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A Prospective, Double Blind, Randomized Clinical Study on Effect of Oral Clonidine Premedication on the Induction Dose of Intravenous Thiopentone Sodium

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Abstract

Background: Preanaesthetic medication significantly modulates intraoperative requirement of anaesthetic agents such as the i.v. anaesthetic Thiopentone sodium.

Objectives: A prospective, randomised, double blind, was done to evaluate the effect of oral Clonidine premedication on the induction dose of Thiopentone sodium. To study hemodynamic and sedative effects of oral Clonidine.

Methods: The study was done on 60 patients of age group 18-60 years and ASA grade I and II scheduled for elective surgeries under general anaesthesia. After obtaining a well informed consent, these patients were randomly divided in two groups A and B with 30 patients each according to whether they receive placebo or Clonidine 4µg/kg orally, 90 min prior to induction as premedication.

Results and interpretation: Clinical parameters as per module of the study were recorded and tabulated for statistical analysis and interpretation was discussed in detail to draw conclusions.

Induction dose of Thiopentone was 5.63±0.46 mg/kg in group A and 4.3±0.22 mg/kg .The mean arterial blood pressure (MABP) and pulse rate were lower in groups receiving Clonidine. Administration of oral Clonidine in a dose of 4µg/kg given 90 min before induction decreases the induction dose of Thiopentone sodium. Clonidine produces clinically significant reduction in sedation score with hemodynamic stability. No significant side effect was seen after premedication with oral Clonidine.

Conclusion: There were no complications or adverse effects during the study period. The oral Clonidine 4µg/kg seems to be better choice for premedication to decrease the induction dose of intravenous Thiopentone sodium.

Keywords: Clonidine, Thiopentone sodium, mean arterial blood pressure (MABP), Preanaesthetic medication, α_2 adrenergic agonist.

Introduction

Preanaesthetic medication forms an integral part of anaesthetic management and some form of premedication is universally administered before any anaesthesia. The primary goal of premedication is to relieve anxiety and produce sedation.[1] The ideal premedicant should be effective and pleasant to be taken orally, have analgesic and non emetic properties, should not impair cardiovascular stability or depress respiration, should have antisialogogueeffect[29] and should effectively alleviate

apprehension of the patient, however, its effect should not be restricted to preoperative period. Preanaesthetic medication significantly modulates intraoperative requirement of anaesthetic agents such as the i.v. anaesthetic Thiopentone sodium.[1]

α_2 adrenergic receptor agonist such as Clonidine produces both preoperative sedation and anxiolysis[5,46] and they have been proposed for premedication.[10,33]The potential advantages of using α_2 adrenergic agonist preoperatively are

- Attenuates sympatho-adrenal response to laryngoscopy.[37]
- Improves intra operative hemodynamic stability.[14,15,18]
- Reduces intraoperative requirement of volatile anaesthetic.[3,18,28]
- Less postoperative pain and shivering.[16,34,35]

However, depending on the dose selected they can induce marked bradycardia, hypotension, and deep sedation and can delay postoperative recovery.

Clonidine, the prototype α_2-adrenergic agonist, was originally developed in the early 1970s for its potential use as a nasal decongestant. Later on it was found as a useful anti-hypertensive agent, however, with the advent of ACE inhibitors and more selective $\alpha_2$adrenergic antagonists, Clonidine has been relegated to no better than third line alternative for this purpose.

It has however, remained an intriguing compound that has been shown to be efficacious in a wide range of applications such as analgesia[2], sedation, reduction in postoperative shivering[34]and control of symptoms during alcohol,[8] nicotine[9] and opioid withdrawal.[20] Clonidine premedication reduces the intraoperative requirement of opioid and volatile anesthetics.[3] Clonidine also reduces the induction dose of i.v. anaesthetic agents.[13]

Its use as a sedative/anxiolytic in the intensive care setting is now relatively common particularly after long-term sedation with opioid and/or benzodiazepines, evidence exists that Clonidine is effective in the relief of withdrawal symptoms from these agents.[20] However, reliable data on i.v. dosing, sedative efficacy and the effect on outcome in the intensive care settings are lacking.

Presence of α_2 receptors has been demonstrated in the substantia gelatinosa of the human spinal cord, often in close association with opioid receptors.[41]

The present study is formulated to study hemodynamic and sedative effects of oral Clonidine and also to evaluate the efficacy of Clonidine as a premedication so as to reduce the induction dose of Thiopentone sodium.

Material and Methods

This study was conducted in the Department of Anesthesiology and Critical Care, Pt. J.N.M. Medical College and Dr. Bhim Rao Ambedkar Memorial Hospital Raipur (C.G.), in the period between January 2018 to August 2018.

After obtaining the consent from Institutional Ethical Committee, the study was carried out as a Prospective, randomized double blind study on 60 patients of age group 18-60 years, of both sexes belonging to ASA grade I and II and posted for elective surgeries under General Anaesthesia.

Inclusion criteria: Male and females between 18-60 years, as well as Patients undergoing general surgery, neurosurgical, orthopaedic procedures under general anaesthesia were selected.

Exclusion criteria: Pregnant or lactating women, Patients receiving analgesics, phenothiazine, tranquilizers, hypnotics or other CNS depressants including alcohol, Patients with body weight >100 kg and< 45 kg, allergic to general anaesthesia, Patients who have received sedative medications in the last 4hrs or on antipsychotic drugs, Patients with unconsciousness (coma) and head injury, Patients with severe cardiac, hepatic, renal,

cerebrovascular disease, chronic uncontrolled systemic disease or any other serious medical illness.

A well informed written consent was taken. A thorough Preanaesthetic checkup was done with complete history, general examination, systemic examination and required investigations.

Baseline pulse rate and blood pressure were recorded before giving oral Clonidine.

All patients were randomly divided into two groups of 30 patients each as -

Group A (**Control group)**: 30 patients received a placebo (tablet vit. C) Orally 90 min before induction.

Group B (**Oral Clonidine group)**: other 30 patients received tablet Clonidine 4 µg / kg 90 min before induction.

- Blood pressure was recorded by sphygmomanometer.
- Pulse rate was recorded by ECG monitor.
- Sedation was assessed on the basis of Chernik sedation score.[7]
  - 0: Completely awake
  - 1: Sleeping but responding to verbal command.
  - 2: Deep sleep but arousable.
  - 3: Deep sleep but not arousable.
- Cardiovascular parameters such as pulse rate, systolic, diastolic and mean arterial pressure were recorded before premedication and at 15min, 30min, 45min and 60 min after administration of study drug and just before and immediately after induction of anaesthesia.

Sedation score was recorded before premedication and at 15min, 30min, 45 min and 60 min after administration of study drug and just before induction of anaesthesia.

Anaesthesia procedure and recording: Patients were preoxygenated with 100% oxygen by face mask for 3 minutes. General anaesthesia was induced with inj. Thiopentone sodium 2.5% intravenous. Loss of eyelash reflex was taken as the end point of induction. The dose of Thiopentone sodium required to produce loss of eyelash reflex was recorded in both the groups. Inj. pentazocine 0.5mg/kg was given after induction. This was followed by inj. succinyl choline 1.5 mg/kg body weight intravenously. IPPV was done for 90 seconds, which was followed by laryngoscopy and endotracheal intubation with appropriate size cuffed endotracheal tube. Endotracheal tube was then checked and fixed. To complete the surgical procedure, anaesthesia was maintained with nitrous oxide (66.6%), Oxygen (33.3%), Halothane (0.5%) and a non depolarizing muscle relaxant on Bain's anaesthetic circuit under controlled ventilation. At the end of surgical procedure residual effect of muscle relaxant was reversed with a combination of Glycopyrrolate 0.4 mg. and Neostigmine 2.5 mg.

Any complication like change in blood pressure, pulse rate and ECG changes during study along with postoperative complications if any was recorded.

The observations were recorded and subjected to statistical analysis using student′s “t” test and chi-square test.

Results

Table - 1 showed division of patients in two groups.

Table - 2 showed age distribution in two groups, Table showing majority of patients in 18-40 years age group. Mean (±SD) age in group A and group B were 35.9±12.16 years and 37.7±12.43years respectively. Mean (± SD) weight in group A and group B were 57.4±9.81 kg and 56.2±7.01 kg respectively. These variables were statistically analysed and found to be comparable. ($p>0.05$). [Table 4]

Table-3 showed gender distribution in two groups, in which, 18 were male (60%) and 12 were female (40%) in group A, while 17 were male (56.7%) and 13 were female (43.3%) in group B.

Types of surgery done on patients in group A were 30% Neurosurgery,36.7% General Surgery and 33.3% Orthopaedic surgery and in group B were 33.3%Neurosurgery,23.4%General Surgery and43.3% Orthopaedic surgery.[table 5]

Table 6 showed dose of Thiopentone sodium in two groups. Also indicated significant reduction in the induction dose of Thiopentone sodium in group B. ($p<0.05$).

Table 7 showed statistical analysis of mean pulse rate in two groups, there were no significant fall in pulse rate in group A. ($p>0.05$) In group B no significant fall before 30 min but significant fall was observed thereafter. ($p<0.05$) On intergroup comparison significant reduction was observed from 30 min after giving study drug in group Bas compared to group A. ($p<0.05$)

Table 8 showed statistical analysis of mean systolic blood pressure (mm of Hg) in two groups. There was no significant fall in SBP in group A. ($p>0.05$).In group B no significant fall was observed before 30 min but significant fall was observed thereafter. ($p<0.05$) On intergroup comparison significant reduction was observed from 30 min after giving study drug in group Bas compared to group A. ($p<0.05$) Table– 9 showed statistical analysis of mean diastolic blood pressure (mm of Hg) in two groups, there was no significant fall in DBP in group A. ($p>0.05$) In group B no significant fall was observed before 30 min but significant fall was observed thereafter. ($p<0.05$) On intergroup comparison significant reduction was observed from 30 min after giving study drug in group Bas compared to group A. ($p<0.05$).

Table 10 showed statistical analysis of mean arterial pressure (mm of hg) in two groups, there was no significant fall in MAP in group A observed.($p>0.05$) In group B no significant fall was observed before 30 min but significant fall in MAP was observed thereafter. ($p<0.05$).On intergroup comparison significant reduction was observed from 30 min after giving study drug in group Bas compared to group A. ($p<0.05$) Table 11denoted stastistical comparison of sedation scores in two groups. Where *-P value cannot be calculated as the data was zero in either group at these intervals of time. In Group B, sedation score of 1 was perceived by 10% patients at 30 minutes, 16.7% patients at 45min, 23.3%patients at 60minutes and30% patients at 90minutes after giving the study drug.

Discussion

The study was done on 60 patients of age group 18-60 years and ASA grade-I and II of both sexes scheduled for elective surgeries under general anaesthesia. Two groups and were made with 30 patients randomly selected in each group according to the study drug given. Group-A received a placebo (tab.vit C) orally 90 min prior to induction and Group-B received 4µg/kg of Clonidine orally 90 min prior to induction. [Table 1]

Demographic profile: Mean (± SD) age in group A and group B were 35.9±12.16 years and 37.7±12.43years respectively. [TABLE 2] Mean (± SD) weight in group A and group B were 57.4±9.81 kg and 56.2±7.01 kg respectively. These variables were statistically analysed and found to be comparable ($p>0.05$). [Table 4]

In the present study, 18 were male (60%) and 12 were female (40%) in group Awhile 17 were male (56.7%) and 13 were female (43.3%) in group B. [Table 3].

Types of surgery done on patients in group A were 30% Neurosurgery,36.7% General Surgery and 33.3% Orthopaedic surgery and in group B were 33.3%Neurosurgery,23.4%General Surgery and43.3% Orthopaedic surgery.[Table 5]

Dosage and timing of premedication: In the present study oral Clonidine in a dose of 4µg/kg was given 90 min prior to induction of anaesthesia. Similar dose was used by

Baskaran N etal[1] two hours prior to induction, to evaluate its effect on induction dose of Thiopentone.

A statistically significant reduction in the induction dose of Thiopentone sodium was observed in group B as compared to group A. ($p<0.05$). [Table6]

The Mean (±S.D.) induction dose of Thiopentone was 5.63±0.46 in group A and 4.3±0.22 in group B and the difference was statistically significant.($p<0.05$)[Table6]The induction dose of Thiopentone sodium was 23.62% less in group B as compared to group A.

The findings of our study are comparable with the following studies-

Tetsu K et al[43] who reported a significant reduction in induction dose of Thiamylal requirement with two different doses of oral Clonidine (5µg/kg and 2.5µg/kg) given 90minutes prior to surgery. **Richards MJ et al**[40] also reported a significant reduction in Protocol requirement in TIVA with 600µg of oral Clonidine premedication prior to surgery.

Baskaran N et al[1] **also showed a significant reduction in Thiopentone requirement in Clonidine group (4.15±1.46mg/kg) as compared to the control group (5.50±1.15mg/kg).**

Carbine UA et al[5] reported a significant reduction of Thiopentone requirements by 15% and 28% with a oral Clonidine dose of 0.625 and 1.25µg/kg respectively.

Nishana K et al[36] studied that in children oral Clonidine dose of 2µg/kg and 4µg/kg reduced the dose of intravenous Thiamylal required to4.5±1.1 and 3.4±0.9mg/kg respectively for induction of anaesthesia. The reduction in the induction dose of Thiopentone was due to inhibitory action of Clonidine over the locus ceruleus involved in the control of sleep/awake cycle, cortical arousal and in modulation and integration of sensory input which modulates the stimuli arriving at central nervous system.[11] Clonidine partially inhibits voltage-gated $Na^+$and K^+ channels and suppresses the generation of action potentials in tonic firing spinal dorsal horn neurons contributing to the reduction of Thiopentone requirements.[13]

Pulse rate: In group A, statistically insignificant change in pulse rate was observed after giving placebo drug but statistically significant rise was observed just after induction. In group B, statistically significant decrease was observed after 30 min of giving study drug and decrease persisted till induction. ($p<0.05$) [Table 7] On intergroup comparison, variation in basal pulse rate was comparable up to 30 min but thereafter statistically significant decrease was observed in group B as compared to group A. ($p<0.05$) **Carbine UA et al**[5] also found a significant decrease in heart rate with oral Clonidine a dose of 0.3 mg as compared to their control groups. **Baskaran N et al**[1] **also** reported in their study a significant decrease in the pulse rate at a oral dose of Clonidine 4µg/kg.

Guyenet PG et al[25] also observed that Clonidine causes decrease in pulse rate due to central α_2 adrenergic agonist activity which enhances parasympathetic nervous system activity and decreases sympathetic nervous system activity at brainstem sites**.**

The cause of increase in heart rate noted after induction with Thiopentone sodium in both the study groups is the baroreceptor mediated sympathetic reflex stimulation of the heart in response to the decrease in output and pressure.[30]

Clonidine reduces heart rate by stimulating presynaptic α2 receptors present in medulla and hypothalamus which decreases sympathetic out flow and partly by a vagomimetic effect.[1125]

Systolic blood pressure: In group A, change in SBP was statistically insignificant upto 90 min of giving placebo

drug but a statistically significant fall in SBP was observed just after induction(P>0.05). In group B, a statistically significant fall in SBP was observed at 30 min, 45 min, 60 min, and 90 min and also just after induction. (p<0.05) [Table 8] On intergroup comparison, variation in basal SBP was statistically insignificant and found to be comparable up to 30 mines but thereafter throughout the study period a statistically significant fall in SBP was observed in group B as compared to group A. (p<0.05)The findings of our study are comparable with the study by **Tetsu K et al[43] who also reported a significant reduction in** systolic blood pressure at a oral Clonidine dose of 5µg/kg and 2.5µg/kg. **Kumar A et al[31] also showed s**ignificant reduction in SBP in Clonidine group as compared to the control group.

The major hemodynamic effects of Clonidine are due to its action on medulla (vasomotor center possibly the nucleus tractus solitarius) and hypothalamus. It stimulates presynaptic α_2 receptors present at these sites which decreases sympathetic outflow resulting in fall in SBP.[11],[33]

Diastolic blood pressure: In group A, change in DBP was statistically insignificant upto 90 min of giving placebo drug but statistically significant decrease was observed just after induction(P>0.05). In group B, statistically significant decrease was observed at 30 min, 45 min, 60 min, 90 min and also just after induction.(p<0.05) [Table 9]

On intergroup comparison, variation in basal DBP was statistically insignificant and found to be comparable up to 30 mines but thereafter statistically significant decrease was observed in group B as compared to group A. (p<0.05) The findings of our study are comparable with the following studies- **Kumar A et al[31] reported a** significant reduction in DBP in Clonidine group as compared to the control group. **Tetsu K et[43]al also found a significant reduction in** diastolic blood pressure in Clonidine group as compared to the control group. Fall in DBP is due to the central α_2 agonist action which enhances parasympathetic nervous system activity and decreases sympathetic nervous system activity at brainstem sites.[27]

Mean arterial pressure: In group A, change in MAP was statistically insignificant upto 90 min of giving placebo drug but statistically significant decrease was observed just after induction(P>0.05). In group B, statistically significant decrease was observed at30min, 45min, 60min, 90min and also just after induction.(p<0.05)[TABLE 10]

On intergroup comparison, variation in basal MAP was statistically insignificant and found to be comparable up to 30 min but thereafter a statistically significant decrease was observed in group B as compared to group A. (p<0.05) [Table 10]

The findings of our study were comparable with the study by **Baskaran N et al[1] who showed a significant reduction** in mean arterial pressure (MAP) in Clonidine group as compared to control group. **Tetsu K et al[43] also reported a significant reduction** in MAP at oral Clonidine dose of 5µg/kg and 2.5µg/kg.

Clonidine decrease MAP by its α_2 adrenergic inhibitory neurons in the medullary vasomotor center which decreases the sympathetic nervous system outflow from the central nervous system (CNS) to the peripheral tissues leading to central and peripheral attenuation of sympathetic outflow and central activation of noradrenergic imidazoline preferring receptors.[11]

The probable cause of fall in blood pressure (SBP, DBP,MAP) after induction with inj. Thiopentone sodium in group A is peripheral vasodilatation that results in pooling of blood in the venous system.[12] A decrease in contractility is another effect, which is related to reduced availability of calcium to the myofibrils. Mechanisms for the decrease in cardiac output include 1. Direct negative inotropic action. 2. decreased ventricular filling owing to

increased capacitance and 3. Transiently decreased sympathetic outflow from the CNS.[3044]

Clonidine is an α_2 adrenoceptor agonist, which interacts with the catecholaminergic neuronal system which modulates tonic and physic (reflex) blood pressure control and reduces the release of nor epinephrine from nerve endings both centrally and peripherally and causes reduction in arterial pressure.[25,26 27]

The sedation score was assessed by **Chernik**[7] sedation score just before premedication and at 15min, 30min, 45 min, 60 min and 90 min after premedication. In group A, no sedation was found in any patients and sedation score remained zero all the time. In Group B, sedation score of 1(sleeping but responding to verbal command) was perceived by 10% patients at 30min, 16.7% patients at 45min, 23.3% patients at 60min and 30% patients at 90 min just before induction. On intergroup comparison sedation scores were significantly higher in group B as compared to group A at 30 min after premedication till 90 min ($p<0.05$) [Table 11] but sedation was clinically insignificant without any respiratory depression or airway compromise. Clonidine produces sedation by its inhibitory activity at pontine locus ceoruleus which is involved in control of sleep/awake cycle, cortical arousal and in modulation of sensory input. The result is a calm patient who can be easily aroused to full consciousness.[17]

There was no side effect or any untoward effect observed during the study period.In our study we used oral Clonidine 4µg/kg, 90 min before induction and we observed statistically significant decrease in the induction dose of intravenous Thiopentone sodium with significant changes in hemodynamic parameters without any serious side effect. Our results are well in accordance to other investigators who have used oral Clonidine to decrease induction dose of Thiopentone sodium.

Conclusion

Administration of oral Clonidine in a dose of 4µg/kg given 90 min before induction decreases the induction dose of Thiopentone sodium.

Clonidine produces clinically significant reduction in sedation score with hemodynamic stability. No significant side effect was seen after premedication with oral Clonidine. In our study we used oral Clonidine 4µg/kg,90 min before induction and we observed statistically significant decrease in the induction dose of intravenous Thiopentone sodium with significant changes in hemodynamic parameters without any serious side effect. Our results are well in accordance to other investigators who have used oral Clonidine to decrease induction dose of Thiopentone sodium.

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Tables

Table 1: Showing Division of Patients in Two Groups

S.No.	Group	(n)	Drug and it's Dose
1	A	30	Placebo 1 tab 90 min before induction
2	B	30	Tab. Clonidine 4µg/kg90 min before induction

Table 2: Table Showing Age Distribution in Two Groups

S.NO	AGE GROUP (in years)	GROUP - A		GROUP – B	
		No. Of Patients (n)	%	No. Of Patients (n)	%
1	18-30	14	46.7	11	36.6
2	31-40	8	26.7	9	30
3	41-50	5	16.6	4	13.4
4	51-60	3	10	6	20
	Mean(±SD)	35.9±12.6		37.7±12.43	
GROUP-A vs GROUP-B		P-value	0.57(NS)		

Table 3: Table Showing Sex Distribution in Two Groups

SEX	GROUP – A		GROUP - B	
	(n)	%	(n)	%
Male	18	60	17	56.7
Female	12	40	13	43.3
Total	**30**	**100**	**30**	**100**

Table 4: Showing Weight Distribution in Two Groups

Weight Group (Kg.)	Group - A	Group – B
41 – 50	11	9
51 – 60	9	14
61 – 70	7	5
71- 80	3	2
Mean(±SD)	57.4±9.81	56.2±7.01
GROUP-A vs GROUP-B	P -value	0.58(NS)

Table 5: Showing Distribution of Types Of Surgery In Two Groups

S. NO	TYPE OF SURGERY	GROUPS			
		GROUP- A		GROUP- B	
		n	%	n	%
1	Neuro Surgery	9	30	10	33.3
2	General Surgery	11	36.7	7	23.4
3	Orthopaedic	10	33.3	13	43.3
	Total	**30**		**30**	

Table 6: Showing Dose of Thiopentone Sodium In Two Groups

Dose of Thiopentone sodium	GROUP-A Mean(±SD)	GROUP- B Mean(±SD)	p-value
(mg/kg)Body weight	5.63±0.46	4.3±0.22	0.00(S)

Table 7: Showing Statistical Analysis Of Mean Pulse Rate In Two Groups

GROUPS		GROUP_A Mean(±SD)	p-value (intragroup)	GROUP_B Mean(±SD)	p-value (intragroup)	GROUP-A vs GROUP-B (intergroup) p-value
Basal value		83.4±10.94		84.6±9.02		0.64(NS)
After Study Drug	15min	83.2±10.22	0.94(NS)	84.4±8.65	0.93(NS)	0.62(NS)
	30min	83.6±10.16	0.94(NS)	77.5±7.32	0.03(S)	0.00(S)
	45min	83.6±10.27	0.93(NS)	74.9±7.13	0.00(S)	0.00(S)
	60min	84.3±9.70	0.73(NS)	71.4±6.82	0.00(S)	0.00(S)
	90min	87.7±9.56	0.11(NS)	67.6±5.92	0.00(S)	0.00(S)
Just after induction		98.0±10.96	0.00(S)	71.6±5.76	0.00(S)	0.00(S)

Table 8: Showing Statistical Analysis of Mean Systolic Blood Pressure (Mm of Hg) In Two Groups

Groups		Group-A Mean(±SD)	p-value (intra group)	GROUP-B Mean(±SD)	p-value (intra group)	Group-A vs Group-B p-value (intergroup)
Basal value		123.6±9.83		125.6±5.82		0.34(NS)
After Study Drug	15 min	123.6±9.71	1.0(NS)	125.6±5.82	1.0(NS)	0.33(NS)
	30 min	123.6±9.71	1.0(NS)	119.4±5.73	0.00(S)	0.04(S)
	45 min	123.8±9.64	0.94(NS)	117.5±5.98	0.00(S)	0.003(S)
	60min	123.8±9.64	0.94(NS)	112.9±5.77	0.00(S)	0.00(S)
	90min	124.2±9.56	0.81(NS)	108.4±5.67	0.00(S)	0.00(S)
Just after induction		113.4±9.45	0.00(S)	104.3±4.85	0.00(S)	0.00(S)

Table 9: Showing Statistical Analysis Of Mean Diastolic Blood Pressure (Mm Of Hg) In Two Groups

Groups		Group-A Mean(±SD)	p-value (intra group)	Group-B Mean(±SD)	p-value (intragroup)	Group-A vs Group-B p-value (intergroup)
Basal value		79.2±4.41		79.8±4.19		0.59(NS)
After Study Drug	15 min	79.2±4.41	1.0(NS)	79.8±4.19	1.0(NS)	0.59(NS)
	30 min	79.2±4.41	1.0(NS)	76.3±3.79	0.00(S)	0.00(S)
	45 min	79.1±4.38	0.93(NS)	76.3±3.79	0.00(S)	0.00(S)
	60min	79.1±4.38	0.93(NS)	75.8±3.27	0.00(S)	0.00(S)
	90min	79.2±4.41	1.0(NS)	75.8±3.27	0.00(S)	0.00(S)
Just after induction		78.2±3.88	0.03(S)	74.9±3.31	0.00(S)	0.00(S)

Table– 10: Table Showing Statistical Analysis Of Mean Arterial Pressure (Mm Of Hg) In Two Groups

Groups		Group-A Mean±(SD)	p-value (intra group)	Group-B Mean±(SD)	p-value (intra group)	GROUP-A vs GROUP-B p-value (intergroup)
Basal value		93.9±5.16		95.1±4.18		0.326(NS)
After Study Drug	15 min	94.0±5.12	0.94(NS)	95.1±4.18	1.00(NS)	0.365(NS)
	30 min	93.9±5.16	1.0(NS)	90.69±3.50	0.00(S)	0.00(S)
	45 min	94.0±5.08	0.93(NS)	90.08±3.53	0.00(S)	0.00(S)
	60min	94.0±5.08	0.93(NS)	88.1±3.17	0.00(S)	0.00(S)
	90min	94.2±5.08	0.82(NS)	86.6±3.20	0.00(S)	0.00(S)
Just after induction		89.8±4.64	0.00(S)	84.6±2.94	0..00(S)	0.00(S)

Table 11: Stastical Comparison of Sedation Scores in Two Groups

Time (min)	Score	Group A		Group B		X^2	P-value	Remarks
		n	%	N	%			
Just Before premedication	0	30	100	30	100	*	*	*
	1	0	0	0	0			
15 min after premedication	0	30	100	30	100	*	*	*
	1	0	0	0	0			
30 min	0	30	100	27	90	10.53	0.001	S
	1	0	0	3	10			
45 min	0	30	100	25	83.3	18.58	0.000	S
	1	0	0	5	16.7			
60 min	0	30	100	23	76.7	24.66	0.000	S
	1	0	0	7	23.3			
90 min (just before induction)	0	30	100	21	70	32.23	0.000	S
	1	0	0	9	30			