Assessing Intravenous Ketamine and Intravenous Dexamethasone Separately and in Combination for Early Oral Intake, Vomiting and Postoperative Pain Relief in Children Following Tonsillectomy

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Background: The aim of the present study is to evaluate the effect of preoperative 0.5 mg/kg i.v. dexamethasone in combination with 0.5 mg/kg i.v. ketamine on pain, early oral intake and vomiting in pediatric patients undergoing tonsillectomy during the first 24 hours of the postoperative period.

Methods: One hundred twenty children who were scheduled for tonsillectomy were randomly assigned to receive a single dose of dexamethasone 0.5 mg/kg i.v. as Group D (n = 30), receive ketamine 0.5 mg/kg i.v. as Group K (n = 30), receive dexamethasone 0.5 mg/kg i.v. and ketamine 0.5 mg/kg i.v. as Group KD (n = 30) and an equivalent volume of saline as Group C (n = 30) 15 minutes before the induction of anesthesia.

Post-operative pain was evaluated using an observational pain score (OPS) on arrival to the post-anesthesia care unit (PACU), at 15, 30, 45, and 60 minutes after that and at 1, 2, 4, 6, 12, and 24 hours after arrival to the ward.

Results: OPS scores were significantly lower at the time of arrival to the PACU, and at 15, 30, 45, and 60 minutes in the Group KD compared with Group C (p < 0.05). Postoperative OPS scores were significantly lower at 1, 2, 4, 6, 12, and 24 hours after operation in Group KD compared with Group C (p < 0.05).

Conclusion: A prophylactic preoperative single dose of i.v. 0.5 mg/kg dexamethasone in combination with a single dose of i.v. 0.5 mg/kg ketamine significantly decreased post-tonsillectomy pain compare with using i.v. ketamine or i.v. dexamethasone separately. Key words: Pain, Postoperative, Tonsillectomy, Dexamethasone, Ketamine.

1. INTRODUCTION

Postoperative pain is one of the most important problems in children undergoing tonsillectomy (1). Effective postoperative pain management can prevent morbidity, minimize crying that increases the risk of postoperative bleeding, facilitate early oral intake and adequate hydration (1, 2).

Aydin et al. (3) showed that the intravenous use of 0.5 mg/kg of ketamine (i.v.) before a tonsillectomy day-surgery had an analgesic effect and significantly reduced postoperative analgesic requirements. Verbal pain scale score in the ketamine group were significantly lower in the early postoperative period in the fourth and sixth hours.

Kaan et al. (4) showed that using a prophylactic intra-operative single dose of 0.5 mg/kg dexamethasone intravenously significantly reduced early post-tonsillectomy pain, improved oral intake and facilitated meeting the discharge criteria without any significant side effects. Their results showed that the pain score in the first 6 hours after operation was significantly lower in the dexamethasone group compared to the control group. However, they didn’t find a significant difference in analgesic requirements between the two groups. Moreover, there was no difference in the incidence of postoperative vomiting among the two groups.

As above studies showed, using dexamethasone or ketamine intravenously separately limited their efficacy to early post-operative period (till 6 hours) after tonsillectomy. Our hypothesis was that using ketamine plus dexamethasone intravenously before surgical incision will probably prolong the duration of postoperative analgesia after tonsillectomy and reduce analgesic requirements while decreasing adverse effects. To the best of our knowledge, there was no study to examine this hy-
and in Combination for Early Oral Intake, Vomiting and Postoperative Pain Relief in Children Following Tonsillectomy

2. METHODS

This randomized, double-blind, and placebo-controlled study was performed after obtaining institutional approval from the Ethic Committee of Isfahan University of Medical Sciences and taking written informed consent from the parents. One hundred twenty children, 2-12 years old, ASA physical status I or II, who were scheduled for a tonsillectomy, were enrolled in the study. Indications for tonsillectomy were tonsillar hypertrophy with obstructive symptoms and recurrent tonsillitis. Children with pulmonary and/or cardiac disease, history of allergy to the study drugs, peritonsillar abscess, and analgesic usage within 24 hours before surgery were excluded from the study. Moreover, patients who received antiemetic, antihistamine, steroids or psychiatric drugs within 24 hours of surgery were not included in the study.

Children were permitted to eat solid food until 12 a.m. on the day before the operation and drink clear fluids until 3 hours before the surgery. An anesthesiologist prepared syringes containing either the study medications or normal saline for each subject. All medications were 2 ml in volume. All children received intravenous midazolam 0.05 mg/kg for premedication 5-10 minutes before induction of anesthesia.

After establishing standard monitoring, the patients were randomly assigned to receive dexamethasone 0.5 mg/kg i.v. and a maximum dose of 8 mg plus 2 ml normal saline as Group D (n = 30), ketamine 0.5 mg/kg i.v. plus 2 ml normal saline as Group K (n = 30), dexamethasone 0.5 mg/kg i.v. and ketamine 0.5 mg/kg i.v. as Group KD (n = 30) and an two equivalent volume of saline as Group C (n = 30) 15 minutes before induction of anesthesia, in a double-blinded fashion.

General anesthesia was induced by using thiopental sodium 5 mg/kg, fentanyl 2 µg/kg, and atracurium 0.6 mg/kg for facilitation of endotracheal intubation. Anesthesia was maintained with isoflurane 1.2 % and a gas mixture of 50 % nitrous oxide and 50% oxygen adjusted to maintain heart rate and blood pressure values within 20% of the baseline induction value. The amount of intravenous fluid administered was 25-30 ml/kg of lactated Ringer’s solution during the intraoperative period. The same surgeon used the dissection and snare technique for all patients. At the end of the surgery neumromuscular blockade was reversed by i.v. neostigmine 0.04 mg/kg and i.v. atropine 0.01 mg/kg. Later, the anesthesia was discontinued and the tracheal tube removed in the operating room when airway reflexes had returned.

Heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP), means arterial pressure (MAP), oxygen saturation (SpO2) were recorded at 15 minute intervals during the operation. After extubation the patients were transferred to the postanesthesia care unit (PACU) where an anesthetist and nurses who were unaware of the study drug observed the patients. The time from anesthesia induction to the discontinuation of anesthetic drugs was considered as duration of anesthesia, and the time between discontinuation of nitrous oxide and extubation was considered extubation time. The time from the first surgical incision to the last mucosal suture was regarded as operation time.

In the PACU, pain was evaluated using a modified Hannallah pain scale5 an observational pain score (OPS) which was considered statistically significant.

Differences among the groups’ mean were compared using one-way analysis of variance (ANOVA) and post-hoc comparisons at various points in time by using Bonferroni’s type I error rate correction for multiple tests of significance. Kruskal-Wallis test was used to compare groups for nonparametric variables. Gender and complication rates were assessed by the Pearson chi-square test and by the Fisher’s exact test when the anticipated number was less than 5, P < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS 16.0 for Windows statistical package.

3. RESULTS

One-hundred twenty patients were included in the study. There was no patient excluded from the study due to any problems. There was no significant difference in the patient characteristics such as gender, ASA, age, weight,
time to tracheal extubation, duration of PACU stay, blood loss, duration of surgery and anesthesia among the four groups (Table 2).

Mean HR, SpO₂, level, SAP, DAP, and MAP values during surgery, in the PACU, and the first 24 hours after operation was not significantly different between the four groups. OPS scores were significantly lower at the time of arrival to the PACU, 15, 30, 45, and 60 minutes in Group KD compared with Group C (p < 0.05) (Figure 1). This variable was significantly lower in Group KD compared with Group K and Group D at these intervals (p < 0.05) (Figure 1). OPS scores were not significantly different between Group K and Group D.

Postoperative OPS scores were significantly lower at 1, 2, 4, 6, 12, and 24 hours after operation in Group KD compared with Group C (p < 0.05) (Figure 2). This variable was significantly lower in Group KD compared with Group K and Group D at these intervals (p < 0.05) (Figure 2). OPS scores were not significantly different between Group K and Group D.

There was no significant difference in median sedation values at any postoperative period among the four groups. Postoperative analgesic requirement was significantly less in Group KD compared with Group C (p < 0.05) (Table 3). This variable was not significantly different between Group D and Group K and Group KD with Group C (Table 3). Postoperative antiemetic requirement was significantly less in Group K, Group D, and Group KD compared with Group C (p < 0.05) (Table 3).

The time duration until the first oral intake was significantly lower in Group KD compared with Group K, Group D, and Group C (p < 0.05) (Table 3). This variable was not significantly different between Group D and Group K and Group KD compared with Group C, which showed the postoperative first hour still remains challenging for physicians.

As our results showed, ketamine 0.5 mg/kg i.v. significantly reduced postoperative pain score compared with placebo in PACU. Our finding is in accordance with the study by Aspinall et al. (11) which showed i.v. ketamine 0.5 mg/kg provides effective analgesia for the immediate postoperative period after adenotonsillectomy without increasing the risk of side-effects. The study by Dal et al. (2) had a similar conclusion.

Our data also showed that dexamethasone 0.5 mg/kg IV didn’t decrease postoperative pain compared with the placebo in PACU. This is in accordance with the study by Aspinall et al. (11) which showed i.v. ketamine 0.5 mg/kg provides effective analgesia for the immediate postoperative period after adenotonsillectomy without increasing the risk of side-effects. The study by Dal et al. (2) had a similar conclusion.

Table 3. Postoperative analgesics and antiemetic use in four groups Values are presented as mean ± SD or number. Group K = ketamine treated patients; Group D = dexamethasone treated patients; Group KD = ketamine-dexamethasone treated patients; Group C = control group. *P < 0.05 vs. Group C. †P < 0.05 vs. Group KD. ‡P < 0.05 vs Group D.
mg/kg significantly reduced postoperative pain in PACU in comparison with groups using placebo, or ketamine or dexamethasone separately without increasing adverse effects. This conclusion is also true when postoperative pain evaluation is extended for 24 hours.

Tonsillectomy can cause damage to the underlying muscle tissue and surrounding tissues mechanically, thermally or both. This causes the activation of an acute inflammatory response in the surrounding tissues and consequently causes spasm of pharyngeal muscles, irritation of nerve endings and in some cases disruption of the mucosa (12). Finally, the tissue damage results in an imbalance in the mechanisms of swallowing, incoordination, dysphagia and pain. Review of the above events shows that if the tissue damage was prevented, the normal physiologic mechanisms could be reestablished (13).

Glucocorticoids decrease the degree of inflammation by inhibition of bradykinin, prostaglandin and leukotrienes. Decrease in inflammatory response results in lessening of accompanying signs and symptoms including pain (13). The efficacy of using 0.5 mg/kg i.v. dexamethasone in combination with i.v. ketamine 0.5 mg/kg ketamine in reducing postoperative pain may be attributed to the anti-inflammatory effect of dexamethasone which may decrease local edema and pain (14). Moreover, dexamethasone can modulate inducible COX-2 (15). The complication following corticosteroid administra-

istration such as increased rate of infection, adrenal suppression and peptic ulcer are usually related to its long term use. The adverse effect of steroid therapy less than 24 hours is insignificant (16). In our study we didn’t have any complications related to the dexamethasone administration.

Perioperative ketamine, an NMDA antagonist, has been shown to decrease rescue analgesic requirements, pain severity, or both (17). Woolf et al. (18) showed that NMDA receptors are located in the dorsal horn of the spinal cord. Activation of these receptors can cause alterations in the central nervous system’s (CNS) response to pain and subsequent postoperative hyperalgesia. Local and regional anesthesia can prevent the transmission of peripheral nociceptive stimuli from the surgical incision to the dorsal horn of the spinal cord (1). This conclusion cannot be attributed to the general anesthesia. As Woolf et al. (19) suggested, blockade of the NMDA receptors may inhibit central sensitization. Using NMDA receptor antagonist at subanesthetic doses can prevent or block central hypersensitivity (3).

Ketamine has side effects such as hallucinations, bad dreams, dysphoria, nausea and vomiting, sedation, and diplopia. These adverse effects of ketamine are usually seen when higher doses (more than 1 mg/kg) are used (20). No case of hallucination was seen in our study. It seems that the anti-inflammatory effect of dexamethasone combined with the anti-nociceptive effect of ketamine caused more analgesic effects compared with using each drug separately.

Two of the most important side effects following tonsillectomy are nausea and vomiting. This can be due to opioid administration, swallowed blood, pain, and direct oropharyngeal irritation. As our findings showed, the use of ketamine in combination with dexamethasone decreased the incidence of nausea and vomiting at the early and late postoperative periods. This can be attributed to antiemetic effect of dexamethasone as described by the study of Fazel et al. (21).

Dexamethasone exerts its antiemetic effect through inhibition of
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Conflict of interests: authors have no conflict of interests.

REFERENCES


