

COMPARATIVE STUDY BETWEEN INTRAVENOUS DEXAMETHASONE VERSUS KETAMINE GARGLE VERSUS INTRAVENOUS DEXAMETHASONE COMBINED WITH KETAMINE GARGLE FOR EVALUATION OF POST-OPERATIVE SORE THROAT AND HOARSENESS IN MIDDLE EAR SURGERY

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ABSTRACT

BACKGROUND

Endotracheal intubation is the common cause of trauma to the airway mucosa, resulting in post-operative sore throat (POST) and hoarseness. This study was done to evaluate and compare the effectiveness of prophylactically used dexamethasone-ketamine combination compared with IV dexamethasone/ ketamine-gargle alone in POST and hoarseness in patients undergoing elective middle ear surgery receiving general anaesthesia with endotracheal intubation.

MATERIALS AND METHODS

This was a prospective, randomised, placebo-controlled and double-blinded clinical study, in which 80 patients (as per convenience as there are 4 groups in my study and availability of patients who meet with the study criteria) aged (16 - 45 yrs.). ASA grade I and II were posted for middle-ear surgery. They were randomly assigned with informed consent into 4 groups (n= 20); Group K: gargled 40 mg ketamine in 30 mL NS for 30 sec; Group D: gargled 30 mL normal saline for 30 sec, received 0.2 mg/kg IV dexamethasone, Group KD: gargled 40 mg ketamine in 30 mL NS for 30 sec and received 0.2 mg/kg IV dexamethasone and Group P: gargled 3 mL NS for 30s, received IV NS (all measures were done 5 mins before induction. POST and hoarseness were graded post-operatively at 0, 1, 6, 12 and 24 hrs.).

RESULTS

The incidence and severity of POST were significantly lower in Group KD compared with other groups at all times during 24 hrs. post-operatively. Also, the incidence and severity of hoarseness were significantly lower in each one of Groups of KD, K and D compared with Group P. But no significant differences between Groups KD with Group K and Group D. Most of the patients of Group P suffered from POST and hoarseness.

CONCLUSION

For reducing incidence and severity of POST and hoarseness, administration of ketamine-gargle combined with IV dexamethasone was more effective than using each of these drugs alone at all times after extubation.

KEYWORDS

Endotracheal Intubation, Post-Operative Sore Throat (POST) and Hoarseness, IV Dexamethasone, Ketamine-Gargle, Middle Ear Surgery.

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BACKGROUND

Endotracheal intubation is the most common cause of trauma to airway mucosa, resulting in post-operative sore throat (POST) and hoarseness. Incidence of sore throat- 21%-65%.^[1] These are the most undesirable outcomes influencing patient's satisfaction and activities, and leaving an unpleasant memory of operation to the patients.

Despite attempts to reduce its incidence and severity, there are currently no effective therapies for the prevention of POST and hoarseness. Various trials (non-pharmacological methods) have been used for reducing POST with variable success. Like smaller sized ET tubes, use of lubricating water-

soluble jelly, careful airway instrumentation, intubation after full relaxation, minimised intracuff pressure, gentle under vision oropharyngeal suctioning and extubation when the tracheal tube cuff is fully deflated. These have been reported to decrease the incidence of POST.^[2]

The pharmacological methods used for reducing POST: Steroid gel,^[3] azulene sulphate,^[4] ketamine gargle and steroid injections.^[5,6,7]

So, we designed this present study to evaluate prophylactic effect of using dexamethasone- ketamine combination compared with using IV dexamethasone or ketamine gargle alone on the post-operative POST and hoarseness.

MATERIALS AND METHODS

The study was a prospective, randomised, placebo-controlled and double-blind clinical study in Dept. of Anaesthesiology at Hamidia Hospital, Bhopal, over a period of 6 months.

After obtaining approval from Ethical Committee and individual written informed consent, 80 consecutive patients aged (16 - 45 yrs.) ASA grade I and II posted for middle ear

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surgery under General Anaesthesia, patients with the help of a computer-generated table of random numbers were randomised into 4 groups-

Group K (n= 20): Who gargled 40 mg ketamine in 30 mL NS for 30 sec.

Group D (n= 20): Who gargled 30 mL NS for 30 sec and received 0.2 mg/kg IV dexamethasone.

Group KD (n= 20): Who gargled 40 mg ketamine in 30 mL NS and received 0.2 mg/kg IV dexamethasone.

Group P (n= 20): Who gargled 30 mL NS for 30 sec and receive IV NS.

Inclusion Criteria

1. ASA grade I and II.
2. Age- 16 to 45 yrs.
3. Mouth opening of > 3.5 cm.
4. Patients w/o history of POST and asthma, known allergies to study drugs, known difficulty with tracheal intubation.

Exclusion Criteria

1. Requirement of mechanical lung ventilation after surgery in ICU.
2. Who required > 1 attempt for tracheal intubation.

Preparation and Procedure

The preparations of 30 mL each were placed in an opaque container by a staff nurse, who also asked patients to gargle with the preparation for 30 sec after their arrival in the operation room and another study drug (Dexamethasone or NS) was injected IV, 5 mins before induction of anaesthesia. The same technique of anaesthesia operated on all patients. Induction of anaesthesia was done after 5 mins.

Monitoring

Non-invasive arterial pressure, Pulse oximetry (SPO₂), Heart Rate, ECG, Et-CO₂.

All Patients underwent a Standardised Anaesthesia Protocol which included-

- IV 0.04 mg/kg midazolam and glycopyrrolate 0.01 mg/kg.
- Induction with propofol (2 mg/kg) and fentanyl (2 µg/kg).
- Atracurium was used as a muscle relaxant. Tracheal intubation was performed with a soft seal cuffed sterile ET tube, an ID of 7 - 7.5 mm for women and 8 - 8.5 mm for men. ET tube cuff pressure was maintained between 18 cm - 22 cm H₂O using hand-held pressure gauge (Endotest; Rüsch, Kern, Germany). No air leakage could be heard with a peak airway pressure at 20 cm H₂O.
- Maintenance with 50% nitrous oxide and 50% O₂ mixture along with isoflurane (0.5% - 1%). Ventilation was adjusted to produce normocapnia. IV fentanyl infusion 0.5 µg/kg/hr in 50 mL NS was given. Reversal at the end of surgery was done with IV glycopyrrolate 0.01 mg/kg and neostigmine 0.05 mg/kg.
- Oropharyngeal suction was done under direct vision to avoid trauma to the tissues before extubation and to confirm that the clearance of secretions was completed.

All patients were carefully extubated when they were able to obey commands and lung ventilation seemed adequate.

The following Variables Regarding Tracheal Intubation were Recorded

- Glottis exposure as defined by Cormack and Lehane score;
- Endotracheal tube size;
- The time to achieve intubation;
- The duration of tracheal extubation.

The patients were interviewed and assessed for recovery by a blinded observer.

On arrival in the post-anaesthesia care unit at 0 hr, 1 hr, 3 hrs., 6 hrs., 12 hrs. and 24 hrs., POST and hoarseness were recorded thereafter.

Post was graded on a Four-Point Scale (0 - 3)

- 0- No sore throat;
- 1- Mild sore throat (Complains of sore throat only on asking);
- 2- Moderate sore throat (Complains of sore throat on his/ her own);
- 3- Severe sore throat (Change of voice/ hoarseness, associated with throat pain).

Hoarseness (As a Change in Voice Quality) was graded on a Four-Point Scale (0-3)

- 0: No hoarseness;
- 1: Hoarseness at the time of interview, but noted only by patient;
- 2: Hoarseness that is readily apparent, but mild;
- 3: Hoarseness that is readily apparent and severe.

Sedation was assessed during interviewing the patients to investigate the POST using the four-point observer's assessment of alertness/ sedation scale.

(Where 0= awake/ alert and 3= deep sleep).

Any complication (e.g. peptic ulcer, frequency of infections and electrolyte imbalance) associated with a single use of dexamethasone was obtained from review of the medical record. Other side effects, if any, were also noted.

Statistical Analysis

Differences in the age and weight among the groups were compared by One-Way Analysis of Variance. Differences in the incidence and severity of POST among the groups were compared with the help of Fisher's exact test. SPSS 16 for windows (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. P < 0.05 was considered as significant.

RESULTS

- The incidence and severity of POST were significantly lower in Group KD (10%) compared with the other groups [K (26%) and D (20%)] at all times during 24 h after the tracheal extubation (p < 0.05) (Diagram 1, Chart 1, Table 3).
- Also, the incidence and severity of hoarseness were significantly lower in each groups of KD (10%) and K (25%) and D (16%) compared with Group P (49%) at all

times after tracheal extubation for up to 24 hrs. (p < 0.05) (Diagram 1, Chart 2, Table 3).

- Most of the patients of Group P suffered from POST (44%) and hoarseness (49%). No local or systemic side-effects were observed. Only one patient in Group P had vomiting.
- Out of the 80 enrolled patients 1 patient from Group P was excluded from the analysis, because of difficulty

during intubation. Demographic data for the 79 patients are shown in Table 1.

- There were no significant differences among the four groups with respect to age, sex, weight, ASA Grade, duration of surgery, duration of anaesthesia, recovery and sedation score (p > 0.05). Variables associated with tracheal intubation are listed in Table 2.

Group Variable	Group K (n= 20)	Group D (n= 20)	Group KD (n= 20)	Group P (n= 19)
Age (Years)	28.8 ± 8.18	27.85 ± 8.02	29.2 ± 7.43	28.6 ± 8.7
Weight (kg)	51.7 ± 10.08	47.85 ± 11.52	46.75 ± 10.37	51.36 ± 12.27
Sex (M/F)	11/9	8/12	13/7	9/10
ASA (I/II)	14/6	12/8	15/5	11/8
Duration of Operation (min)	81.38 ± 13.48	82.5 ± 12.27	84.16 ± 11.66	82.35 ± 10.6
Duration of Anaesthesia (min)	99.4 ± 8.95	100.2 ± 7.52	101.8 ± 6.70	103.31 ± 9.06
Recovery Time (min)	25.5 ± 7.06	23.77 ± 5.61	23.5 ± 6.44	24.52 ± 6.40

Table 1. Demographic Data Related to Surgery

(Data are given as Mean ± SD. ASA- American Society of Anesthesiologists, SD: Standard Deviation)

Group Variable	Group K (n= 20)	Group D (n= 20)	Group KD (n= 20)	Group P (n= 19)
Cormack and Lehane Score (1/2/3)	15/4/1	16/4/0	14/4/2	15/3/1
ET tube size (7/7.5/8/8.5)	6/3/9/2	8/4/4/4	4/3/10/3	6/4/5/4
Time to Achieve Intubation (sec)	19.12±4.07	18.70±4.30	20.24±4.24	18.10±3.87
Extubation Time (sec)	12.85±4.42	10.9±3.46	11.5±4.04	12.26±3.52

Table 2. Variables associated with Tracheal Intubation

(Data are given as Mean ± SD. ET: Endotracheal)

Variables	Group D (n= 20)	Group K (n= 20)	Group KD (n= 20)	Group P (n= 19)	P value
0 hr after Tracheal Extubation	18/2/0/0 (10%)	16/3/1/0 (20%)	19/1/0/0 (5%)	13/4/3/0 (35%)	0.028
Sore Throat (0/1/2/3)	19/1/0/0 (5%)	16/4/0/0 (20%)	19/1/0/0 (5%)	14/3/3/0 (30%)	0.022
Hoarseness (0/1/2/3)	17/3/0/0 (15%)	16/3/1/0 (20%)	19/1/0/0 (5%)	12/6/2/0 (40%)	0.031
1 hr after Tracheal Extubation	18/2/0/0 (10%)	17/3/0/0 (15%)	19/1/0/0 (5%)	14/3/3/0 (30%)	0.034
Sore Throat (0/1/2/3)	18/2/0/0 (10%)	17/3/0/0 (15%)	19/1/0/0 (5%)	14/3/3/0 (30%)	0.023
Hoarseness (0/1/2/3)	16/4/0/0 (20%)	15/4/1/0 (25%)	19/1/0/0 (5%)	12/4/2/2 (40%)	0.020
3 hrs. after Tracheal Extubation	18/2/0/0 (10%)	16/4/0/0 (20%)	18/2/0/0 (10%)	12/6/2/0 (40%)	0.011
Sore Throat (0/1/2/3)	16/4/0/0 (20%)	16/1/2/1 (20%)	19/1/0/0 (5%)	11/6/1/2 (45%)	0.026
Hoarseness (0/1/2/3)	16/4/0/0 (20%)	15/5/0/0 (25%)	20/0/0/0 (0%)	13/3/4/0 (35%)	0.040
6 hrs. after Tracheal Extubation	17/3/0/0 (15%)	16/4/0/0 (20%)	19/1/0/0 (5%)	12/2/4/0 (40%)	0.041
Sore Throat (0/1/2/3)	17/1/2/0 (15%)	16/3/1/0 (20%)	18/2/0/0 (10%)	12/5/2/1 (40%)	0.037
Hoarseness (0/1/2/3)	17/3/0/0 (15%)	16/1/3/0 (20%)	18/2/0/0 (10%)	12/5/1/2 (40%)	0.043
12 hrs. after Tracheal Extubation	16/4/0/0 (20%)	16/4/0/0 (20%)	19/1/0/0 (5%)	13/4/3/0 (35%)	0.037
Sore Throat (0/1/2/3)	17/3/0/0 (15%)	16/1/3/0 (20%)	18/2/0/0 (10%)	12/5/1/2 (40%)	0.043
Hoarseness (0/1/2/3)	16/4/0/0 (20%)	16/4/0/0 (20%)	19/1/0/0 (5%)	13/4/3/0 (35%)	0.037
24 hrs. after Tracheal Extubation	17/3/0/0 (15%)	16/1/3/0 (20%)	18/2/0/0 (10%)	12/5/1/2 (40%)	0.043
Sore Throat (0/1/2/3)	17/3/0/0 (15%)	16/1/3/0 (20%)	18/2/0/0 (10%)	12/5/1/2 (40%)	0.043
Hoarseness (0/1/2/3)	16/4/0/0 (20%)	16/4/0/0 (20%)	19/1/0/0 (5%)	13/4/3/0 (35%)	0.037

Table 3. Severity Score of Sore Throat and Hoarseness

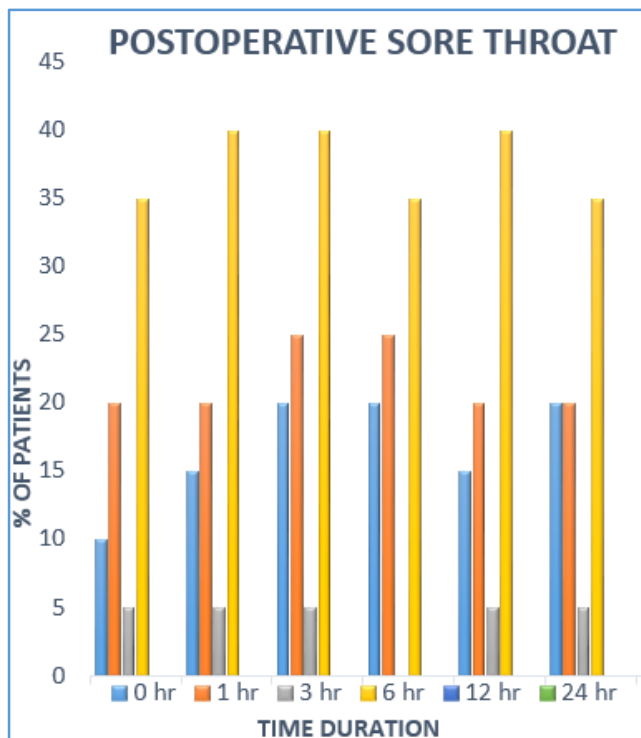


Chart 1

(1st bar is for Group D, 2nd for Group K, 3rd for Group KD and last is for Group P).

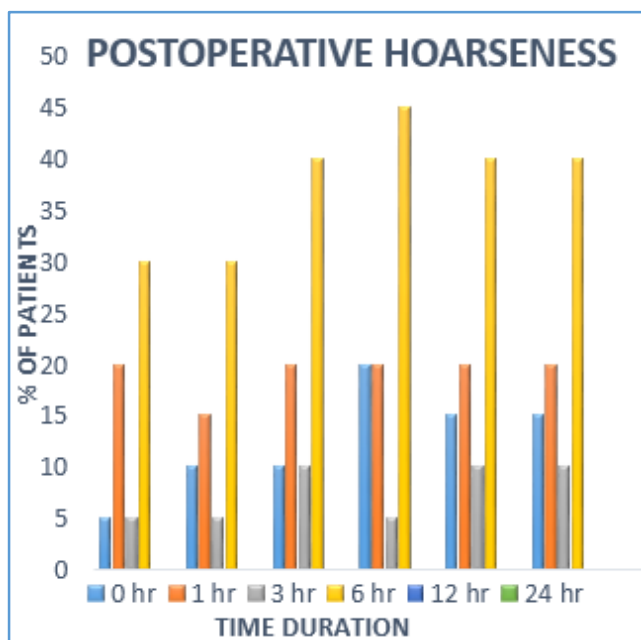


Chart 2

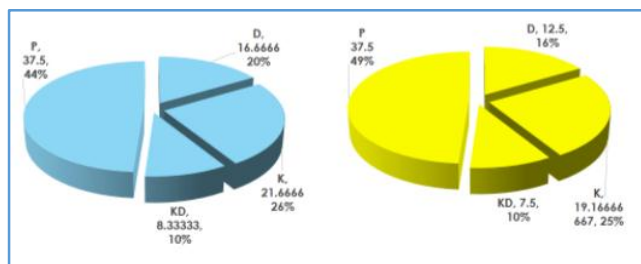


Diagram 1. Pie Diagram showing the Average % of Patients suffering from POST and Hoarseness upto 24 hrs. after Tracheal Extubation

DISCUSSION

- The results of this study demonstrated that the incidence and severity of POST and hoarseness were decreased in each one of Groups of KD and K and D compared with Group P at all times during 24 hrs. after tracheal extubation. So ketamine gargle combined with 0.2 mg/kg of dexamethasone was more effective than using each drug alone for reducing sore throat and hoarseness at all times after tracheal extubation for up to 24 hrs.
- Several contributing factors for sore throat after surgery have been reported including patient’s sex, age, ET tube size, cuff design and intracuff pressure.^[8,9,10] In this study, no correlation was observed between them.
- POST is mediated by an aseptic inflammatory process caused by:
 - Irritation of the pharyngeal mucosa during laryngoscopy,
 - The tracheal mucosa by the cuff of the ET tube, and
 - The trauma to tissues during intubation and extubation.

Ketamine

There is an increasing amount of experimental data showing that NMDA receptors are found not only in the central nervous system but also in the peripheral nerves.^[11,12] Moreover, experimental studies point out that peripherally administered NMDA receptor antagonists are involved with antinociception and anti-inflammatory cascade.^[13,14] Potent antagonist of the NMDA receptor that is currently available for use in humans.^[15] At low, sub-anaesthetic doses, it is relatively selective and potent antagonist of the N-methyl-D-aspartate (NMDA) receptor. In the previous studies, Canbay et al^[16] found that a ketamine gargle (40 mg ketamine in saline 30 mL; gargled for 30s 5 mins before induction) reduced the incidence and severity of POST in patients undergoing septorhinoplasty under general anaesthesia with endotracheal intubation, potentially because of local anti-inflammatory and anti-hyperalgesic effect of ketamine (as a potent antagonist of the NMDA receptor).

Dexamethasone

Potent corticosteroid with analgesic and anti-inflammatory effects have a prophylactic effect on post-operative nausea and vomiting, prescribed for the treatment of a sore throat resulting from tracheal mechanical irritation due to its modulating effects of tissue oedema and pain.^[17]

Mechanism of Anti-Inflammatory Activity

- Inhibition of leukocyte migration.
- Maintenance of cell membrane integrity.
- Attenuation of lysosome release.
- Reduction of fibroblast proliferation.^[18,19]
- On the other hand, Park et al^[20] showed that the prophylactic use of 0.2 mg/kg of dexamethasone significantly decreases the incidence and severity of sore throat and hoarseness 1 hr. to 24 hrs. after tracheal extubation of a DLT.

With respect to these findings, we propose that ketamine gargle plus IV dexamethasone is more effective than using

alone in reducing the incidence and severity of POST and hoarseness, perhaps due to their synergistic effects.

CONCLUSION

For reducing the incidence and severity of POST and hoarseness, the administration of 40 mg ketamine mix with 30 mL NS gargle combined with IV 0.2 mg/kg dexamethasone was more effective than using each of these drugs alone at all times after tracheal extubation upto 24 hrs.

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