Randomized Controlled Trial of Dexamethasone in Infectious Croup

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Abstract

Infectious croup is a common and an important cause of upper airway obstruction in young children. Despite its frequency and potentially serious nature, there is still no definite conclusion regarding the beneficial effect of corticosteroid. A randomized controlled study on the effects of dexamethasone in infectious croup was conducted at the Department of Pediatrics, Ramathibodi Hospital between January 1985 and September 1986.

Thirty-two patients, 2-37 months old, were included in this study. Fourteen patients received dexamethasone (0.5 mg/kg/dose daily for 3 days) and eighteen patients were the control group. The dexamethasone group had significantly lower croup scores at 48 hour ($p < 0.05$), shorter hospital course ($p < 0.005$) and lower incidence of endotracheal intubation ($p < 0.05$) than the control group. Five patients in the control group required endotracheal intubation. Complications included four episodes of pneumonia, one episode of sepsis, and one bacterial tracheitis. Pneumonia and sepsis occurred only in the control group. We concluded that dexamethasone therapy decrease the severity of infectious croup and the risk of complications.

Infectious croup is a common and an important cause of upper airway obstruction in young children[1,2]. "Standard" treatment includes oxygen, hydration and racemic epinephrine but there is no definite conclusion regarding the beneficial effect of corticosteroids[1-5]. This prospective randomized control study aimed to determine the beneficial effect of dexamethasone in children with moderate to severe infectious croup.

PATIENTS AND METHOD

The study was conducted at the Department of Pediatrics, Ramathibodi Hospital from January 1985 to September 1986. The study design

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Table 1. Upper airway obstruction score (Downes JJ and Raphaely R. Pediatric intensive care. Anesthesiology : 1975; 43: 201-50).

Score	0	1	2
- Cough	none	hoarse cry	bark
- Stridor	none	inspiratory	inspiratory + expiratory
- Retraction & nasal flaring	none	suprasternal retraction	intercostal, substernal, and suprasternal retraction
- Inspiratory breath sound	none	harsh with rhonchi	delayed
- Cyanosis	none	in room air	in 40% O_2

score < 3 = mild degree of airway obstruction
score 4-6 = moderate degree of airway obstruction
score > 7 = severe degree of airway obstruction

was a randomized controlled trial involving patients aged below 5 years who had a clinical diagnosis of infectious croup with Downe's upper airway obstruction score not less than 3 (Table 1)[6]. Patients were eligible or included if they had clinical onset of croup i.e. hoarseness or barking cough, or stridor for less than 3 days. Patients who had diphtheria, measles, or foreign body aspiration were excluded from the study.

Initial investigations included complete blood count, nasopharyngeal suction culture for bacteria (blood agar and chocolate agar with supplement for *Hemophilus influenzae*) and virus (rhesus monkey kidney, human lung fibroblast, and HEP_2). Acute and convalescence serum titre for 6 viruses i.e. hemagglutination inhibition test for influenza A, B; complement fixation test for respiratory syncytial virus, adenovirus, and parainfluenza type 1, 3. With informed consent from the parents, the patients were randomized to receive dexamethasone 0.5 mg/kg/d intramuscular/ intravenously for 3 consecutive days or to be a control group. Other treatment i.e. aerosolized adrenaline (1:1000) 0.05 ml/kg/dose (maximum 0.5 ml) *via* face mask, antibiotics, intravenous fluid, and cool mist were left to the decision of the attending physicians.

Downe's scores were determined on admission, 24, and 48 hours after admission consecutively. The patients were intubated when the upper airway obstruction score was 7 or more. Complications were recorded during admission and until 3 weeks after discharge from the hospital. Statistical analysis using Mann-Whitney U test and Fischer's exact test was done to compare upper airway obstruction score, duration of hospital stay and risk of endotracheal intubation in the patients.

RESULTS

Thirty-two patients, male to female ratio = 3:1, were included in the study. The patients were aged 2-37 months, 75 per cent of them were aged between 6 to 18 months. Viral isolation and/or serology were positive in 14 cases i.e. influenza A in 2 cases, parainfluenza type 1 in 6, parainfluenza type 3 in 5, and parainfluenza unknown type in 1. No virus or bacteria was demonstrated in 9 cases and the results were inconclusive in 9 cases. Fourteen patients received dexamethasone and eighteen patients were controls. Mean age, initial upper airway obstruction score, episode of aerosolized adrenaline *via* face mask, and 24 hour-upper airway obstruction score were not different between the control and dexamethasone group ($p>0.05$). The dexamethasone group had lower 48 hour-upper airway obstruction score, shorter hospital stay, and lower incidence of endotracheal intubation than control (Table 2). Complications included pneumonia in 4 controls, *Acinetobacter* sepsis in 1 control, and bacterial tracheitis in 1 cases.

DISCUSSION

Age distribution, male sex preponderance and etiologies found in this study were similar to other studies[1,2,4,7]. The mean age, initial score, and aerosolized adrenaline in the dexamethasone group were not different from controls. Although score at 24 hour in the dexamethasone group was not different from controls, 2 patients from the control group already required endotracheal intubation and thus were not included in the statistical analysis. At 48 hour, dexamethasone group had

Table 2. Comparing control and study group.

	Control (mean ± S.D.)	Dexamethasone (Mean ± S.D.)	t	p
Mean age (month)	16.72 ± 9.34	11.64 ± 4.65	1.9	> 0.05(1)
Initial upper airway obstruction score	5.06 ± 0.99	5.21 ± 0.77	0.568	> 0.05(1)
Adrenaline prescribed (episode)	1.45 ± 1.21	1.21 ± 0.80	0.639	> 0.05(1)
24 hour upper airway obstruction score	3.25 ± 1.34*	3.34 ± 1.28	0.466	> 0.05(1)
48 hour upper airway obstruction score	3.07 ± 1.82**	2.27 ± 1.10$	1.918	< 0.05(1)
Duration of Hospital stay (day)	9.08 ± 7.34	3.18 ± 1.35	3.230	< 0.005(1)
Hospital stay (day)	5.42 ± 3.28*	3.18 ± 1.35	2.426	< 0.025(1)
Endotracheal intubation (case)	5	0	-	< 0.05(2)

* excluding 2 patients who had endotracheal intubation
** excluding 2 patients who were discharged
$ excluding 3 patients who were discharged
(1) Mann Whitney U test
(2) Fischer's exact test

significantly lower obstruction score than the controls, 2 patients from the control group and 3 patients from the dexamethasone group were discharged from the hospital and were not included. Five patients (15%) in this study required endotracheal intubation, notably they were all in the control group. According to Sholnik's, 1-5 per cent croup patients require endotracheal intubation[8]. This difference may be due to the rather small number of cases in this study and also probably because only patients who had moderate to severe obstruction scores were included. The dexamethasone group also had a shorter duration of hospital stay ($p<0.005$), even when endotracheal intubated patients were excluded ($p<0.025$). This study agreed with others that corticosteroid is beneficial for the treatment of infectious croup[4,5,9,10] and dexamethasone does not increase the risk of secondary bacterial infection in this study as well as others [3,11]. The drug may even decrease serious complication e.g. bacterial pneumonia due to prolonged and severe airway obstruction and/or endotracheal intubation.

We conclude that appropriate use of dexamethasone in patients with infectious croup can reduce the risk of endotracheal intubation and the duration of hospitalization without increasing the risk of infections.

(Received for publication on February 28, 1996)

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การศึกษาเปรียบเทียบผลการรักษาโรคครูพ โดยใช้เดกซาเมธาโซน

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Croup เป็นโรคที่พบบ่อยและเป็นสาเหตุสำคัญอย่างหนึ่งของการอุดกั้นทางเดินหายใจส่วนบนในเด็กเล็ก การประเมินประสิทธิภาพของการรักษาโดยการใช้คอร์ติโคสเตียรอยด์ร่วมไปกับการรักษาประคับประคองอย่างอื่นยังไม่มีผลสรุปที่แน่นอน ผู้ทำการศึกษาได้ทำการศึกษาเปรียบเทียบผลการรักษาโรค croup โดยใช้เดกซาเมธาโซนกับกลุ่มควบคุม ในผู้ป่วยโรค croup ที่โรงพยาบาลรามาธิบดี ตั้งแต่เดือนมกราคม 2528 ถึง กันยายน 2529

มีผู้ป่วยร่วมในการศึกษาครั้งนี้ 32 ราย เป็นชาย : หญิง = 3 : 1 อายุระหว่าง 2–37 เดือน กลุ่มที่ได้เดคสาเมธาโซน (14 ราย) มีดัชนีการอุดกั้นทางเดินหายใจส่วนบน ที่ 48 ชม. น้อยกว่า ($p < 0.05$), อยู่โรงพยาบาลเป็นระยะเวลาสั้นกว่า ($p < 0.005$), และต้องใส่ท่อหลอดลมคอน้อยกว่า ($p < 0.05$) กลุ่มควบคุม (18 ราย) มีผู้ป่วยที่อาการรุนแรงถึงต้องใส่ท่อหลอดลมคอ 5 ราย อาการแทรกซ้อนที่พบในผู้ป่วย มีปอดอักเสบ 4 ราย, เซพสิส 1 ราย, หลอดลมอักเสบ 1 ราย อาการแทรกซ้อนรุนแรงเกิดเฉพาะในกลุ่มควบคุมเท่านั้น ผู้ทำการศึกษาเสนอว่าการใช้เดกซาเมธาโซนในขนาดและระยะเวลาที่เหมาะสมร่วมกับการรักษาประคับประคองอื่น ๆ อาจจะสามารถลดความรุนแรงของโรค croup และภาวะแทรกซ้อนที่อาจเกิดตามมาได้

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