



## A COMPARATIVE STUDY OF EFFECTS OF CLONIDINE AND MAGNESIUM SULPHATE ON PROPOFOL REQUIREMENT IN CRANIOTOMY PATIENTS UNDER GENERAL ANAESTHESIA

### Anesthesiology

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### ABSTRACT

**Introduction :** Awareness can be defined as the subjective experience of external or internal stimuli. Recent review of reported cases of awareness suggested the absence of volatile agents or intravenous agents during maintenance of anaesthesia 2.

**Material & Methods :** The study was conducted in SMS Medical College and attached hospital, Jaipur after approval from the institutional ethics committee.

The present study was conducted in 105 patients 35 in each group of ASA physical status 1 & 2 posted for elective spinal surgery under general anaesthesia, age between 20-50 years, Hospital – based, randomized, double blind, comparative interventional study. The sample size was calculated 35 subjects in each group.

**Results:** In recovery period, the time to reach BIS to 80 was found to be significantly more in Group B compared to Group C and Group A [ $P < 0.001$ ].

When the groups were compared, all the three parameters of recovery (extubation time, response to verbal commands and time for orientation) were found to be significantly longer in Group B. There were no significant difference between the other two groups, i.e. Group A and Group C ( $P < 0.001$ ). Propofol Induction and Maintenance dose found to be significantly more in Group C as compared to group B than Group A. ( $P < 0.001$ ). Total Propofol requirement was significantly more in group C as compared to group B than Group A. ( $P < 0.001$ ).

**Conclusion:** Perioperative use of both clonidine and magnesium sulphate significantly reduced the requirement of propofol. They were able to attenuate the haemodynamic response to tracheal intubation. Clonidine was associated with bradycardia and hypotension. Magnesium sulphate caused a delay in recovery.

### KEYWORDS

Clonidine, Magnesium Sulphate, Propofol, Normal Saline, Craniotomy, Bis ,general Anaesthesia

### INTRODUCTION

Awareness can be defined as the subjective experience of external or internal stimuli and one's own existence in space and time at any given moment. In general anaesthesia direct laryngoscopy and tracheal intubation is associated with stimulation of the supra-glottic region, a reflex circulatory responses characterized by an increase in blood pressure and heart rate.<sup>2-8</sup> This study mainly demonstrates use of clonidine and magnesium sulphate to improve intraoperative haemodynamic stability in attenuating sympathoadrenal responses to laryngoscopy and tracheal intubation, reduces intraoperative requirement of anaesthetic agents and reduces postoperative pain and reducing analgesic requirements during the postoperative period.<sup>9, 10</sup>

Clonidine, a centrally acting  $\alpha_2$ -receptor agonist, has attracted increasing interest as an adjunct to anaesthesia. A variety of beneficial effects before, during and after anaesthesia, such as sedation, analgesia, increased cardiovascular stability and improved outcome, have been attributed to clonidine. Clonidine reduced the requirement for volatile anaesthetics when assessed by haemodynamic responses. Because centrally acting  $\alpha_2$ -receptor agonists have effects on the EEG and the bispectral index (BIS) in the awake patient, we thought that the effect of clonidine on depth of anaesthesia might also be monitored using the BIS. This study was conducted to evaluate first whether the sedative effect of clonidine is measurable by BIS analysis during propofol anaesthesia, and secondly whether BIS monitoring allows the maintenance of a constant anaesthetic depth despite a reduced propofol dosage after administration of clonidine.<sup>12</sup> Magnesium sulphate is a mineral that is present in relatively large amounts in body. Magnesium is required for the proper growth and maintenance of bones, proper function of nerves and muscles.

### Materials & Methods

The study was conducted in SMS Medical College and attached hospitals Jaipur after approval from Institutional ethical committee.

The present study was conducted in 105 patients 35 in each group of ASA physical status 1 and 2 age 20-50 years weight 40-80 kg.

### Aim & Objectives

To compare and assess the effect of i.v. clonidine and magnesium sulphate in craniotomy patients in terms of:

1. Changes in heart rate, mean arterial pressure, spo 2 among all the group.
2. Propofol required desired depth of anaesthesia among all the group.

### Study Design

Hospital based, randomised, double blind, comparative interventional study.

### Sample Size –

The sample size was calculated 35 subjects in each group, at Alpha error 0.05 and power 80% assuming the minimum detectable mean difference in the propofol Maintenance during surgery was  $0.68 \pm 0.9$  mg/kg.hr. For the study, purpose 35 subjects in each group was taken.

### Inclusion Criteria –

ASA physical status I/II posted for elective surgery under general anaesthesia, age between 20-50 years, weight 40-80 kg and height > 140cm. Informed consent was taken from each group.

### Exclusion Criteria –

Patient on antihypertensive treatment, history of arrhythmias, uncontrolled hypertension. Known allergy to one of the drugs use, severe renal and hepatic impairment.

### Study Groups

Group	Drug used
A	Group A received clonidine 0.1 ml/kg as a bolus before 15 mins of induction & than IV infusion @ 0.03ml/kg/hr.
B	Group B received MgSO 0.1 ml/kg as a bolus before 15 mins of induction & than IV infusion @ 0.03 ml/kg/hr.
C	Group C received Normal saline 0.1ml/kg/as a bolus before 15 mins of induction & than IV infusion @ 0.03 ml/kg/hr.

### Test drug infusion preparation :-

Group A patients---- clonidine 600  $\mu$ g ( 4 ml ) diluted with 16 ml normal saline in a 20-ml

Group B patients---, magnesium sulphate 12 ml (6000 mg) diluted with 8 ml normal saline, was added to a 20- ml

Group C patients--- Normal saline was used.

Double – blinding was done. Randomized group allocation by chit in box method

#### Technique -

- On arrival in the operation theatre, weight, fasting status, consent and PAC were checked.
- Baseline parameters {SpO<sub>2</sub> Pulse rate ( PR) Systolic blood pressure ( SBP), Diastolic blood pressure (DBP) Mean Arterial Pressure (MAP), baseline BIS) were recorded.

#### Premedication and Induction

Every patients was premedicated with inj. Glycopyrrolate ( 0.005 mg/kg/ i.v. ) + inj. Fentanyl citrate ( 2 µg/kg i.v. ) along with pre oxygenation for 5 min. Before starting induction of anaesthesia. They were induced by injection propofol.

#### Maintenance

Anaesthesia was maintained by nitrous oxide and oxygen with propofol intermittent iv bolus dose 10-20 mg given and intermittent bolus of atracurium

#### Extubation

Propofol infusion was stopped. Residual neuromuscular block was reversed by Neostigmine and glycopyrolate.

### RESULTS

#### Demographic Profile

Particular	Group A	Group B	Group C	P value
Age ( Year )	37.7±11.088	7.37±9.476	40.37±9.347	.467
Weight (kg)	61.0±4.75	61.86±5.47	60.63±5.45	.61
ASA I & II	30/5	28/7	27/8	.649
Surgery Duration hours.	3.229±.9342	3.271±.9263	3.257±.9954	.98

#### Propofol Requirement doses

	Group A	Group B	Group C	P value
Induction	95.14±10.606	98.43±8.975	126.57±7.648	<0.001
Maintenance	99.14±27.15	115.43±28.93	193.43±35.80	<0.001
Total Propofol Requirement	99.00±10.34	103.14±9.00	126.57±7.648	<0.001

#### Mean Arterial Pressure at different time interval among group

Group		Pre op MAP	5 min after bolus of study.	Just after induction	Just after intubation	10	20	30	60	90	120	150	180	210	240	270	300	Postop
Group C	N	35	35	35	35	35	35	35	35	34	32	28	22	18	13	6	1	35
	Mean	97.95	95.69	95.66	100.71	97.37	96.63	95.45	97.16	95.47	96.53	96.53	95.23	95.85	99.22	98.77	99.30	96.93
	SD	4.32	3.57	3.824	3.556	4.25	5.00	4.01	5.57	5.15	4.54	5.62	5.34	5.43	3.25	2.40		2.573
Group A	N	35	35	35	35	35	35	35	35	35	33	30	26	16	12	4	4	35
	Mean	97.79	92.63	90.70	92.55	89.62	88.09	87.21	86.41	86.95	87.89	88.45	86.92	88.17	89.24	93.56	91.35	91.01
	SD	6.80	6.83	6.220	6.157	6.78	6.89	5.81	6.60	5.87	6.55	6.22	6.02	4.04	3.58	5.66	3.63	5.562
Group B	N	35	35	35	35	35	35	35	35	35	34	31	27	18	14	9	5	35
	Mean	98.72	92.97	92.83	92.70	90.87	88.97	88.24	88.97	89.11	89.17	89.50	89.10	90.77	90.01	91.89	91.14	93.85
	SD	5.30	9.89	5.000	4.522	4.60	4.76	5.49	4.76	4.74	4.53	5.23	4.83	5.58	3.13	3.67	3.93	3.409
		.759	.141	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.015	.126	.480
		NS	NS	S	S	S	S	S	S	S	S	S	S	S	S	S	NS	NS

#### Heart Rate at different time interval among group

Group		Pre op MAP	5 min after bolus of study.	Just after induction	Just after intubation	10	20	30	60	90	120	150	180	210	240	270	300	Postop
Group C	N	35	35	35	35	35	35	35	35	34	32	28	22	18	13	6	1	35
	Mean	80.29	82.97	84.17	96.86	84.34	82.77	82.03	83.60	83.82	81.63	83.00	84.14	84.56	88.08	85.00	87.00	80.53
	SD	4.383	3.914	3.494	4.852	4.640	4.747	5.044	5.776	4.783	5.966	5.644	4.368	3.485	5.619	4.336		3.560
Group A	N	35	35	35	35	35	35	35	35	35	33	30	26	16	12	4	4	35
	Mean	81.00	77.83	75.17	72.34	70.36	71.11	71.26	71.94	73.57	70.42	71.83	74.23	71.50	73.08	70.35	72.00	78.31
	SD	9.007	6.224	6.494	6.873	7.352	6.764	8.240	8.073	6.608	6.792	6.075	5.645	6.290	6.103	8.057	6.325	5.274
Group B	N	35	35	35	35	35	35	35	35	35	34	31	27	17	13	9	5	35
	Mean	83.03	79.17	75.69	73.24	72.14	71.83	71.49	72.66	73.64	73.18	73.71	76.22	75.35	73.54	74.78	77.60	79.17
	SD	6.977	5.096	5.598	5.939	6.045	6.866	5.908	6.296	5.578	6.355	7.422	5.086	5.533	3.205	5.563	5.550	4.469
		.245	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.003	.0125	.060	

#### Mean Spo2 requirement during different time interval

Group		Pre op MAP	5 min after bolus of study.	Just after induction	Just after intubation	10	20	30	60	90	120	150	180	210	240	270	300	Postop
Group A	N	35	35	35	35	35	35	35	35	35	33	30	26	16	12	5	4	35
	Mean	99.97	99.69	99.57	99.51	99.77	99.66	99.77	99.71	99.86	99.70	99.63	99.88	99.75	99.67	100.00	99.75	100.00
	SD	0.169	.583	.778	.853	.547	.725	0.646	.789	.355	.637	.718	.326	.775	.888	0.000	.500	.000
Group B	N	35	35	35	35	35	35	35	35	35	34	31	27	18	14	9	5	35
	Mean	99.97	99.83	99.83	99.80	99.74	99.89	99.91	99.77	99.80	99.76	99.84	99.81	99.94	99.93	99.89	99.80	100.0
	SD	.169	.453	.453	.584	.505	.323	.373	.690	.406	.654	.454	.483	.236	.267	.333	.447	0.000
Group C	N	35	35	35	35	35	35	35	35	34	32	28	22	18	13	6	1	35
	Mean	99.97	99.86	99.80	99.91	99.83	99.89	99.89	99.89	99.79	99.94	99.75	99.77	99.78	100.0	99.83	100.0	100.0
	SD	.169	.355	.584	.284	.453	.323	.323	.323	.641	.246	.518	.429	.548	0.000	.408		0.00
		1.000	.271	.169	.200	.769	.088	.406	.516	.834	.197	.380	.644	.537	.252	.687	.895	NA

Mean value of hemodynamic parameters was comparable between all three groups.

All the three groups were comparable with respect to age, sex, body weight and the duration of surgery ( $P>0.05$ ). In recovery period, the time to reach BIS to 80 was found to be significantly more in Group B compared to Group C and Group A [ $P<0.001$ ]. When the groups were compared, all the three parameters of recovery (extubation time, response to verbal commands and time for orientation) were found to be significantly longer in Group B. There were no significant difference between the other two groups, i.e. Group A and Group C ( $P<0.001$ ) Propofol Induction, Maintenance and total propofol requirement dose found to be significantly more in Group C as compared to group B than Group A. ( $P<0.001$ ).

## Discussion

We studied the effects of magnesium sulphate and clonidine as adjuvant for general anaesthesia. When magnesium sulphate or clonidine was given preoperatively the dose of propofol for induction and maintenance was significantly reduced. In the magnesium sulphate group, no hemodynamic and cardiovascular effects were seen, but extubation time was longer and recovery was slower. A craniotomy is a most common surgical processor in neurosurgery in which a bone flap is temporarily removed relieving elevated intracranial pressure and from trepanation, the creation of a burr hole through the cranium in to the dura mater ect.<sup>11</sup> Titrating propofol with BIS monitoring during balanced anaesthesia decreased propofol use and significantly improved recovery. These findings indicate that the use of BIS may be valuable in guiding the administration of propofol intraoperatively. Ray M, Bhattacharjee DP found that the time for BIS to reach 60 was considerably longer in control Group compared to clonidine Group and magnesium group, recovery period significantly longer in magnesium sulphate group and propofol consumption less in clonidine and magnesium groups<sup>10</sup>. In our study extubation time, response to verbal commands and time for orientation were also found to be significantly longer in magnesium sulphate group. There were no significant differences between the other two groups and propofol induction dose, maintenance dose and total propofol requirement was significantly more in control group. In our study, both magnesium sulphate and clonidine lowered the hemodynamic response to intubation but clonidine was more effective in attenuating the sympathetic response. Taittoven and colleagues compared clonidine and midazolam as premedication agents and observed no difference in oxygen consumption, anxiety, energy expenditure and carbon dioxide production.<sup>21</sup> Parenteral magnesium sulphate ( $MgSO_4$ ) has been used for many years as an antiarrhythmic agent and for prophylaxis against seizures in pre-eclampsia. Recently in anaesthetic practice it has been suggested that magnesium (Mg) has got the potential to treat and prevent pain by acting as an antagonist of N-methyl D-aspartate (NMDA) receptors<sup>13</sup>. Preoperative oral clonidine protects against the pressor response to intubation. Hypotension and bradycardia may be encountered with clonidine, and in our study we found more bradycardia and hypotension in the clonidine group than in the other groups. Clonidine has been shown to decrease propofol requirements during anaesthesia and our study confirms this. Preoperative administration of clonidine, in addition to careful anaesthetic management, results in improved perioperative haemodynamic stability in patients with mild or moderate arterial hypertension and a reduction of the anaesthetic requirement, but further studies are necessary to investigate whether this approach may be safely extended to hypertensive patients.

## Conclusion

Perioperative use of both clonidine and magnesium sulphate significantly reduced the requirement of propofol. Clonidine was associated with bradycardia and hypotension. Magnesium sulphate caused a delay in recovery. Therefore, both clonidine and magnesium sulphate need careful management, to be used as adjuvant agents to general anaesthetics.

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