

CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Dexamethasone for the Treatment of Pediatric Croup: Clinical Effectiveness

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Research Question

What is the clinical effectiveness of dexamethasone for the treatment of pediatric croup?

Key Findings

Four systematic reviews and six randomized controlled trials were identified regarding the clinical effectiveness of dexamethasone for pediatric patients with croup.

Methods

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD), Canadian and major international health technology agencies, as well as a focused Internet search. No methodological filters were applied to limit retrieval. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between Jan 1, 2002 and May 26, 2017. Internet links were provided, where available.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Pediatric patients with croup (laryngotracheobronchitis)
Intervention	Dexamethasone (oral, intravenous, or intramuscular administration)
Comparator	Standard of care (e.g., solumedrol, prednisolone, etc)
Outcomes	Clinical effectiveness, impact on patient stay in hospital, impact on epinephrine use, safety
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies

Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials and non-randomized studies.

Four systematic reviews and six randomized controlled trials were identified regarding the clinical effectiveness of Dexamethasone for pediatric patients with croup. No relevant health technology assessments or non-randomized studies were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

Four systematic reviews¹⁻⁴ and six randomized controlled trials⁵⁻¹⁰ were identified regarding the clinical effectiveness of dexamethasone for pediatric patients with croup. One systematic review¹ evaluated the effects of treatments in children with mild croup and moderate to severe croup. This review, which was an update to another publication³ identified in this report, included 19 studies. These studies were assessed by the GRADE evaluation to determine to quality of evidence.¹ Information on the clinical effectiveness and safety of dexamethasone, nebulised budesonide, oral prednisolone, heliox, humidification, and nebulised adrenaline was presented.¹

A second systematic review² was conducted to determine the effectiveness of glucocorticoids (including dexamethasone) for the treatment of croup in children. 38 randomized controlled trials were included (n = 4,299).² The authors concluded that dexamethasone and budesonide decrease the need for return visits and readmissions, decrease the length of time spent in hospital, and are effective in relieving the symptoms of croup as early as six hours after treatment.² This review was an update to a previous systematic review.⁴

A third systematic review³ assessed the effects of treatments in children with mild or moderate to severe croup. 43 studies were included and evaluated using the GRADE approach.³ The author summarized the information regarding the effectiveness and safety of antibiotics, corticosteroids, dexamethasone (intramuscular, oral, single-dose oral, route of administration), heliox, humidification, intermittent positive pressure breathing, L-adrenaline, nebulised adrenaline (epinephrine), nebulised budesonide, nebulised short-acting beta(2) agonists, oral decongestants, oral prednisolone, oxygen, and sedatives in children with croup.³

A fourth systematic review⁴ evaluated the effectiveness of glucocorticoids in children with croup. 31 randomized controlled trials were included in this review (n = 3,736). The authors concluded that dexamethasone and budesonide decrease the need for return visits and readmissions, decrease the length of time spent in hospital, and are effective in relieving the symptoms of croup as early as six hours after treatment. The authors also noted that oral dexamethasone may be superior to intramuscular dexamethasone.⁴

One randomized controlled trial⁵ measured the comparative effectiveness of prednisolone versus dexamethasone in children with mild or moderate croup. 87 children were randomized to a treatment arm and their clinical outcomes (including health care requirements for croup, duration of croup symptoms, nonbarky cough, nights with disturbed sleep for the parent, and days with stress) were recorded.⁵ The authors concluded that there were no detected difference in clinical outcomes between the two croup treatments.⁵

A second randomized controlled trial⁶ allocated children with croup (n = 64) to receive either nebulized L-epinephrine, intramuscular dexamethasone, or inhaled beclomethasone dipropionate. The croup score, heart rate, blood pressure, respiratory rate, and oxygen saturation were monitored up to 120 minutes following treatment.⁶ There was a significant improvement of the croup score in all three groups. The authors concluded that inhaled beclomethasone was as effective in the treatment of croup as dexamethasone and it was associated with a significant reduction in the severity of illness within 24 hours of treatment.⁶

A third randomized controlled trial⁷ compared the effectiveness of dexamethasone (at two different doses) to prednisolone for the treatment of mild to moderate croup in children. The primary outcomes of interest were changes in Westley croup score, rate of return for medical care with ongoing croup, and requirement of further treatment with steroids.⁷ 99 children were recruited to the study. The authors concluded there were no significant differences in the three treatment groups.⁷

A fourth randomized controlled trial⁸ assessed the effectiveness of betamethasone versus dexamethasone for the treatment of mild to moderate croup in children. Croup score, heart rate, respiratory rate, pulse oximetry, and the need for supplemental treatments were monitored in 52 patients included in the study.⁸ The authors concluded that oral betamethasone and intramuscular dexamethasone were equally effective for the management of mild to moderate croup in children.⁸

A fifth randomized controlled trial⁹ compared prednisolone to dexamethasone for the treatment of mild to moderate croup in children. 133 children were recruited and randomized to receive either a single oral dose of dexamethasone (0.15 mg/kg) or single oral dose of prednisolone (1 mg/kg).⁹ The authors concluded that prednisolone was less effective than dexamethasone in reducing unscheduled re-presentation to medical care in children with mild to moderate croup.⁹

The final randomized controlled trial¹⁰ identified compared the efficacy of nebulized budesonide, oral dexamethasone, and intramuscular dexamethasone for the treatment of croup. 60 children were recruited and allocated to receive either nebulized budesonide, oral dexamethasone, or intramuscular dexamethasone, in addition to salbutamol and other supportive measures, or a placebo group (no treatment).¹⁰ The Westley croup score was used to determine the effectiveness of each treatment. The authors concluded that each regimen was effective for the treatment of croup; however there were no statistical differences among the non-placebo groups.¹⁰

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-Analyses

1. Johnson DW. Croup. Clin Evid (Online). 2014 Sep 29;2014, 2014 Sep 29.
[PubMed: PM25263284](#)
2. Russell KF, Liang Y, O'Gorman K, Johnson DW, Klassen TP. Glucocorticoids for croup. Cochrane Database Syst Rev. 2011 Jan 19;(1).
[PubMed: PM21249651](#)

3. Johnson D. Croup. *Clin Evid (Online)*. 2009 Mar 10;2009, 2009 Mar 10.
[PubMed: PM19445760](#)
4. Russell K, Wiebe N, Saenz A, Ausejo SM, Johnson D, Hartling L, et al. Glucocorticoids for croup. *Cochrane Database Syst Rev*. 2004;(1).
[PubMed: PM14973975](#)

Randomized Controlled Trials

5. Garbutt JM, Conlon B, Sterkel R, Baty J, Schechtman KB, Mandrell K, et al. The comparative effectiveness of prednisolone and Dexamethasone for children with croup: A community-based randomized trial. *Clin Pediatr (Phila)*. 2013 Nov;52(11):1014-21.
[PubMed: PM24092872](#)
6. Eboriadou M, Chryssanthopoulou D, Stamoulis P, Damianidou L, Haidopoulou K. The effectiveness of local corticosteroids therapy in the management of mild to moderate viral croup. *Minerva Pediatr*. 2010 Feb;62(1):23-8.
[PubMed: PM20212395](#)
7. Fifoot AA, Ting JY. Comparison between single-dose oral prednisolone and oral Dexamethasone in the treatment of croup: a randomized, double-blinded clinical trial. *Emerg Med Australas*. 2007 Feb;19(1):51-8.
[PubMed: PM17305661](#)
8. Amir L, Hubermann H, Halevi A, Mor M, Mimouni M, Waisman Y. Oral betamethasone versus intramuscular Dexamethasone for the treatment of mild to moderate viral croup: a prospective, randomized trial. *Pediatr Emerg Care*. 2006 Aug;22(8):541-4.
[PubMed: PM16912619](#)
9. Sparrow A, Geelhoed G. Prednisolone versus Dexamethasone in croup: a randomised equivalence trial. *Arch Dis Child*. 2006 Jul;91(7):580-3.
[PubMed: PM16624882](#)
10. Cetinkaya F, Tufekci BS, Kutluk G. A comparison of nebulized budesonide, and intramuscular, and oral Dexamethasone for treatment of croup. *Int J Pediatr Otorhinolaryngol*. 2004 Apr;68(4):453-6.
[PubMed: PM15013613](#)

Non-Randomized Studies

No literature identified.

Appendix — Further Information

Randomized Controlled Studies

Alternate Comparators

11. Chub-Uppakarn S, Sangsupawanich P. A randomized comparison of Dexamethasone 0.15 mg/kg versus 0.6 mg/kg for the treatment of moderate to severe croup. *Int J Pediatr Otorhinolaryngol*. 2007 Mar;71(3):473-7.
[PubMed: PM17208307](#)
12. Duman M, Ozdemir D, Atasever S. Nebulised L-epinephrine and steroid combination in the treatment of moderate to severe croup. *Clin Drug Invest*. 2005;25(3):183-9.
[PubMed: PM17523767](#)
13. Bjornson CL, Klassen TP, Williamson J, Brant R, Mitton C, Plint A, et al. A randomized trial of a single dose of oral Dexamethasone for mild croup. *N Engl J Med*. 2004 Sep 23;351(13):1306-13.
[PubMed: PM15385657](#)
14. Dexamethasone reduced the incidence of children with mild croup who returned for medical care. *Evidence-Based Nursing*. 2005: 8:41. Available from:
<http://ebn.bmj.com/content/8/2/41.full>
15. Donaldson D, Poleski D, Knipple E, Filips K, Reetz L, Pascual RG, et al. Intramuscular versus oral Dexamethasone for the treatment of moderate-to-severe croup: a randomized, double-blind trial. *Acad Emerg Med*. 2003 Jan;10(1):16-21.
[PubMed: PM12511310](#)

Non-Randomized Studies

Alternate Comparators

16. Gill N, Sirizzotti N, Johnson D, Joubert G, Kucey AS, Tieu A, et al. Endogenous glucocorticoid response to single-dose dexamethasone for croup in children: A pharmacodynamic study. *Pediatr Emerg Care*. 2017 Apr 11; 2017 Apr 11.
[PubMed: PM28398936](#)
17. Dobrovoljac M, Geelhoed GC. 27 years of croup: an update highlighting the effectiveness of 0.15 mg/kg of Dexamethasone. *Emerg Med Australas*. 2009 Aug;21(4):309-14.
[PubMed: PM19682017](#)

Mixed Population – Asthma and Croup

18. Aljebab F, Alanazi M, Choonara I, Conroy S. Tolerability of prednisolone and dexamethasone in children in Saudi Arabia. *Arch Dis Child*. 2016 Sep;101(9):e2, 2016.
[PubMed: PM27540233](#)

Review Articles

19. de Benedictis FM, Bush A. Corticosteroids in respiratory diseases in children. *Am J Respir Crit Care Med*. 2012 Jan 1;185(1):12-23.
[PubMed: PM21920920](#)

20. Zoorob R, Sidani M, Murray J. Croup: An overview. Am Fam Physician. 2011 May 1;83(9):1067-73.
[PubMed: PM21534520](#)