Original Articles

1. Comparison of Spinal Anesthetic Effect between Emulsified Isoflurane and Emulsified Nonimmobilizer F6
   Jiao Guo, Cheng Zhou, Peng Liang, Xiao-jia Wang, Yi Zhao, and Jin Liu

2. Effect of Intra-Cuff Tetracaine on Preventing Postoperative Sore Throat after Gynecological Surgery
   Qing Zhu, Hai Wu, Hai-Bo Song, Ting Liu, Bei Liu, Chun-Lan Zheng, Wei Huang, and Han Huang

14. Surgery Induces Activation of Indoleamine 2, 3-Dioxygenase, Increases in Pro-Inflammatory Cytokines and Cognitive Impairment in Old Rats
   Xiao Wang, Li Chen, Hui-Wei Zhang, Chun-Yu Gong, Kang Yi, Zhuo Li, Huai-ming Wang, Jin Liu, Zhongcong Xie, and Jing Yang

Systematic Review and Meta-Analysis

22. Prophylactic Dexamethasone Decreases the Incidence of Postoperative Sore Throat after Tracheal Extubation: A Meta-Analysis
   Bao-Ji Hu, Lu-Long Bo, Jin-Bao Li, and Xiao-Ming Deng

Review Articles

29. The Role of Emulsified Isoflurane in Multi-Organ Protection
   Zhao-Yang Hu, and Jin Liu

36. Organ Dysfunction Following Trauma, Shock and Sepsis: An Update
   Yu-Ren Wang, Hsin-I Tsai, and Huang-Ping Yu

Opinions

45. Lung-Protection Ventilation Strategy in Surgical Patients: Optimal Setting of Positive End-Expiratory Pressure?
   Fu-Shan Xue, Xu Liao, Rui-Ping Li, and Xin-Long Cui

48. Remote Ischemic Preconditioning Protects against Post-Thoracotomy Acute Lung Injury: Chances and Challenges of Translation from Bench to Bedside
   Fu-Shan Xue, Rui-Ping Li, Xin-Long Cui, Gao-Pu Liu, and Chao Sun

For Authors

52. JAPM: Manuscript Types and Instructions
   Journal of Anesthesia and Perioperative Medicine Editorial Office
Prophylactic Dexamethasone Decreases the Incidence of Postoperative Sore Throat after Tracheal Extubation: A Meta-Analysis

Bao-Ji Hu, Lu-Long Bo, Jin-Bao Li, and Xiao-Ming Deng

ABSTRACT

**Background:** Postoperative sore throat (POST) is an undesirable complaint from patients undergoing general anesthesia. Dexamethasone, with its potent immunomodulatory effects, is used to reduce inflammation and tissue damage in a variety of clinical settings. The present study aimed to evaluate the effect of dexamethasone on the incidence of POST systematically.

**Methods:** Two researchers searched MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Google scholar, World Health Organization International Clinical Trials Registry Platform, Chinese BioMedical Literature Database, and China National Knowledge Infrastructure for randomized controlled trials that compared dexamethasone in patients undergoing general anesthesia and reported the outcome of POST.

**Results:** Five studies with a total of 582 patients receiving dexamethasone or placebo were included. The pooled results revealed that patients receiving dexamethasone had a lower incidence of POST at 1 hour (relative risk [RR] = 0.63, 95% confidence interval [CI] 0.40-0.98, P < 0.05) and 24 hours (RR = 0.42, 95% CI 0.30-0.60, P < 0.001) after surgery.

**Conclusions:** Prophylactic dexamethasone is effective in decreasing the incidence of POST after surgery relative to placebo.

**Keywords:** Dexamethasone, POST, Meta-analysis, Immunomodulatory effects.
formed the current meta-analysis to determine whether a single prophylactic dose of dexamethasone could reduce the incidence of POST in adults undergoing surgery under general anesthesia.

**METHODS**

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) recommendations for reporting our results (20). The risk of bias was checked by appraising "random sequence generation", "allocation concealment", "blinding of participants and personnel", "blinding of outcome assessment", "incomplete outcome data", "selective reporting", and "other bias" via valuing "low risk", "high risk" and "unclear risk" by the software of RevMan. In addition, the publication bias was also assessed by funnel plot and Egger's test. The inclusion criteria were defined as follows: randomized, controlled trials (RCTs), general anesthesia, comparing dexamethasone with placebo, drugs were used prophylactically, collecting data of the incidence of POST but not relative number or which can be calculated from the exact number; while exclusion criteria were defined as follows: conducted by Fujii et al., double-lumen tubes, laryngeal mask airway, and drugs not used in vein.

**Data Collection and Presentation**

Two authors (Bao-Ji Hu and Lu-Long Bo) independently conducted a comprehensive literature search to identify relevant studies. The quality of the reviewed RCTs was assessed independently by two of the authors (Bao-Ji Hu and Lu-Long Bo). In addition, the quality of the articles was also assessed by Jadad Scale (23) with a total possible score of 5. While an article with the scale no less than 3 was defined as high quality and included, otherwise the article would be discarded. All authors examined each title and abstract to exclude clearly irrelevant articles. Two authors extracted data independently. Any disagreements were resolved by discussion between two reviewers or with a third reviewer (Jin-Bao Li) available for arbitration if necessary.

The extracted data were entered into a data collection form including the following items: i) type of surgery, ii) number of patients, iii) dose(s) of dexamethasone, iv) comparator(s), v) timing of administration, vi) primary outcome measure of the study (POST), and vii) side-effects related to dexamethasone administration, including wound infection, delayed wound healing, hyperglycemia, and perennial pruritus. Attempts were made to contact the authors of original papers when additional data were required. Data were extracted from figures as needed if not been displayed numerically and the authors did not respond to our request for numerical data. Dexamethasone dose was converted to units in mg/kg using the mean weight reported for the dexamethasone groups. When information about group weight was unavailable, 70 kg was selected to represent the weight of the patient. POST documented at the early (1 hour) and late (24 hours) postoperative periods was included for analysis.

**Statistical Analysis**

Analyses were performed using the Review Man-
Systematic Review and Meta-Analysis

Characteristics of Eligible Trials
Our comprehensive search yielded to 1,006 relevant publications. Of those, five studies were finally included in the current analysis with a total of 582 patients (353 received dexamethasone and 229 received placebo) (15-19). The PRISMA flow diagram detailing the disposition of retrieved publications was shown in figure 1, a template modified from the PRISMA checklist (20). The characteristics and outcomes found in each of the included studies were summarized in the table 1.

Doses of dexamethasone applied in the original studies ranged from 0.05 to 0.2 mg/kg. Multiple doses of dexamethasone were used in three studies (15-17). Studies with doses ≤0.1 mg/kg and >0.1 mg/kg were defined into two subgroups, and then were compared with placebo (saline were used in all trials), respectively. Of the five studies (15-19), two studies (18, 19) had only one subgroup receiving dexamethasone been compared with saline, while the others had two. Dexamethasone was given preoperatively in all included studies. The incidence of sore throat at 1 hour post-operation was reported in four studies (15-18), at 3 hours post-operation in one study (16), at 6 hours post-operation in one study (18) and at 24 hours post-operation in four included studies (15, 17-19). According to the outcomes summarized, we deter-

RESULTS

Table 1. Details Characters of Included Trials and Incidence of POST Treated with Placebo, Low Dose of Dexamethasone (≤0.1 mg/kg) and High Dose of Dexamethasone (0.1 mg/kg) in the 5 studies (15-19). Number of patients included for analysis. Number randomized was 60.

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Study Design</th>
<th>Procedure</th>
<th>Gender</th>
<th>Age (Year)</th>
<th>Adverse Events</th>
<th>Tube size (N)</th>
<th>Duration of Tube Use (hour)</th>
<th>Incidence of POST</th>
<th>Dose of Dexamethasone (mg/kg)</th>
<th>Number Randomized (N)</th>
<th>Time of Administration</th>
<th>Placebo/Dex (minute)</th>
<th>Score</th>
<th>Jadad Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thomas (2007)</td>
<td>Trial</td>
<td>Male</td>
<td>15-17</td>
<td>15-57</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0.1-0.2</td>
<td>0.11</td>
<td>31-35</td>
<td>117-11177</td>
<td>7.0-8.5</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>Park (2008)</td>
<td>Trial</td>
<td>Male</td>
<td>15-17</td>
<td>18-77</td>
<td>0.1-0.2</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0.11</td>
<td>31-35</td>
<td>117-11177</td>
<td>7.0-8.5</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>Bagchi (2011)</td>
<td>Trial</td>
<td>Male</td>
<td>15-17</td>
<td>18-60</td>
<td>0</td>
<td>0</td>
<td>0.2</td>
<td>0.1</td>
<td>36-360</td>
<td>0.05-0.1</td>
<td>36</td>
<td>117-11177</td>
<td>7.0-8.5</td>
<td>11</td>
</tr>
<tr>
<td>Oliveira (2007)</td>
<td>Trial</td>
<td>Male</td>
<td>15-17</td>
<td>25-60</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.11</td>
<td>31-35</td>
<td>117-11177</td>
<td>7.0-8.5</td>
<td>11</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Rubagga (2012)</td>
<td>Trial</td>
<td>Male</td>
<td>15-17</td>
<td>25-60</td>
<td>0</td>
<td>0</td>
<td>0.2</td>
<td>0.1</td>
<td>36-360</td>
<td>0.05-0.1</td>
<td>36</td>
<td>117-11177</td>
<td>7.0-8.5</td>
<td>11</td>
</tr>
</tbody>
</table>
mined to compare the incidence of POST at 1 hour and 24 hours after surgery.

Risk of Bias

Among all selected trials, randomized sequence and allocation sequence concealment were adequately conducted. Blinded fashion was fully stated in all trials. The numbers of patients and reasons for withdrawal or dropout were reported in all trials. An overview of the risk of bias was shown in figure 2 and figure 3. The Cohen κ statistic for agreement on study inclusion was 0.89. Publication bias assessed by Egger's test at 1 hour and 24 hours after surgery was shown in figure 4.

Outcomes

Four studies (529 patients) recorded the occurrence of POST at 1 hour after surgery. Patients receiving dexamethasone had a significant lower incidence of POST (RR=0.63, 95% CI, 0.40-0.98, I²=78%, P=0.04) (Figure 5). Tests for heterogeneity identified the trial by Oliveira et al. (16) for outlying results. Exclusion of this trial resolved the heterogeneity, which did not change the results of POST at 1 hour after surgery (RR=0.68, 95% CI, 0.5-0.84, I²=9%, P<0.001). We performed a subgroup meta-analysis by the doses chosen in each trial. Dexamethasone ≤ 0.1 mg/
kg showed a trend toward a decreased (but not significant) incidence of POST (RR=0.77, 95% CI, 0.54-1.11, I^2=52%, P=0.17), while dexamethasone > 0.1 mg/kg also showed a trend toward a decreased (but not significant) incidence of POST at 1 hour after surgery (RR=0.46, 95% CI, 0.16-1.35, I^2=89%, P=0.16).

Four studies (567 patients) recorded the occurrence of POST at 24 hours after operation. Patients receiving dexamethasone had a significant lower incidence of POST (RR=0.42, 95% CI, 0.30-0.86, I^2=35%, P<0.01) (Figure 6). A subgroup meta-analysis was also done to examine the effect of different doses chosen on the in-
incidence of POST. Dexamethasone ≤ 0.1 mg/kg showed a trend toward a decreased (but not significant) incidence of POST (RR = 0.57, 95% CI, 0.31-1.03, I² = 0%, P = 0.06), while dexamethasone > 0.1 mg/kg showed a significant decrease in incidence of POST at 24 hours after surgery (RR = 0.37, 95% CI, 0.24-0.56, I² = 48%, P < 0.01). None of the studies recorded the side effects or adverse events of dexamethasone administration at 1 hour or 24 hours after surgery.

### DISCUSSIONS

Our meta-analysis suggested that dexamethasone can lead to a statistically significant reduction in the incidence of POST at both 1 hour and 24 hours after surgery when administered to patients undergoing general anesthesia, compared with placebo.

Prophylactic administration of dexamethasone during the intra-operation was considered to be dramatically effective in reducing the incidence of POST by attenuating the occurrence of edema after extubation in patients under general anesthesia (25). The underlying mechanism of its effect was presumably based on its anti-inflammatory activity.

Multiple doses of dexamethasone were chosen in each trial. Although our pooled analysis of multiple doses of dexamethasone indicated that dexamethasone could lead to a decrease in incidence of POST at both 1 hour and 24 hours after surgery, the subgroup analysis exhibited conflicting results, especially at 1 hour after surgery. This could be explained by the relatively small number of patients included in each trial, which might be insufficient to define the effect of a relatively low or high dose of dexamethasone on POST after surgery.

Many factors can affect the incidence and severity of POST, such as the different types of surgical procedure, endotracheal tube size, intra-cuff pressure, gender, and anesthetic protocol, as well as the contributing factors, and the preventive measures. We had proven in a meta-analysis that a smaller size of endotracheal tube was associated with a lower incidence of POST after surgery (26).

Dexamethasone has several potential side-effects, such as hyperglycemia, wound healing, and susceptibility to infection. However, Oliveira et al. (16) demonstrated that a single dose of perioperative dexamethasone did not increase its dose-limiting complications such as wound infection and wound healing delay. All included studies reported no occurrence of any side effect of dexamethasone, which might be explained by its single dose use partly. Meanwhile, the follow-up time of included studies was within 24 hours, which was too short to identify the side effects of its use.

The results of our meta-analysis are subject to several limitations. Firstly, our present meta-analysis included only five RCTs. The sample size was relatively small, with multiple meta-analysis chosen in the original studies. Our combined results might be inconclusive because of wide CIs. Secondly, dexamethasone was administered preoperatively with a single dose, which limited our ability to investigate whether the timing of administration would influence the outcome measures. We could not assess the severity of POST, because the reports of the outcome differed among studies. Thirdly, a multivariable analysis, such as operation duration, gender, tube size and so on, has not been done on the source data allowing us to take into account some potential confounding factors. Another potential limitation is that the duration of most studies was limited to 24 hours with very few reporting beyond 24 hours after operation. Studies investigating dexamethasone in combination with other pharmacological analgesic and non-pharmacological methods for POST therapy are needed.

### CONCLUSIONS

In summary, our current meta-analysis found that prophylactic intravenous administration of dexamethasone was associated with a statistically significant reduction in the incidence of POST after tracheal extubation. Further studies are warranted to determine the dose-ranging effect of dexamethasone and the effect in patients with high risk of POST.

All authors declare no conflict of interest.

Bao-Ji Hu and Lu-Long Bo defined inclusion and exclusion criteria, performed the electronic and manual search of the literature, and drafted and revised the...
manuscript. Jin-Ruo Li contributed to data analysis, manuscript revision and the interpretation of the data with his expertise. Xiao-Ming Deng had full access to all of the data in the study, contributed to the interpretation of the results, and took responsibility for the integrity of the data and the accuracy of the data analysis. We acknowledge all authors whose publications were included in this study.

References