

PRACTICAL SUMMARIES IN ACUTE CARE

A Focused Topical Review of the Literature for the Acute Care Practitioner

Should Steroids Be Used to Treat Croup?

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Introduction

Croup is an acute respiratory illness caused by inflammation and narrowing of the subglottic region of the larynx. It manifests 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 isolates.^{1,2} Other etiological agents include respiratory syncytial virus, influenza viruses A and B, and *Mycoplasma pneumoniae*.

Croup accounts for 15% of respiratory tract infections among children, and during the second year of life, 1-5% of children will need outpatient evaluation for croup.^{3,4} Although, fewer than 2% of children with croup are admitted to the hospital, and only 0.5-1.5% of these require intubation, croup is a frightening disease to parents. Death from croup is rare, with mortality rates in intubated patients of less

than 0.5%.¹ The total economic cost of croup is difficult to quantify. In the United States, 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.⁵

The diagnosis of viral croup is mainly a clinical one based upon the history and physical findings. Diagnostic studies usually are not necessary.

Treatment of children with croup depends upon the severity of the illness. A number of rating scales have been devised to assess the severity of croup; the most commonly used one is the Westley croup score (*Table 1*).^{1,6-10}

The management of croup has changed during the years, particularly with the development of new pharmacological therapies and increased evidence regarding treatment effectiveness. Pharmacological therapies generally aim to improve oxygenation, reduce air-

way narrowing, improve airflow, and/or reverse the inflammatory process. This article will review recent literature concerning the management of viral croup.

Mist Therapy: Old-fashioned Idea?

Source: Neto GM, et al. A randomized controlled trial of mist in the acute treatment of moderate croup. *Acad Emerg Med* 2002; 9:873-879.

This randomized controlled trial (RCT) compared humidified oxygen delivered through a "mist stick" versus controls (no humidified oxygen) in 71 children with moderate croup (Westley croup score 3-7) who had received a single oral dose of dexamethasone 0.6 mg/kg.

The authors found no significant difference between the no-mist (n = 36) and the mist (n = 35) groups in the overall mean change in croup score at 2 hours (mean change from baseline in croup score: humidified

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oxygen vs controls, $P = 0.39$; actual mean score numbers not available). The croup score was reassessed at 30, 60, 90, and 120 minutes after initiation of treatment (all non-significant). The concentration of oxygen used was not stated, and the

actual percentage humidity delivered to each child was not measured. Other measured variables including oxygen saturation, heart rate, and respiratory rate also showed no significant difference between groups.

A systematic review, in the Cochrane Library, summarized the highest quality evidence for the effectiveness of corticosteroids for children with croup. Only randomized, controlled trials using any corticosteroid in the treatment of acute croup were included in the review. Dexamethasone was the most commonly studied corticosteroid, followed by budesonide, methylprednisolone, and fluticasone. Of the 31 trials involving 3726 patients, 17 involved inpatients, and the remaining 14 involved outpatients.

Using Westley croup score as an outcome, treatment with corticosteroids was associated with an improvement at 6 hours (weighted mean difference [WMD]: -1.2; 95% CI = -1.6 to -0.8) and 12 h (WMD: -1.9; 95% CI - 2.4 to -1.3).

The number of return visits for worsening croup was evaluated following the use of corticosteroids, and there were fewer re-admissions in the corticosteroid-treated group (relative risk [RR]: 0.49; 9% CI = 0.34 to 0.71). Time spent in the ED or hospital also was significantly decreased in the corticosteroid-treated group (WMD: 11h; 95% CI = -18 to -4 h). No differences among routes of delivery (e.g., inhaled, oral, and intramuscular) or treatment agents (e.g., budesonide, dexamethasone, and fluticasone) were identified.

Commentary

The focus of this Cochrane review was children who had moderate-to-severe croup scores. The reviewers concluded that corticosteroids produce a clinical improvement in children with croup within 6 hours and that their use is beneficial in both the inpatient and outpatient setting.

The two most common corticosteroids that have been used in croup studies are systemic dexamethasone

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Commentary

Humidity has been presumed to improve airway inflammation and moisten secretions, thereby improving the child's respiratory status. It has been shown that when sputum is exposed to humidity and nebulized water, there is a significant decrease in viscosity. It has been suggested that the narrowing of the subglottic space causes turbulent air flow, which leads to drying and further inflammation of the mucous membranes. The moist air may prevent the drying and thickening of the secretions, thereby improving the flow of air through the trachea.¹⁴¹

Despite the widespread use of mist for many years, few studies have examined the effectiveness of moist air in the treatment of croup. This report by Neto and colleagues is the largest randomized, controlled trial to date on the use of humidified oxygen in the treatment of croup. Although the total number of patients was relatively small, the study was designed to detect a difference in Westley croup score of 1 between the two groups.

Given the costs associated with providing humidified air, or supplemented with oxygen, the inconvenience to the patients and the lack of efficacy, it appears that the use of mist therapy in the treatment of croup could be abandoned.

Improvement with Corticosteroids

Source: Russell K, et al. Glucocorticoids for croup. *Cochrane Database Syst Rev* 2004 (1) CD001955.

Table 1. Westley Croup Scoring System

Symptom	Score
LEVEL OF CONSCIOUSNESS	
Normal (including sleep)	0
Disoriented	5
CYANOSIS	
None	0
Cyanosis with agitation	4
Cyanosis at rest	5
STRIDOR	
None	0
When agitated	1
At rest	2
AIR ENTRY	
Normal	0
Decreased	1
Markedly decreased	2
RETRACTIONS	
None	0
Mild	1
Moderate	2
Severe	3

Adapted from Westley CR, et al. Nebulized racemic epinephrine by IPPB for the treatment of croup: A double blind study. *Amer Dis Child* 1978;132:484-487.

Westley croup scores of 1-2 considered *mild* croup; Westley croup scores of 3-8 considered *moderate* croup. Westley croup scores of > 8 considered *severe* croup.

and inhaled budesonide. Their mechanism of action is thought to be an anti-inflammatory effect on the laryngeal mucosal edema. Interestingly, measurable treatment effects (e.g., a decrease in the severity of symptoms) have been demonstrated as early as 2 hours after treatment with dexamethasone.^{10,13}

Nebulized Budesonide vs Dexamethasone

Source: Cetinkaya F, et al. A comparison of nebulized budesonide, and intramuscular, and oral dexamethasone for

treatment of croup. *Int J Pediatr Otorhinolaryngol* 2004;68:453-456.

Sixty children aged 6-36 months were randomly allocated into four groups. The first three study groups (15 children in each) were given nebulized budesonide, oral dexamethasone, and intramuscular dexamethasone, respectively, in addition to salbutamol and other supportive measures, and these were compared with the placebo group. All patients were evaluated with Westley croup scores on admission to the pediatric ED (0 hours) and at 24, 48, and 72 hours. At the end of the study, the croup scores of all steroid treatment groups were significantly lower than the placebo group, but there was no statistical difference among them.

The authors concluded that nebulized budesonide and oral and parenteral dexamethasone have the same effectiveness for treatment of croup and that the choice depends upon conditions of the patient and the preference of the treating physician.

Commentary

The Cochrane review not only demonstrated the effectiveness of corticosteroids in moderate-to-severe croup, it also demonstrated that both systemic dexamethasone (oral or intramuscular) and nebulized budesonide were equally effective.¹²

Oral dexamethasone is preferred because it is inexpensive, easy to administer, readily available, and relatively well tolerated.^{6,15} As such, intramuscular dexamethasone or nebulized budesonide should be reserved for children unable or unwilling to take the oral form.¹⁶

The major disadvantage of oral use is the unpleasant taste of the drug. Unfortunately, it is often not tolerated well by younger children and can cause vomiting. Qureshi

and colleagues reported that crushed dexamethasone tablets mixed with soft food were more tolerable than prednisolone syrup.¹⁷ The problem of poor acceptance of oral corticosteroids has been used as the rationale for the parenteral use of these medications.¹⁸ Geelhoed has recently demonstrated that the addition of inhaled budesonide (2 mg) to oral dexamethasone (0.15 mg/kg) offers no advantage in the treatment of children hospitalized with croup.¹⁹

Single-dose Oral Dexamethasone

Source: Bjornson CL, et al. A randomized trial of a single dose of oral dexamethasone for mild croup. *N Engl J Med* 2004;351:1306-1313.

In this double-blind trial conducted at four pediatric EDs, 720 children with mild croup, based upon a score of 2 or less on the croup scoring system of Westley and colleagues, were randomized to receive one oral dose of either dexamethasone (0.60 mg/kg body weight) or placebo. The primary outcome was a return to a medical care provider within seven days after treatment for croup, and the secondary outcome was the presence of ongoing symptoms of croup on days 1, 2, and 3 after treatment.

Both groups were similar in baseline clinical characteristics. Compared with the placebo group, the dexamethasone group had significantly lower return rates for medical care (7.3% vs 15.3%; $P < 0.001$), quicker resolution of croup symptoms ($P = 0.003$), less lost sleep ($P < 0.001$), and less parental stress ($P < 0.001$). There were no serious adverse events attributable to treatment.

The authors concluded that all children with croup symptoms,

requiring a visit to the ED, should be treated with dexamethasone.

Commentary

The majority of the trials in the Cochrane review involved children who had moderate-to-severe croup.¹² The authors sought to identify if there were any benefits of dexamethasone treatment for children with mild croup. This study demonstrated a significantly lower return rate for medical care in the dexamethasone group in addition to faster resolution of croup symptoms. The use of a single dose of 0.6 mg/kg of dexamethasone in children with mild croup 1) reduced a patient's return to medical care by 50%, 2) reduced croup symptoms and sleep lost by 30% in the first 24 hours, and 3) decreased the amount of stress experienced by parents in the first 24 hours.

One study limitation included lack of power to exclude the possibility of rare adverse events. The potential for adverse effects following a single dose of systemic dexamethasone is extremely low, and safety is generally not an issue. However, the medication should be used with caution in children with known immune deficiency or recent exposure to chickenpox.²⁰

It is important to note that another randomized clinical trial of dexamethasone in children with croup has been performed.²¹ This study found that, compared with placebo, a single oral dose of dexamethasone 0.15 mg/kg significantly reduced the proportion of children seeking additional medical attention for ongoing croup symptoms within 7 to 10 days.

None of the 48 children treated with dexamethasone and 8 of the 48 children treated with placebo returned to care with continuing symptoms of croup ($P < 0.01$).

Combination Treatment

Source: Duncan M, et al. Nebulized L-epinephrine and steroid combination in the treatment of moderate to severe croup. *Clin Drug Invest* 2005; 25:183-189.

This study compared the effectiveness of nebulized L-epinephrine in combination with systemic or nebulized corticosteroid with that of cool mist and systemic corticosteroids in the treatment of moderate-to-severe croup as determined by the Westley croup score.

Children were eligible for the study if they presented to the ED with a moderate-to-severe croup. Patients were randomly assigned to three groups: group 1, cool mist and intramuscular dexamethasone ($n = 26$); group 2, nebulized L-epinephrine and intramuscular dexamethasone ($n = 31$); group 3, nebulized L-epinephrine and nebulized budesonide ($n = 19$). The croup score, vital signs, and oxygen saturation levels were assessed before and after medication. Adverse events, additional L-epinephrine administration, and hospitalization were recorded.

Age, sex, initial croup score, and vital signs were similar in all groups. Croup scores were significantly decreased over time in all treatment groups, and this decrease was very evident at 30 minutes ($p < 0.05$). Croup scores of groups 2 and 3 were significantly lower than those of group 1 at 30 and 60 minutes, but no difference was observed between groups 2 and 3 at these time points. The numbers of patients who had croup scores less than 2 at 30 and 60 minutes were higher in groups 2 and 3 than group 1 ($p = 0.004$ and $p = 0.032$, respectively). More patients in group 1 received additional L-epinephrine

treatments ($p = 0.014$). Changes in vital signs were not different among groups when assessed over time ($p > 0.05$).

This study demonstrated that with early combination treatment, croup scores improved rapidly and hospitalization rates were low. Patients with moderate-to-severe croup presenting to the ED should receive nebulized L-epinephrine in combination with intramuscular dexamethasone or nebulized budesonide. No significant adverse effects were observed with L-epinephrine. The use of L-epinephrine has been proposed instead of racemic epinephrine in patients with moderate-to-severe croup because it is efficacious, well tolerated, less expensive, and more readily available in many countries.

Commentary

There have been a number of studies comparing epinephrine with either placebo or no treatment for the management of croup.²²⁻²⁵ An additional study included a treatment arm where inhaled racemic epinephrine is compared to placebo.²⁶ All six of these studies showed significant improvements in the croup score in the treated patients versus the controls, at one or more measured times during the course of the trials.¹ Racemic epinephrine is a 1:1 mixture of the dextrorotatory (D) and levorotatory (L) isomers of epinephrine, of which the L form is the active component.⁶ Racemic epinephrine works by stimulation of the alpha-adrenergic receptors in the airway with resultant mucosal vasoconstriction and decreased subglottic edema and by stimulation of the beta-adrenergic receptors with resultant relaxation of the bronchial smooth muscle.^{6,27} The recommended dose is 0.5 mL of a 2.25% solution of racemic epinephrine diluted in 2-3 mL of normal saline

solution.²⁸

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. 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.²⁹ Both groups had an initial improvement in croup score following treatment, but repeated measures revealed no statistical differences in improvement between the two groups at 5, 15, 30, 60, 90, or 120 minutes following treatment. L-epinephrine, thus, appeared to be as efficacious as racemic epinephrine in the management of severe croup.

This study reviewed by Duncan and colleagues demonstrated that with early combination therapy (epinephrine and steroids), croup scores improved rapidly and hospitalization rates were decreased. Therefore, it is recommended that patients with moderate-to-severe croup presenting to the ED should receive nebulized L-epinephrine in combination with dexamethasone. Kelley and Simon reported that patients receiving therapeutic doses of corticosteroids and epinephrine who remained stable following 2 hours of observation could be safely discharged to home.³⁰ Other studies have suggested that approximately 5% of patients discharged from the ED after receiving dexamethasone and epinephrine for symptomatic croup will return to care.¹

Heliox Therapy as a Temporizing Agent

Source: Gupta VK, Cheifetz IM. Heliox administration in the pediatric intensive care unit: An evidence-based

review. *Pediatr Crit Care Med* 2005; 6:204-211.

This paper provides a comprehensive, evidence-based review of helium-oxygen gas mixtures (heliox) in the management of various pediatric respiratory diseases including croup.

From this review, the authors were able to make the following conclusions: Heliox administration is most effective during conditions involving density-dependent increases in airway resistance (e.g., croup), especially when used early in an acute disease process. Any beneficial effect of heliox should become evident in a relatively short period of time. The medical literature supports the use of heliox to relieve respiratory distress, decrease the work of breathing, and improve gas exchange. No adverse effects of heliox have been reported. However, heliox must be administered with vigilance and continuous monitoring to avoid technical complications.

Commentary

Helium is an odorless, tasteless, nonexplosive, noncombustible, and physiologically inert gas. Since helium has no pharmacologic properties of its own, its therapeutic purpose is to lower the total density of the inhaled gas. It is this property that provides the rationale and theoretical basis for using helium with respiratory diseases that are obstructive and promote turbulent airflow. For medical purposes, helium is always mixed with oxygen; the mixture is commonly referred to as heliox. The higher the concentration of helium, the lower the fraction of inspired oxygen (FIO₂) and the less dense the gas mixture.

Heliox has been evaluated for use in children with croup. In an ED pilot study by Terregino and colleagues, 15 subjects (mean age 24 months) presenting with signs

and/or symptoms of croup were enrolled into one of two groups: patients received either 30% oxygen (humidified) or 70:30 heliox (humidified).³¹ These authors found heliox to be safe, well tolerated, and as effective as humidified oxygen in reducing the croup score. The authors concluded that assessment of patients by a croup scoring system and blood gas analysis suggests that heliox is a useful alternative to tracheotomy or tracheal intubation.

Although helium offers an additional tool in the treatment of various airway and pulmonary problems, it has no inherent therapeutic effect.³² As such, it can be used only as a temporizing agent to allow time for therapeutic agents to work or for the natural resolution of the disease.

To be effective, helium must be administered in concentrations of 60-80%.^{1,32} Helium concentrations less than 60% significantly blunt the density advantage.^{1,31,33} 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.

Croup Clinical Pathway

Source: Chin R, et al. Effectiveness of a croup clinical pathway in the management of children with croup presenting to an emergency department. *J Paediatr Child Health* 2002;38:382-387.

The aim of this study was to evaluate the safety and effectiveness of a clinical pathway for croup in the ED.

This before-and-after intervention study on all consecutive children aged 6 months to 10 years who presented to the ED with moderate/severe croup was conducted during a six-month period. Children with a clinical croup score (Westley

croup scale) of 2 or more and resting stridor were considered eligible for entry into the study. Children were treated with either oral dexamethasone or a combination of oral dexamethasone suspension and nebulized adrenaline. Children were clinically assessed, observed in the emergency short-stay ward, and discharged or admitted according to the clinical pathway. The following outcomes were measured: admission rates, hospital re-presentation, length of stay, and adverse clinical events. Children in the post-intervention group were followed up by telephone within 48 hours of discharge. There were 157 patients recruited in the pre-intervention group and 110 in the post-intervention group. Significant reductions were reported in the length of stay (18.9 hours compared with 5.2 hours), hospital admission (52.9% compared with 18.0%), and intensive care admission (10.2% compared with 0.0%) after the introduction of the croup clinical pathway. Follow-up interviews of parents indicated that the new treatment strategy was well received. The authors concluded that the use of the croup clinical pathway in the ED is safe and effective in guiding consistent management, resulting in reduced admission rates, earlier discharge home, and no reported adverse events.

Commentary

This study demonstrated that a croup clinical pathway can be a safe and effective management tool for reducing length of hospital stay and reducing hospital admission rates for ED patients. Length of hospital stay was reduced by 72% and admission to hospital by 60%. There were no admissions to intensive care in the post-intervention group compared with 4.4% of patients in the pre-intervention

Table 2. Management of Viral Croup

Severity of Symptoms	Intervention
Mild croup	<ul style="list-style-type: none"> • Oral dexamethasone (0.15-0.6 mg/kg) • Discharge to home
Moderate croup	<ul style="list-style-type: none"> • Nebulized racemic epinephrine or equivalent dose of L-epinephrine • Oral dexamethasone 0.15-0.6 mg/kg or nebulized budesonide 2 mg • Observation for ≥ 2 hours and discharge to home or admit to hospital ward
Severe croup	<ul style="list-style-type: none"> • Nebulized racemic or L-epinephrine • Dexamethasone 0.15-0.6 mg/kg (oral or IM) • Consider trial of heliox • Observe in ED/ admit to hospital/contact ICU if appropriate

Adapted from Perkin RM, Swift JD. Infectious causes of upper airway obstruction in children. *Pediatr Emerg Med Rep* 2002;7:117-128.

group.

The use of a croup clinical pathway in this ED was useful in selecting those patients requiring admission. It enabled consistent treatment and has been shown to be both safe and effective in reducing length of stay in hospital.

Conclusions / Recommendations

Croup is one of the most common respiratory illnesses seen in the acute pediatric setting. It can be a cause of acute stridor and/or respiratory distress in young children. Research has shown that therapy can reduce complications (e.g., the need for intubation, or hospitalization) and improve quality of life for parents and children. Corticosteroids are the primary treatment option that will accomplish both goals and can be used in outpatient and inpatient settings. Corticosteroids may be given orally, parenterally, or in nebulized form; however, oral administration is the

preferred route. Nebulized adrenaline (racemic or L-adrenaline) is also an effective treatment for more severe cases of croup. Recent studies have shown that mist/humidified air provides no additional symptom improvement, nor does it alter the overall course of the disease process.

Based upon this extensive review of the available and most recent literature, the following recommendations can be made. (See Table 2.)

- Evidence exists to advocate that all children with croup be treated with corticosteroids. Most children can be treated by health care professionals with a single, oral dose of dexamethasone (0.6 mg/kg with a maximum dose of 10 mg) prescribed. Lower doses of oral dexamethasone (0.3 mg/kg and 0.15 mg/kg) appear to be equally effective.

- Patients with moderate-to-severe croup often need to be assessed in an ED. For those who do not tolerate the oral preparation, nebulized budesonide or intramuscular dexamethasone are reasonable alternatives. Nebulized epinephrine

should be reserved for patients with moderate-to-severe croup. Patients should be observed for a minimum of 2 hours after treatment with epinephrine.¹⁰ Simultaneous administration of corticosteroid with epinephrine reduces both the rate of hospitalization and intubation in patients with severe croup and impending respiratory failure.

Using the approach outlined above should lead to fewer hospitalizations and reduce relapses back to care following discharge. Moreover, corticosteroids lead to more rapid symptom improvement, which should improve the quality of life for both patients and their parents.

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Future Issues

- What is the best diagnostic test for nephrolithiasis?
- Is an LP necessary in SAH with new generation scanners?
- Evaluating PE with CT: Is it time for new paradigm?

CME OBJECTIVES

Upon completing this program, participants will be able to:

- Summarize the most recent significant studies in emergency medicine/acute care related to a single topic;
- Discuss up-to-date information about new drugs, techniques, equipment, trials, studies, books, teaching aids, and other information pertinent to the stated topic;
- Evaluate the credibility of published data and recommendations about the stated topic.

CME INSTRUCTIONS

Physicians participate in this continuing medical education program by reading the articles, using the provided references for further research, and studying the CME questions. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity, participants must complete the evaluation form provided at the end of each semester (June and December) and return it in the reply envelope provided to receive a certificate of completion. When an evaluation form is received, a certificate will be mailed to the participant.

CME QUESTIONS

6. Emergency department management of severe viral croup may include all of the following treatments, *except*:

- a. Oxygen
- b. Racemic epinephrine
- c. Ribavirin
- d. Steroids

7. Which one of the following statements regarding the management of viral laryngotracheitis (croup) is true?

- a. Neck radiographs are essential for establishing the diagnosis and assessing the severity of illness.
- b. Racemic epinephrine has a long duration of action and effectively decreases the length of illness.
- c. Corticosteroids are indicated only for severe cases of croup.
- d. Intubation rarely is required.

8. All children evaluated in the ED with croup should be considered for dexamethasone therapy.

- a. True
- b. False

9. The Westley Croup Score takes into account all of the following conditions, *except*:

- a. Stridor
- b. Air entry
- c. Wheezing
- d. Cyanosis

10. Which one of the following statements is true?

- a. Patients with moderate-to-severe croup presenting to the ED should receive nebulized epinephrine in combination with dexamethasone.
- b. When used in patients with croup, dexamethasone must always be given intramuscularly.
- c. Children with croup who receive nebulized epinephrine in the ED must be admitted to the hospital for observation.
- d. Racemic epinephrine is more efficacious than L-epinephrine in the management of croup.

Answers: 6. c; 7. d; 8. a; 9. c; 10. a

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