Preventive effect of ketamine gargling for postoperative sore throat after endotracheal intubation

Hee Yong Kang, Dae-young Seo, Jeong-hyun Choi, Sung-Wook Park, and Wha Ja Kang

Background: Postoperative sore throat (POST) is a relatively common complication after endotracheal intubation, and various methods have been proposed to prevent it. In the present study, we assessed the effectiveness of ketamine gargling for reducing POST.

Methods: This study was conducted in a prospective, randomized, placebo-controlled, and single-blinded manner. The study populations consisted of 40 patients between 20 and 60 years old who were classified as American Society of Anesthesiologists physical status I–II and were scheduled for elective laparoscopic cholecystectomy. Patients in group K received ketamine (1 ml, 50 mg) in normal saline (29 ml), and they gargled with the given solution for 30 s before induction. Patients in group C received normal saline (30 ml) and gargled it for 30 s before induction. All patients were interviewed 1, 6, and 24 h after the operation. The visual analog scale (VAS) score of POST was checked.

Results: The VAS scores of POST were significantly lower in group K than in group C at 1 and 6 h after the operation. However, there were no significant differences in VAS scores at 24 h after the operation.

Conclusions: Preoperative ketamine gargling temporarily reduced POST in patients that underwent laparoscopic cholecystectomy.

INTRODUCTION

Postoperative sore throat (POST) is a common complication in patients undergoing endotracheal intubation due to direct trauma to tracheal mucosa [1,2]. Although POST is minor and self-limiting over time, many patients experience this complication. Ketamine has been traditionally recognized as an intraoperative anesthetic agent. However, it differs from most other drugs used to induce anesthesia because it has a significant analgesic effect. Thus, it is also used to reduce postoperative pain [3]. Ketamine is one of the most potent N-methyl-D-aspartate (NMDA) antagonists [4], and NMDA receptors are present not only in the central nervous system but also in the peripheral nervous system [5,6]. Peripheral administration of NMDA receptor antagonists are associated with the anti-inflammatory cascade [7] and antinociception [8]. In the present study, we compared the effectiveness of preoperative ketamine gargles to a placebo for reducing POST after endotracheal intubation.

MATERIALS AND METHODS

The study was conducted in a prospective, randomized, placebo-controlled, and single-blinded manner, and was approved by the Institutional Review Board of our institution. Written informed consent was received from 40 patients who underwent elective laparoscopic cholecystectomy. Patients were between 20 and 60 years old with American Society of Anesthesiologists physical status I–II. Patients with a history of POST or respiratory tract infection, recent use of analgesics such as non-steroidal anti-inflammatory drugs or opioids, and more than one attempt for tracheal intubation were excluded from this study. All patients were intubated by the same anesthesiologist.
anesthesiologist who was trained for more than 3 years.

Patients were randomly divided into two groups using a computer-generated random number table. Group C was the control group and group K was the trial group. Patients in group C received normal saline (30 ml) and patients in group K received ketamine (1 ml, 50 mg) in normal saline (29 ml). All patients were blinded to what they received. Each patient gargled with the given solution for 30 s before induction, and general anesthesia was induced 5 min after gargling.

All patients were monitored by electrocardiography, noninvasive arterial blood pressure, pulse oximetry, end-tidal carbon dioxide, and the bispectral (BIS) index. Induction was performed with propofol (2 mg/kg) and rocuronium (0.8 mg/kg). After confirming that the BIS fell below 60 and ensuring maximum neuromuscular blocking effect as assessed by a train of four count of 0, endotracheal intubations were accomplished with a direct laryngoscopy using a curved blade. Endotracheal tubes (having low pressure cuffs) with an internal diameter of 7.5 mm for male or 7.0 mm for female patients were used for tracheal intubation. The endotracheal tubes were lubricated with sterile water. The tracheal tube cuff was inflated with room air until no air leakage could be heard with a peak airway pressure at 20 cmH₂O, and cuff pressure was maintained between 15 and 20 cmH₂O using a handheld pressure gauge that measures endotracheal tube cuff pressure. Anesthesia was maintained with FiO₂ 0.5 in air and supplemented with 1.5–2.5 vol% sevoflurane. At the end of surgery, residual muscle relaxation was reversed with glycopyrrolate (0.008 mg/kg) and pyridostigmine (0.2 mg/kg). The lungs were ventilated with 100% O₂ until extubation. Oropharyngeal suction and extubation were gently performed. All anesthetic procedures were performed by the same anesthesiologist. Intravenous fentanyl (1 µg/kg) was administered to all patients for pain control in the post-anesthesia care unit. The visual analog scale (VAS) score (range 0–10) of POST was checked using direct questions at 1, 6, and 24 h after the operation.

We presumed the incidence of POST to be 60% [9]. The sample size was estimated from the assumption that a 50% reduction in the incidence of POST would be clinically relevant. The power analysis (taking α = 0.05 and power = 0.90) suggested that a minimum of 20 patients in each of the two groups would be required.

SPSS (ver. 21.0, SPSS Inc., Chicago, IL, USA) was used for statistical analysis. The unpaired t-test was used for comparisons between groups in age, height, weight, duration of tracheal intubation, and VAS scores of POST. The chi-square test was used for comparison of incidence. P < 0.05 was considered significant.

RESULTS

There were no significant differences in age, sex, height, weight, or duration of intubation between the two groups (P > 0.05) (Table 1). The VAS scores (mean ± SD) of group C at 1, 6, and 24 h were 3.5 ± 1.4, 2.8 ± 1.2, and 1.5 ± 0.8, respectively. Those of group K were 2.5 ± 1.3, 2.0 ± 1.1, and 1.2 ± 0.8, respectively. The VAS scores of POST were significantly lower in group K than in group C at 1 and 6 h after the operation (P < 0.05). However, there were no significant differences in VAS score at 24 h after the operation (P > 0.05) (Fig. 1). No local or systemic side effects were observed.

| Table 1: Patient Characteristics |
|----------------------------------|
|                                  |
| **Age (yr)**                     |
| Group C (n = 20)                  |
| **42.5 ± 11.7**                   |
| Group K (n = 20)                  |
| **42.3 ± 11.9**                   |
| **P value**                       |
| **0.957**                         |
| **Sex (M/F)**                     |
| Group C (n = 20)                  |
| **9/11**                          |
| Group K (n = 20)                  |
| **9/11**                          |
| **Height (cm)**                  |
| Group C (n = 20)                  |
| **165.8 ± 7.1**                   |
| Group K (n = 20)                  |
| **165.9 ± 7.2**                   |
| **P value**                       |
| **0.965**                         |
| **Weight (kg)**                  |
| Group C (n = 20)                  |
| **60.7 ± 8.2**                    |
| Group K (n = 20)                  |
| **61.7 ± 8.7**                    |
| **P value**                       |
| **0.698**                         |
| **Duration of anesthesia (min)**  |
| Group C (n = 20)                  |
| **100.3 ± 12.6**                  |
| Group K (n = 20)                  |
| **100.8 ± 9.8**                   |
| **P value**                       |
| **0.889**                         |
| **Incidence of POST**            |
| Group C (n = 20)                  |
| **18/20**                         |
| Group K (n = 20)                  |
| **17/20**                         |
| **P value**                       |
| **0.633**                         |

Data are shown as the mean ± SD. Group C: normal saline gargle group. Group K: ketamine gargle group. POST: postoperative sore throat.
DISCUSSION

Sore throat associated endotracheal intubation may be the result of localized trauma, leading to inflammation of pharyngeal mucosa. It may also be associated with edema, congestion, and pain [1]. Generally, POST is resolved spontaneously without specific treatment; however, many patients complain of POST after general anesthesia with endotracheal intubation. Several pharmacological and non-pharmacological trials have been performed to decrease POST [1,10-14]. Kalil et al. [15] reported that preoperative ketamine and aspirin gargle was the most promising pharmacological method for providers practicing in the United States.

There are several trials that have examined ketamine gargling [9,16], and they concluded that ketamine gargling reduced the incidence and severity of POST up to 24 h after the operation. Their results showed that severe sore throat in the control group at 24 h after the operation increased, but were typically self-limiting. However, mild and moderate sore throats were similar between the control group and ketamine gargling group at 24 h. Hu et al. [17] reported that a smaller endotracheal tube could reduce the incidence of POST at 24 h after surgery. To reduce the severity of POST at 24 h, we used a smaller endotracheal tube for tracheal intubation than used in previous studies [9,16]. We found that the VAS scores of POST were reduced in the preoperative ketamine gargling group at 1 and 6 h after the operation (P < 0.05). However, VAS scores between the two groups were not significantly different at 24 h after the operation (P = 0.150), and there was no increase in VAS score in either group during 24 h. This may explain why using a smaller endotracheal tube reduced the incidence of severe POST at 24 h after the operation in our study. Furthermore, McHardy et al. [1] reported that the incidence of POST decreased rapidly after the first postoperative day. Thus, we concluded that preoperative ketamine gargling reduced the VAS score during the early phase of POST.

POST was graded on a four-point scale (0-3) in the reports of Rudra et al. [9] and Canbay et al. [16]. However, Littman et al. [18] reported that a pain score of 0 (no pain) on the four-point scale (0-3) was greater than zero on the VAS (0-10). We used VAS scoring (0-10) to measure the incidence and severity of POST. By subdividing the scale, a reduction in POST could be measured more accurately.

The topical effect of ketamine gargling reduces inflammatory reactions [7], which may explain the reduction in VAS scores of POST during the early period of our study. However, peripheral and central action following systemic absorption cannot be excluded. Systemic absorption via submucosa and the possibility of swallowing the residual solution would contribute to the plasma ketamine level. Because we did not measure ketamine levels in the plasma, we could not rule out the influence of a systemic effect of ketamine. However, Park et al. [19] reported that intravenous low-dose ketamine injection was not effective for reducing POST, and Chan et al. [20] reported that systemic absorption during ketamine gargling did not play a major role in the reduction of POST. In the present study, the topical effect (rather than the systemic effect) may have contributed to the outcome.

Although there have been several trials on ketamine gargling, there is no recommended regimen or known side effects. When ketamine is administered systemically, it may cause adverse cardiovascular or respiratory effects, as well as sedation, dreams, hallucinations, and other psychomimetic adverse reactions [4]. Thus, we used topical low-dose ketamine gargling, and none of the patients complained of side effects. However, because there was a risk of aspiration during ketamine gargling, we encouraged the patients to remove ketamine sufficiently from the mouth.

The reported incidence of POST is 21-65% [1,9]. In the present study, the incidence of POST was higher than expected (Table 1). Because the interview method could also affect the results [21], direct questioning may increase the perceived incidence and VAS score of sore throats.

In conclusion, preoperative ketamine gargling reduced POST temporarily in patients that underwent laparoscopic cholecystectomy. However, there was no difference at 24 h after the operation. Therefore, to prevent POST immediately after general anesthesia with endotracheal intubation, preoperative ketamine gargling may be helpful. However, further studies are required to confirm these findings.

REFERENCES

1. McHardy FE, Chung F. Postoperative sore throat: cause, prevention and treatment. Anaesthesia 1999; 54: 444-53.
2. Maruyama K, Sakai H, Miyazawa H, Toda N, Inuma Y, Mochizuki N, et al. Sore throat and hoarseness after total intravenous anaesthesia. Br J Anaesth 2004; 92: 541-3.
3. Lee JH, Kim JI, Son YB, Rim SK. The effect of remifentanil and ketamine on intraoperative hemodynamics and postoperative pain in gastrectomy with sevoflurane based anesthesia. Anesth Pain...
4. Chizh BA. Low dose ketamine: a therapeutic and research tool to explore N-methyl-D-aspartate (NMDA) receptor-mediated plasticity in pain pathways. J Psychopharmacol 2007; 21: 259-71.
5. Carlton SM, Coggeshall RE. Inflammation-induced changes in peripheral glutamate receptor populations. Brain Res 1999; 820: 63-70.
6. Carlton SM, Zhou S, Coggeshall RE. Evidence for the interaction of glutamate and NK1 receptors in the periphery. Brain Res 1998; 790: 160-9.
7. Zhu MM, Zhou QH, Zhu MH, Rong HB, Xu YM, Qian YN, et al. Effects of nebulized ketamine on allergen-induced airway hyperresponsiveness and inflammation in actively sensitized Brown-Norway rats. J Inflamm (Lond) 2007; 4: 10.
8. Davidson EM, Carlton SM. Intraplantar injection of dextrorphan, ketamine or memantine attenuates formalin-induced behaviors. Brain Res 1998; 785: 136-42.
9. Rudra A, Ray S, Chatterjee S, Ahmed A, Ghosh S. Gargling with ketamine attenuates the postoperative sore throat. Indian J Anaesth 2009; 53: 40-3.
10. Loeser EA, Bennett GM, Orr DL, Stanley TH. Reduction of postoperative sore throat with new endotracheal tube cuffs. Anesthesiology 1980; 52: 257-9.
11. El Hakim M. Beclomethasone prevents postoperative sore throat. Acta Anaesthesiol Scand 1993; 37: 250-2.
12. Park SY, Kim SH, Lee AR, Cho SH, Chae WS, Jin HC, et al. Prophylactic effect of dexamethasone in reducing postoperative sore throat. Korean J Anesthesiol 2010; 58: 15-9.
13. Ogata J, Minami K, Horishita T, Shirinishi M, Okamoto T, Terada T, et al. Gargling with sodium azulene sulfonate reduces the postoperative sore throat after intubation of the trachea. Anesth Analg 2005; 101: 290-3.
14. Al-Qahtani AS, Messahel FM. Quality improvement in anesthetic practice--incidence of sore throat after using small tracheal tube. Middle East J Anaesthesiol 2005; 18: 179-83.
15. Kalil DM, Silvestro LS, Austin PN. Novel preoperative pharmacologic methods of preventing postoperative sore throat due to tracheal intubation. AANA J 2014; 82: 188-97.
16. Canbay O, Celebi N, Sahin A, Celiker V, Ozgen S, Aypar U. Ketamine gargle for attenuating postoperative sore throat. Br J Anaesth 2008; 100: 490-3.
17. Hu B, Bao R, Wang X, Liu S, Tao T, Xie Q, et al. The size of endotracheal tube and sore throat after surgery: a systematic review and meta-analysis. PLoS One 2013; 8: e74467.
18. Littman GS, Walker BR, Schneider BE. Reassessment of verbal and visual analog ratings in analgesic studies. Clin Pharmacol Ther 1985; 38: 16-23.
19. Park SY, Kim SH, Noh Ji, Lee SM, Kim MG, Kim SH, et al. The effect of intravenous low dose ketamine for reducing postoperative sore throat. Korean J Anesthesiol 2010; 59: 22-6.
20. Chan L, Lee ML, Lo YL. Postoperative sore throat and ketamine gargle. Br J Anaesth 2010; 105: 97.
21. Harding CJ, McVey FK. Interview method affects incidence of postoperative sore throat. Anaesthesia 1987; 42: 1104-7.