

The Comparison of Oral and IM Dexamethasone Efficacy in Croup Treatment

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Background: Croup, or acute laryngotracheobronchitis, is the most common cause of upper airway obstruction in children.

Objectives: In this study, the efficacies of intramuscular and oral dexamethasone administration are compared for treatment of croup.

Patients and Methods: This is a single-blind randomized trial involving 68 children divided into two groups, the first group received 0.6 mg/kg intramuscular dexamethasone and the second group received 0.6 mg/kg oral dexamethasone. The clinical score, respiratory rate, heart rate, O₂ saturation and clinical response were assessed before and then hourly for four hours after treatment.

Results: The respiratory rate 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.

Conclusions: Oral and intramuscular administrations have the same effectiveness for treatment of croup and oral dexamethasone was proposed because this is a non-invasive procedure.

Keywords: Croup; Corticosteroid; Dexamethasone

1. Background

Croup (or laryngotracheobronchitis) is a respiratory condition that is usually triggered by an acute viral infection of the upper airway ducts. The infection leads to inside throat swelling, which interferes the normal breathing and produces the classical symptoms of a "barking" cough, stridor, and hoarseness. It may produce mild, moderate, or severe symptoms, which often worsen at night. The most important diagnoses to differentiate the croup include bacterial tracheitis, epiglottitis, and inhalation of a foreign body (1). Croup occurs most commonly between the ages of 6 months and 12 years, with a peak incidence being around 2 years of age (2). At least 60% of children who are admitted in the emergency care ward have mild symptoms and are routinely discharged without any observation and treatment. Of these children with mild croup, most have transient symptoms and 15% or less seek additional medical care (2). Cool mist, nebulized racemic epinephrine, and steroids are frequently used in the emergency management of croup (3).

During the past 50 years, there has been considerable controversy regarding croup therapies. Nebulized ste-

roid might work faster than the oral version; according to some reports of animal studies it has fewer side effects, although their occurrence is rare. Direct comparison of different steroids and routes of administration have been sparsely studied. There were no significant differences between dexamethasone and nebulized budesonide regarding short term hospitalization responses. In another study, the children who were treated using oral dexamethasone appeared to need additional treatment with nebulized budesonide. The most recent studies showed that intra-muscular dexamethasone is more effective in reducing croup scores and hospital admissions, compared to nebulized budesonide (3). However, the marked success of corticosteroids in the outpatient management of croup and the effectiveness of nebulized epinephrine in more severe cases have led many controversies to be resolved (4). Dexamethasone is a corticosteroid with a predominant glucocorticoid activity. In terms of anti-inflammatory potential and in comparison with prednisolone, dexamethasone is five to six times more potent. From traditional point of view, dexamethasone is categorized as long-term-activity corticosteroids class with a biological

Implication for health policy/practice/research/medical education:

The purpose of this study was to compare the efficacy of oral and IM dexamethasone in treatment of children with croup in emergency department. We concluded that oral and IM dexamethasone have equal effectiveness in the treatment of mild to moderate croup. As oral dexamethasone has many advantages, we proposed oral dexamethasone administration instead of intramuscular route.

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half-life time of 36 to 72 hours. Suppression of the hypothalamic-pituitary axis by dexamethasone, could take up to 2.5 days. Dexamethasone is well and quickly absorbed by the gastrointestinal tract, binds to the plasma points easily and is extracted from the urine (4, 5).

The literature around the croup which supported the use of steroids was mostly based on hospitalized patients who were mainly treated with IM (intramuscular) doses. The PO route of administration has as effective assumed serum concentration as the IM route, and its absorption and bioavailability are approximately 80% (2). Since the majority of children with croup showed mild symptoms and a transient, uncomplicated course, we thought it is essential to have clear evidences before advocating corticosteroid treatment for this large subgroup of children.

2. Objectives

The purpose of this study was to compare the efficacy of oral and IM dexamethasone in treatment of children with croup in emergency department.

3. Patients and Methods

This is a randomized controlled clinical trial. From January 2009 to March 2010, all patients from 6 months to 6 years were admitted to emergency ward of Ali-Ebne Abitaleb Hospital with barking cough, stridor, hoarseness and respiratory distress were enrolled in this study. Exclusion criteria were chronic pulmonary disease, severe croup (croup score > 7), recurrent croup, allergy to corticosteroids, contraindication of corticosteroid (history of tuberous sclerosis, history of varicella infection during the past three weeks), history of corticosteroid administration during the last four weeks, foreign body, epiglottitis, bacterial tracheitis and immune deficiency. The patients were randomly divided into two groups. Ethical approval was obtained from the relevant local ethics committees. All parents were thoroughly informed about the study and received information leaflets.

All patients were treated with cool mist therapy. The patients were divided into two groups: Group A received 0.6 mg/kg IM dexamethasone and group B received 0.6 mg/kg oral dexamethasone. Main investigators (Gh. Soleimani) randomly divided patients into two groups. Responses to the treatment were measured by A. Daryadel who was blinded to the study groups. To access the severity of croup, Westley croup score was used (Table 1). Croup score, respiratory rate, heart rate, O2 saturation were recorded before treatment and on the first, second, third and fourth hours after treatment. Variables were expressed as means ± standard deviation. All data analysis was performed using SPSS version 16. Table 1 shows Westley croup scoring system as following (5).

Table 1. Westley Croup Scoring System

Indicator of Disease Severity	Score
Stridor	
None	0
Only with agitation or excitement	1
At rest with stethoscope	2
At rest without stethoscope	3
Retraction	
None	0
Mild	1
Moderate	2
Sever	3
Air entry	
Normal	0
Decreased	1
Severely decreased	2
Cyanosis	
None	0
With agitation	4
At rest	5
Level of consciousness	
Normal	0
Alerted mental status	5

4. Results

One hundred patients enrolled into the study. Twenty patients had exclusion criteria: severe croup (6 patients), foreign body (2 patients), previous treatment with corticosteroid (6 patients) and immunodeficiency due to chemotherapy (6 patients). Twelve patients did not finish the study. Eighty six patients (between 6 months to 6 years) finished the study. The mean age of patients was 26.3 ± 1.5 months. Thirty six (53%) were male and 32 (47%) were female. There were no significant statistical differences between groups in case of age, gender, and croup scores (Table 2). The hourly respiratory rates in 4 hours are showed in Table 3. The respiratory rate was not significantly different statistically except at the first hour after treatment (P value: 0.02).

The mean changes of heart rates after each measuring time were not significantly different (P values 0.65, 0.16, 0.28, 0.21 for the 1st, 2nd, 3rd and 4th hours of treatment, respectively). The mean changes of O2 saturation after 1, 2, 3 and 4 hours were not statistically significantly different (P values 0.27, 0.70, 0.80, 0.19 on 1st, 2nd, 3rd and 4th hours of treatment, respectively). At the same way the mean changes of croup score after each measurement time did

Table 2. Comparison of Basic Characteristic Between Two Groups

	Group A (IM)	Group B (Oral)	P Value
Male/Female	19/17	17/15	
Age, y, mean ± SD	27.6 ± 3.8	25.7 ± 2.1	0.81
Croup Score, Mean ± SD	1.81 ± 0.59	2.03 ± 0.47	0.51
Respiratory Rate, mean ± SD	49.30 ± 7.5	52.56 ± 8.13	0.92
Heart Rate, mean ± SD	134.58 ± 21.44	134.66 ± 19.08	0.98
O2 Saturation, mean ± SD	89.80 ± 4.6	90.65 ± 5.03	0.471

Table 3. The Respiratory Rate After Treatment

Hour	1	2	3	4
Group A, mean ± SD	41.66 ± 6.44	40.00 ± 6.65	36.72 ± 5.64	35.61 ± 6.01
Group B, mean ± SD	45.53 ± 7.12	42.00 ± 7.94	39.03 ± 6.52	36.75 ± 4.05
P Value	0.02	0.26	0.12	0.36

not have significant statistical difference (P values 0.65, 0.63, 0.32, 0.24 for the 1st, 2nd, 3rd and 4th hours of treatment, respectively). One patient from group A (2.7%) and one patient from group B (3.1%) were admitted to the pediatric ward because of no response to the treatment.

5. Discussion

Croup is a disease caused due to the acute obstruction of the laryngeal area. Croup is mainly among the laryngotracheobronchitis caused by a viral agent such as parainfluenza virus, and acute spasmodic croup, which usually occurs recurrently as a mild disorder without a viral prodrome and fever (2). Spasmodic croup has been related to hyperactivity of the upper airway and allergic disease, thought this view has been challenging. It has been suggested that the two entities represent two ends of a board spectrum in the clinical presentation of a single disease (3). Corticosteroid therapy is now routinely recommended by all experts (4). Compared to the placebo, IM dexamethasone accelerates the recovery (4, 5). The ordinary and routine treatment with humidification is not effective, however it is traditional. Nebulized adrenaline is effective, but because of its short-term action and severe side effects, it is not recommended for general use. As shown in some trails and meta-analyses, when the oral and intra-muscular steroid treatments are administrated in proper doses, they can be effective in curing moderate to severe croups. Since nebulized administration has fewer side effects and more rapid action, it is preferred to oral or intra muscular route. However, the debates on the effectiveness of nebulized steroid administration still

exist. There are many trials that compare different routes of corticosteroid administration (1, 6-10).

This is a randomized controlled trial comprising 68 children between six months to six years with mild to moderate croup that received oral or intramuscular dexamethasone and their respiratory rate, heart rate, O2 saturation and croup score was assessed after the treatment. A meta-analysis has shown that treatment with glucocorticoids is effective in improving the symptoms of croup in children in the first 6 hours up to at least 12 hours of treatment (1). Steroids can be used orally and intramuscular as well as nebulized form (3). In Cetinkaya F. et al. study, which compared the nebulized budesonide, and IM and oral dexamethasone for treatment of croup, the croup score of these three regiments were reported significantly lower than the placebo group, but there were no statistical differences among them (3).

In the meta-analysis of Kayris et al. there appeared to be a dose-response effect of steroids in croup (11). In both meta-analysis and studies of Kuusela and Super et al., which used high doses of steroids and both of which showed a beneficial effect from drug treatment (12, 13). In the similar way Donalsidson et al. mentioned that no statistical differences for any parameters were observed between IM and PO dexamethasone treatment for children with moderate to severe croup at 24 hours or at any time of a week after treatment (6). In the present study, except the respiratory rate after one hour, no statistical significant differences between two groups in none of parameters were observed. In a study that assessed the efficacy of oral versus intramuscular dosing of dexamethasone in the outpatient treatment of moderate croup, no statistically difference was found in the need for subsequent interventions after a single dose of either IM or PO dexamethasone (2).

Children with mild croup who enrolled in Luria et al. study received oral dexamethasone are less likely to seek subsequent medical care and demonstrate more rapid symptoms resolution compared with children who received nebulized dexamethasone or placebo treatment (7). One patient from each group of this study needed more treatment than the other ones admitted in pediatric ward (P < 0.05). In a prospective randomized trial, intramuscular dexamethasone (as an effective but painful treatment) was compared with betamethasone (an oral and equally potent glucocorticoid) for the treatment of mild to moderate viral croup. Finally the results were shown no difference between oral betamethasone and intramuscular dexamethasone in the management of mild to moderate viral croup (8).

In our investigation and similar studies, both oral and intramuscular dexamethasone has advantages and disadvantages. The advantages of oral dexamethasone are easy to apply, and more widely available for the office physician. It is inexpensive, has no risks like infection at the injection site, and it is also does not cause pain and

anxiety which may occur during intramuscular administration (3). The major disadvantage of oral use is its unpleasant taste that causes vomiting (3). In Kristine et al., reported one patient vomited the initial dose of PO dexamethasone and later tolerated a repeated dose of PO medicine (2). Oral dexamethasone preparations were well tolerated by all patients studied by Cetinkaya et al. (3). In our study, there was no evidence from vomiting among the group B patients.

We conclude that oral and IM dexamethasone is equally effective in the treatment of mild to moderate croup. As oral dexamethasone has many advantages, we purposed oral dexamethasone administration instead of intramuscular route.

5.1. Limitations

Although the research has reached the defined aims, there were some unavoidable limitations. First because of the time shortage, this research was conducted only on a small size of population. It was difficult to gain significant results for our primary outcome measures.

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Authors' Contribution

Study concept and design: Gholamreza Soleimani and Alireza Daryadel. Analysis and interpretation of data: Gholamreza Soleimani, Alireza Daryadel and Mohammad Reza Sharif. Manuscript drafting: Mohammad Reza Sharif. Critical revision of the manuscript for important intellectual content: Gholamreza Soleimani. Statistical analysis: Alireza Ansari Moghadam.

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