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Introduction to Clinical Answers: Croup

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Croup, a common respiratory illness of childhood, is the focus of this issue's 'Clinical Answers'. Croup (laryngotracheobronchitis) affects up to 3% of children under the age of six years every year (1) and is also occasionally seen in older children and rarely in adolescents and adults (2). Croup is most commonly caused by parainfluenza type 1 and 3 viral infection, but other viruses have been implicated including influenza A and B, respiratory syncytial virus, adenovirus, coronavirus, rhinovirus and human metapneumovirus, among others (1, 3–7). The infection leads to inflammation and oedema of the upper airway mucosa and narrowing of the subglottic region, causing varying degrees of airway obstruction. Classic symptoms include the sudden onset of barky cough and hoarse voice, and in more severe cases, stridor and chest wall indrawing. The majority of children have mild, short-lived symptoms (6). However, a small proportion of children have moderate to severe symptoms which can result in hospital admission (8–10), and in the most severe cases, intubation (11–14).

Croup is a clinical diagnosis, based upon careful history and physical examination in a child presenting with typical symptoms. In general, the diagnosis is straightforward, but rare alternate causes of stridor and respiratory distress should be considered and excluded (15). The most likely alternate diagnoses include bacterial tracheitis and epiglottitis, especially in a child who has atypical symptoms, does not respond as anticipated to treatment or who shows deterioration (15, 16).

There are several practical management aspects in croup that are not evidence based but are clinically sensible. In any child with possible airway obstruction, it is important to take care to minimize distressing procedures and to maintain a calm and reassuring environment (15). Although there is no published evidence that oxygen should be administered, it is routinely given to children who are showing signs of respiratory distress. Blow-by oxygen can be administered by the parent via tubing held a few centimetres from the child's nose and mouth. Children should not be treated with humidified air (mist), as there is now definitive evidence showing no benefit (17, 18).

During the initial treatment of the child with croup, other important decisions need to be considered, the evidence for which seems not as clearly defined. For example, how does one decide on whether to admit a child with croup to hospital? Minimal published evidence is available regarding which children should be hospitalized. However, clinical practice guidelines advise admission for the child who has persistent stridor at rest and sternal indrawing four or more hours after treatment with glucocorticoids, as these findings are markers for more severe illness (15, 19). Relative indications to be considered include a child living a long distance from hospital care, concerns about observation at home, significant parental anxiety and recurrent Emergency Department visits within 24 hours (15, 19). A retrospective review of 527 consecutive children seen in an Emergency Department in Australia found that children who show sternal and chest wall retractions upon presentation are at increased risk for longer hospitalization, need for more medical therapies and need for airway intubation (20). Inpatients must be closely monitored and frequently re-evaluated for changes in respiratory status. Criteria for discharge from hospital are also not informed by published evidence; however, clinical guidelines suggest that a child should be free of significant signs of airway obstruction for a minimum of two hours after epinephrine dosing (15). This observation period is recommended as the clinical effect of epinephrine has disappeared by two hours following administration (21). There is clinical trial data documenting that a child's symptoms do not worsen after epinephrine's effect has worn off, but rather, return to baseline severity at most (21, 22).

The cornerstones of pharmacological management for children with croup include nebulized epinephrine for those with signs of acute airway obstruction (moderate to severe croup) and glucocorticoids (mild, moderate and severe croup). The 'Clinical Answers' presented in this month's issue addresses and summarizes evidence on these two treatments. To provide a broader context and background for this data, let us consider two possible scenarios that a clinician will face: first a child with moderate to severe croup and

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then a child with mild croup. How does the evidence apply, and what questions remain to be answered?

A child should be considered to have moderate croup if they present with a persistent barking cough, accompanied by stridor and suprasternal and sternal chest wall retractions when at rest. In severe croup, there is also significant inspiratory and occasionally expiratory stridor, decreased air entry upon auscultation and evidence of agitation or distress.

Firstly, should epinephrine be used? Epinephrine has a long history of use in the child with croup and signs of airway obstruction. The data is derived from eight small clinical trials (21–28), each measuring slightly different clinical outcomes at differing time intervals following the intervention, and in both inpatient and outpatient settings. Analysis of each outcome contains data from one or two of these eight trials; however, it is important to note that results for each of these outcomes consistently favoured epinephrine to placebo. These results support the role of epinephrine for short-term relief of airway obstruction in children with signs of airway obstruction.

Secondly, is there evidence to guide size of the glucocorticoid dose? The conventional dose of dexamethasone is 0.6 mg/kg, with doses of 0.15 and 0.3 mg/kg also receiving study. Four randomized controlled trials comparing different doses of dexamethasone in children in the inpatient and outpatient setting have been published (29–32). Although all studies were small and none were designed as non-inferiority studies, none showed a significant difference in outcome measures between the smaller and larger glucocorticoid doses. However, in a meta-analysis of six studies in children hospitalized for croup, there appeared to be a dose–response effect favouring higher doses of glucocorticoid (33). Therefore, while there is evidence that 0.15 mg/kg may be adequate, it is not yet definitive.

Finally, in a child who is hospitalized with croup, is a single dose of glucocorticoid sufficient? There are no randomized trials addressing repeated doses of glucocorticoids compared with a single dose. As croup symptoms typically resolve within 72 hours and the anti-inflammatory effect of dexamethasone is thought to last between two and four days (34), in most cases repeated doses are not likely to be needed. However, studies are needed to formally address this question.

What about the child with mild croup? This subset of children will comprise the majority of cases seen by clinicians. Data from 24 general Emergency Departments in the province of Alberta, Canada, classified 85% of all children as having mild croup (unpublished data), defined clinically as presence of barky cough, but no stridor or chest wall indrawing at rest. In a tertiary care Children's Hospital Emergency Department in the same province, the percentage of children with mild croup was found to be somewhat lower at 65% (unpublished data), but still accounted for the majority of cases. Although no randomized controlled trial has studied the use of epinephrine in children with mild croup, since the therapeutic effect of epinephrine does not extend beyond a few hours, there would seem to be little rational basis for treatment with epinephrine. Glucocorticoid treatment in children with mild croup specifically has been studied in two randomized controlled trials which included only children presenting with mild croup, as defined by clinical scores. The first trial in 100 children ranging in age from four to 10 years compared dexamethasone to placebo and found that the group treated with dexamethasone (0.15 mg/kg) were significantly less likely to seek medical attention for ongoing croup symptoms within seven to 10 days after treatment (35). The second trial in 720 children found that a single dose of dexamethasone (0.6 mg/kg) reduced return for medical care for ongoing croup symptoms and reduced croup symptom severity (36). The systematic review included subgroup analysis of outcomes by croup severity and found no significant differences between mild and moderate croup trials, consistent with the randomized controlled trials (37). Thus, there is good evidence that children with mild croup derive benefit from a single oral dose of dexamethasone.

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