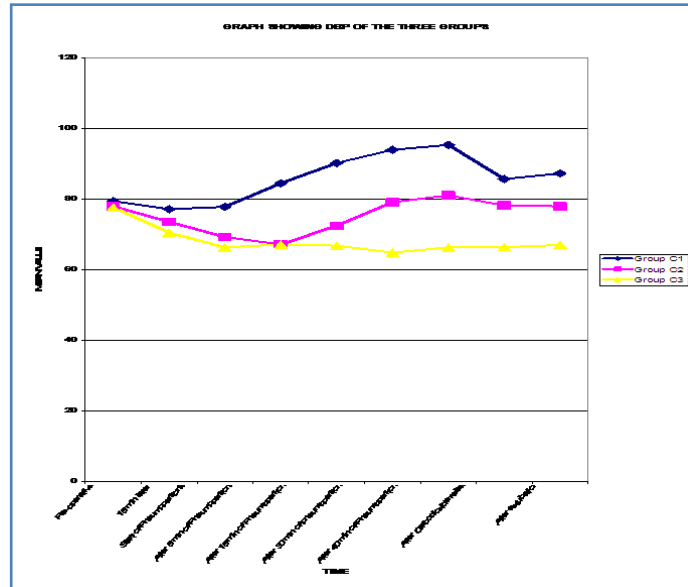


TABLE NO. 6: Comparison of Diastolic Blood Pressure

Comparison of Mean Arterial Pressure: C1 had significantly higher Mean Arterial Pressure than C2 and C3, C2 had significantly higher Mean Arterial Pressure than C3. However the difference was insignificant, 15 min later of giving the dose, and start of pneumoperitonium.

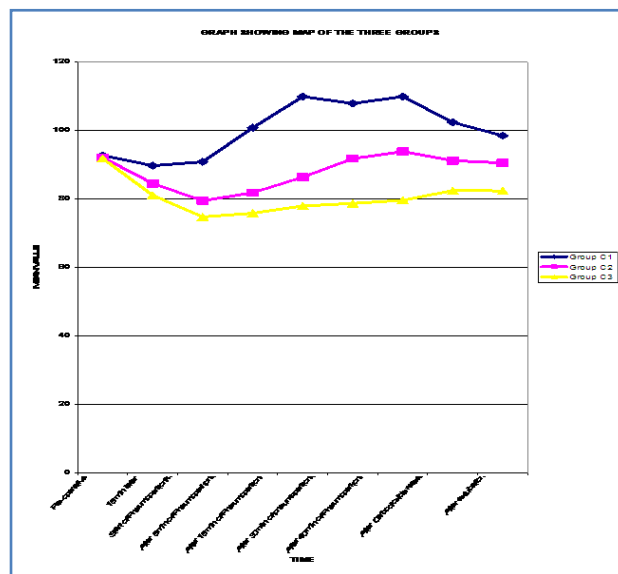


TABLE NO. 7: Comparison of Mean Arterial Pressure

Comparison of incidence of Post-Operative Nausea and Vomiting: Incidence was significantly less in C3. Group C2 had significantly lower incidence compared to C1.

Sedation Score: Higher in group C3 compared to C1 and C2 at all points of observation.

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	s.no.	Group	p-value
Nausea	1	C1 vs. C2	0.90
	2	C2 vs. C3	0.15
	3	C1 vs. C3	0.02
Vomiting	1	C1 vs. C2	0.29
	2	C2 vs. C3	0.31
	3	C1 vs. C3	0.07

Table No. 8: Comparison of Incidence of Post Operative Nausea and Vomiting.

Time	Group	p-value
15 min after extubation	C1	0.53±0.51
	C2	0.93±0.59
	C3	2.20±0.45
30 min after extubation	C1	0.13±0.35
	C2	0.40±0.50
	C3	1.13±0.59
1 Hr after extubation	C1	0
	C2	0.06±0.25
	C3	1.53±0.51
2Hrsafter extubation	C1	0
	C2	0
	C3	0.33±0.48

Table No. 9: Sedation Score

DISCUSSION: In our study mean heart rate, 15 min after giving the dose in group C1 was 84.13 ± 7.06 whereas in Group C2 was 79.2 ± 5.10 . Difference was insignificant between C1 and C2. In group C3 the mean heart rate was 76.33 ± 7.57 which was significantly less as compared to C1 but not C2. The difference was significant between C3 and C2, C3 and C1 and between C2 and C1 throughout pneumoperitonium. Thus the mean heart was highest in Group C1 throughout pneumoperitonium.

Joris et al used 3 microgram per kilogram given intravenously over period of 15 min before induction and 1 microgram per kilogram/min by continuous infusion. Found bradycardia and hypotension in their study.¹

Yu HP, Hseu et al observed that clonidine preserves heart rate control during pneumoperitonium and recovery periods.²

Dyne, Struys assessed effect of intravenous clonidine 3 microgram per kilogram given 15 min before induction and observed statistically significant better perioperative hemodynamic stability.³

The difference in mean systolic blood pressure among the three groups was insignificant. 15 min after giving the dose mean systolic blood pressure of C1 was 113.6 ± 6.94 , C2 and C3 were 105.33 ± 8.61 and 100.47 ± 10.47 respectively. Thus C1 had significantly higher systolic blood pressure than both the other groups. While the difference between C2 and C3 was insignificant. Mean systolic blood pressure of C1 was significantly higher compared to both the groups and C2 was higher than C3 during pneumoperitonium.

D. Tripathi and K. S .Shah observed the systolic blood pressure with 2 microgram per kilogram of clonidine decreased from baseline values within 15 min of giving the dose. This was consistent with our study.⁴

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Ray et al used 3 microgram per kilogram of intravenous clonidine over a period of 15 minutes before induction and 1 microgram per kilogram per minute by continuous infusion intraoperative observed significant incidence of bradycardia and hypotension in their study.⁵

The difference between the mean diastolic blood pressure of group C1 and C2, and the group C2 and C3 was insignificant and C1 and C3 were significant. During the pneumoperitonium the mean diastolic blood pressure of C1 was 77.86 ± 5.15 to 95.40 ± 5.34 , in group C2 it ranged from 67.2 ± 4.45 to 81.13 ± 2.20 whereas in C3 it ranged from 66.40 ± 4.45 . Thus C3 had significantly lower mean diastolic blood pressure compared to C1 during pneumoperitonium.

N K Kalra et al observed that the diastolic blood pressure of the group receiving 1.5 microgram per kilogram of clonidine was significantly lower than the group receiving 1 microgram per kilogram. This was consistent with our study.⁶

Raval DL, Mehta MK observed that 2 microgram per kilogram of clonidine prevented stress response to pneumoperitonium that approaches to baseline values within 20 min of pneumoperitonium.⁷

The Mean arterial pressure of the three groups was comparable preoperatively. 15 min after giving the dose there was fall in mean arterial pressure in all the three groups. Mean arterial pressure of C3 was 81.16 ± 4.93 which was less than C1 having mean arterial pressure of 89.81 ± 5.47 . Group C2 had mean of 84.62 ± 4.87 which was comparable to both the groups. During pneumoperitonium the Mean arterial pressure of C1 was greater than 20% of preoperative values and required Nitro-glycerine infusion for maintenance, whereas C2 and C3 do not required infusion.

Altan and Turgot observed significant incidence of hypotension with i.v clonidine 3 microgram per kilogram. This was consistent with our study.⁸

Aho M et al observed that 4.5 microgram per kilogram of clonidine significantly decrease in mean arterial pressure before induction of anaesthesia, so they recommended 3 microgram per kilogram for perioperative stability.⁹

Postoperative Nausea and Vomiting in C1 was 33% and 20% and C2 was 13.33% and 6.66% respectively and the difference was insignificant. None of the patient nauseated or vomited in C3. This difference was significant to C1 but not C2.

JavaherFroosh.F, M.Raza et al also observed reduction in postoperative nausea and vomiting after clonidine administration.¹⁰

Laisalmi M, Koivusalo AM et al observed that premedication with 150 microgram oral clonidine has been found to reduce post-operative nausea vomiting and shivering.¹¹

Sedation lasted less in C1 as compared to C2 and C3, thus C3 had maximum sedation score and at times it was >2. None of the patients in C1 and C2 had score >2 at any point of observation. No respiratory depression was observed in any of the three groups.

Legrain C, Nkiko G, et al also observed sedation lasting longer in group receiving clonidine.¹²

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