The management of croup

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Croup is a common paediatric respiratory illness involving inflammation and narrowing of the subglottic region of the larynx, frequently precipitated by viral infections. Treatment is aimed at decreasing symptoms and reducing inflammation. Glucocorticoids are effective by oral, parenteral or nebulized routes, and continue to provide the mainstay of therapy. The common oral dexamethasone dose (0.6 mg/kg) may exceed the dose required for good clinical efficacy. Nebulized epinephrine provides effective additional therapy for more severe cases. L-epinephrine appears to be comparable to racemic epinephrine, although further study is warranted. Limited data suggest that heliox is also effective in the short-term management of refractory croup. The use of humidified oxygen remains controversial, as good data are lacking.

Croup is an acute respiratory illness caused by inflammation and narrowing of the subglottic region of the larynx. It manifests variously as a barking cough, hoarseness, stridor and respiratory distress, with or without concomitant symptoms of viral upper respiratory infection. Parainfluenza viruses account for most cases of viral croup, with types 1, 2 and 3 identified in three-quarters of all isolates1. Other aetiological agents include respiratory syncytial virus, influenza viruses A and B, and Mycoplasma pneumoniae. In general, the symptoms and signs of croup can be differentiated clinically from those of epiglottitis, foreign body aspiration and anatomical upper airway obstruction. When the diagnosis is uncertain, croup should be considered a diagnosis of exclusion, after appropriate evaluation for these alternate diagnoses.

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Croup is a common childhood illness, resulting in 30 primary care visits per 1000 children per year in the US. Fewer than 2% of cases are admitted to hospital and only 0.5–1.5% of these require intubation. Death from croup is rare, with mortality rates in intubated patients of less than 0.5%. The total economic cost of croup is difficult to quantify. In the US, emergency visits and hospitalizations resulting from parainfluenza virus types 1 and 2 alone result in annual costs of $20 million and $56 million, respectively, and about 25% of these visits are due to croup.

Traditionally, researchers emphasized differences between spasmodic (recurrent) croup and laryngotracheitis (viral croup). Some argued that
spasmodic croup might be due to an allergic reaction to viral antigens rather than a direct result of a viral infection. However, viral and spasmodic croup are poorly differentiated clinically, can both be associated with recent viral infections, and can have similar clinical presentations. The pathology of the two entities is the same. For these reasons, most authors currently consider these two entities as part of a continual spectrum of disease. Few clinical trials have differentiated between viral and spasmodic croup, so differences in treatment responsiveness by croup type are impossible to determine.

The management of croup has changed over the years, particularly with the development of new pharmacological therapies and increased evidence regarding treatment effectiveness. Pharmacological therapies generally aim to improve oxygenation, reduce airway narrowing and/or reverse the inflammatory process.

Evaluating therapies for croup

Clinical studies of therapies for croup must have some measure of treatment efficacy. There is no single parameter that can be used as an accurate marker of clinical improvement. Researchers have developed croup scores, summarizing numerous symptoms and signs, as objective measures of clinical symptoms. A variety of croup scores have been devised, the most commonly used being the Westley and the modified Westley croup scores (Table 1).

Ideally, croup scores should be consistent between different examiners (good inter-rater reliability), comparable to other measures of disease severity (good construct validity), and able to demonstrate anticipated decreases with effective therapy (good responsiveness to change). The

<table>
<thead>
<tr>
<th>Name of score</th>
<th>Validated?</th>
<th>Total points</th>
<th>Stridor</th>
<th>Retractions</th>
<th>↓ Air entry</th>
<th>Cyanosis</th>
<th>↓ LOC</th>
<th>Cough</th>
<th>Dyspnoea</th>
<th>↑ HR</th>
<th>↑ RR</th>
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<td>Westley</td>
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<td>17</td>
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<td>0, 4 or 5</td>
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<td>Modified Westley</td>
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<td>17</td>
<td>0–4</td>
<td>0–3</td>
<td>0–3</td>
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<td>0–3</td>
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<td>0–3</td>
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<tr>
<td>Muhlendahl</td>
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<td>18</td>
<td>0–3</td>
<td>0 or 2</td>
<td>0–3</td>
<td>0, 4 or 5</td>
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<tr>
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<td>10</td>
<td>0–2</td>
<td>0–2</td>
<td>0–2</td>
<td>0–4</td>
<td>0–2</td>
<td>0–2</td>
<td>0–2</td>
<td>0–2</td>
<td></td>
</tr>
<tr>
<td>Geelhood</td>
<td>Y</td>
<td>6</td>
<td>0–3</td>
<td>0–3</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Kuusela</td>
<td>N</td>
<td>3</td>
<td>0–2</td>
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<td>Syracuse</td>
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<td>11</td>
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<td>0–3</td>
<td>0–3</td>
<td>0–3</td>
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</tbody>
</table>

↑, Increased; ↓, decreased; LOC, level of consciousness; HR, heart rate; RR, respiratory rate.
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validation of croup scores has been considered in four studies\textsuperscript{7–10}. The Geelhoed score was twice assessed for inter-rater reliability. In the first study, triage nurse \textit{versus} researcher assessments for 17 randomly selected patients were retrospectively compared. The weighted kappa was 0.85, indicating reasonable inter-observer agreement\textsuperscript{7}. In the second study, two workers prospectively assigned croup scores to 15 children not in the clinical trial. The weighted kappa statistic was 0.87\textsuperscript{8}. The Syracuse croup score was tested prospectively on 165 croup patients in an intensive therapy unit (ITU) to assess how well scores below 6 predicted suitability of transfer from the ITU to the general wards (responsiveness to change).\textsuperscript{10} The authors found that this score had 80% sensitivity and 100% specificity for testing suitability for transfer. The Westley croup score was evaluated with respect to inter-rater reliability, construct validity and responsiveness to change, using 54 patients with croup, none of whom had cyanosis or changes in level of consciousness.\textsuperscript{9} It performed well in all areas of assessment. Inter-rater reliability between three research assistants was assessed prospectively. The weighted kappa was 0.90 for the total croup score, 0.47 for air entry, 0.93 for stridor and 0.87 for retractions. Construct validity was assessed by correlating the change in croup score during the course of treatment with other measures, including a parental global assessment of change (correlation coefficient, \( r = 0.51 \)), the treating physician’s global assessment of change (\( r = 0.51 \)), the research assistant’s global assessment of change (\( r = 0.76 \)), length of time spent in the emergency department (\( r = 0.44 \)), change in heart rate (\( r = 0.19 \)) and change in respiratory rate (\( r = 0.32 \)). Responsiveness to change was assessed by testing the sensitivity of the change in croup score to final patient disposition (mean [SD] change in croup score was 1.7 (1.7) in patients discharged and 0.3 (1.0) in patients admitted, \( P = 0.006 \)).

\textbf{Therapies for croup}

\textit{Glucocorticoids – effectiveness}

A systematic review published by the Cochrane collaboration\textsuperscript{11,12} summarizes the numerous studies that have evaluated the effectiveness of glucocorticoids in attenuating the clinical course of croup. This systematic review is high quality evidence, level 1a, based on the Centre for Evidence Based Medicine’s Levels of Evidence and Grades of Recommendations (http://cebm.jr2.ox.ac.uk/docs/levels.html). An update of this systematic review is expected within the next year.

Of the 29 trials included, 17 studied dexamethasone, 9 studied budesonide and 3 studied methylprednisolone. Patients ranged from 4 months to 12 years, with mean ages of 13–45 months. Fourteen trials involved
Most of the studies were small with a median of 40 (interquartile range 36, 60) patients. Overall, glucocorticoids were associated with a significant improvement in the croup score with an effect size of –1.0 (95% confidence interval [CI] –1.5, –0.6) at 6 h and –1.0 (95% CI, –1.6, –0.4) at 12 h (see Fig. 1). By 24 h, this improvement was no longer statistically significant, effect size –1.0 (95% CI, –2.0, 0.1). Compared with placebo-treated children, children treated with glucocorticoids were also statistically less likely to need epinephrine compared to those who did not receive glucocorticoids, with a decrease of 9% (95% CI, 2%, 16%) in the budesonide group and 12% (95% CI, 4%, 20%) in the dexamethasone group. Children receiving glucocorticoids also had significantly shorter stay in both the emergency department, where stay was reduced by 11 (–18, –4) h and in the in-patient setting, where stay was reduced by 16 (–31, –1) h.

The authors of the meta-analysis assessed publication bias by a combination of graphical methods including funnel plots and a rank correlation test. A funnel plot indicated the presence of publication bias, suggesting that smaller, statistically negative studies were not identified and subsequently included in this systematic review. The effect size of the primary outcome croup score varied by study size, with the largest effect size of –1.4 (95% CI, –2.3, –0.4) for the smallest trials (≤ 38 patients), and the smallest effect size of –0.5 (95% CI, –0.8, –0.2) for the largest trials (> 62 patients). However, there was still evidence of benefit in the largest trials that were the least vulnerable to publication bias.

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**Table 1**

<table>
<thead>
<tr>
<th>Treatment Comparison</th>
<th>Time (hours)</th>
<th># Studies</th>
<th># Patients</th>
<th>Effect Size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Budesonide vs Placebo</td>
<td>6</td>
<td>5 / 327</td>
<td>–0.9 (–1.4, –0.4)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>2 / 142</td>
<td>–0.7 (–1.1, –0.3)</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone vs Placebo</td>
<td>6</td>
<td>8 / 739</td>
<td>–1.1 (–1.8, –0.5)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>5 / 339</td>
<td>–1.2 (–2.1, –0.3)*</td>
<td></td>
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<tr>
<td></td>
<td>24</td>
<td>4 / 189</td>
<td>–1.1 (–2.6, 0.4)*</td>
<td></td>
</tr>
<tr>
<td>Bud. or Dex. vs Placebo</td>
<td>6</td>
<td>13 / 1066</td>
<td>–1.0 (–1.5, –0.6)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>7 / 481</td>
<td>–1.0 (–1.8, –0.4)*</td>
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<tr>
<td></td>
<td>24</td>
<td>5 / 256</td>
<td>–1.0 (–2.0, 0.1)*</td>
<td></td>
</tr>
</tbody>
</table>

**Fig. 1** Meta-analysis of randomized controlled trials according to type of corticosteroids and time of assessment. The pooled effect sizes of corticosteroids versus placebo (derived from the change in croup score using random effect models) are given with their 95% confidence intervals. Pooled estimates with significant heterogeneity among trials are marked with asterisks. Reprinted with permission from BMJ Publishing Group.
This meta-analysis supports the use of corticosteroids in both the in-patient and the out-patient setting. These conclusions are supported by additional outcomes research: in a hospital that established a policy of mandatory dexamethasone therapy for all children admitted with croup, transfer rates to the intensive care unit dropped from 12% to 3%.

**Glucocorticoids – route of administration**

Most studies involving corticosteroids used dexamethasone, which has the advantages of a long biological half-life (36–54 h). Traditionally, dexamethasone was given by intramuscular injection at a dose of 0.6 mg/kg. More recently, oral dexamethasone and nebulized budesonide have been evaluated as alternative routes of corticosteroid administration.

Six clinical trials have compared oral corticosteroids with placebo for the treatment of croup. All of these studies showed a positive effect of oral corticosteroids. To compare directly oral and intramuscular administration of dexamethasone, Rittichier and Ledwith studied all children between 3 months and 12 years of age seen in the emergency department with moderate croup symptoms and less than 48 h of illness. Moderate croup was defined as a clinical syndrome of hoarseness or barking cough combined with a history of or presence of stridor at rest, and/or retractions. Enrolled children were randomized to receive dexamethasone 0.6 mg/kg by either the intramuscular or the oral route. There was allocation concealment at the time of randomization, although nurses and parents were subsequently aware of the medication route used. The physicians remained blinded, and parents were advised not to indicate how the medication was delivered. The primary outcome was the need for further therapy based on telephone follow-up at 48–72 h. Secondary outcomes were caretaker reports of improvement in or resolution of symptoms.

The researchers enrolled 277 children with a median age of 2.1 ± 1.8 years. All patients received telephone follow-up. Rates of unscheduled return visits in those who received an intramuscular injection (32%) and oral administration (25%) of dexamethasone were not statistically different: RR 0.78 (95% CI, 0.54–1.14). Rates of treatment failure (need for additional steroids, racemic epinephrine and/or hospitalization) were also similar between those who received intramuscular injection (8%) and oral (9%) administration.

Caretakers reported resolution of symptoms in 56% and 48% of patients who received intramuscular and oral administration of dexamethasone, respectively. Symptoms were improved in 42% and 47% of patients who received intramuscular and oral administration of dexamethasone, respectively. Oral administration of dexamethasone appears to be as effective for the treatment of croup as intramuscular administration, and is easier and cheaper to administer.
Glucocorticoids – nebulized

Numerous studies have compared nebulized budesonide with other routes of glucocorticoid administration. Geelhoed and Macdonald evaluated 80 patients over 3 months of age admitted to hospital with croup. Patients were randomized to receive oral dexamethasone 0.6 mg/kg with nebulized saline placebo, nebulized budesonide 2 mg with oral placebo, or double placebo. The Geelhoed croup score was measured at 0, 1, 2, 3, 4, 8, 16, 20 and 24 h from study entry. Duration of admission, duration of croup score greater than 1, and use of racemic epinephrine were also measured. Although corticosteroid-treated children had improved outcomes over placebo treated children for all measured outcomes, there were no statistically significant differences in any outcomes for children in the oral dexamethasone and nebulized budesonide arms of the study.

Johnson et al randomized 144 children aged 3 months to 9 years and with a Westley croup score of 3–6 to receive i.m. dexamethasone 0.6 mg/kg, nebulized budesonide 4 mg or nebulized placebo. All patients received nebulized racemic epinephrine. Hospitalization rates were measured, as well as changes in Westley croup score and need for additional racemic epinephrine. Rates of hospitalization after treatment were highest in the placebo group (67%), intermediate in the budesonide group (35%) and lowest in the dexamethasone group (17%). Unadjusted rates of hospitalization were not significantly different between the dexamethasone and budesonide groups (P = 0.18).

Klassen et al evaluated 198 children aged 3 months to 5 years presenting to the emergency department with croup. Patients who had a croup score of 2 or greater following 15 min of mist therapy were randomized to receive oral dexamethasone 0.6 mg/kg with nebulized saline placebo, nebulized budesonide 2 mg with oral placebo, or both oral dexamethasone 0.6 mg/kg and nebulized budesonide 2 mg. The Westley croup score was measured at baseline and hourly until the patient received racemic epinephrine, had a croup score less than 2, had been discharged or had been observed for 4 h, whichever occurred first. All three therapies were equally effective in reducing the croup score from baseline. The estimated treatment difference between dexamethasone and budesonide was −0.12 (95% CI, −0.53, 0.29). There was no statistical difference in median time to discharge from the emergency department (127.5 min in the dexamethasone group versus 155 min in the budesonide group, P = 0.65). Co-intervention with racemic epinephrine was evenly distributed amongst the three groups. Physician follow-up for croup symptoms after discharge occurred in 27% of patients treated with dexamethasone, 60% of the patients treated with budesonide, and 38% of patients treated with both (P = 0.06). Only one patient, from the dexamethasone group, was subsequently hospitalized.
The evidence from these three studies suggests that aerosolized budesonide is an effective alternative to oral or i.m. dexamethasone for the management of croup. In additional research, Geelhoed noted that the oral medication was easier to administer to children with croup than the nebulized treatment, and that many children found the nebulized treatment distressing in its own right. For this reason, he advocated the use of oral dexamethasone rather than inhaled budesonide.

**Glucocorticoids – dosing**

Regardless of administration route, the most commonly studied dexamethasone dose is 0.6 mg/kg, with a maximum dose of 10 mg. This dose is equal to a typical daily dose of dexamethasone for the treatment of meningitis, which is usually given as four divided doses. It has equivalent glucocorticoid activity to approximately 6 mg/kg of prednisolone, and is arguably a larger dose than is needed for adequate treatment of croup. Recently, the effectiveness of lower doses of oral dexamethasone have been evaluated. Two clinical trials by Geelhoed show that lower doses of dexamethasone are effective in the treatment of croup. In his first randomized trial, Geelhoed evaluated 120 children greater than 3 months of age admitted for croup, over two separate study periods. He compared dexamethasone 0.6 mg/kg with dexamethasone 0.3 mg/kg during the first study period (n = 60) and dexamethasone 0.3 mg/kg with dexamethasone 0.15 mg/kg during the second study period (n = 60). In both study periods, there were no differences and no trends towards differences in a six-point croup score at 1, 2, 3, 4 or 8 h post-treatment, nor were there differences or trends towards differences in duration of hospitalization or need for racemic epinephrine. These studies may have been too small to detect a clinically important difference in efficacy between the higher and lower dose groups.

Geelhoed also performed a randomized trial of 100 children over 3 months of age who were evaluated in an emergency department and treated as out-patients for croup with placebo or oral dexamethasone 0.15 mg/kg. None of the 48 children treated with dexamethasone and eight of the 48 children treated with placebo returned to care with continuing symptoms of croup (P < 0.01). Even if the 2 patients in the treatment group who were lost to follow-up had both sought further treatment, and the two in the placebo group had not, the relative risk of returning to care would be 4.0 times higher for the placebo-treated children compared with the dexamethasone treated children (95% CI, 0.89, 17.91).

Finally, Geelhoed published an observational study reporting adverse events in a hospital that switched from 0.6 to 0.15 mg/kg of oral dexamethasone for all croup patients other than those in intensive care. In
1993, this hospital established a routine policy of administering a single oral dose of dexamethasone, 0.6 mg/kg, to all children admitted to the hospital with croup. This dose was decreased to 0.3 mg/kg and then 0.15 mg/kg after 1994. The intensive care admission and intubation rates fell dramatically after the introduction of steroids, but did not show an increase when the steroid dose was subsequently decreased. The number of children presenting with croup did not change during this time, and many came from other parts of the country where corticosteroids were not used. In summary, these three studies suggest that lower doses of dexamethasone are equally effective in reducing acute symptoms of croup.

**Humidification**

Treatment with moist air probably stems from the late 19th century, when parents used steam from tea kettles or hot tubs to treat croup in their children. Hospitals adopted the practice of ‘croup kettles’ long before clinical trials were routine\(^6\). The use of hot steam at home has never been studied, and there are case reports of scald injury resulting from this therapy\(^24\). Cool mist and humidified oxygen are used by some hospitals, although there are limited data to support their use. The only published randomized, controlled trial evaluating mist therapy in croup was a study of 16 children that compared delivery of 87–95% relative humidity for 12 h via a perspex covered cot, with no treatment\(^25\). The two groups were compared using the Westley croup score, plus pulse rate, respiratory rate, transcutaneous oxygen and transcutaneous carbon dioxide, at 0, 1, 2, 3, 4, 5, 6, and 12 h. The study failed to demonstrate statistically significant associations between the method of treatment and the above measurements. However, the study size was small, increasing the chance of missing a true difference between the two groups (beta error). In addition, the initial croup scores were low (means 3.75 and 3.00 for the humidity and control groups, respectively, out of a possible 17 points), limiting the potential for improvement with therapy.

There is a currently unpublished, blinded, randomized controlled pilot study of 27 patients comparing treatment with a Mist stick (humidified oxygen) to no treatment\(^26\). The groups were comparable at baseline, and both received 0.6 mg/kg (maximum 10 mg) of dexamethasone at the onset of mist therapy. Two patients in each group received racemic epinephrine. The two groups were compared using the Westley croup score, pulse rate, respiratory rate, transcutaneous oxygen at 0, 0.5, 1, 1.5 and 2 h. The study failed to demonstrate statistically significant associations between the method of treatment and croup score at any of the time intervals, or overall \((P = 0.27)\). However, there was a consistent
trend towards a decrease in croup score in the mist treated group \((n = 13)\) compared with the no mist group \((n = 14)\). Given the small numbers studied and the low initial croup scores (means 4 out of 17 points in each group), a true difference in effect may have been missed (beta error). The role of humidification remains unclear. Further study is in progress to evaluate this subject further.

**Racemic epinephrine**

There are four randomized trials comparing racemic epinephrine with either placebo\(^{27-29}\) or no treatment\(^{30}\) for the management of croup. Two additional studies include treatment arms where inhaled racemic epinephrine is compared to placebo\(^{31,32}\). A meta-analysis of these studies has not been done, and it would be difficult to combine the results since they all measured effectiveness at different times using different croup scores and allowing for different co-interventions. In some cases\(^{30-32}\), repeated epinephrine treatments were permitted as needed for continued symptoms. However, all seven studies showed significant improvements in croup score in the treated patients *versus* the controls, at one or more measured times during the course of the trials.

Traditionally, children with croup who were symptomatic enough to require racemic epinephrine treatment in addition to glucocorticoids were admitted to the hospital for observation, for concerns that their symptoms would relapse as the effect of epinephrine waned. In a randomized trial of nebulized racemic epinephrine administration, 35% of patients who received racemic epinephrine had a relapse of symptoms within 2 h of treatment\(^{33}\). Glucocorticoids were not given in this trial. No child was clinically worse 2 h after treatment than before treatment. More recently, out-patient management is being considered for a subset of emergency department patients who receive racemic epinephrine and dexamethasone and are asymptomatic following a period of observation. The optimal duration of observation following epinephrine treatment, to ensure that symptoms will not return, is uncertain, and the data are limited to two observational studies.

One prospective cohort study evaluated 174 children less than 13 years of age treated in an emergency department for moderate or severe croup\(^{34}\). Patients met study criteria if they were discharged from the emergency department after receiving a single dose of racemic epinephrine and dexamethasone 0.6 mg/kg (maximum 10 mg). Among 82 eligible discharged patients, 11 required follow-up within 48 h of discharge, 6 for croup and 5 for either asthma or bronchiolitis. One patient was lost to follow-up. Four patients required admission to hospital within 48 h, 2 for croup and 2 for bronchiolitis. The authors
used their own croup score, and did not comment on the initial or discharge croup scores for those patients who returned to care.

In an additional prospective cohort study of 60 children aged 3 months to 6 years presenting to the emergency department with viral croup, all eligible children received mist and intramuscular dexamethasone. Children with continued symptoms after 30 min received racemic epinephrine and were followed. Sixty children received racemic epinephrine, and 20 had continued symptoms and were admitted. All admitted patients who did not receive further racemic epinephrine treatments within 2 h (16/20) had modified Westley croup scores ≥ 2 at 2 h. Forty patients were discharged, 32 with a croup score of 0 or 1 and only 1 with a croup score of 3 (the remaining 7 presumably had a croup score of 2). Thirty-eight patients were followed-up. Two patients returned 32–36 h following racemic epinephrine treatment with worsening symptoms of croup and were admitted. The croup scores of these two patients at discharge were not mentioned. The sensitivity and specificity of the croup score at 2 h for predicting admission after observation for 4 h could not be determined from the data provided.

Although these studies are not conclusive, it appears that roughly 5% of patients discharged from the emergency department after receiving dexamethasone and racemic epinephrine for symptomatic croup will return to care. Relapse within 24 h is unlikely in patients with minimal symptoms (croup score 0–1) 2 h after racemic epinephrine treatment.

**L-epinephrine**

The use of L-epinephrine has been proposed as a less expensive and more readily available treatment for croup. Many practitioners who do not routinely stock racemic epinephrine have L-epinephrine available as a resuscitation medication. One randomized controlled trial has compared L-epinephrine, 5 mg of a 1:1000 dilution in normal saline with racemic epinephrine 0.5 cc of 2.25% (5 mg) in normal saline. All patients aged 6 months to 6 years presenting with croup were evaluated and those with a Downes and Raphaely croup score of ≥ 6 after 20–25 min of mist therapy were included. Patients with a croup score > 8 or oxygen saturation < 95% also received i.m. dexamethasone. Sixteen patients were treated with racemic epinephrine and 15 with L-epinephrine. Both groups had an initial improvement in croup score following treatment, but repeated measures ANOVA revealed no statistical differences in improvement between the two groups at 5, 15, 30, 60, 90 or 120 min following treatment. L-epinephrine thus appears to be as efficacious as racemic epinephrine in the out-patient management of severe croup, although the number of patients studied is small and clinically important differences between the two groups could have been missed.
Heliox

Heliox is a metabolically inert, non-toxic gas that combines helium with oxygen. It has low viscosity and low specific gravity, which allows for greater laminar airflow through the respiratory tract. It was first described by Barach for use in ameliorating airway obstruction associated with asthma, chronic obstructive pulmonary disease and upper airway disorders. It has more recently been evaluated for use in the paediatric setting, for post-extubation stridor and croup. In a pilot study, Terregino et al randomized 15 children aged 6 months to 4 years with signs and/or symptoms of croup to receive either 30% humidified oxygen or heliox in a 70% helium/30% oxygen ratio. Heliox was well tolerated and croup scores were similarly reduced in both groups (P = 0.32). The study may have been underpowered to detect important differences in efficacy between the two groups. Nelson et al followed 14 children between 3–21 months of age who were admitted to the ICU with severe croup and treated with heliox after failing to improve with racemic epinephrine. Glucocorticoids are not mentioned in the report. Rapid improvement in clinical symptoms was noted in 11 of the 14 patients immediately following heliox treatment. Additional studies have shown benefit using heliox for post-extubation stridor.

Heliox is commercially available in an 80% helium/20% oxygen ratio or a 70% helium/30% oxygen ratio, and is administered with a tight-fitting mask. The benefits improved laminar flow are lost if the gas holds more than 40% oxygen. The improvements in air exchange appear to outweigh this limitation. More studies are needed to determine better the indications for heliox therapy.

Future research

There is limited evidence in many areas of croup therapy. In particular, studies have not clearly established the roles of humidified oxygen and lower doses of dexamethasone, or the optimal duration of observation following treatment with epinephrine. Further research is also needed to determine the efficacy of prednisolone versus dexamethasone for acute croup and the efficacy and safety of repeated doses of dexamethasone after 24 or 48 h, for patients with continued symptoms. Although we are likely to continue to manage croup for years to come, early intervention with corticosteroids and new therapies for severe disease will likely continue to lower morbidity and mortality due to this common childhood illness.
Key points for clinical practice

- Glucocorticoids are the mainstay of therapy for croup
- Glucocorticoids can be given orally, parenterally or as nebulized medications
- Oral dexamethasone 0.6 mg/kg (maximum dose 10 mg) is commonly prescribed. Lower doses of oral dexamethasone, 0.3 mg/kg and 0.15 mg/kg appear to be equally effective
- There are insufficient data to evaluate the efficacy of humidification for the treatment of croup
- Nebulized epinephrine is an effective adjunctive therapy for the short-term treatment of respiratory distress due to croup
- L-epinephrine appears to be as efficacious as racemic epinephrine
- Heliox appears to be an effective short-term treatment for refractive respiratory distress due to croup. It should be used in conjunction with glucocorticoids.

Acknowledgement


References