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WEST AFRICAN JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Attenuating the Pressor Response to Laryngoscopy and Endotracheal Intubation in Controlled Hypertensives: The Effect of Combining Lidocaine and Magnesium Sulphate

Atténuation de la Réponse Pressive à la Laryngoscopie et à l'Intubation Endotrachéale chez les Hypertendus Contrôlés : Effet de L'association de la Lidocaïne et du Sulfate de Magnésium

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ABSTRACT

BACKGROUND: Laryngoscopy and intubation result in a pressor response which may be deleterious especially in hypertensives, resulting in potentially harmful effects. Many drugs have been used to attenuate this undesirable pressor response to laryngoscopy and intubation in hypertensives; amongst them are magnesium alone in different doses or in combination with lidocaine. However, drug combinations have been found to be more effective than single drug therapy.

OBJECTIVE: This study compared the different doses of magnesium sulphate and its combination with lidocaine for the attenuation of the pressor response.

METHODS: A prospective, randomized, double-blinded study. Nighty-six controlled hypertensives (ASA physical status II) scheduled for elective surgery under general anaesthesia and who required endotracheal intubation were recruited and randomized into either Group I (they received 30mg/kg of IV $MgSO_4$ plus 1.5mg/kg of 2% lidocaine) or Groups II and III who received 30mg/kg and 40mg/kg of IV $MgSO_4$ alone, respectively. The outcome was the change in the systolic blood pressure (SBP) from the baseline following administration of study medication and after laryngoscopy and endotracheal intubation. The side effects of study medication and changes in serum magnesium level prior to and after 30 minutes of administering study medication were documented.

RESULTS: The post-intubation SBP was attenuated in patients in groups I and III only. However, five patients in group III had hypotension. Serum magnesium levels were higher than their respective baseline values in all the groups.

CONCLUSION: The combination of 1.5 mg/kg of 2% lidocaine and 30 mg/kg of $MgSO_4$ is more effective than 30 mg/kg of $MgSO_4$ alone and even $MgSO_4$at the higher dose of 40 mg/kg. **WAJM 2023; 40(2): 129–136.**

Keywords: Magnesium sulphate, Lidocaine, Laryngoscopy and endotracheal intubation, Haemodynamic response, Serum levels of $MgSO_4$.

RÉSUMÉ

CONTEXTE: La laryngoscopie et l'intubation entraînent une réponse pressive, qui peut être délétère, surtout chez les hypertendus, entraînant des effets potentiellement dangereux. De nombreux médicaments ont été utilisés pour atténuer cette réponse pressive indésirable à la laryngoscopie et à l'intubation chez les hypertendus, parmi lesquels le magnésium seul à différentes doses ou en association avec la lignocaïne. Cependant, les associations de médicaments se sont avérées plus efficaces qu'un traitement médicamenteux unique.

OBJECTIF: Cette étude a comparé les différentes doses de sulfate de magnésium et son association avec la lidocaïne pour l'atténuation de la réponse pressive.

MÉTHODES: Une étude prospective, randomisée, en double aveugle. Six hypertendus contrôlés (statut physique ASA II) prévus pour une chirurgie élective sous anesthésie générale et nécessitant une intubation endotrachéale ont été recrutés et randomisés dans le groupe I, ils ont reçu 30mg/kg de MgSO4 1V plus I,5mg/kg de lidocaïne à 2%, les groupes II et III ont reçu respectivement 30mg/kg et 40mg/kg de MgSO4 IV seul. Les résultats étaient les changements de la pression artérielle systolique (PAS) par rapport à la ligne de base après l'administration du médicament étudié et après la laryngoscopie et l'intubation endotrachéale. Les effets secondaires du médicament à l'étude et les changements du taux de magnésium sérique avant et après 30 minutes d'administration du médicament à l'étude ont été documentés.

RÉSULTATS: La PAS après intubation a été atténuée chez les patients des groupes I et III seulement. Cependant, cinq patients du groupe III ont présenté une hypotension. Les niveaux de magnésium sérique étaient plus élevés que leurs valeurs de base respectives dans tous les groupes.

CONCLUSION: L'association de 1,5 mg/kg de lidocaïne à 2 % et de 30 mg/kg de MgSO4 est plus efficace que 30 mg/kg de MgSO4 seul et même à la dose supérieure de 40 mg/kg. **WAJM 2023; 40(2): 129–136.**

Mots clés: Sulfate de magnésium, Lidocaïne, Laryngoscopie et intubation endotrachéale, Réponse hémodynamique, Taux sériques de MgSO4.

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INTRODUCTION

Laryngoscopy with tracheal intubation is an integral component of general anaesthesia. This procedure, though beneficial (prevents aspiration and aids ventilation), may be harmful.[1] The increase in blood pressure and heart rate (pressor response) during laryngoscopy and endotracheal intubation is transient, occurring 30 seconds after intubation and lasting up to 10–15 minutes.[2] It can be deleterious in patients with systemic hypertension and may result in potentially harmful effects like myocardial infarction, stroke or arrhythmias.[3]

A wide variety of pharmacological agents have been used to attenuate the haemodynamic responses to laryngoscopy and endotracheal intubation – including lidocaine, propofol, dexmedetomidine, fentanyl, alfentanyl, remifentanil, nifedipine, beta-blockers, gabapentin, magnesium sulphate, verapamil, nicardipine, and diltiazem - with varying results.[4] Some of these agents are not without drawbacks. Increasing the doses of these agents is associated with increasing efficacy and side effects. However, some drug combinations at reduced doses have been found to be more effective in addition to having a reduced incidence of side effects than single drug therapy.[5]

Magnesium and lidocaine are easily accessible in our environment; hence, this study compared increasing doses of magnesium sulphate (30 mg/kg and 40 mg/kg) to a combination of 30 mg/kg of magnesium sulphate and 1.5 mg/kg of lidocaine for the attenuation of the pressor response in controlled hypertensive patients.

MATERIALS AND METHODS

This study was a prospective, randomized, double-blinded study. The study was carried out in a tertiary hospital in Nigeria. The study population was 96 individuals who were known hypertensive patients between the ages of 30–55 years. Patients recruited were controlled hypertensives (ASA physical status II) scheduled for elective surgery under general anaesthesia and who required endotracheal intubation.

Sample size estimation resulted in 28 patients in each group using the formula [6] $n=2[(a+b)^{2\partial 2}]/(\mu_1-\mu_2)$: where n is the sample size for each group, a is the value of alpha or type 1 error at 0.05, b is the value of beta at 0.20 or power of 0.80, ∂^2 is the population variance (SD) while $\mu_1-\mu_2$ is the effect size. We assumed a 10% reduction in blood pressure equivalent to 11.50mmHg when a combination of magnesium and lidocaine was used to obtund the pressor response, as against the blood pressure of 110.50 ±14.1mmHg obtained by Chaithanya *et al*[7] when 30 mg/kg of $MgSO_4$ was used alone in obtunding pressor response. A total of 96 patients – 32 in each group – were recruited when 15% loss due to protocol violation was factored in.

Socio-demographic data and perioperative events were obtained using a structured questionnaire. Inclusion Criteria: Adults of both sexes, aged between 30–55 years, ASA II controlled hypertensives, patients with blood pressure less than 160/90mmHg (British Heart Society)[8] undergoing elective surgeries under general anaesthesia with endotracheal intubation. Exclusion Criteria: patient's refusal, pregnancy, emergency surgery, patients with known allergies to the study drugs, morbid obesity, impaired cardiac, renal or liver function, anticipated difficult airway, neuromuscular diseases and arrhythmias.

Ethical clearance was obtained from the Research and Ethics Committee of the Hospital. Randomization was by blind balloting which was carried out by a registrar without any other task in this study. The patient was to pick among sealed opaque envelopes of equal sizes from a bag and was randomly assigned into one of the three groups – I, II, or III.

Procedure

During the preoperative evaluation, investigations were carried out which included full blood count, blood grouping and cross-matching, serum electrolytes/urea/creatinine, urinalysis, chest x-ray and electrocardiography. The study and its protocol were explained to the patients and written consent was obtained. Patients were all fasted according to the ASA fasting guideline and they received preoperative oral diazepam 10 mg and their antihypertensive drugs in the morning on the day of the surgery with a sip of water. Nonetheless, angiotensin-converting enzyme inhibitors were withheld and replaced with amlodipine tablets.

On arrival of the patient in the operating theatre, baseline parameters were taken and recorded. Intravenous access was established and blood sample collected for baseline serum magnesium level. The study drugs were prepared by an assistant (first assistant) while a second assistant administered it with no other task thereafter.

Group I patients (ML) received 30 mg/kg of 50 % magnesium sulphate in 100 ml of normal saline which ran as an infusion over 10 minutes. At the end of the infusion, 1.5 mg/kg of 2% lidocaine was also diluted to 10 ml with sterile water and was given as a bolus over 30 seconds. Group II (M30) patients received 30 mg/kg of 50 % magnesium sulphate diluted in 100 ml of normal saline that ran as an infusion over 10 minutes. Group III patients (M40) received 40 mg/kg of 50 % magnesium sulphate in 100 ml of normal saline which ran as an infusion over 10 minutes. However, Groups II and III both had 10 ml of sterile water which was given as bolus over 30 seconds at the end of the infusion of their study drug.

Patients were induced with 4 mg/kg of intravenous sodium thiopentone while laryngoscopy and endotracheal intubation was facilitated with 1.5 mg/kg of intravenous suxamethonium. After fasciculation, laryngoscopy was carried out and the trachea was intubated (5 minutes post-administration of study drug) with an appropriate-sized endotracheal tube. Laryngoscopy and endotracheal intubation were performed by an anaesthetist of at least a senior registrar cadre who was skilled in the procedure of laryngoscopy. After the confirmation of the endotracheal tube placement, the patient was connected to the anaesthetic machine via a closed-circuit system.

Time taken after fasciculation and apnoea to achieve endotracheal intubation was noted, as well as the number of attempts at intubation. An attempt at intubation was described by ability or inability to pass the endotracheal tube

through the glottic opening after insertion of the laryngoscope into the mouth. Patients whose duration of laryngoscopy was greater than 30 seconds or had more than two attempts were excluded from the study.

Anaesthesia was maintained using 1.2% of isoflurane in 100 % oxygen and intravenous atracurium 0.5 mg/kg was used for neuromuscular paralysis. Analgesia was achieved using fentanyl 1–2 mcg/kg (repeated after 30–45 minutes if surgery continued), paracetamol 15 mg/kg and ketorolac 0.5 mg/kg (except when contraindicated).

Patient vital signs were measured at the beginning (as baseline) and subsequently every 2 minutes up to 10 minutes during the administration of study drug (pre-induction) and after intubation at the 1st, 2nd, 3rd, 4th, 5th, 10th and 15th minute after intubation. During this period surgery was not allowed to commence. Data collection, collation and analysis were done by the investigator. Blood sample for serum magnesium was taken 30 minutes post-administration (peak serum concentration) and analysed. At the end of surgery, the oropharynx was suctioned under direct vision. Residual neuromuscular paralysis was antagonized with 0.04 mg/kg neostigmine and 4 mcg/kg glycopyrrolate. The volatile agent was discontinued and the trachea was extubated. Supplemental oxygen was administered after extubation for a few minutes and the patient was then transferred to the recovery room.

Hypotension and hypertension were taken as either a decrease or increase in systolic blood pressure of more than 20% from the baseline. Hypotension was treated by reducing the concentration of the volatile agent or by increasing the intravenous fluid (500 ml over 30 minutes) and/or the administration of 3 mg aliquots of ephedrine. Hypertension was managed by increasing the concentration of the volatile inhalational agent, reducing intravenous fluid or by giving intravenous labetalol in 10 mg aliquots slowly. Bradycardia was taken as a decrease in heart rate of more than 20 % from the baseline which was treated with 0.6 mg atropine.

The primary outcome was the percentage change in the SBP from the baseline following laryngoscopy and endotracheal intubation while the secondary outcomes were the percentage change in the HR from the baseline following laryngoscopy and endotracheal intubation, the incidence of side effects (hypotension, bradycardia, tachycardia, ST segment changes) following administration of lidocaine and magnesium sulphate, and the difference between the pre-administration and 30 minutes post-administration levels of serum magnesium.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 20.0 (IBM SPSS Modeler). Categorical variables were expressed as actual numbers and percentages. Continuous variables such as weight and height were tested for normal distribution with the Kolmogorov-Smirnov test and were expressed as mean ± standard deviation (SD) or median (minimum ± maximum). One-way analysis of variance (ANOVA) was used to identify significant differences between group means. Differences among the three group medians were estimated by the Kruskal Wallis test. Paired t test was used to check the difference in values before and after induction within the same group; $p < 0.05$ was considered statistically significant. Bonferroni correction was made to control type I error in all sub-analyses.

RESULTS

A total of 96 patients were recruited into the study. However, thirty in each group successfully completed this study. Six patients were excluded due to protocol violation, multiple attempts at laryngoscopy and incomplete data documentation.

The combination of 30 mg/kg $MgSO_4$ and 1.5 mg/kg of lidocaine (Group I) resulted in better attenuation of systolic blood pressure when compared to 30 mg/kg (Group II) or 40 mg/kg $MgSO_4$ (Group III). The incidence of hypotension was highest in Group III with 16.67%, amounting to 5.56 % of the total number of patients recruited in the study.

Table 2 shows the mean baseline SBP, pre-induction SBP (post-administration of study drugs), their mean differences from baseline and percentage difference in the three study groups. The post-administration (pre-induction) SBP in Group 1 (ML) was 123.37±16.82mmHg (mean difference from baseline of 21.86). This represents a 15% decrease from baseline. Following laryngoscopy and endotracheal intubation, the SBP rose above the pre-induction value (141.90±10.27mmHg at 1 minute post-intubation) and then subsequently reduced from 2 minutes up till 5 minutes post-intubation before beginning to rise from 10 minutes to 15 minutes post-intubation. The peak rise (141.90 ± 10.20mmHg $p<0.001$) was at 1 minute post-intubation. This represents a 2.14% drop in mean baseline with a mean difference of 3.33±7.22.

In Group II (M30) patients, the pre-induction SBP was 126.57±10.99mmHg with a mean difference of 13.17 (9.5% decrease from baseline). Following laryngoscopy and endotracheal intubation, the SBP rose above the pre-induction value (134.27±11.58mmHg at 1 minute), then continued to rise till 4 minutes post-intubation, reaching its peak at this time (148.43±16.14mmHg $p = <0.0001$, 6.58% rise). It subsequently reduced from 5 minutes to 15 minutes.
In Group III (M40) patients, the post-administration SBP was 114.50 ±

Table 1: Patient Demographics

Parameters	Group I Mean± SD	Group II Mean± SD	Group III Mean± SD	*P*-Value	Level of significance
Patients	n = 30	n = 30	n = 30	1.00	NS
Age (yrs)	50.10 ± 13.82	50.87 ± 4.79	47.67 ± 6.83	0.06	NS
M/F n (%)	25(83.33) 5(16.67)	21(70.0) 9(30.0)	25(83.33)	0.35	NS
Weight(kg)	83.46±9.33	84.83±10.80	75.63±11.49	0.00	S
Height(m)	1.67±0.06	1.65±0.06	1.65±0.07	0.04	S

Values are expressed as mean ± SD or n (%).

Table 2: Systolic Blood Pressure changes

Time (Minutes)	Group I n =30 mean± SD	Group II n =30 mean± SD	Group III n =30 mean± SD	P-Value*	Level of Significance
Baseline	145.23±9.50	139.27±12.99	142.17±8.81	0.10	NS
Pre induction	123.37±16.82	126.57±10.99	114.50±14.15	<0.0001	S
*	21.86±3.01	13.17±7.35	27.67±5.30		
**	15%↓	9.5%↓	19.5%↓		
1 min	141.90±10.27	134.27±11.58	128.33±8.90	<0.0001	S
*	3.33±7.22	5.00±6.26	13.83±8.06		
**	2.14%↓	3.59%↓	9.73%↓		
2 min	139.97±10.67	138.27±11.63	135.83±8.81	0.30	NS
*	5.27±6.56	1.00±5.73	6.33±5.37		
**	3.47%↓	0.72%↓	4.46%↓		
3 min	135.87±9.69	143.80±12.36	138.20±8.49	0.01	S
*	9.37±6.69	–4.53±7.56	3.27±4.11		
**	6.30%↓	3.25%↑	2.79%↓		
4 min	132.57±11.58	148.43±16.14	138.90±9.73	<0.0001	S
*	12.67±10.22	–9.17±10.20	3.97±5.38		
**	8.57%↓	6.58%↑	2.30%↓		
5 min	128.90±13.91	145.80±14.63	136.20±9.28	<0.0001	S
*	16.33±13.07	–6.53±8.01	5.97±5.95		
**	11.10%↓	4.69%↑	4.20%↓		
10 min	135.83±8.53	139.80±13.19	133.40±10.82	0.08	NS
*	9.40±6.28	–0.53±13.53	8.77±6.79		
**	6.32%↓	0.38%↑	6.17%↓		
15 min	140.67±9.17	138.83±12.01	136.86±8.85	0.35	NS
*	4.57±5.47	0.43±10.01	5.30±6.65		
**	2.99%↓	0.32%↓	3.73%↓		

**, Mean difference from baseline; **, Percentage difference from baseline; ' ↑, Increase from baseline, ↓, Decrease from baseline*

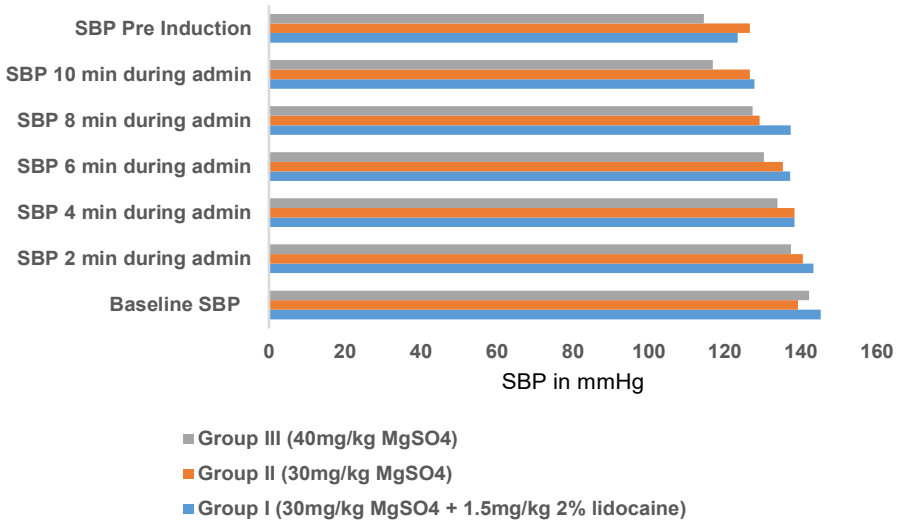

Fig. 1: Baseline SBP (mmHg) and SBP (mmHg) at different times during Administration of Study Drugs.

14.15mmHg (mean difference of 27.67 and 19.5% decrease). Following laryngoscopy and endotracheal intubation, the SBP rose above pre-induction value at 1 minute (128.33 ± 8.90mmHg), then continued to rise till 4 minutes post-intubation, reaching its peak at this time (138.90±9.73 p< 0.001, 2.30% decrease). It subsequently decreased from 5 minutes to 10 minutes and then began to rise again. The post-administration SBP reduced in the 3 groups with the highest percentage reduction in Group III (15% vs. 9.5% vs. 19.5%).

Following laryngoscopy and endotracheal intubation, the SBP rose in the 3 groups above the pre-induction value. The peak rise in Group I patients was at 1 minute post-intubation while those of Groups II and III were at 4 minutes post-intubation. Unlike patients in Group II in which there was failure to achieve attenuation (peak rise above baseline), Group I and III patients achieved attenuation and this was statistically significant.

Table 3 shows the mean baseline pulse rate (PR), pre-induction PR (post-administration of study drugs), their mean differences from baseline and percentage difference in the three study groups. The pre-induction PR decreased below their respective baseline values in the three groups – Group I (80.03±9.78 vs. 76.37bpm, mean difference = 3.66, 4.5% decrease from baseline), Group II (82.27±13.22 vs. 79.97±9.16bpm, mean difference = 2.3, 2.8% decrease), and Group III (76.03±10.67 vs. 74.13±6.78, mean difference = 1.9, 2.5% decrease). Following laryngoscopy and endotracheal intubation, mean PR rose in the 3 groups reaching peak at 2 minutes in Group I patients (92.20±7.30, mean difference = –12.17, 15% increase from baseline), 1 minute in Group II (86.27±5.51, mean difference = –4, 4.86% increase from baseline) and 15 minutes in Group III (89.27 ± 4.14, mean difference = –13.24, 17.4% increase from baseline). There was failure of attenuation in the three groups with the highest increase from baseline value occurring in Group III (17.4% increase) as compared to Groups I and II.

Table 4 compares the baseline (pre-administration) serum magnesium with 30 minutes after (post) administration serum magnesium. In the three groups, the 30 minutes post-administration serum magnesium levels were higher than their corresponding baseline serum values – Group 1 (1.82±0.23 vs. 2.09±0.21), Group II (1.80±0.24 vs. 2.08±0.21) and Group III (1.78±0.20 vs. 2.11±0.20).

Table 3: Pulse Rate changes at different Times

	Group I n =30 mean± SD	Group II n =30 mean± SD	Group III n =30 mean± SD	P-Value*	Level of Significance
Baseline	80.03±9.78	82.27±13.22	76.03± 10.67	0.38	NS
Pre induction	76.37±8.74	79.97±9.16	74.13±6.78	0.03	S
*	3.66±9.10	2.3±7.15	1.9±6.08		
**	4.5%↓	2.8%↓	2.5%↓		
1 min	90.47±7.62	86.27±5.51	85.13±6.15	<0.0001	S
*	–10.44±9.29	–4.00±9.13	–9.10±7.74		
**	13.05%↑	4.86.16%↑	11.97%↑		
2 min	92.20±7.30	85.87±5.18	86.20±6.92	<0.0001	S
*	–12.17±9.24	–3.60±6.71	–10.18±6.72		
**	15.21%↑	4.62%↑	13.38%↑		
3 min	92.07±8.06	85.83±4.34	86.47±5.49	<0.0001	S
*	–5.70±9.83	–3.56±6.06	–10.44±6.55		
**	15.04%↑	4.33%↑	13.73%↑		
4 min	89.37±10.67	79.97±9.16	78.20±11.61	<0.0001	S
*	–9.34±11.99	2.30±10.08	2.17±11.54		
**	11.67%↑	2.79%↓	2.85%↑		
5 min	90.77±9.46	85.10±4.46	85.63±5.25	<0.0001	S
*	–10.74±11.07	–2.83±6.11	–9.60±6.06		
**	13.42%↑	3.44%↑	12.63%↑		
10 min	90.97±8.92	85.26±5.13	85.57±5.67	<0.0001	S
*	–4.03±11.17	–2.99±6.52	–9.54±5.63		
**	13.67%↑	3.63%↑	12.55%↑		
15 min	90.40±9.61	85.47±7.66	89.27±4.14	<0.0001	S
*	–10.37±7.21	–3.20±10.08	–13.24±4.11		
**	12.96%↑	3.89%↑	17.41%↑		

Table 4: Serum Magnesium Level

	Group I n =30	Group II n =30	Group III n =30	P value
Baseline(pre) mg/dl	1.82±0.23	1.80±0.24	1.78±0.20	0.001
30 min(post) mg/dl	2.09±0.21	2.08±0.21	2.11±0.20	0.001

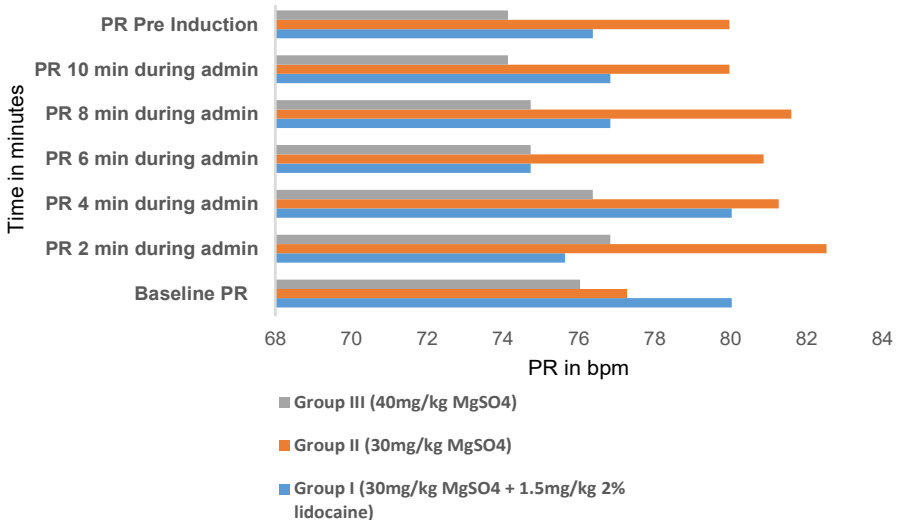

Fig. 2: Baseline PR (bpm) and PR (bpm) at different times during Administration of Study Drugs.

DISCUSSION

This study revealed that a combination of 30 mg/kg $MgSO_4$ and 1.5 mg/kg of lidocaine resulted in better attenuation of systolic blood pressure when compared to the 30 mg/kg or 40 mg/kg $MgSO_4$. This is because it resulted in lower mean pre-induction (post-administration) and lower mean peak systolic blood pressure values after intubation than their mean baseline values with no side effect.

This superior outcome in the combination group could be because lidocaine is a membrane stabilizer which prevents the stimulation of nerve endings by blocking action potential generation and propagation which would have resulted in stimulation of the sympathetic nervous system while magnesium sulphate prevents the stimulation of the sympatho-adrenal gland to block the release of catecholamines by inhibition of calcium. Catecholamine release and the direct stimulation of the sympathetic nervous system are both responsible for the increase in blood pressure and heart rate seen after laryngoscopy and intubation. Secondly, these agents also cause vasodilatation and myocardial depression; their combination results in more pronounced reduction in the haemodynamic parameters compared to the individual agent. However, increasing the doses of these drugs attenuates the haemodynamic response better but not without increasing the side effect profile. So, the combination of different agents at lower doses results in a superior outcome with fewer side effects.[9,10] The superiority of these two drugs in combination could be because they have different mechanisms of action and their ultimate effects might be synergistic or additive in obtunding the laryngoscopic response.

Various doses of magnesium sulphate have been used to obtund pressor response but the use of 30 mg/kg of magnesium sulphate alone has been found to be the optimal dose from a previous study, as increasing the dose beyond this optimal value causes increased side effects.[10] The outcome of our study corroborated this assertion that increasing the dose of $MgSO_4$ beyond 30 mg/kg is associated with the

possibility of more side effects. When $MgSO_4$ was administered at 40 mg/kg it had more side effects (hypotension) compared to 30 mg/kg $MgSO_4$ but attenuated the pressor response better.[10]

The outcome of this study is similar to that by Mollick,[11] and Gupta;[5] they used drug combinations to attenuate the laryngoscopic response and it provided better haemodynamic response. In Mollick's study,[11] the lidocaine and pethidine combination group attenuated the pressor response to laryngoscopy with a 5 % decrease in mean SBP from baseline ($p< 0.001$). Whereas the group that received lidocaine alone failed to attenuate the pressor response to laryngoscopy, rather there was a 4 % increase in mean SBP from baseline ($p<0.01$). However, in a study by Singh *et al.*[12] the combination of dexmedetomidine and esmolol did not reduce patients' blood pressure during laryngoscopy and intubation in patients undergoing coronary bypass graft. This observation could be because patients were on preoperative β-blockers,[13] and the duration of laryngoscopy and post-intubation time were 20 seconds and 5 minutes, respectively, unlike ours that were 30 seconds and 15 minutes, respectively. Mechanical stimulation of the airway leads to reflex activation of the cardiovascular and respiratory systems; this reflex peaks within 1 minute and ends in about 5–10 minutes after intubation.[12] Furthermore, the age range of patients recruited was between 21–65 years unlike in ours that was 30–55 years. Cardiovascular response to tracheal intubation is influenced by the age of the patient. Ismail *et al*[14] observed exaggerated increase in the systolic blood pressure following laryngoscopy and intubation in elderly and middle-aged patients as compared to the young. This may be due to the predominance of the parasympathetic nervous system/ outflow in the younger age group.

After laryngoscopy, Group I (30 mg/kg $MgSO_4$ + 1.5 mg/kg lidocaine) and Group III patients (40 mg/kg $MgSO_4$) attenuated the post-intubation rise in systolic blood pressure up to 15 minutes, whereas in group II (30mg/kg $MgSO_4$) the post-intubation systolic blood pressure readings were all higher than baseline except at the 1st, 2nd and 15th minute after intubation. Groups I and III had decreases in systolic blood pressure below its baseline value unlike group II with increasing pressure from baseline. Group I had the highest percentage decrease (11 %) in systolic blood pressure at the 5th minute when compared to those of Group II (3.6 % at 1st minute) and Group III (9.73 % at 1st minute). Both Group II and III had the highest percentage decrease occurring at 1st minute while that of Group I was at 5th minute post-intubation. The higher percentage decrease in Group I patients could mean better attenuation in this group. The superior outcome of Group I patients in our study who had 11 % decrease from baseline systolic blood pressure is clear when compared to that by Olatosi and colleagues[15] with a 21.6 % increase from baseline systolic blood pressure. This is hypothesised to be due to the addition of 30 mg/kg of magnesium sulphate to lidocaine in Group I patients which was absent in the study by Olatosi and colleague.[15]

The type of induction agent could also be contributory to the ability of pressor agents to attenuate the laryngoscopy response. The greater the effect of the induction agent used on the cardiovascular system (blood pressure and heart rate) the better its ability to obtund the pressor response. These agents counter the effect of catecholamine release from both the sympathoadrenal gland and the nerve ending in the hypo-pharynx during laryngoscopy. This is the rationale behind the use of second dose thiopentone in obtunding the laryngoscopic response.

Honarmand and colleagues[8] used propofol for induction while in this study sodium thiopentone was used. Propofol causes a significant dose dependent decrease in arterial blood pressure during induction of anaesthesia. The effect of propofol on the cardiovascular system is more marked than other intravenous induction agents. However, systemic vascular resistance and arterial blood pressure remain relatively unaltered following a normal induction dose in healthy patients. Hence, the use of propofol for induction of anaesthesia, as opposed to thiopentone in our study, could be contributory to the more favourable outcome in their study**.** Its use attenuated the rise in the systolic blood pressure in the 30 mg/kg group in their study when compared to the 30 mg/kg group in the present study.

Beside pressor responses, heart rate also increases during laryngoscopy and tracheal intubation. This ultimately causes an increase in cardiac output which is a product of the stroke volume and heart rate. It is clinically necessary to mitigate increases in heart rate which may ultimately lead to better control of the patient's haemodynamics. Following laryngoscopy and tracheal intubation, there was an increase in heart rate above baseline up to 15 minutes post-intubation in Group I and Group III patients. The highest increase in percentage heart rate was seen in Group III patients (17.41 %) at 15 minutes post-intubation. This finding is similar to that of Olatosi and colleague[15] in which they recorded a 25.7 % increase in heart rate in the group that received lidocaine in their study. However, in Group II there was a decrease from baseline heart rate at the 4th minute post-intubation with 2.79 % decrease. The rise in heart rate in the three study groups from baseline was statistically significant ($p < 0.05$). However, they all reached the baseline after 20 minutes post-intubation. Failure to attenuate the heart rate has been demonstrated by other researchers. Kotwani and colleagues[16] compared 30 mg/kg and 40 mg/kg of magnesium sulphate. The mean baseline versus 5 minutes post-laryngoscopy and tracheal intubation in the two groups were: 84.32±9.67 vs 95.76±12.61bpm and 89.92±11.76 vs. 100.24±13.20bpm, respectively. Similarly, Kiran and colleagues[17] demonstrated failure of attenuation of PR 5 minutes post-intubation when patients received 50mg/kg of $MgSO_4$.

On the contrary, Singh *et al*[12] observed no significant increase in heart rate at all time intervals while Sachin and colleague[18] demonstrated a return to baseline at 5 minutes post-intubation after an initial rise in heart rate. Sachin *et al*[18] combined benzodiazepine, a premedicant which acts as an anxiolytic/sedative/ amnesic agent to prevent sympathetic discharge from the anxiety of surgery with another sedative agent pentazocine.

This combination is additive and further depresses the sympathetic nervous system but, in our study, only diazepam was used as premedication for anxiolysis. Similarly, Honarmand and colleagues[8] also demonstrated a favourable attenuation of the heart rate 10 minutes post-intubation. There was an initial increase in heart rate which returned below baseline in all the three study groups. The favourable outcome in their study can be attributed to the selection criteria and methodology. They recruited ASA I-II (normotensive and controlled hypertensive patients) normotensive patients who are typically less sensitive to the laryngoscopic response, and induction of anaesthesia was achieved with 2 mg/kg propofol and 3 mcg/kg fentanyl. Co-administration of high dose opioid also results in effective attenuation rather than the effect of the study drug itself. This is because opioids suppress the hypothalamic-pituitary-induced release of catecholamine to noxious stimuli (laryngoscopy and tracheal intubation). The use of combined induction agent was possibly more effective in blunting the laryngeal reflexes with no reflex tachycardia. In this study, only 4 mg/kg sodium thiopentone was used to induce anaesthesia.

The reasons for failure of attenuation of PR in the index study could be due to selection of only ASA II patients, induction with thiopentone which causes rebound tachycardia,[2] and maintenance of anaesthesia with isoflurane which similarly causes rebound tachycardia.[19] Tachycardia leads to an increase in oxygen consumption of the myocardium, decreased diastolic filling, and reduced coronary blood supply, thereby causing more stress on the myocardium as compared to hypertension.[20]

Thirty minutes post-administration of study drug, serum magnesium was higher in all the three groups when compared to baseline but was highest in the 40 mg/kg group. These higher values obtained were still within the acceptable normal range of 1.7–2.2 mg/dl. It is therefore possible to use any of the doses used in this study without exceeding the normal serum concentration. Toxic levels of serum $MgSO_4$ can cause nausea and vomiting, muscle weakness, hypotension, respiratory depression, and decreased tendon reflexes.

The only side effect noted in the present study was hypotension (>20 % drop from baseline). This occurred in five patients in the 40 mg/kg $MgSO_4$ group. This value represents 16.7% of the total number of patients in that group and 5 % of the total number of patients recruited in this study. It can be said that the side effect profile of $MgSO_4$ increases as the dose increases. This assertion is corroborated by the findings of the study by Panda and colleagues[10] in which patients who received 30 mg/kg magnesium sulphate did not develop hypotension while the groups that received 40 mg/kg and 50 mg/kg had 6 (30 %) and 16 (80 %), respectively. The incidence of hypotension observed in the 40 mg/kg group in our study could have been due to a high serum magnesium concentration of 2.11 mg/dl which was highest among the three groups. However, this did not exceed the normal range. Hypotension is a premonitory sign of impending toxicity which was managed with favourable outcome.

CONCLUSION

The combination of intravenous 1.5 mg/kg of lidocaine and 30 mg/kg of magnesium sulphate attenuates the pressor response of laryngoscopy and tracheal intubation better than either intravenous 30 mg/kg or 40 mg/kg of magnesium sulphate alone in controlled hypertensive patients with no side effect. In low resource countries where availability and affordability of drugs like dexmedetomidine, clonidine, alfentanyl, and remifentanyl is limited, a combination of lidocaine and $MgSO_4$ could be used as drugs to attenuate the haemodynamic responses to laryngoscopy and intubation in controlled hypertensive patients. These drugs are affordable and readily available and are equally safe in therapeutic range with minimal side effects.

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