Do Glucocorticoids Improve Symptoms and Reduce Return Visits or Admission Rates Among Children With Croup?

TAKE-HOME MESSAGE

Compared with placebo, glucocorticoids improve symptoms of croup at 2 through 24 hours and reduce rates of return visits and admissions among children with croup.

METHODS

DATA SOURCES

Authors searched the Cochrane Central Register of Controlled Trials, Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Ovid MEDLINE, Ovid EMBASE, ClinicalTrials.gov, and the World Health Organization International Trials Registry Platform. Authors searched ClinicalTrials.gov and apps.who.int/trialsearch for ongoing studies. All searches ran from database inception through April 3, 2018. Authors also scanned the reference lists of relevant systematic reviews and all included studies.

STUDY SELECTION

The review included randomized controlled trials of patients (0 to 18 years) with a diagnosis of croup, defined as a syndrome of hoarseness, barking cough, and stridor, that compared outcomes of glucocorticoids versus pharmacologic alternatives, including placebo. Authors included studies of both outpatients (including emergency department [ED] patients) and inpatients. Included studies needed to report

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Editor's Note: This is a clinical synopsis, a regular feature of the *Annals'* Systematic Review Snapshot (SRS) series. The source for this systematic review snapshot is: **Gates A, Gates M, Vandermeer B, et al. Glucocorticoids for croup in children. *Cochrane Database Syst Rev.* 2018;8:CD001955.**

Michael Brown, MD, MSc, Jestin N. Carlson, MD, MS, and Alan Jones, MD, serve as editors of the SRS series.

Results

Results of included trials.

Outcome	No. of Studies (No. of Patients)	Relative Effect (95% CI)	Evidence Quality (GRADE)	Heterogeneity (I^2), %
Decrease in croup score (SMD), h				
2	7 (426)	SMD −0.65 (−1.13 to −0.18)	Moderate	81
6	11 (959)	SMD −0.76 (−1.12 to −0.40)	Moderate	83
12	8 (571)	SMD −1.03 (−1.53 to −0.53)	Moderate	86
24	8 (351)	SMD −0.86 (−1.40 to −0.31)	Low	81
Return visits, admissions, or both	10 (1,679)	RR 0.52 (0.36 to 0.75)	Moderate	52

GRADE, Grading of Recommendations Assessment, Development and Evaluation; *SMD*, standard mean difference; *RR*, risk ratio.

at least one of the following outcomes: changes in croup score; return visits, admissions, or both; hospital length of stay; patient improvement; use of additional treatments; and adverse events. There were no exclusion criteria based on language, publication status, trial conduct, reporting quality, or risk of bias. Two authors independently reviewed the full text of all potentially relevant articles. A third author arbitrated any disagreements in regard to study inclusion.

DATA EXTRACTION AND SYNTHESIS

One author extracted data from each study, whereas a second independently verified extraction to identify errors or omissions. Included studies used alternative croup scores, including the Westley score,[1] the Downes score,[2] or author-created scores. Consequently, the meta-analysis authors calculated treatment effect in regard to croup scores, using a standardized mean difference. They compared the binary outcome of return visits or admissions as a risk ratio with 95% confidence intervals (CIs). For return visits or admissions, authors calculated the number needed to treat for an additional beneficial outcome. Two review authors independently assessed risk of bias for each study by using the Cochrane Risk of Bias Tool,[3] quality of evidence with the Grading of Recommendations Assessment, Development and Evaluation approach,[4] and heterogeneity with the I^2 statistic.[5] They also evaluated treatment effect in subgroup analyses stratifying calculations according to inpatient versus outpatient settings (including the ED), as well as sensitivity analyses.

Authors included 43 randomized controlled trials comprising 4,565 patients from an initial 79 studies discovered during the literature search. Of these, 21 (48.8%) evaluated ED patients, 21 (48.8%) evaluated hospitalized patients, and 1 (2.3%) evaluated patients presenting to a physician outpatient office. Twenty-nine studies (67.4%) measured croup scores; of these, 17 (58.6%) used the Westley score, 11 (37.9%) used author-created scales, and 1 (3.4%) used the Downes score. Compared with placebo, glucocorticoids improved symptoms of croup as measured by standardized mean difference at intervals from medication administration at 2 hours (standardized mean difference −0.65; 95% CI −1.13 to −0.18) to 24 hours (standardized mean difference −0.86; 95% CI −1.40 to −0.31). Compared with placebo, glucocorticoids also reduced the rate of return visits, admissions, or both (risk ratio 0.52; 95% CI 0.36 to 0.75) (Table). There were no significant differences in these findings in subgroup analyses stratifying treatment effect by inpatient versus outpatient study settings (including the ED). Data comparing different glucocorticoid agents and alternative dexamethasone doses (ranging from 0.15 to 0.60 mg/kg) were limited, and hence these comparisons were of generally low or very low certainty, precluding definitive conclusions. Most studies (98%) demonstrated high or unclear risk of bias.

Commentary

Although the term *croup* may colloquially refer to myriad upper respiratory infections in children, the medical literature generally accepts the definition of a viral illness affecting the larynx and trachea (laryngotracheitis).[6] This disease process is common in children, particularly those aged 6 months to 3 years. Diagnosis is clinical and based on symptoms including inspiratory stridor, barking cough, and hoarseness caused by inflammation in the larynx and subglottic airway.[7] Although the viral cause is typically self-limited, croup can cause severe respiratory distress requiring hospitalization, including treatment in an ICU setting.[8]

The mainstay of treatment for croup is glucocorticoids.[9] As demonstrated by this meta-analysis, glucocorticoids decrease the severity of croup symptoms at 2 through 24 hours and reduces the risk of return visits and need for hospital admission. The number needed to treat for an additional beneficial outcome to reduce return visits (or readmissions) was 7 (95% CI 5 to 12) for the mean placebo baseline rate of 30.62%.

An important limitation of this meta-analysis was the unclear or high risk of bias in all but one of the included studies. For many studies, this determination was due to inadequate detail in regard to randomization and blinding methodology. Many studies also lacked sufficient detail relating to recruiting and enrollment to assess for the possibility of selection bias. A related issue is the potential for limited generalizability, given that a substantial proportion of the included studies examined inpatients. That said, the overall meta-analysis findings did not change in subgroup analyses stratified by study setting. Next, there was significant heterogeneity across the included studies, as

reflected in the calculated I^2 values. This heterogeneity arose in part from the different scores used by the included studies.[1,2] The use of a croup score in general is a limitation, given that measurements by health care providers can be subjective, with only fair to moderate interrater reliability.[10] The analysis of croup scores in this case was further problematic, given the use of different scores by the included studies, thus requiring the use of standardized mean difference to quantify treatment effect. The clinical relevance of croup score reduction as measured by standardized mean difference is unclear.

According to the results of this meta-analysis,[11] glucocorticoids improve symptoms of croup at 2 through 24 hours and reduce rates of return visits and admissions among young patients with croup. With data from the 2005 National Hospital Ambulatory Medical Care Survey reporting that only 31% of children presenting to the ED with croup receive glucocorticoids,[12] there exists a need for studies examining potential barriers to this intervention. Given the prevalence of unclear or high risk bias of the included studies, the literature would also benefit from studies evaluating the use of glucocorticoids in croup, with attention to best study practices, including preregistration with full reporting of salient methodology to include recruitment, randomization, and blinding.

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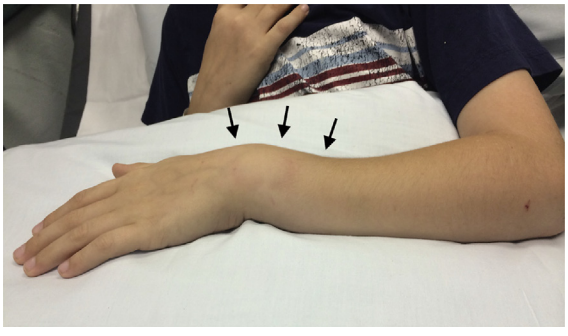

"Child With Dinner Fork Deformity" by Kardouni, February 2016, Volume 67, #2, pp. 165, 188.