**Comparison of Usefulness of Ketamine and Magnesium Sulfate Nebulizations for Attenuating Postoperative Sore Throat, Hoarseness of Voice, and Cough**

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**Abstract**

**Context:** Postoperative sore throat (POST) is a complication that is unresolved in patients undergoing endotracheal intubation. **Aim:** To compare the effects of ketamine and magnesium sulfate nebulizations in two strengths, on the incidence and severity of POST, hoarseness, and cough. **Settings and Design:** Sixty surgical patients undergoing elective abdominal and lower limb surgeries under combined epidural and general anesthesia were included in this prospective, randomized, double-blinded study. **Subjects and Methods:** Patients in each group were nebulized with the respective study drug 15 min prior to the surgery, i.e., ketamine in Group K, magnesium sulfate 250 mg, and 500 mg in Group M1 and Group M2, respectively, and normal saline as control in Group C. A standardized anesthesia protocol was followed for all patients. After extubation, the patients were asked to grade POST, hoarseness, and cough at 0, 2, 4, 12, and 24 h. **Statistical Analysis Used:** One-way analysis of variance, Chi-square test, Fisher’s exact test, paired t-tests, and Wilcoxon’s signed-rank test as applicable. **Results:** Ketamine and magnesium sulfate 500 mg demonstrated a statistically significant decrease in POST at 0, 2, and 4 h, and postoperative hoarseness at 0 h. There was decrease in the incidence and severity of sore throat, hoarseness, and cough at all periods in the study groups as compared with control. **Conclusion:** Nebulization with ketamine 50 mg and magnesium sulfate 500 mg, 15 min before induction of general anesthesia and intubation, reduce the incidence and severity of POST and hoarseness of voice.

**Keywords:** Hoarseness of voice, ketamine, magnesium sulfate, nebulization, postoperative sore throat

**INTRODUCTION**

After any surgery performed under general anesthesia with endotracheal intubation, postoperative sore throat (POST) is still a complaint that has never been eradicated completely, despite the best measures we have instituted over the years. This is even more amplified in surgeries that are prolonged in nature and remains as a problem that is yet to be addressed in an effective and reliable manner. The high variability of incidence is due to a large number of factors implicated in POST. It was rated by patients as the 8th most undesirable outcome in the postoperative period.\(^1\) Although the symptoms resolve spontaneously without any treatment, prophylactic management for decreasing its frequency, and severity is desirable.\(^2\)

Besides monitoring of intracuff pressures, a multimodal approach consisting of nonpharmacological and pharmacological interventions has been advocated to attenuate POST. Ketamine and magnesium sulfate are shown to be promising agents to reduce POST.\(^3\)-\(^8\) This study was undertaken with the need to evolve a suitable agent and method to bring down the incidence of sore throat following tracheal intubation.

The primary aim of the study was to compare the effects of ketamine and magnesium sulfate nebulizations in a preemptive manner, on the incidence and severity of POST. Secondary objectives included comparison of the incidence of postoperative hoarseness and postoperative cough and also to evaluate the effects on these nebulizations on the hemodynamic parameters and oxygen saturation (SpO\(_2\)).

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**Subjects and Methods**

This prospective, randomized, double-blinded study was conducted between June 2013 and March 2015. After obtaining approval from the Hospital Ethical Committee, sixty consenting surgical patients aged 18–80 years were included in the study. All patients belonged to the American Society of Anesthesiologists physical status 1–3, had Mallampati Grade of 1–2, and were undergoing elective abdominal and lower limb surgeries under combined epidural and general anesthesia with endotracheal intubation. Epidural was mainly meant to reduce the postoperative pain at the surgical site so that the subjects could appreciate postoperative throat pain if at all it was present. Patients with difficult airway, who needed more than three attempts at intubation, nasogastric tube insertion, and those with reactive airway disease were excluded from the study.

Based on the results on attenuation of sore throat, hoarseness, and cough, with respect to the specific modalities used from existing literature and with 90% power and 95% confidence, minimum sample size was computed to be 25 in each of the four groups. However, as the availability of cases that fulfilled the inclusion and exclusion criteria were limited, the sample size had to be truncated to a number lower than the stipulated total of 100 cases. Hence, the sample size was recalculated with 80% power and 95% confidence, and an altered sample size of 15 per group was decided.

Randomization was performed in blocks of twenty cases apiece to avoid disparity in the number of cases in each group that are being performed, in case the number of cases for the sample size was not obtained. The patients were divided into four equal groups. Fifteen minutes before induction of anesthesia, all the patients were nebulized with either 5 mL normal saline or one of the study drugs diluted to 5 mL with normal saline. Patients allotted to Group C received normal saline, Group K ketamine 50 mg, Group M1 magnesium sulfate 250 mg, and Group M2 magnesium sulfate 500 mg.

In the premedication room, a large-bore intravenous (IV) cannula was inserted under local anesthesia and monitors such as electrocardiogram, noninvasive blood pressure and pulse oximeter were attached to the patient. Heart rate (HR), mean arterial pressure (MAP), and SpO\textsubscript{2} were noted. Immediately after nebulization, a set of values for the above-mentioned parameters were taken.

After shifting the patient to operation theater, an epidural catheter was inserted under strict aseptic precautions using an 18-gauge Tuohy needle, at the level desirable for the incision as per the surgery. After negative aspiration, a test dose of 3 mL of lignocaine 2% with adrenaline (1/200,000) was injected, and negative response to the test dose was confirmed. Then, a bolus of 6 mL 1% lignocaine was given, and the dermatomal level of the epidural block achieved was confirmed using an ice pack. An infusion of 0.25% bupivacaine with fentanyl 2 μg/mL was started as a continuous epidural infusion at a rate of 4–6 mL/h.

There were four categories of doctors who routinely intubate in the operating theaters – 1\textsuperscript{st} year (PG1), 2\textsuperscript{nd} year (PG2), and 3\textsuperscript{rd} year (PG3) postgraduates, and staff anesthetists (AP), who may be senior lecturers, fellows, associate professors, associate professors, and professors, who all were broadly classified under the staff category.

The patients were then preoxygenated with 100% oxygen, glycopyrrolate 5–10 μg/kg, midazolam 0.05–0.1 mg/kg, and fentanyl 2–3 μg/kg were given intravenously. Induction was performed with propofol 1.5–2.5 mg/kg till there was loss of response to verbal commands after which mask ventilation with oxygen and isoflurane (0.5–1.5%) was performed for 3 min.

Vecuronium 0.1 mg/kg was administered after the induction as skeletal muscle relaxant, and the patient was intubated following a gentle and quick laryngoscopy with a soft seal cuffed sterile poly vinyl chloride endotracheal tube (ET) (low-pressure, high-volume cuff). In males 8 mm or 8.5 mm, and in females 7 mm or 7.5 mm, internal diameter tube was used. ET cuffs were filled with the minimal volume of room air required to prevent an audible leak. Correct ET placement was confirmed with auscultation and end-tidal capnography. Patients who required three or more attempts of laryngoscopy were excluded from the group. A Ryle’s tube was also inserted gently through the nose, and if it required three or more attempts or instrumentation, the patient was excluded from the study.

The cuff pressure was checked immediately after intubation and 2 hourly during surgery using cuff inflator/pressure gauge PORTEX (Smiths Medical) cuff pressure monitor and was maintained between 20 and 25 cm of H₂O. Postinduction at 5 min HR, MAP, and SpO\textsubscript{2} were recorded before the surgical stimulus. Anesthesia was maintained using oxygen in air (1:2) with isoflurane 0.5–1.5% and intermittent positive pressure ventilation. Further skeletal muscle relaxation was provided using vecuronium at 1/5\textsuperscript{th} the induction dose at ½ h intervals.

Toward the end of the surgery ondansetron, 4 mg was given intravenously. Residual muscle relaxation was reversed with neostigmine 0.05–0.07 mg/kg and glycopyrrolate 10 μg/kg on completion of surgery. Extubation was performed after gentle oropharyngeal suctioning under laryngoscopic vision. Postoperative analgesia was provided using an epidural infusion of 0.125% bupivacaine and fentanyl 2 μg/mL in the Intensive Care Unit (ICU).

POST, cough, and hoarseness monitoring and grading were performed in the ICU by a nursing staff, who was blinded to the preoperative nebulization. The responses were noted at 0, 2, 4, 12, and 24 h in the questionnaire based on the scales described in Table 1. The rescue therapy for POST, especially in patients with Grade 3 score throat, was with the use of a dispersible aspirin 75 mg gargoyle which was repeated as many number of times as needed till patient got relief from the symptoms. The number of times the modality had been used was also taken into account.
The rescue therapy for surgical site pain, when any patient complained of breakthrough pain, was by epidural bolus – with 4–6 mL of 1% lignocaine as and when the patient complained of pain at the surgical site. If this was ineffective, repeat bolus doses were given for each episode of breakthrough pain till the end of 24 h. If the patient had pain, despite epidural boluses, tramadol was given as 100 mg IV boluses along with 4 mg of ondansetron. The boluses were repeated every time patient complained of breakthrough pain. If the above two modalities had failed to control surgical site pain, IV fentanyl 10–30 μg boluses were given and if pain still persisted, fentanyl infusion at 10–20 μg/h was initiated.

The number of times rescue therapy had been initiated for POST, the number of times rescue therapy had been initiated for postoperative pain, and the modality used were also noted.

Demographic data were analyzed with one-way analysis of variance for continuous variables and Chi-squared test for categorical variables. The incidence of postoperative symptoms was analyzed by Fisher’s exact test. To test the statistical significance of the difference in the values of the variable between the pre- and the post-operative periods for each group, paired t-test was applied. In case of comparatively large standard deviation values, comparison was done by applying Wilcoxon’s signed-rank test. All statistical analyses were performed with IBM SPSS statistics 20 software (Bengaluru, India). P values < 0.05 were considered statistically significant.

### Results

Comparison of demographic data showed no significant difference between the groups. Majority of the study subjects had a Mallampati scoring of 2 (63.33%), but the distribution was similar in both groups. The duration of surgery and intraoperative fentanyl consumption (both IV and epidural) were comparable in all the groups.

All the groups were comparable with respect to attempts at intubation (68.3% of the cases were intubated in the first attempt), use of bougie prior to intubation (18.3%), attempts at nasogastric tube insertion (70% of the cases, nasogastric tube was inserted in the first attempt), and experience of the intubating doctor [Table 2].

Statistically significant increase in HR was seen in Group M2, when baseline and prenebulization HR were compared with the postintubation HR ($P = 0.003$ and $P = 0.012$, respectively). All other groups showed no statistically significant change in HR, before and after the nebulization, and after intubation [Table 3]. The MAP of all groups showed no statistically significant change when baseline and prenebulization MAP were compared with the postintubation MAP [Table 3]. The SpO$_2$ preoperatively, postnebulization, and postintubation in all the groups were comparable.

The incidence of sore throat was assessed at 0, 2, 4, 12, and 24 h postoperatively. As demonstrating statistical significance in such small samples could be erroneous, it was advised that the incidence of nil and mildly severe sore throat to be combined and the incidence of moderate and severe throat pain to be combined and to compare the values in Group C with the values obtained from each respective group. This format has been followed for assessing the incidence of POST, hoarseness, and cough at all time intervals.

There was a statistically significant reduction in the incidence of sore throat in Group K and Group M2 at 0, 2, and 4 h after extubation as compared to the control group. Although Group M1 also had decreased incidence, the difference was not statistically significant. All the groups exhibited decreased incidence at 12 and 24 h but insignificant statistically. The maximum decrease in incidence was observed in Group K, followed by Group M2 and finally Group M1 [Table 4 and Figure 1].

There was a decrease in the incidence of hoarseness in Groups K, M1, and M2 at 0, 2, 4, and 12 h. The maximum decrease in incidence was observed in Group K consistently, followed by Group M2 and Group M1. Statistically significant decrease was only observed in Group K and Group M2, in comparison to Group C at 0 h. There was no incidence of hoarseness in any subject 24 h after extubation [Table 5].

There was a definite decrease in the incidence of cough in Groups K, M1, and M2 at 0, 2, and 4 h, though not statistically significant. However, there was no instance of cough at 12 and 24 h post extubation in all four groups [Table 6].

There was no statistical significance in the incidence of postoperative pain in any group when compared with control group. Fentanyl infusion for postoperative pain relief has demonstrated no significant difference among all four groups.

### Table 1: Grading severity of postoperative sore throat, cough, and hoarseness

| Grade | Severity                                      |
|-------|-----------------------------------------------|
| 0     | No sore throat at any time since the operation |
| 1     | Minimal Patient answered in the affirmative when asked about sore throat |
| 2     | Moderate Patient complained of sore throat on his/her own |
| 3     | Severe Patient is in obvious distress          |
| 0     | No cough at any time since the operation      |
| 1     | Minimal Minimal change in quality of speech. Patient answers in the affirmative only when enquired about |
| 2     | Moderate Moderate change in quality of speech of which the patient complains on his/her own |
| 3     | Severe Gross change in the quality of voice perceived by the observer |

*P* values < 0.05 were considered statistically significant.
DISCUSSION

Most of the general anesthetic procedures in the modern anesthetic practice are carried out with endotracheal intubation. POST is a well-recognized complication after general anesthesia in the postoperative period.\(^1\)

Ketamine and magnesium sulfate are shown to be promising agents to reduce POST.\(^1,3-8\) Peripherally administered \(N\)-methyl-D-aspartate (NMDA) receptor antagonist like ketamine is involved with antinociception and anti-inflammatory cascade,\(^1,9\) by reducing nuclear factor kappa-light-chain-enhancer of activated B-cells activity, and tumor necrosis factor alpha production.\(^10\) It diminishes the expression of inducible nitric oxide synthase,\(^11\) serum C-reactive protein, and interleukins 6 and 10.\(^12\) Pharmacological studies have shown that low-dose ketamine has antihyperalgesic, anti-allodynic, and opioid tolerance-protective effect due to an additive effect with opioids, and postsynaptic NMDA blockade which reduces wind up and central sensitization. Magnesium is an antagonist of the NMDA receptor ion channel.\(^7\)

Several studies had recommended gargle as the method of distribution of drug whereas we have tried to use nebulization as it ensures that the drug is equally and effectively distributed all over the pharynx and up to the beginning of the respiratory tract. In addition, nebulization prevents the user variability associated with gargling and confounded the issue of taste of the medications. Moreover, we have assessed two drugs in three different strengths in the same study, all conducted in a single center, by a single investigator, thus ensuring uniformity in method and equipment. This is the key difference in our study in comparison with the other studies.

In our study, there was a significant decrease in the incidence of POST seen at 0, 2, and 4 h in both ketamine and magnesium

| Table 2: Comparison of attempts at intubation, nasogastric tube insertion, usage of bougie, experience of intubating doctor |
|---|---|---|---|---|---|---|---|
| **Attempt number** | **Group C** | **Group K** | **Group M1** | **Group M2** | **Total** | **P** |
| **n** | **Percentage** | **n** | **Percentage** | **n** | **Percentage** | **n** | **Percentage** |
| **Comparison of attempts at intubation** | | | | | | | |
| 1 | 8 | 53.3 | 11 | 73.3 | 12 | 80 | 10 | 66.7 | 41 | 0.441 |
| 2 | 7 | 46.7 | 4 | 26.7 | 3 | 20 | 5 | 33.3 | 19 | |
| **Comparison of attempts at nasogastric tube insertion** | | | | | | | |
| 1 | 11 | 73.3 | 10 | 66.7 | 12 | 80 | 9 | 60 | 42 | 0.662 |
| 2 | 4 | 26.7 | 5 | 33.3 | 3 | 20 | 6 | 40 | 18 | |
| **Comparison of usage of bougie for intubation** | | | | | | | |
| **Yes** | 3 | 20 | 4 | 26.7 | 2 | 13.3 | 2 | 13.3 | 11 | 0.747 |
| **No** | 12 | 80 | 11 | 73.3 | 13 | 86.7 | 13 | 86.7 | 49 | |
| **Comparison of experience of intubating doctor** | | | | | | | |
| **PG1** | 1 | 6.7 | 3 | 20 | 4 | 26.7 | 2 | 13.4 | 10 | 0.969 |
| **PG2** | 5 | 33.3 | 4 | 26.7 | 3 | 20 | 5 | 33.3 | 17 | |
| **PG3** | 4 | 26.7 | 3 | 20 | 3 | 20 | 3 | 20 | 13 | |
| **Staff** | 5 | 33.3 | 5 | 33.3 | 5 | 33.3 | 5 | 33.3 | 20 | |

| Table 3: Comparison of hemodynamics |
|---|---|---|---|---|---|---|---|
| **Group** | **Mean±SD** | **P** |
| **Prenebulization** | **Postnebulization** | **Postintubation** | **Prenebulization versus postnebulization** | **Postnebulization versus postintubation** | **Prenebulization versus postintubation** |
| **Comparison of heart rate** | | | | | | |
| C | 78.87±17.97 | 76.53±15.27 | 81.67±16.54 | 0.13 | 0.124 | 0.451 |
| K | 82.4±14.85 | 82.27±11.24 | 83.73±9.31 | 0.912 | 0.324 | 0.586 |
| M1 | 79.67±12.45 | 79.67±11.48 | 84.27±13.15 | 1.00 | 0.144 | 0.173 |
| M2 | 75.13±14.31 | 72.93±11.48 | 82.93±12.16 | 0.098 | 0.003* | 0.012* |
| **Comparison of mean arterial pressure** | | | | | | |
| C | 101.9±14.87 | 100.5±12.9 | 101.3±11.69 | 0.505 | 0.786 | 0.882 |
| K | 99±14.29 | 98.73±12.1 | 97.73±11.99 | 0.854 | 0.673 | 0.641 |
| M1 | 97.13±11.11 | 96.67±8.93 | 95.4±11.78 | 0.694 | 0.643 | 0.54 |
| M2 | 100.3±13.80 | 99.87±12.34 | 95.33±12.84 | 0.832 | 0.22 | 0.229 |

*Statistically significant. SD=Standard deviation
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There was no incidence of POST at 12 and 24 h for ketamine and 24 h for magnesium sulfate 500 mg. This could be because of the persistent local action of ketamine and magnesium even at that time.

Although in this study, magnesium sulfate 250 mg group had decreased the incidence of POST at all time points, it was not statistically significant. Hence, it can be inferred that for prevention of POST, magnesium sulfate in a dose of 250 mg may not be sufficient, but there are no published data to support this hypothesis.

In this study, there was a significant decrease in the incidence of postoperative hoarseness in ketamine group and magnesium sulfate 500 mg group at 0 h. However, at 2, 4, 12, and 24 h, though the incidence of hoarseness was reduced with respect to the control group, it was not statistically significant in all three study groups. Possible explanation could be that the action of drugs had worn off, and incidence of hoarseness following intubation is not common. However, in a study by Gojendra et al.,[14] it was found that significant reduction in hoarseness occurred only at 24 h though there was reduction of incidence at 0, 2, and 4 h following ketamine gargle. The author had not given any reasoning for this observation.

The observation of reduced incidence of postoperative cough in all three study groups up to 24 h, statistically insignificant, is in agreement with the previous study by Park et al.[4] who had also reported no significant difference in the incidence of cough postoperatively following ketamine gargle.

We presumed that the position of the tube was optimal and endeavored to place the cuff below the level of the vocal cords. There was minimal or no tube movement during abdominal surgery. The concurrent epidural analgesia prevented any sudden coughing or bucking on the tube. Although air was used to fill the cuff, we did not find any increase in intracuff pressure as the surgery progressed.

In our study, nebulization with 500 mg magnesium sulfate resulted in significant increase in the HR following intubation. We are uncertain about the impact of magnesium on this hemodynamic response, but there was no decrease in blood pressure. We have tried to find other studies which could help us validate this finding. However, it has been proved

| Table 4: Comparison of incidence of postoperative sore throat |
|-------------------------------------------------------------|
| Time (h) | Severity | Group C | Group K | | Group M1 | Group M2 |
|----------|----------|---------|---------|----------------|---------|
| 0        | Nil      | 0       | 0       | 66.7          | 0.0017* | 3       | 20     | 0.272  | 5       | 33.3    | 0.0077* |
|          | Mild     | 5       | 33.3    | 4       | 26.7          | 6       | 40     | 8       | 53.3    |
|          | Mod      | 6       | 40      | 1       | 6.6           | 4       | 26.7   | 1       | 6.7     |
|          | Severe   | 4       | 26.7    | 0       | 0             | 2       | 13.3   | 1       | 6.7     |
| 2        | Nil      | 0       | 0       | 13      | 86.7          | 0.0022* | 3       | 20     | 0.128  | 7       | 46.6    | 0.014*  |
|          | Mild     | 7       | 46.6    | 2       | 13.3          | 9       | 60     | 7       | 46.6    |
|          | Mod      | 5       | 33.4    | 0       | 0             | 3       | 20     | 1       | 6.7     |
|          | Severe   | 3       | 20      | 0       | 0             | 0       | 0      | 0       | 0       |
| 4        | Nil      | 2       | 13.3    | 14      | 93.3          | 0.042*  | 7       | 46.7   | 0.168  | 10      | 66.7    | 0.042*  |
|          | Mild     | 8       | 53.3    | 1       | 6.7           | 7       | 46.7   | 5       | 33.3    |
|          | Mod      | 4       | 26.7    | 0       | 0             | 1       | 6.6    | 0       | 0       |
|          | Severe   | 1       | 6.7     | 0       | 0             | 0       | 0      | 0       | 0       |
| 12       | Nil      | 4       | 26.7    | 15      | 100           | 0.224   | 10      | 66.7   | 0.224  | 14      | 93.3    | 0.224   |
|          | Mild     | 8       | 53.3    | 0       | 0             | 5       | 33.3   | 1       | 6.7     |
|          | Mod      | 3       | 20      | 0       | 0             | 0       | 0      | 0       | 0       |
|          | Severe   | 0       | 0       | 0       | 0             | 0       | 0      | 0       | 0       |
| 24       | Nil      | 9       | 60      | 15      | 100           | 1       | 15     | 93.3   | 1      | 15      | 100     | 1       |
|          | Mild     | 5       | 33.3    | 0       | 0             | 1       | 6.7    | 0       | 0       |
|          | Mod      | 1       | 6.7     | 0       | 0             | 0       | 0      | 0       | 0       |
|          | Severe   | 0       | 0       | 0       | 0             | 0       | 0      | 0       | 0       |

*Statistically significant
The fact that there was no variation in the blood pressure after the administration of magnesium sulfate nebulization reinforces that this could not be due to systemic absorption, which would have been evidenced by the fall in blood pressure. Hence, the only possible explanation for an increase in HR could be the stress response to laryngoscopy and intubation in that group studied.

One of the major limitations of our study was that the sample size was limited as the patients who had to undergo surgeries with the need for both epidural and general anesthesia, who met the rigorous exclusion criteria were minimal. Moreover, the drugs we were using are known to have hemodynamic effects when administered intravenously. Hence, the patients whose safety may be compromised in the unlikely event of

### Table 5: Comparison of incidence of postoperative hoarseness of voice

| Time (h) | Severity | Group C | Group K | Group M1 | Group M2 |
|----------|----------|---------|---------|----------|----------|
|          |          | n       | Percentage | n       | Percentage | P  | n       | Percentage | P  | n       | Percentage | P  |
| 0        | Nil      | 2       | 13.3     | 12      | 80        | 0.0022*  | 8    | 53.4     | 0.050      | 10 | 66.6     | 0.0142*    |
|          | Mild     | 5       | 33.3     | 3       | 20        |          | 5    | 33.3     | 4          | 26.7 | 1        | 6.7        |
|          | Mod      | 7       | 46.3     | 0       | 0         |          | 2    | 13.3     | 1          | 4    | 26.7     | 1          |
|          | Severe   | 1       | 6.7      | 0       | 0         |          | 0    | 0        | 0          | 0    | 0        | 0          |
| 2        | Nil      | 5       | 33.3     | 14      | 93.4     | 0.099    | 11   | 73.3     | 0.099      | 12 | 80       | 0.099      |
|          | Mild     | 6       | 40       | 1       | 6.6       |          | 4    | 26.7     | 3          | 20   | 1        | 0          |
|          | Mod      | 4       | 26.7     | 0       | 0         |          | 0    | 0        | 0          | 0    | 0        | 0          |
|          | Severe   | 0       | 0        | 0       | 0         |          | 0    | 0        | 0          | 0    | 0        | 0          |
| 4        | Nil      | 8       | 53.3     | 15      | 100      | 1        | 14   | 93.4     | 1          | 14 | 93.4     | 1          |
|          | Mild     | 7       | 46.7     | 0       | 0         |          | 1    | 6.6      | 1          | 6.6   | 1        | 6.6        |
|          | Mod      | 0       | 0        | 0       | 0         |          | 0    | 0        | 0          | 0    | 0        | 0          |
|          | Severe   | 0       | 0        | 0       | 0         |          | 0    | 0        | 0          | 0    | 0        | 0          |
| 12       | Nil      | 12      | 80       | 15      | 100      | 1        | 15   | 100      | 1          | 14 | 100      | 1          |
|          | Mild     | 3       | 20       | 0       | 0         |          | 0    | 0        | 1          | 6.6   | 0        | 0          |
|          | Mod      | 0       | 0        | 0       | 0         |          | 0    | 0        | 0          | 0    | 0        | 0          |
|          | Severe   | 0       | 0        | 0       | 0         |          | 0    | 0        | 0          | 0    | 0        | 0          |
| 24       | Nil      | 15      | 100      | 15      | 100      | 1        | 15   | 100      | 1          | 15 | 100      | 1          |
|          | Mild     | 0       | 0        | 0       | 0         |          | 0    | 0        | 0          | 0    | 0        | 0          |
|          | Mod      | 0       | 0        | 0       | 0         |          | 0    | 0        | 0          | 0    | 0        | 0          |
|          | Severe   | 0       | 0        | 0       | 0         |          | 0    | 0        | 0          | 0    | 0        | 0          |

*Statistically significant

### Table 6: Comparison of incidence of postoperative cough

| Time (h) | Severity | Group C | Group K | Group M1 | Group M2 |
|----------|----------|---------|---------|----------|----------|
|          |          | n       | Percentage | n       | Percentage | P  | n       | Percentage | P  | n       | Percentage | P  |
| 0        | Nil      | 9       | 60       | 14      | 93.3     | 1    | 12      | 80        | 1    | 13      | 86.7       | 1    |
|          | Mild     | 5       | 33.3     | 1       | 6.7      | 3    | 20      | 2        | 13.3  | 2        | 13.3       | 1    |
|          | Mod      | 1       | 6.7      | 0       | 0        | 0    | 0       | 0        | 0    | 0        | 0          | 0    |
|          | Severe   | 0       | 0        | 0       | 0         | 0    | 0        | 0        | 0    | 0        | 0          | 0    |
| 2        | Nil      | 12      | 80       | 15      | 100      | 1    | 14      | 93.3     | 1    | 14      | 93.3       | 1    |
|          | Mild     | 3       | 20       | 0       | 0        | 0    | 0       | 0        | 0    | 0        | 0          | 0    |
|          | Mod      | 0       | 0        | 0       | 0         | 0    | 0        | 0        | 0    | 0        | 0          | 0    |
|          | Severe   | 0       | 0        | 0       | 0         | 0    | 0        | 0        | 0    | 0        | 0          | 0    |
| 4        | Nil      | 14      | 93.3     | 15      | 100      | 1    | 15      | 100      | 1    | 15      | 100        | 1    |
|          | Mild     | 1       | 6.7      | 0       | 0        | 0    | 0       | 0        | 0    | 0        | 0          | 0    |
|          | Mod      | 0       | 0        | 0       | 0         | 0    | 0        | 0        | 0    | 0        | 0          | 0    |
|          | Severe   | 0       | 0        | 0       | 0         | 0    | 0        | 0        | 0    | 0        | 0          | 0    |
| 12 and   | Nil      | 15      | 100      | 15      | 100      | 1    | 15      | 100      | 1    | 15      | 100        | 1    |
| 24       | Mild     | 0       | 0        | 0       | 0         | 0    | 0        | 0        | 0    | 0        | 0          | 0    |
|          | Mod      | 0       | 0        | 0       | 0         | 0    | 0        | 0        | 0    | 0        | 0          | 0    |
|          | Severe   | 0       | 0        | 0       | 0         | 0    | 0        | 0        | 0    | 0        | 0          | 0    |
systemic absorption from the nebulized drug were excluded prior to the nebulization itself.

The reasons that we did not have any cases excluded during the study are multifactorial. We had not excluded any patients with regard to the incidence of POST or its treatment modalities or the rescue analgesia provided in the case of a nonfunctional epidural as per study protocols. Similarly, all cases being conducted in our institution are accompanied by senior consultants. In the event of noninsertion of ET or Ryle’s tube in the first attempt, the consultant takes over and performs the procedure. This is the reason why no cases were excluded as the procedures were performed successfully within the stipulated number of tries.

The anesthetic techniques used for all the cases were as per the protocol, and there was no difference in administering the same. The surgeries that were selected for the study were different but anesthetic technique and analgesia provided were very similar in nature. Moreover, all these cases were related to the gastrointestinal tract, and Ryle’s tube insertion was mandatory, so that was one bias we could not avoid unfortunately. Moreover, in an unfortunate dearth of cases, nonexclusion of a case for a repeat insertion of Ryle’s tube or ET was seen as acceptable at the time of conducting the study.

**Conclusion**

It is concluded that nebulization with ketamine 50 mg and magnesium sulfate 500 mg, 15 min before the intubation, effectively reduces the incidence, and severity of POST and postoperative hoarseness of voice.

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**Conflicts of interest**

There are no conflicts of interest.

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