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Comparison of Intravenous Magnesium Sulphate and Clonidine in Attenuating Hemodynamic Responses during Laryngoscopy and Tracheal Intubation

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Abstract

Background: Laryngoscopy and endotracheal intubation is essential to maintain patent airway during surgery under general anaesthesia but results in reflex sympathoadrenal stimulation leading to elevated blood pressure and heart rate. The present study was undertaken to compare the efficacy of intravenous magnesium sulphate and clonidine in attenuation of these haemodynamic responses. *Materials and Methods*: This is a prospective randomized double-blind study conducted over a period of one year in patients undergoing elective open abdominal surgery under general anaesthesia at our centre. A total of 80 normotensive patients were randomized into two groups, Group M received intravenous magnesium sulphate 30mg/kg, and Group C received intravenous clonidine 2 µg /kg. All patients received standard induction with propofol, vecuronium, fentanyl and O2:N2O (50:50). Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were recorded from baseline until ten minutes after intubation at specific intervals. *Results*: There was a significant decrease in HR, SBP, DBP and MAP compared to baseline value at ten minutes after tracheal intubation in both Group M and Group C. The difference between the two groups was also statistically significant with p value of 0.006, 0.037 and 0.036 for SBP, DBP and MAP respectively with greater attenuation noted in group M. *Conclusion*: Intravenous Magnesium sulphate given at 30mg/kg was found to be significantly more effective than intravenous clonidine given at 2 µg /kg in attenuating the pressor response to laryngoscopy and tracheal intubation

Keywords: Clonidine, Haemodynamic response, Intubation, Laryngoscopy, Magnesium sulphate.

INTRODUCTION

Laryngoscopy and endotracheal intubation are essential to maintain patent airway during surgery under general anaesthesia and in intensive care unit for mechanical ventilation. However, they result in reflex sympathoadrenal stimulation with increase in catecholamines, norepinephrine and epinephrine [1] leading to elevated blood pressure and heart rate. These sympathetic effects are short acting but can be detrimental in high-risk patients especially in patients with cardiovascular disease. Therefore, it is imperative to effectively attenuate sympathetic response to laryngoscopy and intubation with anaesthetic management that simultaneously fulfills other criteria; there should be no effect on cerebral blood flow, prevent patient arousal, not time consuming, not affecting the duration or modality of anaesthesia, and must be applicable irrespective of patient co-operation. Many drugs are known to produce this effect, namely inhalational anaesthetics,[2,3] opioids,[4] short acting β-adrenergic blockers,[5] calcium channel blockers,[6] α-agonists,[7] and their combinations.[1,8] Magnesium sulphate[9] is effective in attenuating the

pressor response to tracheal intubation by inhibiting catecholamine release from adrenal medulla and adrenergic nerve endings. Clonidine [10] is a centrally acting α_2-adrenergic agonist. It stimulates pre-synaptic α_2 – adrenoreceptors, increases reuptake of nor-adrenaline and hence decreases central sympathetic outflow.

Aims and objectives: To compare the efficacy of intravenous (IV) 30mg/kg Magnesium sulphate [9] and IV 2 µg/kg clonidine [10] administered before induction of anaesthesia, in attenuating hemodynamic response to laryngoscopy and tracheal intubation in normotensive patients.

MATERIALS AND METHODS

This is a prospective, randomized, double blind study conducted in 80 patients undergoing elective open abdominal surgical procedure under general anaesthesia requiring endotracheal intubation. Inclusion criteria: Patients aged between 18 and 60 years with American Society of Anaesthesiologists (ASA) physical status grades 1 and 2. Exclusion criteria: Patients with ASA physical status grade 3 or higher, hypertensives, patients with anticipated difficult intubation (Mallampatti grade 4 or more), patients in whom intubation required multiple attempts, BMI > 30 kg/m^2, pregnant and lactating women, patients who had raised intracranial pressure, coronary artery diseases, impaired renal function, neuromuscular diseases, increased intraocular pressure, cardiac arrhythmias, GERD, hiatal hernia, patients who are allergic to the study drugs and patients not willing to participate in the study. Institutional Ethics Committee approval was obtained. Written informed consent was taken from each patient participating in the study.

Patients were randomly divided in to two groups, each comprising 40 patients. Randomization was done before start of the study by using a computer-generated random number table and sealed opaque envelope technique. The random drug was administered to the patient by the anaesthetist who was blinded to the nature of the drug and who made the observations. Group 'M' received Injection magnesium sulphate 30 mg/kg[9] added in 100 ml NS intravenously over 10 minutes before induction. Group 'C' received Injection Clonidine 2 µg/kg[10] in100 ml NS intravenously over 10 minutes, before induction.

Pre-operative evaluation was done a day before surgery and once determined fit for surgery, the patients were kept nil per oral 6 hours for solids and 2 hours for clear liquids, premedicated with tablet Alprazolam 0.25mg oral on the night before surgery and tablet Ranitidine 150 mg oral on the night before surgery as well in the morning on the day of surgery. In the operating room, patient monitoring was done with Electro cardiogram (ECG), Non-invasive blood pressure (NIBP), pulse oximeter (SpO_2), End tidal CO_2 ($ETCO_2$). Intravenous access was achieved with 18G cannula under local anaesthesia. Baseline values of hemodynamic parameters, heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP) were noted.

The study drug was given to the patient over a period of 10 minutes, before induction of anaesthesia and patient was monitored adverse effects hypotension, restlessness, agitation, confusion, and respiratory depression. Patient was ventilated by facemask using 100 % oxygen for 3 minutes to maintain adequate oxygenation and normocapnia. Anaesthesia was induced with fentanyl 2 µg/kg and propofol 2mg/kg until loss of verbal contact. Vecuronium 0.1mg/kg intravenously was given to facilitate endotracheal intubation. Analgesia was maintained with Fentanyl 1 µg/kg given every one hour intravenously. Laryngoscopy and intubation was done 3 minutes after administration of vecuronium. When laryngoscopy procedure exceeded 30 seconds or required multiple attempts for intubation, the patient was excluded from the study. Maintenance of anaesthesia was achieved with Isoflurane 0.5-2% depending on hemodynamic variations and Isoflurane inhalation rate was altered according to blood pressure variations. Vecuronium 0.02 mg/kg intravenously was given every 30 minutes for optimum muscle relaxation

The haemodynamic parameters heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were recorded at each of the following points: baseline (BL), at the end of study drug infusion, after induction of anaesthesia, immediately after intubation, and at 1 minute, 2 minutes, 3 minutes, 4 minutes, 5 minutes, 7 minutes and 10 minutes after intubation. Episodes of hypotension were defined as MAP < 20% of baseline for >60 seconds. Episodes of hypertension were defined as MAP > 20% of baseline for >60 seconds. Episodes of Tachycardia were defined as HR>

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100bpm. Episodes of Bradycardia were defined as HR<50bpm. Study period ended in 15 minutes after start of administration of study drugs. During the study period, other stimuli were avoided like bladder catheterization, nasogastric tube insertion, change in position or surgical incision.

Statistical analysis

Statistical analysis was performed using SPSS 17.0 software. Quantitative variables age, weight, HR, SBP, DBP, MAP was expressed as Mean and Standard deviation. Inter group data was analyzed using unpaired student's t-test. Intra group data was analyzed using repeated measures ANOVA (analysis of variance) and appropriate post hoc test. For Qualitative variables, chi-square test was used. Pearson's correlation-coefficients were calculated between different quantitative variables. A p value of < 0.05 was considered statistically significant.

RESULTS

The study included 80 patients. The demographic characteristics, mean age, weight, height, BMI, sex ratio, ASA physical status was comparable between the two groups with no statistically significant differences (Table 1). The differences in Mallampati grade among patients in the two groups were not statistically significant (p value 0.232) (Figure 1).

The baseline values of HR, SBP,DBP and MAP were comparable between group M and group C (p value >0.05).

Heart Rate (HR): Intergroup difference**:** HR showed difference at all time intervals between the two groups. However, these differences were not statistically significant. Intragroup difference**:** In both Group M and Group C, HR varied compared to baseline at all the time intervals within each individual group, with statistically significant observations between 4 and 10 minutes in Group M and at intervals between 5 and 10 minutes after intubation in Group C, as shown in Table 2.

Systolic Blood Pressure (SBP): Intergroup difference**:** SBP differed between the two groups at all intervals of time, however these differences were statistically significant only at 10 minutes after intubation. SBP was 101.15±10.327 in group M and 108.35±12.257 in group C with a p value of 0.006. Intragroup difference: SBP varied compared to baseline value, at all the time intervals within each individual group, however they were statistically significant at 1 minute after intubation in group C and, at end of infusion, after induction and intervals between 2 and 10 minutes in both group M and group C as shown in Table 3.

Diastolic Blood Pressure (DBP): Intergroup difference**:** Diastolic blood pressure varied between the two groups, at all the time intervals. However, this difference between the two groups is statistically significant only at 10 minutes after intubation. DBP was 63.88±7.852 in Group M and 67.90±9.035 in Group C; p value=0.037. Intragroup difference: DBP varied when compared to baseline value, at all the time intervals within each individual group, however they were statistically significant only at intervals between 3 and 10 minutes after intubation in Group M and at 4, 7 and 10 minutes after intubation in Group C, as shown in Table 4.

Mean Arterial Pressure (MAP): Intergroup difference: Mean arterial pressure (mm of Hg) showed difference at all the time intervals between the two groups, however, this difference is statistically significant only at 5 minutes after intubation (Group M=76.28±7.54, Group C=80.10±8.512; p value=0.037) and 10 minutes after intubation (Group M=73.53±8.970, Group C=77.68±8.456; p value=0.036). Intragroup difference: In both Group M and Group C when compared to baseline value, MAP showed difference at all the time intervals within each individual group, however they were statistically significant at end of infusion for Group M, at 2 minutes after intubation for Group C, after induction and at intervals between 3 and 10 minutes for both Group M and Group C, as shown in Table 5.

The maximal increase in HR, SBP, DBP and MAP compared to baseline value occurred immediately after tracheal intubation in both the groups and there was no statistically significant difference between the groups. Among all 80 patients, none developed hypertension, hypotension, tachycardia, bradycardia.

DISCUSSION

The efficacy of intravenous Magnesium sulphate in attenuation of haemodynamic response during laryngoscopy and endotracheal intubation was assessed at different doses by various investigators, Elsharnouby NM and Elsharnouby MM[11] (40mg/kg),

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Puri GD et al[12] (50mg/kg), James MF et al[13] (60 mg/kg) and Trivedi V and Patel RA[14] (30 mg/kg).

In a study by Elsharnouby NM and Elsharnouby MM[11] the authors administered intravenous magnesium sulphate before induction of anaesthesia at 40 mg/ kg bolus, and as 15 mg/kg/hr by continuous infusion during the surgical procedure, in patients undergoing functional endoscopic sinus surgery. They observed that the drug was effective in reducing MAP, HR apart from having effect on reducing loss of blood and the time duration of surgery. In addition, episodes of hypotension (MAP<50mmHg), reflex tachycardia or arrhythmia were not seen neither was there rebound hypertension. In our study, we gave magnesium sulphate 30 mg/kg only before induction and noted significant efficacy in attenuation of HR, SBP, DBP and MAP with no episodes of hypotension, bradycardia, hypertension or tachycardia. Puri GD et al[12] studied the efficacy of 50mg/kg magnesium sulphate before induction in cardiac patients who underwent elective coronary artery bypass grafting. They observed significant benefits with respect to HR, MAP and systemic vascular resistance. James MF et al[13] employed pre-treatment with 60 mg/kg of intravenous magnesium sulphate. After intubation, compared to the control group, in the magnesium group, heart rate and epinephrine levels were unchanged, while SBP and norepinephrine levels were less elevated and all these differences were found statistically significant. Panda NB et al[9] did a study in controlled hypertensives posted for elective surgery to assess the effect of magnesium sulphate infusion at doses of 30, 40 and 50 mg/kg administered to patients randomized into 3 groups respectively. They observed that variations in HR were comparable among the groups, MAP remained within normal limits in 30mg/kg group while it showed a significant decrease compared to baseline in patients given 40 or 50 mg/kg with a p value of 0.01. Among patients administered 30, 40, 50mg/kg and controls, none, 30%, 80%, and 5% patients respectively needed intervention to control episodes of hypotension. They concluded that in controlled hypertensive patients, the optimum dose of magnesium sulphate to attenuate pressor response to intubation is 30mg/kg and increased doses could lead to hypotension. In the present study, we found magnesium sulphate to be efficacious at a dose of 30 mg/kg, in normotensive patients, similar to the study by Trivedi V and Patel RA[14] who compared the efficacy of intravenous magnesium sulphate 30 mg/kg with buprenorphine 3 µg/kg and placebo (normal saline) given 3 minutes before intubation in normotensive patients needing general anaesthesia. They found magnesium sulphate to be more efficacious than buprenorphine in attenuating pressor response to laryngoscopy and intubation. Bandey S and Singh V [15] compared efficacy of 30 mg/kg magnesium sulphate with 1.5mg/kg lidocaine administered 1 minute prior to intubation and noted significant benefits with magnesium and no adverse effects.

Kulka PJ et al[16] noted that the efficacy of IV clonidine is dose related in attenuating stress response to laryngoscopy and intubation but mentioned that an increase beyond 4 µg/kg does not provide added benefit. In our study we used intravenous clonidine at a dose of 2 µg/kg. In their study, Zalunardo et al[17] compared IV clonidine 3 µg/kg given just before induction, oral clonidine 4 µg/kg given before induction, and placebo. They noted that the rise in MAP and cardiac output, during intubation, was significantly lower in the IV clonidine group than in oral clonidine group and placebo. However MAP, HR and cardiac output were similar among the three groups, ten minutes after intubation. No episodes of hypotension or bradycardia were noted. In a study by Chatrapathi S et al[18] in patients undergoing elective surgery, premedication with IV clonidine 3 µg/kg resulted in significantly lower increase in HR, SBP, DBP, MAP and rate pressure product from baseline values after laryngoscopy and tracheal intubation compared to control group ($p< .05$). Sameenakousar et al[10] found that 2µg/kg IV clonidine administered 5 minutes before laryngoscopy and intubation was more effective than fentanyl and there were no side effects. They observed in the clonidine group the attenuation of HR, SBP, DBP, MAP was significant ($p<0.001$) compared to fentanyl and control group, immediately after laryngoscopy and at 7 and 10 minutes from preinduction. On the other hand, Arora S et al[19] in a study on patients undergoing breast surgery concluded that IV clonidine 1 µg/kg administered with 2 µg/kg fentanyl was effective and clonidine 2 µg/kg resulted in hypotension.

Ray M et al[20] assessed the impact of intravenous clonidine 3 µg/kg bolus prior to induction and 1µg/kg/hour infusion intraoperatively and compared it with magnesium 30 mg/kg bolus prior to induction and

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10 mg/kg/hour by infusion intraoperatively in patients undergoing elective upper limb orthopaedic surgery. They noted that both drugs significantly reduced the need for propofol and fentanyl citrate, significantly attenuated haemodynamic response to intubation but were also associated with episodes of bradycardia and hypotension and Magnesium sulphate resulted in a delayed recovery. Altan A et al[21] reported that magnesium sulphate and clonidine attenuated HR, MAP in response to intubation with no statistically significant differences between the two groups. They employed MgSO4 30mg/kg before induction and 10 mg/kg/hr by infusion to one group and 3mg/kg clonidine IV at induction along with 2mg/kg/hr as maintenance intraoperatively to the other group of patients. Further they noted bradycardia and hypotension in clonidine group. In our study we administered 30mg/kg magnesium sulphate or 2 µg/kg clonidine only before induction with no maintenance doses, both attenuated hemodynamic response to laryngoscopy and tracheal intubation but magnesium sulphate resulted in greater decrease in SBP, DBP, MAP from baseline ($p<0.05$) with no episodes of hypotension or bradycardia in either group. In a study by Palak PS et al[22] in patients undergoing laproscopic surgery they compared the efficacy of IV clonidine 1.5 µg/kg given 30 minutes before surgery and 1µg/kg/hr intraoperatively with IV magnesium sulphate 50mg/kg given 30 minutes before surgery and 10mg/kg/hr intraoperatively before creation of pneumoperitoneum. They concluded that, at the dose given in their study, IV clonidine is more effective than IV magnesium sulphate to attenuate haemodynamic response to laryngoscopy and intubation but found the both drugs to be equally effective for the same purpose in response to pneumoperitoneum

CONCLUSIONS

We conclude that 30mg/kg magnesium sulphate and 2 µg/kg clonidine are effective in attenuating hemodynamic response to laryngoscopy and tracheal intubation with no episodes of bradycardia, hypotension, tachycardia or hypertension. Magnesium sulphate appeared to be significantly more effective than clonidine in attenuating the hemodynamic response as it resulted in greater decrease in SBP, DBP, MAP from baseline.

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TABLES

Table 1: Comparison of demographic data between the study groups

Variables	Group M (n=40)	Group C (n=40)	p value
Age (years)	45.88±10.8	46.23±9.4	0.878
Sex (Male/Female)(n)	24/16	21/19	0.499
Weight (Kg)	56.20±12.0	54.35±9.9	0.457
Height (Cms)	158.13±6.1	156.75±7.1	0.359
BMI(kg/m^2)	22.32±3.7	22.13±3.3	0.808
ASA grade I/II(n)	33/7	37/3	0.176

Table 2: Effects on Heart Rate: Intragroup and intergroup comparison

HR (beats/min)	Group M	Intragroup p value (from BL)	Group C	Intragroup p value (from BL)	Intergroup p value
BL	85.80±14.864	1.000	87.53±15.702	0.326	0.615
End of infusion	85.03±14.350	1.000	85.88±14.092	0.326	0.790
After induction	83.48±13.882	0.216	84.60±13.046	0.060	0.710
Immediately after intubation	89.48±12.683	0.062	90.73±11.739	0.794	0.649
1 min	86.28±11.921	1.000	88.28±11.241	1.000	0.442
2 min	83.80±11.574	1.000	85.78±10.776	1.000	0.432
3 min	82.30±11.757	0.711	83.83±10.130	1.000	0.536
4 min	80.23±12.050	0.003	81.70±9.635	0.091	0.547
5 min	78.80±12.327	0.000	79.85±9.852	0.008	0.675
7 min	76.85±12.450	0.000	77.43±9.145	0.000	0.815
10 min	75.90±12.659	0.000	75.93±9.752	0.000	0.992

Table 3: Effects on SBP: Intragroup and intergroup comparison

SBP (mm Hg)	Group M	Intragroup p value (from BL)	Group C	Intragroup p value (from BL)	Intergroup p value
BL	126.53±17.257		131.35±15.408		0.191
End of infusion	121.35±15.666	0.003	125.33±14.577	0.001	0.244
After induction	114.20±13.975	0.000	119.68±13.501	0.000	0.079
Immediately after intubation	127.63±17.009	1.000	131.13±17.511	1.000	0.367
1 min	118.65±13.229	0.220	121.20±16.028	0.000	0.440
2 min	112.50±14.399	0.000	114.18±13.156	0.000	0.589
3 min	109.45±11.565	0.000	111.53±12.780	0.000	0.449
4 min	106.80±13.294	0.000	108.08±10.774	0.000	0.639
5 min	105.03±10.151	0.000	108.60±10.947	0.000	0.134
7 min	101.15±17.401	0.000	107.23±12.219	0.000	0.075
10 min	101.15±10.327	0.000	108.35±12.257	0.000	0.006

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Table 4: Effects on DBP: Intragroup and intergroup comparison

DBP(mm hg)	Group M	Intragroup p value (from BL)	Group C	Intragroup p value (from BL)	Intergroup p value
BL	75.28±8.869	1.000	77.23±13.124	1.000	0.439
End of infusion	73.18±10.741	1.000	75.03±9.810	1.000	0.424
After induction	70.20±10.191	0.368	73.33±10.209	1.000	0.175
Immediately after intubation	79.38±10.930	1.000	78.68±10.264	1.000	0.769
1 min	73.50±9.298	1.000	74.60±10.005	1.000	0.612
2 min	70.25±8.877	0.429	71.10±9.915	0.146	0.687
3 min	68.18±9.766	0.043	69.70±9.592	0.055	0.483
4min	66.78±8.810	0.007	68.28±8.990	0.003	0.453
5 min	66.23±7.898	0.002	69.70±9.699	0.160	0.083
7 min	64.88±8.410	0.000	66.83±8.427	0.002	0.303
10 min	63.88±7.852	0.000	67.90±9.035	0.018	0.037

Table 5: Effects on MAP: Intragroup and intergroup comparison

MAP (mm hg)	Group M	Intragroup p value (from BL)	Group C	Intragroup p value (from BL)	Intergroup p value
BL	88.20±11.145	1.000	90.45±12.736	1.000	0.403
End of infusion	85.05±11.101	0.000	87.73±9.785	1.000	0.256
After induction	82.15±11.201	0.039	85.20±10.385	0.016	0.210
Immediately after intubation	91.48±11.580	1.000	92.15±10.654	1.000	0.787
1 min	85.18±9.462	1.000	86.13±10.031	0.915	0.664
2 min	81.23±8.628	0.098	82.10±10.233	0.002	0.680
3 min	78.35±10.047	0.002	80.40±10.056	0.001	0.365
4 min	76.65±8.592	0.000	78.08±8.383	0.000	0.455
5 min	76.28±7.541	0.000	80.10±8.512	0.001	0.037
7 min	75.53±9.165	0.000	77.38±8.408	0.000	0.350
10 min	73.53±8.970	0.000	77.68±8.456	0.000	0.036

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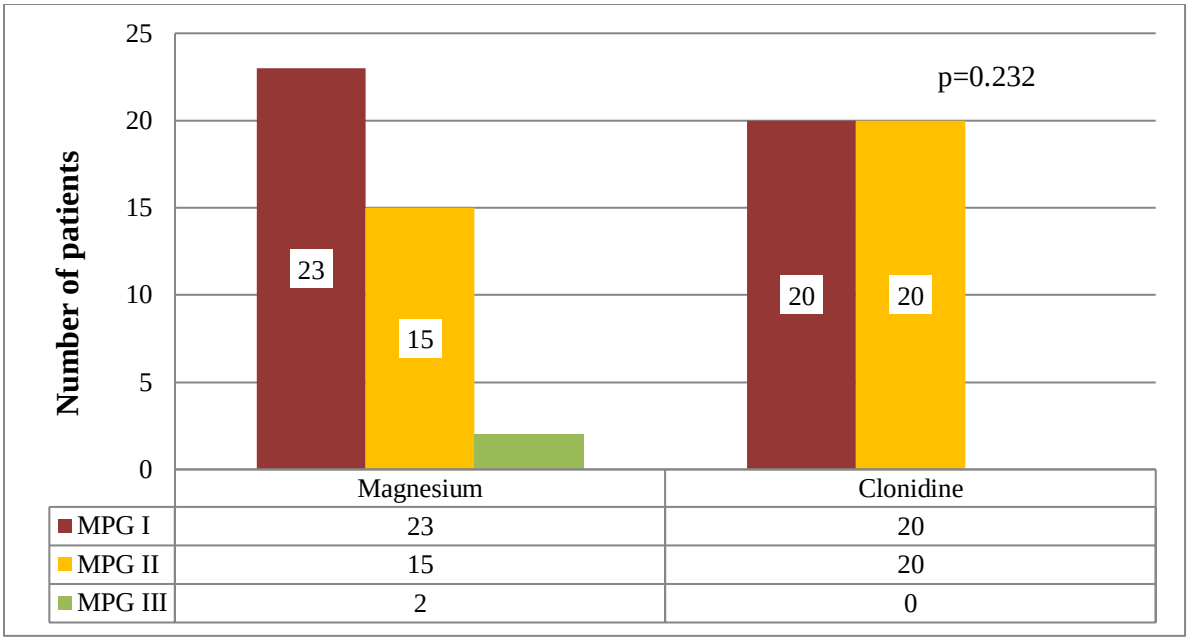
FIGURES

Figure 1



	Magnesium	Clonidine
MPG I	23	20
MPG II	15	20
MPG III	2	0

FIGURE LEGENDS

Figure 1: Comparison of Mallampati grade between study groups.

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