

SUPPLEMENTS

Table S1. Main available randomized clinical trials on pharmacological treatment of croup in childhood.

First author	Year of publication	Country	Number and age of Subjects	Interventions (drugs, dosage and administration route)	Primary outcome	Secondary Outcome	Main results	Comments
Slowron PN	1966	Canada	200 children with acute laryngotracheitis, average age 2.3 years	Randomly assigned to i) subcutaneous dexamethasone 21-phosphate (0.4-0.5 mg/kg); ii) placebo	Normalization of HR, RR, fever, length of hospital stay, time to disappear of stridor and respiratory fatigue		Statistical difference ($p < 0.05$) in the time to disappear of stridor and respiratory fatigue, and number of days spent in hospital in the dexamethasone group	The Authors conclude that in view of the risks inherent in steroid therapy, the degree of difference is not sufficient to warrant routine use of this drug
Gardner HG	1973	USA	20 children with moderate croup	Randomly assigned to 0.5 mL of 2.25% racemic epinephrine (containing 5 mg L-epinephrine) in 3.5 mL of saline ($n = 10$) or 4.0 mL of saline ($n = 10$)	Change in croup score (10 points: cough score 0 to 2 points, anxiety/air hunger 0 to 2 points, stridor 0 to 2 points, retractions 0 to 2 points, cyanosis 0 to 2 points)	Additional treatment of study drug		
Westley CR	1978	USA	20 children admitted with moderate croup aged 4 months to 5 years	Randomly assigned to 0.5 mL of 2.25% racemic epinephrine (containing 5 mg L-epinephrine) ($n = 10$) or nebulized saline	Change in Westley croup score	Change in respiratory rate and pulse	Clinical scores were significantly improved ($p < 0.01$) at 10 and 30 minutes following the treatment with racemic epinephrine but not at 120 minutes	The Authors conclude that nebulized racemic epinephrine is an effective treatment for the acute signs of croup
Corkey CW	1981	Canada	14 children hospitalized with croup	Randomly assigned to 0.5 mL of 2.25% of inhaled racemic epinephrine (containing 5 mg L-epinephrine) with 3.5 mL of distilled water or 4 mL of placebo	Change in a clinical score based on stridor and recession (mild, moderate, severe)	Change in tracheal diameter	Racemic epinephrine is significantly ($p < 0.005$) more effective than distilled water in the acute relief of upper airway obstruction	The Authors conclude that nebulized racemic epinephrine is an effective treatment for the acute signs of croup
Fogel JM	1982	USA	14 children (aged 4 months to 4.7 years) admitted to hospital with persistent inspiratory stridor at rest after 20 to 30 minutes of mist therapy	Children remained in a mist tent during the study period and received supplemental oxygen as indicated. Randomly assigned to 0.25 mL of 2.25% racemic nebulized epinephrine diluted to 1:3 with isotonic saline ($n = 5$) or the same dose of nebulized racemic epinephrine with IPPB ($n = 9$). 2 hours after first treatment, children were then crossed over to the other treatment	Change in modified Westley croup score	Change in heart rate, respiratory rate, supplemental oxygen, intubation, adverse reactions	There was a highly significant reduction ($p < 0.001$) in croup scores with administration of racemic epinephrine by either nebulization alone or nebulization with IPPB	The Authors conclude that nebulized racemic epinephrine is an effective treatment for the acute signs of croup



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Super DM	1989	USA	29 hospitalized patients with moderate to severe acute laryngotracheitis. Mean (SD) age in months: treatment: 15.5 (5); control: 15.8 (12)	Randomly assigned to i) Parenteral dexamethasone (16 pts); ii) saline placebo (23 pts)	Change in modified Westley croup score	Need of racemic epinephrine, oxygen saturation, respiratory rates, or duration of hospitalization	Statistically significant decline in median croup score from 4.5 to 1.0 (p less than 0.001) in patients receiving dexamethasone. By 24 hours, decline of 2 or > points of the total croup score in 85% of the patients in the dexamethasone group compared with 33% of the patients in the placebo group ($p = 0.027$). Less need of two or more racemic epinephrine treatments (19% in the steroid group; 62% in the placebo (p less than 0.05). No statistical difference between the two groups in improvement in oxygen saturation, respiratory rates, or duration of hospitalization	Dexamethasone is beneficial in reducing the overall severity of moderate to severe acute laryngotracheitis during the first 24 hours after injection
Tibbals J	1992	Australia	70 children aged ≥ 6 months with severe croup requiring intubation	Randomly assigned to i) Prednisolone 1 mg/kg (38 pts); ii) or placebo (32 pts) every 12 h given by nasogastric tube until 24 h after extubation	The duration of intubation and the need for reintubation		Reintubation in 11 (34%) placebo-treated and 2 (5%) prednisolone-treated patients ($p = 0.004$, odds ratio 8.9, 95% CI 1.7-59.3). Shorter duration of intubation with steroid therapy ($p < 0.003$). The median duration of intubation was 138 (95% CI 118-160) h in children who received placebo and 98 (85-113) h in the prednisolone group	Steroid therapy reduces the duration of intubation and the need for reintubation in children intubated for croup
Waisman Y	1992	USA	66 children aged 6 months - 6 years, hospitalized for moderate or severe croup	All patients received mist therapy prior to randomization to either inhaled 2.25% racemic epinephrine ($n = 16$) or 5 mL of 1:1000 L-epinephrine ($n = 15$) (each containing 5 mg L-epinephrine	Change in a modified Downes and Rappaeley croup score at 5, 15, 30, 60, 90 and 120 minutes	Respiratory rate, dexamethasone treatment, supplemental oxygen, intubation	Patients in both groups showed significant transient reduction of the croup score and respiratory rate following the aerosol. No differences in croup score, heart rate, blood pressure, and respiratory rate were assessed over time	L-epinephrine is at least as effective as racemic epinephrine in the treatment of laryngotracheitis and does not carry the risk of additional adverse effect
Husby S	1993	Denmark	36 children (0.4-4.9 years of age) admitted to hospital with croup with a modified WCS > 5	Randomly assigned to receive either 2 mg nebulized budesonide or placebo	Change in modified WCS from baseline to 2 hours; use of antibiotics		2 h after treatment there was a significant improvement in the total score and overall clinical severity in those receiving budesonide	Nebulized budesonide is effective in children and infants with moderate to severe croup



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Klassen TP	1994	Canada	54 children 3 months to 5 years of age were eligible for the study with mild-to-moderate croup	Randomly assigned to receive either 2 mg of nebulized budesonide (27 children) or 4 ml of nebulized normal saline (27 children)	Change in Westley croup score and length of ED stay		The median score was significantly lower in the budesonide group (1 vs. 3, $p = 0.005$); length of ED was also shorter ($p = 0.002$). One week after enrollment, 21 pts assigned to placebo had received dexamethasone, as compared with 15 pts assigned to budesonide ($p = 0.10$), and 7 patients assigned to placebo had been admitted to the hospital, as compared with 1 patient assigned to budesonide ($p = 0.05$)	Authors conclude that nebulized budesonide leads to a prompt and important clinical improvement in children with mild-to-moderate croup
Kristjansson S	1994	Sweden	54 children (0.4-10.8 years) with mild to moderately severe croup	Randomly assigned to 0.5 mg/kg of 2.25% inhaled racemic epinephrine (containing 0.25 mg/kg of L-epinephrine) ($n = 25$) or placebo ($n = 29$)	Change in a modified Westley croup score	Respiratory rate, heart rate, length of stay, additional treatments, betamethasone treatment, re-admission	In both groups, a significant improvement in total mean clinical scores was seen 30 min after inhalation, compared with before inhalation ($p < 0.001$). However, racemic adrenaline was significantly better than placebo in terms of improvement in total clinical score, inspiratory stridor, retractions and air entry	Authors conclude that racemic adrenaline should be used as first-line treatment
Geelhoed GC	1995 a	Australia	80 children (aged 5 to 158 months) hospitalized with croup	Randomly assigned to either 2 mg of nebulized budesonide , dexamethasone syrup (0.6 mg/kg) or a placebo	Length of hospital stay	Change in croup scores	Shorter hospitalization with dexamethasone (12 hr) and budesonide (13 hr) compared to placebo (20 hr) ($p < 0.03$), with no difference between dexamethasone and budesonide. Median time to a croup score of ≤ 1 was shorter with dexamethasone (2 hr) or budesonide (3 hr) compared to placebo (8 hr) ($p < 0.01$). Group scores for both steroids were lower than placebo	Authors conclude that oral dexamethasone and inhaled budesonide are both effective in reducing symptoms and duration of hospitalization in children with croup
Geelhoed GC	1995 b	Australia	120 children hospitalized with croup, aged 6 to 160 months	Randomly assigned to i) oral dexamethasone 0.6 or 0.3 mg/kg (60 pts trial A); ii) oral dexamethasone 0.3 or 0.15 mg/kg (60 pts, trial B)	Duration of hospitalization, reduction in modified Westley croup scores	Need for nebulized adrenaline, numbers of patients admitted to intensive care, rate of return to medical care with recurrence of croup, and readmission to hospital with croup	Similar median duration of hospitalization for children in Trial A (7 and 8 h), and in Trial B (9 and 9 h). Croup scores following treatment did not differ and were significantly lower than initial scores for all groups and in each trial. Other outcome measures were similar for the two groups in each trial	Oral dexamethasone in a dose of 0.15 mg/kg is as effective as 0.3 or 0.6 mg/kg in relieving symptoms and results in a similar duration of hospitalization in children with croup



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Cruz MN	1995	USA	38 patients with acute viral croup, croup score of at least 2 (range 0 to 17), aged 6 months to 5 years	Randomly assigned to: i) Single intramuscular dexamethasone 0.6 mg/kg (19 pts); ii) or an equal volume of normal saline (19 pts)	Lack of improvement or worsening of symptoms 24 hours and 7 to 10 days after discharge	Parents' perception of how the child was doing at 24 hours, based on a 4-point ordinal scale: worse (1), same (2), improved (3), symptoms resolved (4), and the number of days it took for complete recovery	The need of racemic epinephrine was similar in both groups. Five patients required additional medical attention within 48 hours after discharge [4 (21%) from placebo group and 1 (5%) from dexamethasone group]. At the 24-hour telephone follow-up, significantly more patients in the dexamethasone group had a score consistent with improvement compared with placebo (84% vs 42%, $P = .003$). No difference in the number of days for complete resolution of symptoms between the two groups	The use of dexamethasone in the outpatient management of viral croup was associated with a reduction in severity of illness within 24 hours after treatment. Patients with viral croup of moderate severity should be considered as candidates for the use of dexamethasone before discharge from the ED
Geelhoed GC	1996	Australia	100 children with mild croup, aged 4 to 122 months	Randomly assigned to: i) Single dose of oral dexamethasone 0.15 mg/kg; ii) placebo	Return to medical care with ongoing croup	Admission to hospital with croup, duration of croup symptoms, duration of viral symptoms, return to medical care for other reasons	8 children from the placebo group returned to medical care with ongoing croup, 1 being admitted $P < 0.01$. No statistical difference between the two groups for the other outcomes	Oral dexamethasone in a dose of 0.15 mg/kg is effective in reducing return to medical care with ongoing croup in children with mild croup
Klassen TP	1996	Canada	Children 3 months to 5 years of age with a croup score ≥ 3 after at least 15 minutes of mist therapy	All children received 0.6 mg/kg oral dexamethasone and then were randomly assigned to receive 2 mg inhaled budesonide or saline	Change in modified Westley croup score during the 4 hours after treatment		84% ($n = 21$) of the patients who received budesonide had clinically important responses, compared with 56% ($n = 14$) in the placebo group	Children with mild to moderate croup have added, clinically important improvement in symptoms after receiving treatment with budesonide following oral dexamethasone
Fitzgerald D	1996	Australia	Children 0.5 to 6 years of age at the ED with moderate or severe croup	36 pts received budesonide (2 mg/4 mL) and 31 received L-adrenaline (4 mg/4 mL) via nebulization	Change in the total modified Westley croup symptom score to 2, 12, and 24 hours	Readmission to the hospital; intubation, use of epinephrine, and use of additional steroids	All patients had significant improvement from baseline. No significant difference between the two treatments	This study does not show any difference in efficacy and safety between nebulized budesonide and nebulized adrenaline
Godden CW	1997	United Kingdom	87 children admitted to hospital aged 7-116 months	Randomly assigned to: i) initial 2 mg nebulized budesonide followed by repeating dose of 1 mg every 12 hours; ii) initial 4 mL dose of nebulized placebo, followed by a repeating dose of 2 mL placebo every 12 hours	Length of hospital stay and change in WCS at 30 minutes, one, two, four, 12, and 24 hours	Use of epinephrine; intubation rate	Budesonide was associated with a significant improvement in symptoms at 12 hours (95% CI 1 to 3) and 24 hours (95% CI 0 to 3). Patients with WCS above 3 demonstrated a significant improvement in symptoms at 2 hours (95% CI 1 to 3). Nebulized budesonide was associated with a 33% reduction in the length of stay (95% CI 2% to 63%)	Authors conclude that repeated doses of nebulized budesonide are an effective treatment for children admitted to hospital with croup



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Klassen TP	1998	Canada	199 patients with mild or moderate croup presenting at the ED, aged 3 months to 5 years	Randomly assigned to i) Oral dexamethasone , 0.6 mg/kg, and nebulized placebo (69 pts); ii) oral placebo and nebulized budesonide , 2 mg (65 pts); iii) oral dexamethasone , 0.6 mg/kg, and nebulized budesonide , 2 mg (64 pts)	Change in WCS	Oxygen saturation, heart rate, respiratory rate, hospital admission rates, time spent in the ED, return visits to the ED, or ongoing symptoms at 1 week	No difference in the croup score and secondary outcomes among the 3 glucocorticoid regimens. Mean change in WCS was -2.3 (95% CI, -2.6 to -2.0) in the budesonide group, -2.4 (95% CI, -2.6 to -2.2) in the dexamethasone group, and -2.4 (95% CI, -2.7 to -2.1) in the budesonide and dexamethasone group ($p = 0.70$)	Authors recommend that mild-to-moderate croup patients should receive oral dexamethasone or nebulized budesonide in the ED (on the basis of availability of treatment, cost of the drugs, and ease of administration)
Johnson DW	1998	Canada	144 children with moderately severe croup, aged 3 months to 9 years	Randomly assigned to racepinephrine and a single dose of 4 mg of nebulized budesonide (48 children), 0.6 mg/kg of intramuscular dexamethasone (47 children), or placebo (49 children)	Hospitalization rate	Number of additional racepinephrine treatments administered	The overall rates of hospitalization were 71% in the placebo group (35 of 49 children), 38% in the budesonide group (18 of 48 children), and 23% in the dexamethasone group (11 of 47 children) (unadjusted $p = 0.001$ for budesonide vs placebo, $p < 0.001$ for dexamethasone vs placebo, and $p = 0.18$ for budesonide vs dexamethasone). Children treated with budesonide or dexamethasone had greater improvement in croup scores ($p = 0.03$ and $p < 0.001$), and those treated with dexamethasone had a greater improvement than those treated with budesonide ($p = 0.003$)	The Authors conclude that both budesonide and dexamethasone reduce hospitalization rates and are effective in moderate - severe croup, with dexamethasone offering the greatest clinical improvement
Roorda RJ	1998	The Netherlands	17 children aged 4 to 52 months hospitalized with moderate croup	Randomly assigned to 2 doses of 1000 mcg of fluticasone propionate administered by metered dose inhaler or placebo	Change in modified Westley croup symptom score from baseline to 2, 6, and 24 hours	Need for administration of nebulized corticosteroids with a nebulizer, need for intubation, and duration of hospitalization	In all children the clinical course was favorable, without any significant differences between the actively treated and placebo-treated group	Small group of patients. This study did not demonstrate therapeutic benefits of fluticasone propionate when administered with an MDI and a spacer compared with placebo
Pedersen LV	1998	Denmark	59 children aged 3 months to 6 years (mean 20 months)	Randomly assigned to inhalations of 1000 micrograms budesonide or dexamethasone 0.6 mg/kg i.m	Change in a modified Westley-score		Improvement for all children after 3, 6 and 12 hours, with better scores with dexamethasone after 6 and 12 hours	Article in Danish: Authors recommend dexamethasone 0.6 mg/kg intramuscularly



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Roberts GW	1999	Australia	82 children hospitalized with croup aged 6 months to 8 years, croup score of ≥ 4 ;	Randomly assigned to either 2 mg of inhaled budesonide or placebo 12 hourly (maximum four doses)	Change in modified Liepzig croup score at 0, 2, 6, 12, 24, h from initial nebulization	Revisits to the hospital for follow-up; 2: use of epinephrine	Improvement was observed in the budesonide group ($p = 0.04$). 3 days after discharge 7/ 32 placebo-treated pts and 1/ 34 budesonide-treated pts had sought further medical follow-up ($p = 0.02$)	Twelve-hourly dosing with inhaled budesonide significantly improved symptoms of croup as well as decreased relapse rates when compared with placebo
Rittichier KK	2000	USA	277 children with moderate croup, aged 3 months to 12 years	Randomly assigned to i) Single dose of intramuscular (139 pts) or ii) oral dexamethasone (138 pts) (0.6 mg/kg, maximum 8 mg)	Need for further therapy or evaluation after the initial ED visit	Parental report of improvement at the follow-up phone call	At phone follow-up, 141 (51%) had total resolution of symptoms (75 in IM, 66 in PO). Eighty patients (29%) returned for further evaluation (45 in IM, 35 in PO). Twenty-three (8%) received either more steroids, racemic epinephrine, or admission (11 in IM, 12 in PO)	No statistically significant difference was found in the need for subsequent interventions after a single dose of either IM or PO dexamethasone. A single PO dose can be effectively and safely used for the outpatient treatment of moderate croup
Donaldson D	2003	USA	96 children with moderate-to-severe croup, aged 3 to 84 months	i) Intramuscular dexamethasone 0.6 mg/kg and an oral placebo; ii) oral dexamethasone 0.6 mg/kg	Resolution of symptoms at 24 hours after treatment administration	Resolution of symptoms at 10 days; interval to complete resolution of symptoms	At 24 hours and 10 days after the visit, there were no statistical differences between the groups for the proportion with stridor, expiratory sounds, barking cough, sleep pattern, the degree of improvement, or the proportion with complete resolution of symptoms at one day	No statistical differences for any parameters were observed between IM and PO dexamethasone treatments for children with moderate-to-severe croup at 24 hours or at any time the week after treatment
Cetinkaya F	2004	Turkey	60 children aged 6 to 36 months	Randomly assigned to i) nebulized 500 mcg budesonide + a single dose of oral placebo + 2 mL intramuscular placebo; ii) 2 mL nebulized placebo + a single dose oral placebo + 0.60 mg/kg intramuscular dexamethasone ; iii) 2 mL nebulized placebo + a single dose of oral Dexamethasone 0.60 mg/kg + 2 mL intramuscular placebo; iv) 2 mL intramuscular placebo + 2 mL nebulized salbutamol solution with saline + oral placebo	Change in WCS		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	Details are missing on the protocol and especially on any measures taken to blind participants and personnel from treatment. Authors conclude that the three treatments have the same effectiveness, and the choice depends on conditions of the patient and the physician



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Bjornson C	2004	Canada	720 children with mild croup aged 3 months to 9 years	i) Single dose of oral dexamethasone (0.6 mg/kg); ii) or placebo	Return to a medical care provider for croup within seven days after treatment	Presence of ongoing symptoms of croup on days 1, 2, and 3 after treatment; economic costs, hours of sleep lost by the child, and parent's stress	Return to medical care was significantly lower in the dexamethasone group (7.3 percent vs. 15.3 percent, $p < 0.001$). In the dexamethasone group, there was quicker resolution of croup symptoms ($p = 0.003$), less lost sleep ($p < 0.001$), and less stress on the part of the parent ($p < 0.001$)	For children with mild croup, dexamethasone is an effective treatment that results in consistent and small but important clinical and economic benefits
Geelhoed GC.	2005	Australia	72 children (aged 3 to 126 months) hospitalized with croup	Randomly assigned to either 2 mg of nebulized budesonide or placebo, with all children receiving a single oral dexamethasone dose of 0.15 mg/kg	Length of hospital stay	Change in croup scores, use of nebulized epinephrine, duration of croup symptoms, duration of viral symptoms, and return to medical care after discharge	No difference in any outcome measures for the 2 groups	The Authors conclude 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
Alshehr M	2005	Saudi Arabia	72 children with acute laryngotracheobronchitis, moderately severe respiratory distress, aged 3 months to 9 years	Randomly assigned to i) Oral dexamethasone (0.15 mg/kg); ii) oral dexamethasone (0.6 mg/kg)	Change in Westley croup score per 12-hour; classification of patients as having a favorable clinical response at 12 and 24 hours after treatment	Reduction in croup score, hospitalization rate (also in ICU) and admission, duration of hospital stay, adrenaline usage, change in RR and O2 saturation	Twelve hours from the time of treatment, the patients in group A (0.6 mg/kg oral dexamethasone) as well as the patients in group B (0.15 mg/kg oral dexamethasone) had statistically significant decline in median croup score from 4.5 to 2 ($p = 0.01$) and from 5 to 2 ($p = 0.01$), respectively. The overall rate of hospitalization after treatment in group A was 15/36 children (41.6%) and in group B it was 14/36, (38.9%) ($p = 0.36$). The median hospital stay (hours) for group A was 28 h (12-50) and for group B was 26 h (14-48) ($t = -0.32$, $p = 0.64$)	Oral dexamethasone in a dose of 0.15 mg/kg is as effective as a dose of 0.6 mg/kg in relieving symptoms of acute croup in children and results in similar reduction in the croup score, the adrenaline usage and the overall hospital admission rate and the duration-stay
Amir	2006	Israel	52 children presenting to the ED, with a modified Westley croup score of 0 to 11, aged 6 months to 6 years	Randomly assigned to i) IM dexamethasone 0.6 mg/kg; ii) PO betamethasone 0.4 mg/kg	Changes in the Westley croup score	Need for additional treatment in the ED, hospitalization rate, need for additional treatments, and the rate of follow-up physician visits after discharge	Significant reduction in the croup score after treatment in both groups; no significant differences between croup scores at 4 hours ($p = 0.18$). No differences between groups in the hospital admission rate, time to resolution of symptoms, need for additional treatments, or number of return ED visits	PO betamethasone and IM dexamethasone have similar efficacy in the management of mild to moderate viral croup



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Sparrow A	2006	Australia	133 children, with mild to moderate croup, aged 3 to 142 months	Randomly assigned to i) Single oral dose of dexamethasone 0.15 mg/kg (68 pts); ii) or single oral dose of prednisolone 1 mg/kg (65 pts)	Re-presentation to medical care at 7 to 10 days	Croup score, adrenaline use, time spent in the ED, duration of croup and viral symptoms	19 of 65 children (29%) from prednisolone group reattended medical care compared with 5 of 68 (7%) from the dexamethasone group. The confidence intervals around this 22% difference in outcome were 8% to 35%, outside the 0% to 7.5% range of equivalence. There were no significant differences in other outcomes	A single oral dose of prednisolone is less effective than a single oral dose of dexamethasone in reducing re-presentation to medical care in children with mild to moderate croup
Filbot AA	2007	Australia	99 children presenting to the ED with WCS ≥ 2 , aged 6 months to 6 years	i) Single oral dose of prednisolone 1 mg/kg (34 pts); ii) single oral dose of dexamethasone 0.15 mg/kg (34 pts); or single oral dose of dexamethasone 0.6 mg/kg (31 pts)	The magnitude and rate of reduction in WCS, rate of return for medical care	The proportion of subjects requiring admission or salvage therapy (nebulized adrenaline)	There were no significant differences in primary or secondary outcome measures between the three treatment groups	Both prednisolone 1 mg/kg and low-dose dexamethasone 0.15 mg/kg were found not to differ in efficacy from the currently recommended 0.6 mg/kg dexamethasone
Chut-Uppakarn S	2007	Thailand	41 children admitted to hospital, with moderate to severe croup, aged 6 months to 5 years	Randomly assigned to i) Single intravenous injection of dexamethasone 0.6 mg/kg (maximum dose 12 mg); ii) or dexamethasone 0.15 mg/kg (maximum dose 3 mg)	The difference of WCS at the end of the study	Time to WCS equal or less than two	The mean WCS were significantly reduced from baseline values in both groups at 1h after injection ($p < 0.01$). No difference in the mean WCS between the two groups at any time. Median times to croup scores equal or less than two in both high- and low-dose groups were 8 and 7.9 h, respectively	Dexamethasone 0.15 and 0.6 mg/kg are equally effective in the treatment of moderate to severe croup
Eboriadou M	2010	Greece	64 Children 6 months to 5 years of age, with a croup score of at least 2	Randomly assigned to receive either 5 mL nebulized epinephrine (1:1000), a single intramuscular injection of dexamethasone 0.6 mg/kg, or inhaled beclomethasone dipropionate 200 mcg, via aerochamber device	Change in a modified Downes and Raphaely croup score	Return visits to the ED	Significant improvement of the croup score was noticed at the end of observation time in all groups: beclomethasone was found as effective as intramuscular dexamethasone	The Authors conclude that the use of inhaled beclomethasone could be useful in the treatment of croup
Dobrovoltac M	2012	Australia	70 children with mild-moderate croup, aged above 6 months	Randomly assigned to i) Oral dexamethasone 0.15 mg/kg (35 pts); ii) or oral placebo solution (35 pts)	Change in WCS at 10 min intervals over 1 h		Growing trend to a lower WCS in the dexamethasone group, evident from 10 min and statistically significant from 30, 40, 50 and 60 min (mean of 1 vs 1.9)	An oral dose of 0.15 mg/kg dexamethasone offers benefit by 30 min
Garbutt JM	2013	USA	87 children with mild-moderate croup, aged 1 to 8 years	Randomly assigned to i) Oral prednisolone 2 mg/kg/d for 3 days (41 pts); ii) 1 oral dose of dexamethasone 0.6 mg/kg; iii) and 2 doses of placebo (46 pts)	Additional health care for croup within 11 days of randomization	Duration of croup symptoms, nights with disturbed sleep, parental stress	No differences for patients treated with dexamethasone or prednisolone for additional health care for croup (2% vs 7%, $p = 0.34$), duration of croup symptoms (2.8 vs 2.2 days, $p = 0.63$), non-barky cough (6.1 vs 5.9 days, $p = 0.81$), nights with disturbed sleep for the parent (0.68 vs 1.21 nights, $p = 0.55$), and days with stress (1.39 vs 1.56 days, $p = 0.51$)	No differences in patient or parent outcomes between one oral dose of dexamethasone 0.6 mg/kg and a 3-day course of oral prednisolone 2 mg/kg once per day



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Soleimani G	2013	Iran	86 children with croup score < 7, aged 6 months to 6 years (mean age 26.3 ± 1.5 months)	Randomly assigned to i) Intramuscular dexamethasone 0.6 mg/kg; ii) oral dexamethasone 0.6 mg/kg	Changes in clinical score, RR, HR, O2 saturation and clinical response assessed before and then hourly for four hours after treatment		The RR of two groups was significantly different at the first hour of treatment ($p = 0.02$), but it did not vary between study groups at the second, third, and fourth hour of treatment. There was no statistical difference among clinical score, heart rate, O2 saturation and clinical response in any of the measurement times	Oral and intramuscular administrations of dexamethasone have the same effectiveness for treatment of croup
Parker CM	2019	Australia	1231 children with croup, aged > 6 months	Randomly assigned to: i) Oral dexamethasone 0.6 mg/kg (410 pts); ii) oral dexamethasone 0.15 mg/kg (410 pts); iii) oral prednisolone 1 mg/kg (411 pts)	Changes in WCS 1-hour after treatment and unscheduled medical re-attendance during the 7 days after treatment	Total hospital stay, ED length of stay, vomiting, use of nebulized epinephrine, endotracheal intubation, need for additional steroid doses, and need for admission to an inpatient ward, emergency short-stay unit, or ICU	Mean WCS at baseline was 1.4 for dexamethasone, 1.5 for low-dose dexamethasone, and 1.5 for prednisolone. Adjusted difference in scores at 1 hour, compared with dexamethasone, was 0.03 (95% confidence interval -0.09 to 0.15) for low-dose dexamethasone and 0.05 (95% confidence interval -0.07 to 0.17) for prednisolone. Re-attendance rates were 17.8% for dexamethasone, 19.5% for low-dose dexamethasone, and 21.7% for prednisolone (not significant) [$P = .59$ and $.19$]. No differences for the other outcomes were recorded between groups	Non inferiority was demonstrated for both low-dose dexamethasone and prednisolone

Legend: ED, emergency department; pts, patients; WCS, Westley Croup Score; CI, confidence interval; HR, heart rate; RR, respiratory rate; IM, intramuscular; PO, per os; h, hours.

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