



## ORAL CLONIDINE PREMEDICATION – ITS EFFECT ON INDUCTION DOSE OF THIOPENTONE SODIUM AND PERIOPERATIVE HEMODYNAMICS

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### ABSTRACT

**Background:** Proper premedication is important in general anaesthesia cases to reduce anxiety, to produce sedation analgesia, amnesia and to maintain hemodynamical stability during peri operative period. We studied the effect of oral clonidine premedication on the induction dose of intravenous thiopentone sodium and its effect on perioperative haemodynamics.

**Methods:** Sixty ASA Grade 1 and Grade II patients were divided in to two groups, Group I (study group) pre medicated with oral clonidine 4mcg/kg/body wt, Group II (control group) (no study drug administered). Dose of thiopentone sodium required and perioperative comparison of systolic blood pressure, diastolic blood pressure and heart rate in both groups assessed. **Statistical analysis:** the data was analysed using two tailed tests for differences between means of two samples (Z test) and in needed situation using  $\chi^2$  test. significant level for rejecting null hypothesis was taken  $p < 0.05$ .

**Results:** The induction agent thiopentone sodium dose requirement is significantly reduced in group I (study group) clonidine pre medicated patient compared to control group (Group II) ( $p$  value  $< 0.0001$ ). There was a very significant rise of systolic blood pressure, diastolic blood pressure and heart rate in control group (group II) compared to group I (study group).

**Conclusion:** Pre medication with clonidine 4mcg/kg body weight ninety minutes before induction with thiopentone decreases the requirement of thiopentone and also attenuates the pressor response during gentle and smooth direct laryngoscopy and intubation.

### KEYWORDS

Clonidine, thiopentone sodium, perioperative haemodynamics

### INTRODUCTION:

Pre anaesthetic medication begins with a night sedative. The patient receives an oral sedative such as alprazolam 0.5mg or diazepam 10 mg for sedation and anxiolysis. Now clonidine is also found suitable as a premedicant given in a dose of 4-5 mcg/kg 90 minutes before surgery. Clonidine is an alpha 2 receptor agonist that acts centrally to reduce sympathetic outflow. It has been used as a centrally acting anti hypertensive, but in the field of anaesthesiology clonidine is making a come back as premedicant used selectively in particular group of patients. Clonidine acts by stimulating alpha 2 receptors and then by reducing the central sympathetic out flow with consequent reduction in catecholamines and thus cause a fall in blood pressure. It produces sedation, anxiolysis and smooth induction of anaesthesia. It reduces salivation, induction dose of intravenous anaesthetics and post operative shivering. The pharmacodynamic profile of clonidine suggests that it may also be suitable for this purpose especially because it produces minimal respiratory depression. It is also proven to attenuate the pressor response to intubation and ameliorate post operative hypertension and tachycardia.

### METHODS:

Sixty ASA Grade I and Grade II Patients posted for elective surgery were selected for the study. The patients were between the age group of 20-40 years. Patients receiving sedative and opiate medication affecting the cardio vascular system were excluded. During the pre anaesthetic evaluation, The anaesthetic procedure to be undertaken was explained to the patient and an attempt was made to allay their anxiety. Routine laboratory examination was conducted. An informed written consent was obtained from the patients and his/her relatives. A period of a over night fasting was advised. All the patients were pre medicated with tablet Alprazolam 0.5 mg

on the night before surgery. On the day of surgery, base line blood pressure and heart rate of all the patients were recorded. The patients were randomly divided in to two groups of thirty patients each using computer generated random numbers.

Group I: patients were given oral clonidine 4 mcg/kg body weight 90 minutes before induction (study group)

Group II: patients were not given any study drug (control group).

Blood pressure and heart rate were recorded at half an hour interval for three hours. After the arrival of the patient in the operation theatre, an 18 gauge canula was secured and connected to i.v line. Patient was connected to a cardiac monitor for recording ECG in Lead II. All patients were given inj. glycopyrrolate 0.2 mg IV, inj. ranitidine 50 mg IV and inj. ondansetron 4 mg IV. After pre-oxygenation with 100% oxygen for 3 minutes the patient were induced with freshly prepared thiopentone solution diluted to 2.5% at a rate of 1 ml/2sec. The dose of thio pentone sodium required to produce loss of eyelash reflexes was recorded in all cases. This was immediately followed by succinylcholine 1.5 mg/kg/body weight intravenously. A smooth and gentle direct laryngoscopy was done and appropriate sized cuffed oro tracheal tube was kept in place within fifteen seconds. Then the patient was given a mixture of 33% oxygen in N<sub>2</sub>O with a rate of 14-15 ventilations per minute. No volatile anaesthetics was used which would possibly have caused myocardial depression. Blood pressure and heart rate were also monitored before and after intubation.

### STATISTICAL ANALYSIS:

The data was analysed using two tailed tests for differences between means of two samples (Z test) and in needed situations using  $\chi^2$  test. Significant level for rejecting null hypothesis was taken as  $p < 0.05$ .

**RESULTS:**

Sixty patients in the age group of 20-40 years of either sex had been selected in this study in the study Group I denotes the study patients and Group II the control patients

**Table 1: Age distribution**

GROUP-I			GROUP-II		
Age	No. of cases	Percentage (%)	Age	No. of cases	Percentage (%)
20-25	5	16.67	20-25	7	23.37
25-30	11	36.67	25-30	10	33.34
30-35	7	23.34	30-35	6	20.0
35-40	7	23.33	35-40	7	23.33

Both Group I and Group II had a higher percentage of patients in the age group of 25-30 years.

Sex distribution: In Group I, 18 patients were male and 12 were female. In Group II, 17 patients were male and 13 were female. In both group I and Group II a predominance of male patients is seen over female and sex distribution was comparable in both groups. In both group I and group II the weight of the patients between 45-60 kg. Mean body weight in group I was  $49.5 \pm 5.1$  kg and in group II was  $50.1 \pm 4.9$  kg and was comparable in both the groups.

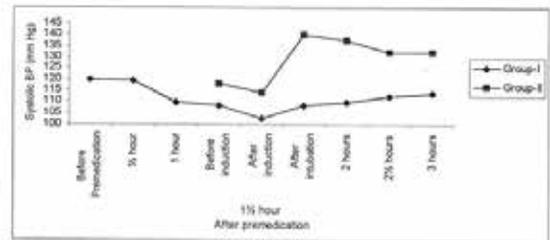
**Table 2: Thiopentone requirement**

	GROUP-I		GROUP-II		Z value	P value	Remarks
	Mean	SD	Mean	SD			
Thiopentone requirement mg / kg	3.73	0.35	5.68	0.52	17.03	< 0.0001	Very highly significant

The above comparison reveals that there is a significant reduction in the dose requirement of thiopentone in group I than in group II patients.

**Table 3: COMPARISON OF SYSTOLIC BLOOD PRESSURE IN GROUP I AND GROUP II**

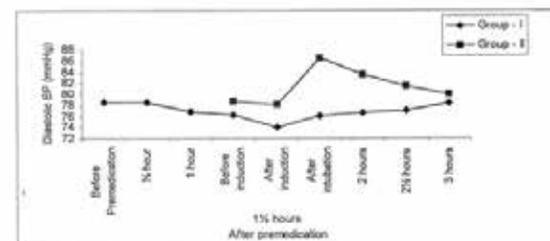
Time Mean	Group-I		Group - II		Z score	Remarks	
	SD	Mean	SD	Mean			
Before premedication	120	6.24	-	-	-	-	
AFTER PREMEDICATION	½ hour	119.6	5.997	-	-	-	-
	1 hour	109.8	6.04	-	-	-	-
	Before induction	108.53	5.73	118.27	5.98	6.44	$P < 0.0001$ VHS
	After induction	102.73	6.4	114.07	5.86	7.15	$P < 0.0001$ VHS
	After intubation	108.2	6.98	140.27	9.1	15.31	$P < 0.0001$ VHS
	2 hours	109.67	7.05	137.53	7.35	14.9	$P < 0.0001$ VHS
	2½ hours	112.33	5.8	132.13	6.41	12.54	$P < 0.0001$ VHS
	3 hours	113.73	5.87	132	6.62	11.31	$P < 0.0001$ VHS



The above data shows that while there is a very significant rise of systolic blood pressure in group II following intubation, the systolic blood pressure of group I remained controlled except for a drop after induction

**Table 4: Comparison of diastolic blood pressure in Group I and Group II**

Time Mean	Group-I		Group - II		Z score	Remarks	
	SD	Mean	SD	Mean			
Before premedication	78.53	4.03	-	-	-	-	
AFTER PREMEDICATION	½ hour	78.6	4.04	-	-	-	-
	1 hour	78.67	4.26	-	-	-	-
	Before induction	76.27	4.06	78.73	3.73	2.45	$P < 0.05$ SS
	After induction	74.13	4.3	78.13	3.71	3.86	$P < 0.01$ HS
	After intubation	76.13	4.03	86.53	3.32	10.91	$P < 0.001$ VHS
	2 hours	76.6	4.7	83.47	4.2	6.35	$P < 0.001$ VHS
	2½ hours	77.07	4.39	81.47	3.28	4.4	$P < 0.001$ VHS
	3 hours	78.3	3.79	80.07	3.17	2.14	$P < 0.05$ SS

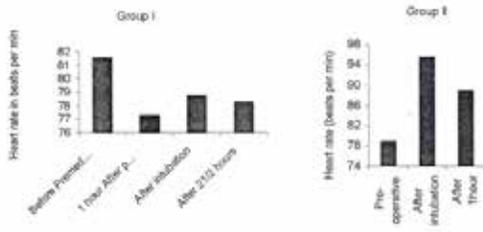


The above data shows that there is a very significant rise of Diastolic blood pressure in Group II following intubation and the diastolic blood pressure of group I remained controlled. This shows that oral clonidine pre medication attenuates rise of diastolic blood pressure.

**Table 5: Comparison of heart rate in group I and group II**

Time	Group - I		Group-II		Z score	p-value	Remarks
	Mean	SD	Mean	SD			
Before premedication	81.53	5.67	78.87	7.02	-1.62	>0.05	NS
1hr after premedication	77.33	5.47	-	-	-	-	-
After intubation	78.73	5.74	95.43	7.09	10.023	<0.0001	VHS
After 2½hrs	78.27	5.14	89	6.66	6.98	<0.0001	VHS

**Heart Rate Variations**



The above data shows that while there is a significant rise in the heart rate in group II following intubation. The heart rate in the group I remained controlled after a small fall following premedication.

#### DISCUSSION :

Several drugs have been used as premedication perioperatively to produce sedation, anxiolysis and for attenuation of pressor response during laryngoscopy and intubation. Clonidine offers unique pharmacological profile with sedation, sympatholysis, analgesia, opioid and anaesthetic sparing effect, cardiovascular stability with great advantage to avoid respiratory depression. Polypharmacy has to be used for premedication to produce all the effects which clonidine alone can do.

In our study both study and control group were also in the same age group limits and in both the group the male and female ratio is also maintained same even though both groups showed a male predominance. Weight of the patient in both group also falls in the same range. Hence all these factors which can effect the dose requirement of thiopentone were tried to be eliminated and this was succeeded to a great extent. Our study shows significant reduction in the thiopentone requirement in the study group (group I). Group I required only  $3.73 \pm 0.35$  mg/kg/body weight of thiopental, whereas (Group II) control group required  $5.68 \pm 0.52$  mg/kg/body weight. The Z score was  $< 0.0001$  which shows very highly significant reduction in the thiopentone dose. In the study of Pradeep et al and Baskaran et al the induction dose of thiopentone was decreased by clonidine premedication. Nishina et al also observed decrease in thiopentone requirement in patients premedicated with clonidine. Mark D peterson et al found that clonidine reduced peak isoflurane requirement, while providing superior haemodynamic stability during coronary artery surgery. Aloka Samantray et al found that clonidine premedication reduces post operative pain and reduces fentanyl requirement.

In group I (study group) systolic blood pressure before pre medication was  $120 \pm 6.24$  mm. hg which dropped to  $108.53 \pm 5.73$  mm .hg after pre medication . And further dropped to  $102.73 \pm 6.4$  mm hg after induction and then rose

to  $108 \pm 6.98$  mmhg and slowly rose back to the base line  $113.73 \pm 5.87$  mm hg within one and half an hour after induction and then was maintained so. In group II pre operative systolic blood pressure was  $118.27 \pm 5.98$  mm hg which showed a slight drop after induction to  $114.07 \pm 5.86$  mm hg. During intubation it shoot up to  $140.27 \pm 9.1$  mm hg which was highly significant and then remained high throughout the procedure at  $132 \pm 6.62$  mm hg even after one and half hour. Laurido CE et al, Ghignone M et al, Nishikawa et al and Dipak et al found that clonidine reduced systolic blood pressure following intubation.

Diastolic blood pressure in group I showed a drop after pre medication from  $78.53 \pm 4.03$  mm hg to  $76.27 \pm 4.06$  mm hg and after induction further dropped to  $74.13 \pm 4.3$  mm hg and then rose to  $76.13 \pm 4.03$  mm hg after intubation..The pre operative diastolic blood pressure was  $78.73 \pm 3.73$  mm hg which showed sudden rise to  $86.53 \pm 3.32$  mm hg during intubation and slowly dropped to pre-operative level within one and half hour after induction. Laurido CE et al, Ghignone M et al, Nishikawa et al and Dipak et al found that clonidine reduced diastolic blood pressure following intubation.

The heart rate also showed rise in group II after intubation from  $78.87 \pm 7.02$  to  $98.43 \pm 7.09$  beats/minute, where as in group I following a small drop after pre medication, the heart rate did not show a sudden rise after intubation. Even after one and half hour after surgery also heart rate remained at  $89 \pm 6.56$  beats/minute in group II as compared to  $78.27 \pm 5.14$  beats in group I. . Laurido CE et al, Ghignone M et al, Nishikawa et al and Dipak et al found that clonidine reduced heart rate following intubation.

#### CONCLUSION:

Following the study, we concluded that pre medication with clonidine 4mcg/kg body weight ninety minutes before induction with thiopentone decreases the requirement of thiopentone and also attenuates the pressor response during gentle and smooth direct laryngoscopy and intubation. It also maintains hemodynamic stability peri operatively.

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