Prophylactic Dexamethasone Decreases the Incidence of Postoperative Sore Throat after Tracheal Extubation: A Meta-Analysis

Bao-Ji Hu1,2*, Lu-Long Bo2*, Jin-Bao Li2, and Xiao-Ming Deng2

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.

Postoperative sore throat (POST) is a common complication after general anesthesia, with its incidence ranging from 40 to 90% (1-3). It is important to prevent POST to decrease the patients’ dissatisfaction. Many factors including gender, history of smoking or lung diseases, postoperative nausea, endotracheal tube size and cuff pressure, and duration of surgery (1, 2), contribute to the occurrence of POST. Despite efforts devoted to reduce its incidence and severity, effective therapies were rarely determined for the prevention of POST in patients.

Dexamethasone, with its potent immunomodulatory effects, has been used to reduce inflammation and tissue damage in a variety of clinical settings. Previous studies demonstrated that dexamethasone can be safely used for the prevention of postoperative nausea and vomiting (PONV) (4-6). The efficacy of dexamethasone in reducing pain and inflammation after surgery has also been explored (7-12). Dexamethasone is also widely applied in the therapy for sore throat resulting from tracheal mechanical irritation (13, 14). Recently, several studies have explored the efficacy of dexamethasone in reducing the incidence of POST (15-19). Thus, we per-

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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", "complete 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.

**Literature Search**

The databases of MEDLINE (updated to July 2013), EMBASE (updated to July 2013), Cochrane Central Register of Controlled Trials (updated to July 2013), Google scholar, World Health Organization International Clinical Trials Registry Platform (July 2013), Chinese Biomedical Literature Database (1978 to July 2013), and the China National Knowledge Infrastructure (1994 to July 2013) were searched. Full reports of RCTs in which a single dose of dexamethasone was given intravascularly preoperatively to adult patients undergoing surgery under general anesthesia and was compared with placebo were identified. The Medical Subject Heading and the appropriate corresponding keywords "dexamethasone", "steroids" AND "postoperative sore throat" were used. We restricted the findings of the above restrictions with a highly sensitive search strategy recommended by the Cochrane Collaboration for identifying RCTs (21). Considering the validity of the data, studies conducted by Fujii et al. (22) were not included in the present meta-analysis. We also checked the reference lists of RCTs and previous meta-analyses to include any further potential eligible trials.

**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-
Characteristics of Eligible Trials

Our comprehensive search yielded 1,006 relevant publications. Of those, five studies were included in the analysis with a total of 229 patients (15-19). The PRISMA flow diagram detailing the disposition of retrieved publications was shown in figure 1. The characteristics and outcomes found in each of the included studies were summarized in table 1.

Table 1. Detailed characteristics 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).

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Trial</th>
<th>Gender (n)</th>
<th>DEX (mg/kg)</th>
<th>Procedure (minute)</th>
<th>Anesthesia</th>
<th>Study Groups</th>
<th>Adverse Events</th>
<th>Time of administration</th>
<th>Preoperative, DEX (ug/ml)</th>
<th>Baseline, DEX (ug/ml)</th>
<th>Postoperative, DEX (ug/ml)</th>
<th>Preoperative</th>
<th>Baseline</th>
<th>Postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bagchi (2012)</td>
<td>India</td>
<td>male, 67</td>
<td>0.2</td>
<td>General</td>
<td>7.8-8.5</td>
<td>10-11</td>
<td>Postoperative</td>
<td>4</td>
<td>151-155</td>
<td>35-70</td>
<td>45-90</td>
<td>0.2</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Park (2008)</td>
<td>Korea</td>
<td>male, 47</td>
<td>0.05, 0.1</td>
<td>General</td>
<td>7.5-8.0</td>
<td>3-5</td>
<td>Preoperative</td>
<td>4</td>
<td>56-110</td>
<td>36</td>
<td>3-5</td>
<td>0.05, 0.1</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Huangsin (2012)</td>
<td>China</td>
<td>male, 20</td>
<td>0.1</td>
<td>General</td>
<td>7.0-8.5</td>
<td>111-117</td>
<td>Preoperative</td>
<td>4</td>
<td>151-155</td>
<td>45-90</td>
<td>45-90</td>
<td>0.1</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Oliveira (2011)</td>
<td>USA</td>
<td>female 72</td>
<td>0.02</td>
<td>General</td>
<td>9-10</td>
<td>111-117</td>
<td>Pretreatment</td>
<td>4</td>
<td>35-37</td>
<td>36</td>
<td>35-37</td>
<td>0.02</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Baegil (2012)</td>
<td>India</td>
<td>male, 49</td>
<td>0.2</td>
<td>General</td>
<td>7.8-8.5</td>
<td>35-37</td>
<td>Preoperative</td>
<td>4</td>
<td>151-155</td>
<td>45-90</td>
<td>45-90</td>
<td>0.2</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

Results

Characteristics of Eligible Trials

Our comprehensive search yielded 1,006 relevant publications. Of those, five studies were included in the analysis with a total of 582 patients (353 received dexamethasone and 229 received placebo) (15-19).

The fixed-effect model was used as the overall heterogeneity had no significant difference, while a random-effect model was employed in case of significant heterogeneity, i.e., P value of chi-square test was less than 0.10 and I² was greater than 50% (24). Potential sources of heterogeneity were identified by sensitivity analyses conducted by omitting one study in each turn and investigating the influence of a single study on the overall pooled estimate. Publication bias was assessed by visually inspecting funnel plot and Egger's test. P value less than 0.05 was considered statistically significant.
minded 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 k 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, I² = 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, I² = 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, I² = 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 signi-
nificant) incidence of POST (RR=0.57, 95% CI, 0.31-1.03, I²=0%, P=0.06), while dexametha-
sone > 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 ef-
fects or adverse events of dexamethasone admin-
istration at 1 hour or 24 hours after surgery.

DISCUSSIONS

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

Prophylactic administration of dexametha-
sone during the intra-operation was considered
to be dramatically effective in reducing the inci-
dence 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-in-
flammatory activity.

Multiple doses of dexamethasone were cho-
en 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 sur-
gery. 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 dexametha-
sone on POST after surgery.

Many factors can affect the incidence and se-
verity of POST, such as the different types of sur-
gical procedure, endotracheal tube size, intra-
cuff pressure, gender, and anesthetic protocol,
as well as the contributing factors, and the pre-
ventive measures. We had proven in a meta-analy-
sis that a smaller size of endotracheal tube was
associated with a lower incidence of POST after
surgery (26).

Dexamethasone has several potential side-ef-
fects, such as hyperglycemia, wound healing,
and susceptibility to infection. However, Olivei-
ra et al. (16) demonstrated that a single dose of
perioperative dexamethasone did not increase
its dose-limiting complications such as wound in-
fected 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 doses
chosen in the original studies. Our combined re-

results might be inconclusive because of wide CIs.

Secondly, dexamethasone was administered pre-
operatively 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 dif-
fered 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 po-
tential limitation is that the duration of most
studies was limited to 24 hours with very few re-
porting beyond 24 hours after operation. Stud-
ies 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 statistical-
ly significant reduction in the incidence of
POST after tracheal extubation. Further studies
are warranted to determine the dose-ranging ef-
fect of dexamethasone and the effect in patients
with high risk of POST.
References


We acknowledge all authors whose publications were included in this study.