Effectiveness of Oral Dexamethasone in the Treatment of Moderate to Severe Pharyngitis in Children

Robert P. Olympia, MD; Hnin Khine, MD; Jeffrey R. Avner, MD

Objective: To determine the effectiveness of a single dose of oral dexamethasone in reducing the pain associated with moderate to severe pharyngitis in pediatric patients.

Design: Prospective, randomized, double-blind, placebo-controlled clinical trial.

Setting: Large, urban pediatric emergency department between March 2002 and November 2003.

Patients: Children aged 5 to 18 years with moderate to severe pharyngitis (odynophagia or dysphagia, moderate to severe pharyngeal erythema or swelling, and a McGrath Facial Affective Scale score of 0.75 or higher [scale 0.0-1.0]).

Interventions: Study patients were randomly assigned to receive 1 dose of either oral dexamethasone suspension (0.6 mg/kg with a maximum of 10 mg) or placebo of the same volume. All participants were tested for group A β-hemolytic streptococcal pharyngitis and treated accordingly. Daily telephone follow-up was conducted until complete resolution of sore throat.

Main Outcome Measures: Primary outcome variables included hours to initial relief of sore throat and time to the complete resolution of pain. Secondary outcome variables included changes in the McGrath Facial Affective Scale score at 24 and 48 hours, persistence of associated symptoms, use of anti-inflammatory or antipyretic medication, and subsequent use of medical resources for dehydration or pain.

Results: A convenience sample of 150 patients was randomized to receive either dexamethasone (n=75) or placebo (n=75). Twenty-five patients were lost to follow-up, leaving 125 patients available for data analysis; 57 received dexamethasone and 68 received placebo. Patients who received dexamethasone reported earlier onset of pain relief (9.2 vs 18.2 hours; P=.001), fewer hours to complete resolution of sore throat (30.3 vs 43.8 hours; P=.04), and larger changes in the McGrath Facial Affective Scale score in the first 24 hours (−0.58 vs −0.43; P=.002). Children who tested negative for group A β-hemolytic streptococci had greater pain relief with dexamethasone compared with placebo (onset of pain relief, 8.7 vs 24 hours; P=.001), less time to complete resolution of sore throat (37.9 vs 70.8 hours; P=.006), and greater changes in the McGrath Facial Affective Scale score in the first 24 hours (−0.50 vs −0.21; P=.001).

Conclusion: Children with moderate to severe pharyngitis had earlier onset of pain relief and shorter duration of sore throat when given oral dexamethasone.

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A CUTE PHARYNGITIS IS ONE of the most frequent illnesses for which children seek medical care, and it is the second most common childhood illness diagnosed in the ambulatory setting.1 The pain associated with pharyngitis can be reduced minimally by nonsteroidal anti-inflammatory drugs and acetaminophen2 and, if group A β-hemolytic streptococci (GABHS) are present, by antibiotics.3-5 Nevertheless, continued odynophagia might result in absence from school or work for the child or the child's guardian and the risk of dehydration from reduced oral intake. A recent article found that children with pharyngitis usually miss at least 2 days of school because of their illness.6

Intramuscular and oral glucocorticoids have been shown to reduce pain in adults with acute severe exudative pharyngitis.7-10 In contrast, in a study of children with acute pharyngitis, there was no significant difference in time to onset of clinically significant pain relief or time to complete pain relief in children who received oral dexamethasone.11 Another study showed that a single oral dose of dexamethasone provided only short-lived pain relief in children with suspected infectious mononucleosis who had acute pharyngitis.12 However, in both these pediatric studies,11,12 the authors in-
cluded children with mild complaints of sore throat and did not quantify the amount of pharyngeal erythema or edema to be included in the study, which might be the reason why a difference was not detected.

The objective of this study was to determine the effectiveness of a single dose of oral dexamethasone in reducing the pain associated with moderate to severe pharyngitis in pediatric patients.

METHODS

PATIENTS

A prospective, randomized, double-blind, placebo-controlled clinical trial was conducted in a large, urban pediatric emergency department (PED) (with a census of 48,000 patients per year) between March 2002 and November 2003. A convenience sample of children, aged 5 to 18 years, was eligible if they came to the PED with moderate to severe pharyngitis, defined as having all of the following: presence of odynophagia or dysphagia, moderate to severe pharyngeal erythema or swelling as determined by the pediatric emergency medicine physician, and a McGrath Facial Affective Scale (FAS) score of “F” (0.75) or higher. The McGrath FAS, validated in measuring pain as determined by the pediatric emergency medicine physician, and a McGrath Facial Affective Scale (FAS) score of “F” (0.75) or higher. The McGrath FAS, validated in measuring pain as determined by the pediatric emergency medicine physician.

STUDY PROTOCOLS

Study patients were randomly assigned to receive 1 dose of either oral dexamethasone suspension (0.6 mg/kg with a maximum of 10 mg) or placebo of the same volume. A research pharmacist at our institution used a computerized random numbers table for block randomization (groups of 30) to maintain similar numbers in the 2 groups throughout the study. The study medication was dexamethasone sodium phosphate injection (10 mg/mL, Elkins-Sinn Inc, Cherry Hill, NJ); isotonic sodium chloride solution was used for placebo. Both the dexamethasone and isotonic sodium chloride solution were flavored with cherry syrup to minimize the taste difference and make their appearance indistinguishable. The research pharmacist then placed 1.5-mL aliquots of study medication (1 mL of dexamethasone or isotonic sodium chloride solution with 0.5 mL of flavoring) into brown syringes. The syringes were numbered sequentially. After consent was obtained, the study medication was administered orally by the pediatric emergency medicine physician. If the child vomited the medication, another syringe was given a copy of the McGrath FAS with the face corresponding to the initial pain score circled. Patients were instructed to use a weight-appropriate dose of nonsteroidal anti-inflammatory drugs or acetaminophen as needed for fever or pain at home. The child or child’s guardian was contacted by telephone daily by 1 of 2 of us (R.O. or H.K.) from the time of discharge to the time of complete resolution of the sore throat. Follow-up information obtained daily included (1) the pain score on the McGrath FAS (“Which face shows how your feel about your throat?”); (2) the time to inception of pain relief (“When did your throat start feeling better?”); (3) the time to complete resolution of pain (“When did your throat feel completely better?”); (4) the presence or absence of fever; (5) the type, dosage, and frequency of anti-inflammatory or antipyretic medications; (6) the need to obtain further medical care; and (7) the persistence of associated symptoms or potential side effects of dexamethasone.

We considered a potential side effect of dexamethasone to include headache, nausea or vomiting, abdominal pain, myalgia, mood changes, dizziness, and swollen legs. Participants were excluded if we could not attain daily follow-up until complete resolution of the sore throat.

STATISTICAL ANALYSIS

Outcome variables included time to the inception of pain relief, changes in McGrath FAS score at 24 and 48 hours, persistence of associated symptoms, time to the complete resolution of pain, use of anti-inflammatory or antipyretic medication, and subsequent use of medical resources for dehydration or pain.

To achieve a power of 0.80 and detect a 12-hour difference to complete resolution of sore throat between the dexamethasone and placebo groups, we determined that we needed a total of 384 subjects (192 in each treatment group). At the completion of each block randomization, we performed interim analysis on the data for all enrolled patients. Randomization continued through each successive block until either statistical significance (considered at P < .05 in this study) was achieved or the projected sample size was reached. Data organization and analysis were done using Epi Info version 2000 (EpiInfomatics, Doraville, Ga).13 We used analysis of variance to compare continuous data and χ2 to compare categorical data. We used 95% confidence intervals to compare the magnitude of differences between the dexamethasone and placebo groups.
RESULTS

CHARACTERISTICS OF THE PATIENTS

A convenience sample of 150 patients (Figure) was randomized to receive either oral dexamethasone or placebo. Eighteen patients were lost to telephone follow-up: we were unable to contact 15 patients at the first 24-hour follow-up telephone call because of disconnected telephones, and we lost 3 patients to follow-up after the first follow-up telephone call at 24 hours. Seven patients were excluded because of improper data collection. Recruitment was completed at 150 patients because, after that block randomization, a statistically significant difference was detected for complete resolution of sore throat between the dexamethasone and the placebo groups. Study medication was easily tolerated; no subject refused to swallow the study medication or placebo groups. Study medication was easily tolerated; no subject refused to swallow the study medication or placebo. Seventy patients tested positive for GABHS (27 in the dexamethasone group and 43 in the oral placebo group), and 55 patients tested negative for GABHS (25 in the dexamethasone group and 27 in the placebo group). Table 1 describes the baseline study group characteristics.

Efficacy

Table 2 describes the clinical course of patients following the administration of study medication. Five patients were hospitalized, all owing to dehydration secondary to poor oral intake from extreme odynophagia (3 received dexamethasone and 2 received placebo). Of the 3 patients who developed a peritonsillar abscess, 2 developed the abscess within 48 hours (1 from each study group), and the third case (placebo group) developed a peritonsillar abscess 6 days after the initial PED visit. The groups did not differ in the presence of fever or potential side effects.

Table 3 outlines the clinical response of each treatment group and the responses stratified by the presence or absence of GABHS. In patients with GABHS, there was a significant difference between the dexamethasone and placebo groups in the onset of pain relief, but we detected no differences in the hours to complete resolution of sore throat or in the change in pain score in the first 24 hours. In patients without GABHS, there was a significant difference in the onset of pain relief, in total duration of sore throat, and in the change in pain score in the first 24 hours between patients given dexamethasone and placebo.

Using a computer tracking system, none of the 18 patients lost to telephone follow-up were seen in our PED or hospitalized in the following 2 months after enrollment secondary to sore throat or dehydration. One child was seen 1 month after enrollment in the outpatient clinic with a chief complaint of sore throat. Another child was admitted 4 days after enrollment from our PED because of an asthma exacerbation.

COMMENT

Several studies in adults have investigated the role of glucocorticoids in managing pain associated with acute pharyngitis. In a placebo-controlled trial in adults, a single intramuscular dose of dexamethasone shortened the time

Table 1. Study Group Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients</th>
<th>Positive for GABHS</th>
<th>Negative for GABHS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dexamethasone Sodium Phosphate Group (n = 57) (95% CI)</td>
<td>Placebo Group (n = 68) (95% CI)</td>
<td>Dexamethasone Group (n = 27) (95% CI)</td>
</tr>
<tr>
<td>Mean age, y</td>
<td>12.7 (11.7 to 13.7)</td>
<td>11.3 (10.4 to 12.3)</td>
<td>11.6 (9.9 to 13.3)</td>
</tr>
<tr>
<td>Female, %</td>
<td>54 (41 to 66)</td>
<td>62 (50 to 73)</td>
<td>56 (38 to 73)</td>
</tr>
<tr>
<td>Duration of sore throat, h</td>
<td>72.0 (43.9 to 81.3)</td>
<td>53.1 (40.7 to 65.5)</td>
<td>49.4 (29.2 to 69.6)</td>
</tr>
<tr>
<td>Temperature, °C</td>
<td>37.7 (37.5 to 37.9)</td>
<td>38.0 (37.7 to 38.3)</td>
<td>37.6 (37.3 to 37.9)</td>
</tr>
<tr>
<td>Initial McGrath FAS score*</td>
<td>0.84 (0.82 to 0.86)</td>
<td>0.83 (0.81 to 0.85)</td>
<td>0.85 (0.81 to 0.89)</td>
</tr>
<tr>
<td>Positive for GABHS, %</td>
<td>47</td>
<td>63</td>
<td>63</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; FAS, Facial Affective Scale; GABHS, group A β-hemolytic streptococci.

*The McGrath FAS ranges from 1 (maximum negative affective value, sad face) to 0 (maximum positive affective value, happy face).
to initial pain relief (a difference of 6.1 hours) and to complete resolution of pain (a difference of 20.4 hours). Similarly, a single intramuscular dose of betamethasone in adults with acute exudative pharyngitis led to earlier initial pain relief (a difference of 4.9 hours) and time to complete resolution of pain (a difference of 14 hours). More recently, a study comparing the effectiveness of dexamethasone with placebo for adults with acute pharyngitis showed that both dexamethasone groups (subjects received it via either oral or intramuscular routes) were equally effective and superior to placebo. However, these adult studies included few pediatric patients, so the results might not be generalizable to children.

Two recently published studies have investigated the use of dexamethasone in children with pharyngitis. In a prospective, randomized, double-blind, placebo-controlled study of oral dexamethasone (0.3 mg/kg; maximum dose, 15 mg) for the treatment of pharyngitis in children aged 8 to 18 years with suspected infectious mononucleosis, Roy et al found a significantly greater proportion of children who received oral dexamethasone achieved pain relief within the first 12 hours compared with placebo (12/20 vs 5/19; \( P = .03 \)). However, this difference did not exist at subsequent follow-up. In a prospective, randomized, double-blind, placebo-controlled study of oral dexamethasone (0.6 mg/kg; maximum dose, 10 mg) for 184 children aged 5 to 16 years presenting with acute pharyngitis, Bulloch et al noted that a subgroup of children without GABHS did not show any benefits from oral dexamethasone in terms of hours to initial pain relief or complete resolution of sore throat. For children with GABHS, oral dexamethasone showed a beneficial effect in terms of the number of hours to initial relief of sore throat (difference, 5.5 hours; 95% confidence interval, 1 to 10), but there was no difference in the number of hours to complete resolution of sore throat.

Our results are similar to those of Bulloch et al for the subgroup of children with GABHS. For these chil-

Table 2. Characteristics of Clinical Course

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients</th>
<th>Dexamethasone Sodium Phosphate Group (n = 57) 95% CI</th>
<th>Placebo Group (n = 68) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Required IVF in the PED</td>
<td></td>
<td>3 (5) 2 to 14</td>
<td>7 (10) 5 to 19</td>
</tr>
<tr>
<td>Hospitalization in first 24 h</td>
<td></td>
<td>2 (4) 1 to 13</td>
<td>2 (3) 1 to 10</td>
</tr>
<tr>
<td>Returned to PED/PCP in first 24 h</td>
<td></td>
<td>1 (2) 0 to 10</td>
<td>0 0 to 5</td>
</tr>
<tr>
<td>Used NSAIDs in first 24 h</td>
<td></td>
<td>14 (25) 16 to 38</td>
<td>20 (29) 20 to 41</td>
</tr>
<tr>
<td>Used acetaminophen in first 24 h</td>
<td></td>
<td>5 (11) 5 to 22</td>
<td>8 (12) 6 to 22</td>
</tr>
<tr>
<td>Hospitalization after 24 h</td>
<td></td>
<td>1/24 (4) 1 to 20</td>
<td>0/39 0 to 9</td>
</tr>
<tr>
<td>Returned to PED/PCP after 24 h</td>
<td></td>
<td>0/24 0 to 14</td>
<td>0/39 0 to 9</td>
</tr>
<tr>
<td>Used NSAIDs after 24 h</td>
<td></td>
<td>2/24 (8) 2 to 25</td>
<td>13/39 (33)† 20 to 49</td>
</tr>
<tr>
<td>Used acetaminophen after 24 h</td>
<td></td>
<td>1/24 (4) 1 to 20</td>
<td>3/39 (8) 3 to 21</td>
</tr>
<tr>
<td>Develop peritonsillar abscess</td>
<td></td>
<td>1 (2) 0 to 10</td>
<td>2 (3) 1 to 10</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; IVF, intravenous fluids; NSAIDs, nonsteroidal anti-inflammatory drugs; PCP, primary care physician; PED, pediatric emergency department.
*Values are number (percentage).
†Values are number (percentage).
‡Values are number (percentage).

Table 3. Characteristics of Clinical Response

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients</th>
<th>Positive for GABHS</th>
<th>Negative for GABHS</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Dexamethasone Sodium Phosphate Group (n = 57) 95% CI</td>
<td>Placebo Group (n = 68) 95% CI</td>
<td>Placebo Group (n = 43) 95% CI</td>
</tr>
<tr>
<td>Time to initial relief of sore throat, h</td>
<td>9.2 ± 7.5 (3.9 to 14.1)</td>
<td>9.0 (3.9 to 14.1)</td>
<td>9.7 ± 5.6 (4.2 to 14.4)</td>
</tr>
<tr>
<td>Time to complete relief of sore throat, h</td>
<td>30.3 ± 27.8 (15.4 to 63.1)</td>
<td>13.5 (12.0 to 46.6)</td>
<td>21.9 ± 20.6 (19.1 to 41.6)</td>
</tr>
<tr>
<td>Change in McGrath FAS score in first 24 h</td>
<td>0.58 ± 0.26 (0.05 to 0.52)</td>
<td>0.15 (0.05 to 0.25)</td>
<td>0.06 (0.05 to 0.17)</td>
</tr>
<tr>
<td>Change in McGrath FAS score in next 24 h</td>
<td>0.31 ± 0.23 (0.05 to 0.50)</td>
<td>0.06 (0.05 to 0.17)</td>
<td>0.34 ± 0.23 (0.05 to 0.52)</td>
</tr>
</tbody>
</table>

Abbreviation: FAS, Facial Affective Scale; GABHS, group A β-hemolytic streptococci.
*Unless otherwise indicated, values are mean ± SD.
†The McGrath FAS ranges from 1 (maximum negative affective value, sad face) to 0 (maximum positive affective value, happy face).
‡In the evaluation of patients after 24 hours, 24 remained in the dexamethasone group and 39 remained in the placebo group.
children, oral dexamethasone provided an earlier onset of pain relief, but because children with GABHS usually have a shorter duration of pain after receiving antibiotics, the effect of oral dexamethasone was not apparent at subsequent follow-up. However, in contrast to previous pediatrie studies, we found that children without GABHS who received oral dexamethasone experienced greater beneficial effects in both the number of hours to initial pain relief and the number of hours to complete resolution of symptoms. We believe the reason for this difference between our study and previous studies is due to the difference in enrollment criteria. Previous studies of pediatrie patients did not distinguish between mild and moderate-to-severe pharyngeal erythema and edema when enrolling patients, or did not use a minimum score in their pain scales. Thus, those studies might have included children with very mild symptoms, making the ability to detect improvements in pain scores more difficult. In fact, when asked to classify their pain as mild, moderate, or severe in the Bulloch et al study, 39 (27%) of 145 children reported their pain as mild. In contrast to the findings of our study, 2 adult studies also did not detect a difference between the group receiving corticosteroids and the placebo recipients in patients who tested negative for GABHS in terms of the number of hours to initial pain relief and the number of hours to complete resolution of symptoms.

We believe the reason for this difference between our study and previous adult studies in the subgroup testing negative for GABHS is also due to the differences in enrollment. The adult studies did not quantify the minimum degree of odynophagia and pharyngeal erythema or edema required for the enrollment of patients in their studies. This inclusion of patients with milder symptoms might have diluted the beneficial effect of the corticosteroid.

There are several limitations to our study. Our study involved a convenience sample; however, patient characteristics that might have influenced the effect of dexamethasone were distributed evenly between the groups. We discontinued daily follow-up telephone calls when patients reported complete resolution of pain. Although we did not detect any immediate complications attributed to dexamethasone, we do not know whether a single oral dose of dexamethasone affected the subsequent clearance of bacteria and potential relapses or complications (rhabdomyolysis or peritonsillar abscess). Therefore, long-term follow-up would have been important in detecting these potential complications. Because no scoring system exists for defining mild, moderate, or severe pharyngeal erythema or swelling, inclusion was based on the subjective findings of the pediatric emergency medicine physician. We addressed this potential limitation by adding a minimum score on the McGrath FAS to our enrollment criteria. Children and their guardians were contacted daily, and therefore, they might not have noted the exact time of pain relief but rather reported a time estimate. Although it is a limitation, this lack of accuracy in determining exact time intervals should have been distributed evenly between the 2 groups. When children were stratified based on the presence of GABHS, we did not detect a statistically significant difference in the number of hours to complete relief of sore throat and changes in the McGrath FAS score in the first 24 and 48 hours between the dexamethasone and placebo groups. The inadequate power of a small sample size in this subgroup might be the reason we did not find a difference.

Our data demonstrate that immunocompetent children with moderate to severe pharyngitis benefited from the use of oral dexamethasone in achieving earlier onset of pain relief and shortened duration of pain. Children with moderate to severe pharyngitis who received oral dexamethasone did not experience any persistence of symptoms or any potential short-term side effects attributable to dexamethasone. Thus, the use of oral dexamethasone appears to be a safe adjunct to nonsteroidal anti-inflammatory drugs or acetaminophen, and if necessary, antibiotics, in the treatment of moderate to severe pharyngitis in children.

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REFERENCES


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