Zagazig University Medical Journal
www.zumj.journals.ekb.eg

https://doi.org/10.21608/zumj.2024.334456.3679 Volume 31, Issue 1, January. 2025

ManuscriptIDZUMJ-2411-3679
DOI10.21608/zumj.2024.334456.3679

ORIGINAL ARTICLE

Nebulized Ketamine or Magnesium Sulphate for Attenuating Stress Response to Laryngoscopy and Intubation in Patients Undergoing Elective Surgeries

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Submit Date: 06-11-2024
Revise Date : 08-11-2024
Accept Date: 10-11-2024

ABSTRACT

Background: The response of stress to intubation and laryngoscopy among patients undergoing different types of surgeries is a regular phenomenon that is observed every day in the surgical setting because of the ejection of endogenous catecholamines.

Objectives: The current study aimed to attenuate the stress response to intubation and laryngoscopy in patients undergoing elective surgeries employing either nebulized ketamine or magnesium sulfate.

Subjects and methods: This double-blinded prospective randomized controlled clinical trial was conducted on 63 patients. The patients were equally divided arbitrarily into Group C (Control): patients were nebulized using normal saline. Group K (Ketamine): patients were nebulized using ketamine. Group M (Magnesium Sulphate): patients were nebulized using magnesium sulfate.

Results: There was statistically significant increase in intraoperative HR, SBP, DBP, and MAP at 3, 5, 8 and 10 minutes after intubation in group C compared to group K, M ($P<0.0001$), also group K show statistically significant increase compared to group M ($P<0.01$), also Regrading postoperative HR, SBP and DBP there was statistically significant increase at 15 and 30 min in group C compared to groups K and M ($P<0.001$) while MAP show statistically significant increase at 15 and 30 min in groups C and K compared to group M ($P<0.01$). moreover, Blood cortisol level was statistically significant increase at 10 min after intubation in groups C and K compared to group M ($P<0.000$) and in group C compared to group K ($P<0.000$). also, Blood glucose level was statistically significant decrease at 5 and10 min after intubation in groups M compared to group C and K ($P<0.000$) and in group C compared to group K ($P<0.000$). and according to number of patients needed fentanyl intraoperative there was statistically significant increase group C compared to group K and M respectively($P<0.05$).

Conclusion: Both interventions were found to significantly blunt the increases in HR, SBP, DBP, MAP, blood cortisol level, and blood glucose level. However, mg sulfate is more effective in blunting stress response than ketamine. Also, mg sulfate decreases the incidence of postoperative sore throat more than ketamine.

Keywords: ketamine, Magnesium sulfate, Intubation, Stress response, Laryngoscopy

INTRODUCTION

Direct laryngoscopy (DL), endotracheal intubation (ETI), and surgical stimulation induce significant sympathetic responses. These responses are correlated with temporary but significant hemodynamic alterations, termed stress/hemodynamic response, which is represented by an abrupt increase in mean arterial pressure (MAP) and heart rate (HR) after DL and ETI and returning to the starting point within 10 minutes [1]. The adrenaline rush that generated from both DL and ETI resulting in hemodynamic variations. This temporary outburst may trigger cardiac ischemia/arrhythmias, Hypertensive episodes, or intracranial hypertension in sensitive patients [2].

The need to attenuate these unpleasant responses impact may cause employing treatment agents like beta-adrenergic blockers, intravenous opioids, calcium channel blockers, α2 agonists, local anesthetics, and topical sprays, volatile agents. Intranasal and nebulizers have also been utilized to prevent this stress response, with varied success rates [1,2].

Nebulized medication administration is strongly recommended over intranasal delivery because it reduces cough, temporary nasal discomfort, and vocal cord irritation [3].

N-methyl-D-aspartate (NMDA) receptors had a crucial part in inflammation and nociception in the body. NMDA receptors exist in both peripheral nervous system (PNS) neurons and the central NS (CNS) [4]. Ketamine, an NMDA receptor antagonist, is commonly administered as a gargle or nebulizer to decline the severity and frequency of postoperative sore throat owing to its antinociceptive and anti-inflammatory properties. Ketamine nebulization is better to ketamine gargling since the second type is utilized in higher volumes and may entail the danger of aspiration if unintentionally consumed, as well as its bitter taste [5].

When the sympathetic nervous system stimulates the adrenergic nerve terminals and adrenal medulla, calcium helps to release catecholamines. Magnesium and calcium compete for interaction with membrane channels. Magnesium is a calcium antagonist and can change calcium-mediated responses; magnesium sulfate ($MgSO_4$) inhibits catecholamine production and reduces responses to adrenergic stimuli. Mg is also an NMDA receptor antagonist. It is utilized as an oral lozenge or nebulizer; it is readily accessible in hospitals, and nebulization will minimize the stress reaction during surgery [6].

The present work aimed to attenuate the stress response of ETI and laryngoscopy in patients receiving elective surgeries using either nebulized ketamine or magnesium sulfate

Stress response of laryngoscopy and ETI in patients regarding systolic blood pressure (as 1ry outcome) and Stress response of laryngoscopy and ETI in patients regarding heart rate, diastolic blood pressure, mean arterial pressure, blood glucose level and cortisol levels in blood (as 2nd outcome).

METHODS

This double blinded prospective randomized controlled clinical trial was conducted from the start of September 2023 till the end of February 2024 in the operating room of Zagazig university hospitals, after obtaining approval from Institutional Review Board (101019-13/8/2023) and written informed consent from all patients.

The included patients were 63 patients who were scheduled for elective surgeries under general anesthesia with the age between 21 and 45, both Male and female, Patients belonged to the American Society of Anesthesiologists (ASA) I or II, BMI (18-30 kg/m2) and the duration of the surgery was about 1.5 hours. The study excluded patients who were hemodynamically unstable, chest infection within two weeks, known allergy or sensitivity to ketamine or magnesium sulfate, airway tumor, mandibular or maxillary fracture, suspected difficult airway (Mallampati class >2), patients on cortisol treatment or receiving nasal Surgeries, diabetic, hypertensive patient and pregnant woman. All the patients had the right to withdraw from the study at any time without any negative consequences or harm on their medical treatment plan.

By Using computer generated randomization tables, the patients were randomly allocated into three equal groups (each of 21 patients) in which Group C (Control group) (n=21): Patients in this group were nebulized using 3 ml of normal saline (0.9%). Group K (Ketamine group) (n=21): Patients in this group were nebulized using ketamine (1ml/kg) completed to 3 ml using normal saline. Group M (Magnesium Sulphate group) (n=21): Patients in this group were nebulized using magnesium sulfate (2.5 ml) with (0.5ml) normal saline. All groups were received nebulizer (by Jet nebulizer) 10 minutes before shifting to operating room.

Sample size:

Assuming that the median of postinduction SBP among patients receiving magnesium sulphate was 97 mmgh versus 103 mmgh in controls [7], so a minimal sample size of 19 patients will be included in each group at power 95% and 0.05 significant level. A drop out rate of 10% will be added. So, the estimated sample size will be 63 patients, 21 in each group.

Sample size was calculated using OpenEpi, Version 3, open-source calculator.

Study protocol:

Preoperative data:

All patients of the studied groups were subjected preoperatively to complete history taking, routine pre-anesthetic examination, and Laboratory tests (Complete blood picture, kidney and liver function tests, Hb A1c, and blood grouping and typing).All patients were fasting 6-8 hours for food and 4 hours for clear fluids. Cortisol and blood sugar levels in blood were measured by all patients 45 minutes before the operation. A nebulizer was applied to each patient according to random group 10 minutes before transfer to operating room.

Intraoperative:

On arrival in the operating room patients were connected to a multiparameter monitor, which records baseline HR, systolic blood pressure (SBP), diastolic BP (DBP), mean arterial blood pressure (MAP), Electrocardiography (ECG) and peripheral oxygen saturation, a suitable-sized intravenous cannula was inserted, and intravenous fluid was started according to the perioperative fluid protocol. SBP, DBP, MAP and HR were recorded before anesthesia induction.

Standard general anesthesia was given to all patients. After preoxygenation (with 100% oxygen for 3 minutes), induction using fentanyl (1 µg /kg), propofol (2mg/kg), and atracurium besylate (0.5 mg/kg) to facilitate tracheal intubation was performed and time taken for intubation was recorded (it's the time between inserting laryngoscopy and insertion of the tube in trachea) Maintenance with isoflurane (0.7) MAC and atracurium (0.1 mg/kg) was performed every 30 minutes. Mechanical ventilation parameters were changed to preserve an end-tidal CO2 between 35 and 40 mmHg.SBP, DBP, MAP and HR were recorded just before induction, just before intubation, then 1, 2, 3, 5, 8, and 10 min after intubation, and every 15 minutes until the end of the surgery. Blood sugar was measured just after endotracheal intubation by glucometer and recorded 1, 5 and 10 mins after intubation. Blood cortisol level was recorded 10 mins after intubation.

If hypertension (SBP > 20% of baseline value) or tachycardia (HR > 25% of baseline value) occurred, fentanyl (1µg /kg) was given and number of patients who needs rescue fentanyl and the total amount of fentanyl needed for tachycardia and hypertension during surgery was recorded.

If hypotension (SBP ≤ 20% of baseline value) occurs, ephedrine (0.1 to 0.2 mg/Kg) will be given and if bradycardia (HR ≤ 20% of baseline value) occurs, atropine (0.01 mg/kg) will be given.

At the end of the surgery, the residual impact of the neuromuscular blocker was reversed with neostigmine (0.05mg/kg) and atropine (0.02mg/kg), and extubation was performed when respiration was adequate, and the patient obeyed simple commands.

Postoperative:

Patients were monitored in the recovery room, where their vital signs (HR, SBP, DBP and MAP) were recorded every 15 minutes for 2 hours. Then, they were discharged to the ward.

Study outcomes:

Stress response of laryngoscopy and ETI in patients regarding systolic blood pressure (as 1ry outcome)

Stress response of laryngoscopy and ETI in patients regarding heart rate, diastolic blood pressure, mean arterial pressure, blood glucose level and cortisol levels in blood (as 2nd outcome), The total amount of Fentanyl consumed intraoperative, number of patients taking fentanyl intraoperative after induction and Postoperative sore throat incidence.

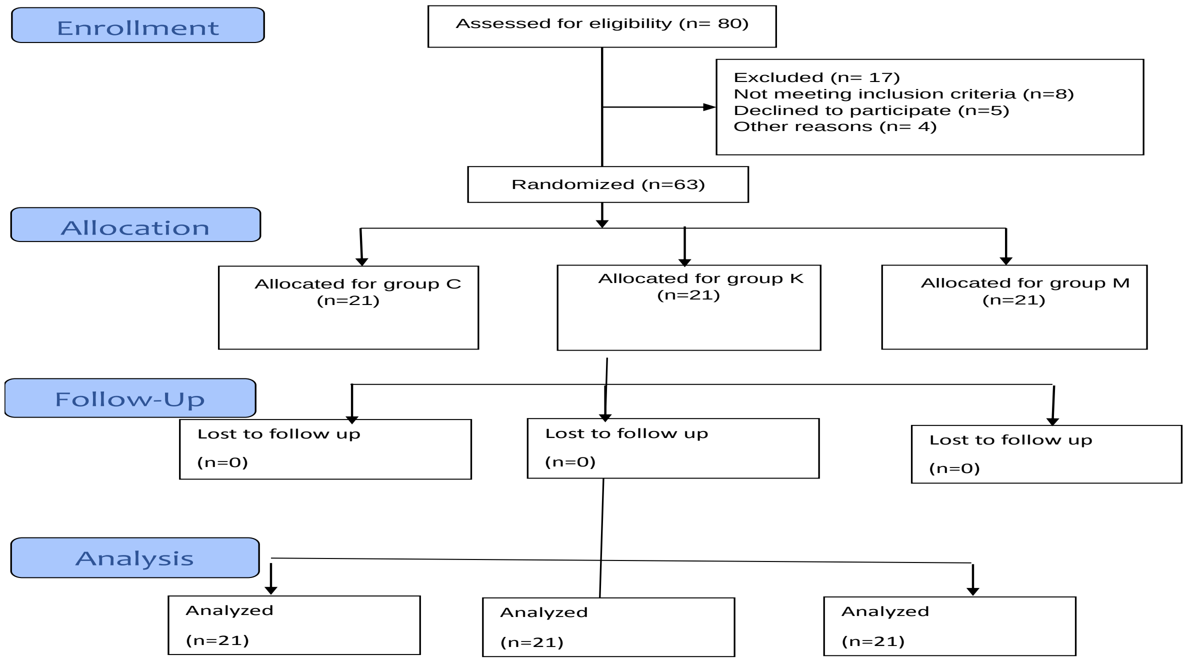

Figure 1: flow chart of the patients in the study

Statistical Analysis:

All statistical analyses were done by employing SPSS version 27. Normality was tested using the shiparo-wilk test and the Kolmogorov-Smirnov Normality Test. Normally distributed continuous data were represented as mean and standard deviation. One-way ANOVA was used to compare the continuous data between groups. Not-normally distributed continuous data were described as median and IQR. Kruskal Wallis test, followed by Mann-Whitney, was used to compare the constant data that was not generally distributed between groups. Categorical data were expressed as events and percentages. Comparing both groups regarding categorical data was performed utilizing the Chi-square test or Fisher Exact test. A mixed linear model assessed repeated measurements of normally distributed data. Data with $P<0.05$ is considered significant.

RESULTS

The study initially included 80 patients that were scheduled for elective surgeries under general anesthesia and assessed for enrollment. Among them 17 patients were excluded (8 patients did not meet inclusion criteria, 5 patients declined to participate, 4 patients for other reasons). The remaining 63 patients were randomly distributed into equal groups for each of 21 patients. (Figure1).There was no statistically significant difference among the three studied groups regarding patient characteristics, Mallampati classification, time for intubation and duration of surgery. ($P>0.05$). (Table 1)

Regarding preoperative and intraoperative measurement of HR, SBP, DBP, and MAP There were no statistically significant difference ($P>0.05$) among three studied groups at baseline, before induction, just before intubation and at all interoperative time except at 3, 5, 8 and 10 mins after intubation there were statistically significant increase in control group compared to both ketamine and magnesium sulphate groups, also there was statistically significant increase in ketamine group compared to magnesium sulphate group at the same time ($P<0.0001$).moreover, there was no statistically significant difference on HR, SBP, DBP and MAP when comparison within the same group on three study groups except at time 3, 5, 8 and 10 mins after intubation there were statistically significant increase in both group C and K while the was statistically significant decrease at the same time on M group (Figure 2).

Regarding Blood cortisol level there was no statistically significant difference among the three studied groups at 45 mins before operation (P=0.693) but there was statistically significantly increased 10 minutes after intubation in Groups C and K than group M (P=0.000). Also, there was statistically significant increase of blood cortisol level at 10 mins in group C compared to K (P=0.000), moreover among the same group there was a statistically significant increase in blood cortisol levels between 45 minutes before the operation and 10 minutes after intubation in groups C and K (P=0.000), on the contrary at M group there was statistically significant decrease in blood cortisol level (P4<0.05) (Table 2) .

There was no statistically significant difference regarding blood glucose level among the three studied groups at 45 minutes before operation and 1 minute after intubation (P=0.828, 0.956) respectively. However, there was statistically significant increase at 5 mins and 10 mins after intubation in group C compared to group K & M respectively (P=0.000), also regarding blood glucose level within the same group there was statistically significant increase in BGL after 5 and 10 mins compared to BGL 45 mins before intubation in all three groups (P <0.001). (Table 3) .

There was statistically significant difference among the three studied groups as regard to number of patients who needed fentanyl intraoperative as most of the patients among group C (85.7%) needed fentanyl in comparison to (38.1%) among group K and one of the patients among group M (P<0.001), however Regarding to amount of fentanyl used intraoperative There was no statistically significant difference among the three studied groups (P>0.05). (Table 4) .

Regarding postoperative HR, SBP and DBP there were statistically significant difference among the three studied groups at 15 and 30 minutes as there was a statistically significant increase in group C and K comparing to group M (P2, P3<0.001), while there was no statistically significant in both group C and K (P1>0.99), when comparing postoperative MAP there was statistically significant increase in group C comparing to group K and group M at 15 and 30 minutes while there was a statistically significant increase (P3<0.001) in MAP in group K than M at 15 minutes with no statistically significant at 30 min postoperatively (P3>0.68). (Figure 3) .

When comparison postoperative HR, SBP, DBP and MAP within the same group there was statistically significant increase on both C and K groups while there was no statistically significant increase in M group. (Figure 3) .As regard post operative sore throat, there was statistically significant increase in the incidence of postoperative sore throat in group C and K compared to group M (P=0.000 and 0.011 respectively) with no statistically significant difference between group C and K (P=0.3) (table 5).

Table 1: Patient characteristics, Mallampati classification, time for intubation and duration of surgery among three studied groups:

Variables	Group C (n=21)	Group K (n=21)	Group M (n=21)	P value
Age (years) Mean ± SD	35.2 ± 9.68	35.2 ± 4.92	33.1 ± 7.59	0.592
Sex (N. %) – Male – Female	8 (38.1%) 13 (61.9%)	13 (61.9%) 8 (38.1%)	13 (61.9%) 8 (38.1%)	0.2
BMI (Kg/m^2) Mean ± SD	26.6 ± 2.93	25.9 ± 2.62	26.8 ± 2.22	0.685
Physical state (N. %) – ASA – ASA	17 (81%) 4 (19%)	16 (76.2%) 5 (23.81%)	13 (61.9%) 8 (38.1%)	0.35
Mallampati class (N. %) – 1 – 2	9 (42.9%) 12 (57.1%)	11 (52.3%) 10 (47.6%)	8 (38.1%) 13 (61.9%)	0.73

Variables	**Group C (n=21)**	**Group K (n=21)**	**Group M (n=21)**	**P value**
Time for intubation (sec) Mean ± SD	17.11±3.09	17.77±3.79	17.04±3.90	٠.٧٧١
Duration of surgery (min) Mean ± SD	75.89±4.58	78.59±5.54	76.51±4.28	0.188

Non-significant: P >0.05, data was expressed as Mean ± SD or number (percentage) using one way ANOVA & Chi square test- Group C= control group - N= number - Group k = ketamine group - BMI= body mass index - group M= magnesium sulphate group - ASA = American Society of anesthesia

Table 2: Blood cortisol level changes among the three studied group

	Group C (n=21)	**Group K (n=21)**	**Group M (n=21)**	***P Value**	**Post Hoc test**
Blood cortisol level 45 minutes before operation (mcg/dl)	13.06±0.65	13.21±1.14	12.97±0.84	0.693	**-------**
Blood cortisol level 10 minutes after intubation (mcg/dl)	15.04±0.51	14.56±0.48	12.24±0.99	0.000	**P1, P2, P3=0.000**
Difference in Blood cortisol level	2.88±0.82	1.36±1.30	-0.72±1.13	0.000	**P1, P2, P3=0.000,**
P 4	0.000	0.000	0.000		

Data were expressed as mean±SD; using one way ANOVA followed by Post Hoc test, Non-significant: P >0.05, Significant: P ≤0.05P1=Comparison between group C and group K; P2=Comparison between group C and group M; P3=Comparison between group K and group M, P4= comparison within the same group between blood cortisol level 45 minutes before intubation and blood cortisol level 10 minutes after intubation (mcg/dl)

Table 3: Blood glucose level change among the studied groups

Blood glucose level mg/dl	**Group C (n=21)**	**Group K (n=21)**	**Group M (n=21)**	***P Value**	**Post Hoc test**
45 minutes before operation	92.2 ± 4.62	93.4 ± 5.28	92.64 ± 8.61	0.828	
1 minute after intubation	95.2 ± 9.62	94.4 ± 7.28	95.64 ± 8.61	0.956	
5 minutes after intubation	112.1 ± 3.37	107.5 ± 3.64	98.2 ± 3.13	**0.000**	P1= **0.0002** P2 =**0.000** P3= **0.000**
10 minutes after intubation	115.3 ± 4.48	109.9 ± 2.83	98.8 ± 2.1	**0.000**	P1=**0.000** P2 =**0.000** P3 =**0.000**
**P value	**<0.001**	**<0.001**	**<0.001**		

Data were expressed as mean and SD using one way ANOVA followed by Post Hoc test when significant*P=Comparison between the three groups, -P1=Comparison between group C and group K, -P2=Comparison between group C and group M, -P3=Comparison between group K and group M
**P=Comparison within the same group

Table 4: Number of patients need intraoperative fentanyl and total amount of fentanyl among the studied groups

Variables	Group C (n=21)	Group K (n=21)	Group M (n=21)	P value	
Number of patients needed fentanyl (N. %)					
– No	3 (14.3%)	13 (61.9%)	20 (95.2%)	**<0.001**[1]	**P1= 0.004,**
– Yes	18 (85.7%)	8 (38.1%)	1 (4.8%)		**P2= 0.000** **P3= 0.02**
Amount of fentanyl (µg)					
Median (IQR)	75 (5)	75 (30)	75		
Range	(60 – 90)	(60 – 90)		1.00[2]	

Data were expressed as number (percentage) or median (Interquartile range) using [1]Fisher exact test, [2]Mann-Whitney U test, Non-significant: P >0.05, Significant: P ≤0.05; P1=Comparison between group C and group K, -P2=Comparison between group C and group M, -P3=Comparison between group K and group M

Table 5: Post-operative sore throat among the studied groups

Variables	Group C (n=21)	Group K (n=21)	Group K (n=21)	P value	
Post operative sore throat (N. %)					**P1= 0.306**
– No	4 (19%)	8 (38.1%)	17 (81%)	**<0.001**[1]	**P2= 0.000**
– Yes	17 (81%)	13 (61.9%)	4 (19%)		**P3= 0.011**

Data were expressed as number (percentage) using *1Fisher exact test, Non-significant: P >0.05, Significant: P ≤0.05; P1=Comparison between group C and group K, -P2=Comparison between group C and group M, -P3=Comparison between group K and group M

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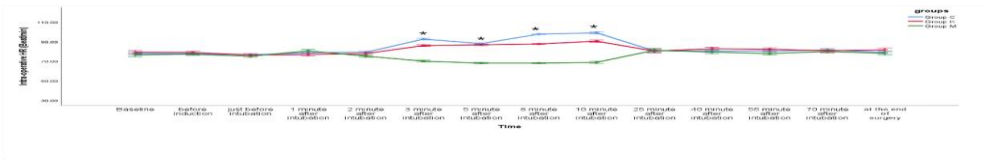

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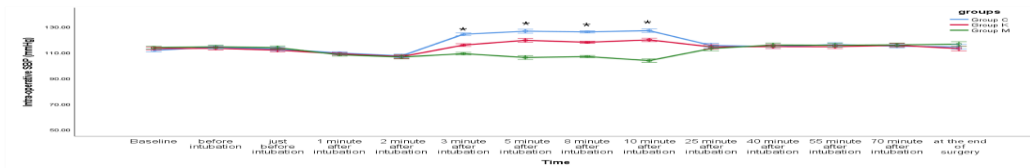

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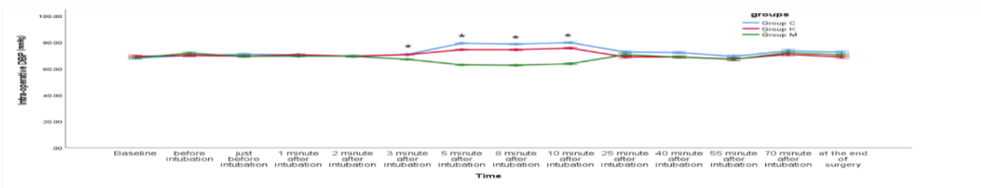

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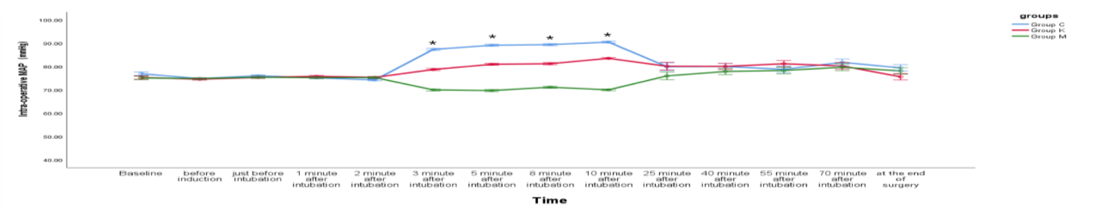

Fig (2). Line charts for repeated intraoperative measurement (A) heart rate. (B) systolic blood pressure. (C) diastolic blood pressure. (D) mean arterial pressure.

Data was expressed as Mean ± SD, C= control group, k = ketamine group M= magnesium sulphate group,

Fig (3). Line charts for repeated postoperative measurement (A) heart rate. (B) systolic blood pressure. (C) diastolic blood pressure. (D) mean arterial pressure.

Data was expressed as Mean ± SD, C= control group, k = ketamine group M= magnesium sulphate group, *= statistically significant difference between groups.

DISCUSSION

Various pharmacological interventions have been assessed to attenuate the stress response to DL and ETI. Intravenous administration of agents such as opioids, lidocaine, and antihypertensive medications has demonstrated some efficacy, but they can be linked to undesirable side effects. Nebulized medications offer a potential alternative approach, with the advantage of targeted delivery to the airway and potentially fewer systemic side effects [8].

Our study used either nebulized ketamine or magnesium sulfate to attenuate the stress response to laryngoscopy and ETI in patients receiving elective surgeries.

There was statistically significant difference in HR among the three studied groups at 3,5,8 and 10 mins after intubation as group (M) showed significant decrease in HR after intubation while in groups (C and K) there were significant increase in HR after intubation.

With our study, Elmeligy and Elmeligy [7] used mg sulfate nebulization and normal saline nebulization and demonstrated a s significant decrease of HR at 3,6 and 10 mins after ETI in Mg sulphate group. Also, Sawan et al. [9] used MgSO4 versus lidocaine to reserve hemodynamic response to ETI and found a significant decrease in heart rate at 3, 5 and 10 mins after intubation in MgSo4 than lidocaine group.

As our study, Abd Ellatif and Mowafy [10], using pre-emptive nebulized ketamine versus nebulized lidocaine for endoscopic nasal operations, stated that nebulized ketamine was found to increase HR at 3, 5, and 10 min after intubation comparing to lidocaine nebulizer.

In contrast with our study, Alshame et al. [11], assessing Preemptive nebulization of dexmedetomidine versus ketamine for postoperative analgesia in nasal surgeries, found that there was a statistically remarkable decline in HR in the ketamine group post-induction till the end of surgery. This may be due to using fentanyl (2 microgram/kg), and anesthesia was maintained with isoflurane from 1.5% up to 2.5% and special techniques to induce hypotension in ENT surgeries.

Concerning our study heart rate changes postoperatively, there was statistically significant difference among the studied groups at 15 and 30 postoperative days, as group M showed statistically significant attenuation in HR while in groups C and K, there was a significant increase in HR, more increase in group C.

Likewise, Seetharamaraju et al. [12] assessed lidocaine versus pre-emptive nebulized ketamine for post-tonsillectomy pain treatment in children and found that HR was increased in the ketamine group postoperatively.

In disagreement, Alshame et al. [11] reported statistically significant decrease HR postoperative in the ketamine group. This may be due to using of ketoprofen as analgesia postoperative.

Our current findings regarding systolic blood pressure changes during operation found that there was a statistically significant increase in SBP from 3 mins till 10 mins after intubation in group C compared to groups K and M with significant increase at the same time in group K comparing to group M.

Similar findings were obtained by Elmeligy and Elmeligy [7], who reported that regarding SBP, there was a notable impact of MgSO4 nebulization on decreasing SBP 3 min later, 6 min after intubation.

Also, Abdel-Ghaffar and Salem [13] revealed that Intranasal ketamine substantially raised SBP after anesthetic induction and at 3 and 5 minutes after intubation compared to intranasal fentanyl.

Regarding SBP postoperatively, there was statistically significant difference among the three studied groups as group M showing statistically significant attenuation in SBP increase compared to groups K and C. There was a statistically significant increase in SBP at 15 and 30 mins postoperatively between groups C and K compared to group M. There was a statistically significant increase in SBP at 15 and 30 minutes postoperatively between groups K and M.

With our study, Ali et al. [14] found that SBP was statistically significantly decreased in the magnesium sulfate group regarding postoperative readings, but the effect was prolonged time postoperative and that may be due to the use of mg sulfate intravenously, which has a longer duration of action, even postoperatively.

Regarding DBP changes during operation there was a statistically significant increase in groups C and K from 3 mins to 10 mins after intubation, while in group M, it was statistically remarkable to lower from 3 mins to 10 mins after intubation.

This was in line with Elmeligy and Elmeligy [7]. Regarding DBP changes, there was a statistically significant decrease in DBP using mg so4 nebulization at 3, 5 and 6 mins after intubation.

Also, regarding DBP changes, Abdel-Ghaffar and Salem [13] showed a statistically significant increase in DBP using intranasal ketamine 3, 5, and 10 mins after intubation.

Regarding DBP postoperatively, there was a statistically significant increase in DBP in groups C and K compared to group M at 15 and 30 minutes without a significant difference between the C and K groups.Following Alshame et al. [11], they found a notably elevation in DBP postoperative in the ketamine group, also with our study, Ali et al. [14] found that DBP show statistically significant decrease in the magnesium sulfate group regarding postoperative readings, but the effect was prolonged postoperative and that may be due to using mg sulfate intravenously. Hence, the duration of action was longer, even postoperatively.

As regards MAP intraoperatively, group C showed that the MAP recorded was statistically significantly increased at 3, 5, 8 and mins after intubation compared to group K and M, with a substantial rise in group K compared to group M.

The intragroup comparison showed that in groups C and K, the MAP recorded significantly increased at 3,5,8 and 10 minutes after intubation. Regarding group M the MAP recorded significantly decreased at 3,5,8 and 10 minutes after intubation.

In line with our study, Mostafa et al. [15] employed a MgSO4 nebulizer compared to ketamine to reduce the frequency of postoperative sore throats in adults. They demonstrated that there was a statistically significantly increased in MAP at 3,5,8 and 10 minutes after ETI in the ketamine and saline groups and statistically significantly decreased in MAP in the MgSO4 group.

Furthermore, Alshame et al. [11] stated a statistically significant increase in MAP in the ketamine group after 3 mins of intubation.

Regarding MAP postoperatively, there was a statistically significant increase in MAP in groups C and K compared to M at 15 and 30 mins postoperatively, without statistically significant difference between groups C and K.In agreement with our study, Alshame et al. [11] stated a statistically significant increase in MAP regarding the ketamine group postoperatively.

Also, Gad et al. [16] investigated the impact of MgSO4 on perioperative hemodynamic reactions in hypertensive individuals having laparoscopic cholecystectomy and found that MAP postoperatively wasn't changed in the mg sulfate group compared to the ketamine group the same as us, Ali et al. [14] found that MAP was statistically substantially decline in MgSO4 group postoperatively compared to the baseline mg sulfate group and regular saline group.

In the present study, there was a statistically significant difference between the groups as regards the number and percentage of patients who needed fentanyl for tachycardia and hypertension, as most of the patients in group (C) (85%) needed fentanyl in comparison to (38.1%) among group (K) and 4.8% of the patients among group (M).

In line with our study, Gad et al. [16] found that the use of fentanyl intraoperative was more in the ketamine group compared to the mg sulfate group. Also, Alshame et al. [11] found that using opioids was more common in the ketamine group.

In the current study, blood cortisol levels were not remarkable among the three studied groups at 45 minutes before intubation, but there was a statistically significant decrease in the mg sulfate groups compared to groups K and C 10 minutes after intubation.Following our study results, Elmeligy and Elmeligy [7] found that serum cortisol levels decreased in the mg sulfate group after intubation compared to baseline reading.In contrast with our findings, Jee et al. [17] used magnesium sulfate to attenuate MAP rise during laparoscopic cholecystectomy and found that the two groups had identical baseline cortisol readings. In the control and mg sulfate groups, cortisol values were higher at 5 and 10 minutes post-pneumoperitoneum and post-operatively compared to baseline.

Concerning blood glucose level, there was no statistically significant difference at 45 minutes before intubation and one minute after intubation among three studied groups, but there was a statistically significant increase in BGL at 5 minutes and 10 minutes after intubation in group K and C than in group M, with a remarkable increase in group C than in group K.

Sahoo et al. [18] illustrated Ketamine elevated blood sugar levels after 30 and 60 minutes of induction at 2 mg/kg. Alterations in glucoregulatory hormones cause ketamine's acute hyperglycemic impact. The observed elevation in blood sugar levels in this research is most likely due to increased plasma catecholamines caused by sympathetic activation. Because novo gluconeogenesis and glycogenesis are intricately tied to sympathetic activation, ketamine is predicted to influence glucose metabolism considerably.

Furthermore, Elmeligy and Elmeligy [7] concluded that the nebulized mg sulfate group attenuates blood glucose levels 3 minutes and 6 mins after intubation, which agrees with our study.

According to incidence of postoperative sore throat, there was increase in the incidence of postoperative sore throat in group C and K compared to group with no statistically significant difference between group C and K.In agreement with our findings, Mostafa et al,[15] stated that there was statistical difference between groups regarding incidence of post operative sore throat (POST). There was a significant decrease in Magnesium sulfate group in comparison to Ketamine group and saline group at 0, 2 postoperative and significant decrease of incidence of POST in ketamine group in comparison to normal saline group.These results were compatible with Teymourian et al,[19] who concluded that number of patients with sore throat were significantly lower in the magnesium gargle group compared to ketamine gargle group at 2hr, 4hr and 24 hours after operation.With contrast with our study Ahuja et al,[5] found that ketamine nebulization significantly attenuated the incidence and severity of sore throat, especially in the early post-operative period, with no adverse effects compared to saline neubolizer.

Conclusions:

The administration of nebulized ketamine (1 mg/kg) or magnesium sulfate (250 mg magnesium sulfate) prior to laryngoscopy and intubation can effectively attenuate the hemodynamic stress response in patients undergoing elective surgery. Both interventions were found to significantly blunt the increases in heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, blood cortisol level and blood glucose level. However, mg sulphate is more effective to blunt stress response than ketamine. Also, mg sulphate decreases the incidence of post operative sore throat more than ketamine.

Conflict of interest:

The authors declare no conflict of interest.

Financial Disclosures:

This study was not supported by any source of finding.

Sources of funding:

No specific grant was obtained for this research from governmental, private, or nonprofit funding organizations

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Citation

Abdelrazek, M., Masoud, S., Elattar, H., Galal El din, A. Nebulized Ketamine or Magnesium Sulphate for Attenuating Stress Response to Laryngoscopy and Intubation in Patients Undergoing Elective Surgeries. *Zagazig University Medical Journal,* 2024; (208-219): -. doi: 10.21608/zumj.2024.334456.3679