

Controlled Delivery of High vs Low Humidity vs Mist Therapy for Croup in Emergency Departments

A Randomized Controlled Trial

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VIRAL CROUP, THE MOST COMMON cause of acute upper airway obstruction in children, is diagnosed in up to 5% of children younger than 6 years, of whom approximately 1% are hospitalized.^{1,2} The infection leads to inflammation of the upper airway and subglottic obstruction. Corticosteroids reduce the frequency and duration of hospitalization and³⁻⁵ the need for intubation^{6,7} and inhaled epinephrine³⁻⁵ in children with severe croup and result in a lower rate of return for medical care compared with placebo in milder cases.⁸

Humidity has long been a treatment for croup, using kettles,⁹ blow-by humidity, croup tents, and face masks, and humidity is still used, despite the lack of scientific evidence.¹⁰⁻¹² It may help in croup by the associated warmth and comfort improving patients' respiratory status.¹⁰ Aerosolized water may soothe inflamed laryngeal mucosa and decrease the viscosity of secretions, and purulent mucus has been shown in vitro to gain water and to decrease in viscosity after exposure to 100% humidity.¹³ Some suggest that subglottic narrowing causes turbulent air flow and drying of the airway and that moisture may

Context Children with croup are often treated with humidity even though this is not scientifically based, consumes time, and can be harmful. Although humidity using the traditional blow-by technique is similar to room air and no water droplets reach the nasopharynx, particles sized for laryngeal deposition (5-10 μm) could be beneficial.

Objective To determine whether a significant difference in the clinical Westley croup score exists in children with moderate to severe croup who were admitted to the emergency department and who received either 100% humidity or 40% humidity via nebulizer or blow-by humidity.

Design and Setting A randomized, single-blind, controlled trial conducted between 2001 and 2004 in a tertiary care pediatric emergency department.

Participants A convenience sample of 140 previously healthy children 3 months to 10 years of age with Westley croup score of more than 1 or 2 or higher (scoring system range, 0-17); 21 families refused participation.

Intervention Thirty-minute administration of humidity using traditional blow-by technique (commonly used placebo, n=48), controlled delivery of 40% humidity (optimally delivered placebo, n=46), or 100% humidity (n=46) with water particles of mass median diameter 6.21 μm .

Main Outcome Measure A priori defined change in the Westley croup score from baseline to 30 and 60 minutes in the 3 groups.

Results Groups were comparable before treatment. At 30 minutes the difference in the improvement in the croup score between the blow-by and low-humidity groups was 0.03 (95% confidence interval [CI], -0.72 to 0.66), between low- and high-humidity groups, 0.16 (95% CI, -0.86 to 0.53), and between blow-by and high-humidity groups, 0.19 (95% CI, -0.87 to 0.49). Results were similar at 60 minutes. Differences between groups in pulse and respiratory rates and oxygen saturation changes were insignificant, as were proportions of excellent responders; proportions with croup score of 0 at study conclusion; and proportions receiving dexamethasone, epinephrine, or requiring additional medical care or hospitalization.

Conclusions One hundred percent humidity with particles specifically sized to deposit in the larynx failed to result in greater improvement than 40% humidity or humidity by blow-by technique. This study does not support the use of humidity for moderate croup for patients treated in the emergency department.

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prevent the drying and facilitate air flow.¹⁴⁻¹⁶

Some studies have failed to show any benefit from humidity^{17,18} while others have demonstrated improvement.¹⁹ However, they are limited by small sample size, lack of blinding, and use of sedation. A recent more rigorous trial using blow-by humidity did not demonstrate any benefit.²⁰ This method is not suited to controlling the delivery of humidity with respect to temperature, gas flow, and oxygen concentration.

Previous studies have not taken into account the particle size of the aerosolized water. While particles that are larger than 10 µm in diameter deposit in the nose and mouth, particles smaller than 5 µm, reach the lower airway,^{21,22} where they may cause bronchospasm.^{23,24} Particles 5 to 10 µm in diameter have the greatest probability of reaching the larynx, making this particle size the most appropriate choice for croup therapy. The primary objective of our study was to compare the efficacy of controlled delivery of 100% humidity, using optimally sized water particles, with controlled delivery of 40% humidity and humidity delivered with the blow-by technique, in children with moderate to severe croup in the emergency department (ED).

METHODS

The study population consisted of a convenience sample of children with croup presenting to the ED at The Hospital for Sick Children, Toronto, recruited when 1 of 3 study nurses was on duty. The study nurses recruited from 6 PM to 8 AM during February-April and September-November, from fall 2001 through spring 2004. These times and months were chosen because this is when the majority of patients with croup present. Children were eligible if they were 3 months to 10 years of age, with a croup score of 2 or higher^{17,25} after a prestudy 30-minute resting period. The items in the Westley croup score include stridor, retraction

of the intercostal and subcostal regions, entry of air into the lungs, cyanosis on room air, and level of consciousness. It varies from 0 to 1 in mild, 2 to 6 in moderate, and 7 to 17 in severe croup.³ Children were excluded if they required immediate intervention with nebulized epinephrine or intubation, had a history or examination suggesting an alternative cause of stridor, had a history of chronic pulmonary disease other than asthma, coexistent systemic disease, previous intubation, duration of present illness for more than a week, had received systemic or inhaled glucocorticoids in the previous 48 hours or epinephrine in the previous 4 hours, or if caregivers had inadequate command of English. The study was approved by the human research ethics board of our institution and parents of all participants provided written informed consent. A log book was kept of all ED croup patients, noting all exclusions and refusals, to assess the study's generalizability.

Baseline Assessment

Before treatment we measured the Westley croup score,^{4,17,25} respiratory and heart rates, and arterial oxygen saturation in room air using an oximeter (Nellcor, Engelwood, Calif). Sociodemographic information, medical history, symptoms, and pharmacotherapy prior to arrival were documented.

Randomization

A statistician not involved in the study generated a computer-generated random block allocation sequence with block size of 9 to ensure comparable group assignment of patients. He also placed the study codes in opaque, sequentially numbered envelopes in the locked ED research office to be retrieved and subsequently destroyed only by the assistant preparing and administering the assigned experimental therapy. The allocation sequence was locked away by the research coordinator until enrollment and all decisions regarding study analysis were finalized.

Blinding

Two research assistants were used to ensure that croup score measurements were blinded. The first assistant (one of several respiratory therapists, nurses, or pediatric residents) was not blinded and was responsible for setting up the apparatus and administering the experimental treatment for 30 minutes. This person remained in the room during the entire treatment ensuring that study conditions were being continually adhered to. The second assistant, 1 of 3 trained study nurses, measured study outcomes while blinded to the intervention. This person also initially enrolled patients into the study and obtained informed consent. To ensure blinding, the first assistant put the study equipment for all 3 study groups in the room, covered with a sheet, wiped each participant's face to eliminate evidence of the mode of delivery, and ensured that ED physicians and nurses did not enter the room while the experimental therapy was being delivered. Parents were requested not to reveal their child's treatment to the study nurse. At no time did the first assistant or the parents reveal the identity of the intervention to either the second assistant or to the ED medical and nursing staff.

Intervention

Following baseline assessment, the participating children were randomly assigned to receive 1 of the 3 interventions for 30 minutes. Blow-by humidity was used because it represents a current standard of care. The amount of humidity delivered to the nose and mouth with this technique is variable, and because of the amount of room air entrained, it is tantamount to inspiring room air. Therefore, this group can be considered a placebo equivalent. In contrast, humidity in the 40% group was delivered in a fully controlled and monitored fashion. Because most air-conditioned buildings control humidity at approximately 40%, this group actually represents optimally delivered placebo. Humidity in Toronto in the spring and fall is about 40%, although

it is lower indoors in winter. The 100% humidity group was provided humidity as water particles in the 5- to 10- μm size range that reaches the larynx, thus representing an optimally delivered humidity intervention group.

The blow-by humidity set-up consisted of a back pressure compensated oxygen flowmeter, which was calibrated at 21°C and 345 kPa inlet pressure (Precision Medical Inc, Northampton, Pa). A high-output nebulizer, set at 100% oxygen (Airlife Nebulizer Cap and Sterile Water for Inhalation, USP 1000-mL bottle, Allegiance Healthcare Corp, McGaw Park, Ill) was connected to the oxygen flowmeter. The oxygen was humidified and delivered to the patient at 10 L/min via 2 m of corrugated flexible tubing of 2.2 cm internal diameter. The tubing, held by the parents, was pointed directly at the patient's face from a distance of 20 cm. This flow, directed at the sensor of a digital hygrometer from a distance of 20 cm (Thermo-Hygro, RadioShack, Barrie, Ontario), showed the same humidity as ambient room air.

Children in both the low- and high-humidity groups received the same total gas flow of 20 L/min, at temperature 21°C, and using 40% oxygen. Based on a normal respiratory rate of 25/min²⁶ and an expected tidal volume of 10 mL/kg for toddlers,²⁷ minute ventilation would be 0.25 L/min per kilogram. The respiratory rate and tidal volume will change in opposite directions. Assuming a maximal respiratory rate of 40/min and a ratio of inspiratory time to total respiratory cycle of 0.42,²⁷ the flow of 20 L/min would exceed the peak inspiratory flow for all children up to 47 kg of body weight. Prior to the study, measurements of relative humidity, temperature, and oxygen percentage were performed at the mask to confirm the stated conditions.

The low-humidity group received 40% relative humidity and 40% oxygen. The 40% oxygen was controlled by an air-oxygen blender (Secrist Corp, Anaheim, Calif). Two oxygen flowmeters calibrated at 21°C and 345 kPa in-

let pressure (Precision Medical) were attached to the blender outlet. Humidity was generated by a high-output nebulizer set at 100% oxygen to prevent entrainment of ambient air (Airlife Nebulizer Cap and Sterile Water for Inhalation, USP 1000-mL bottle). This was connected to 1 of the flowmeters set at a flow of 6 L/min. A 2-m oxygen tube was attached to the other flowmeter set to deliver dry gas at 14 L/min. The dry and humidified gases were mixed to achieve 40% relative humidity and delivered via a 2-m corrugated flexible tubing and a plastic face mask. The relative humidity was verified by a hygrometer.

The high-humidity group received 100% humidity and water droplets with a mass median diameter of 6.21 μm . A small-volume nebulizer with the baffle removed (WhisperJet, Marquest, Englewood, Colo) was kept filled with 3 to 6 mL of sterile water at all times to ensure consistent humidity and particle size during treatment. Two oxygen flowmeters were attached to a blender, as before, set at 40% oxygen. The 2-m oxygen tubing connected to the nebulizer was attached to one of the flowmeters set at 8 L/min, and a Y connector at the nebulizer was used to deliver an additional gas flow of 12 L/min to maintain a constant total flow of 20 L/min. A 2-m corrugated tube and mask were used to deliver this treatment.

Particle Size

To create a droplet size appropriate for pharyngeal and laryngeal deposition, various devices were manipulated to generate the particle size distribution believed most appropriate.²⁸ Particle size measurements were made by laser diffraction using a MasterSizerX (Malvern Instruments, Worcestershire, England) and techniques described elsewhere.²⁹ A WhisperJet nebulizer, with the baffle removed, was used because it generated larger particles with a mass median diameter (geometric SD) of 6.21 (1.02) μm ,³⁰ making it suitable for controlled delivery of droplets to the site of pathology in croup.

To ensure the nebulizer would deliver a consistent particle size during treatment, each WhisperJet nebulizer was tested at minutes 1, 5, 10, 20, and 30 of the procedure using the Malvern Mastersizer X.

Other Treatments and Follow-up

All decisions about further treatment and hospitalization were made by attending physicians uninvolved in the study, absent from the room during experimental therapy and unaware of outcome data. The first assistant was to call the attending physician should any additional treatment be required during the study period. The experimental equipment was removed from the room by the study assistant prior to the physicians' assessment. The parents of all enrolled children were telephoned by the research nurse 72 hours after discharge to ascertain if any further medical intervention had been required.

Outcome Measures

The primary outcome measure was change in the croup score, developed by Westley et al,¹⁸ from baseline to 30 and 60 minutes. We reasoned that for the humidity to be beneficial, its effect should last at least 30 minutes after the end of the intervention. This score has been used in other clinical croup trials and has been shown to be valid, reliable, sensitive to change,^{4,31} with an excellent interrater reliability.^{3,25,32} The 3 research nurses were senior ED practitioners, experienced in assessing respiratory distress in children and trained in the measurement of the croup score by the primary investigator prior to the study. Their weighted κ equivalent was 0.54, equating to moderate agreement, and they did not disagree on any Westley croup score by more than 1 point. Croup scores were measured with children in an awake but quiet state. Secondary outcomes consisted of changes in respiratory rate, heart rate, and oxygen saturation at these times; proportions of children with excellent improvement arbitrarily defined as a decrease in the

croup score of 2 or more points by 60 minutes; and proportions of children with a score of 0 at 60 minutes. We also compared proportions of children in each group receiving nebulized epinephrine or oral dexamethasone after the study and of those hospitalized or returning for medical care by 72 hours.

Statistical Analysis

Prior to the start of the study sample sizes were estimated. Sample sizes of 43 patients per group were needed to detect a difference of 1 point or more^{3,32} between the changes in the croup score at 60 minutes, with an estimated SD of 1.4, at a power of 80%, and an α of .017. A reduced level of significance was considered to adjust for the 3 pairwise comparisons being tested.

The primary analysis of the changes in croup score from baseline to 30 and 60 minutes consisted of a mixed-model approach to the repeated measures design of the study. The baseline croup scores were not significantly different; hence, the results presented did not use baseline croup scores as a covariate. However, for completeness, the analysis was run adjusting for the baseline croup score. As expected, the results, ie, the predicted means, changed only minimally. The analysis considered 2 types of correlation structures to estimate within-subject variation: compound symmetry and first-order autoregressive. Because time was 30 minutes apart, the compound symmetry structure was considered plausible; however, we also thought that this correlation may decrease with time; hence, a first-order autoregressive structure was also considered. Both models of correlation gave very similar results, and the simpler compound symmetry was selected.

The secondary analyses of the comparisons of the changes in pulse and respiratory rate and oxygen saturation over time also used mixed-model analysis. Differences in proportions between the groups were compared with the χ^2 test. Relevant 95% and 99% confidence intervals (CIs) were calculated for the

point estimates and were appropriately (for 6 tests an adjusted 99% CI was used) adjusted for multiple testing. PROC MIXED, version 9.1 (SAS Institute Inc, Cary, NC) was used to analyze the data.

RESULTS

Patient Characteristics

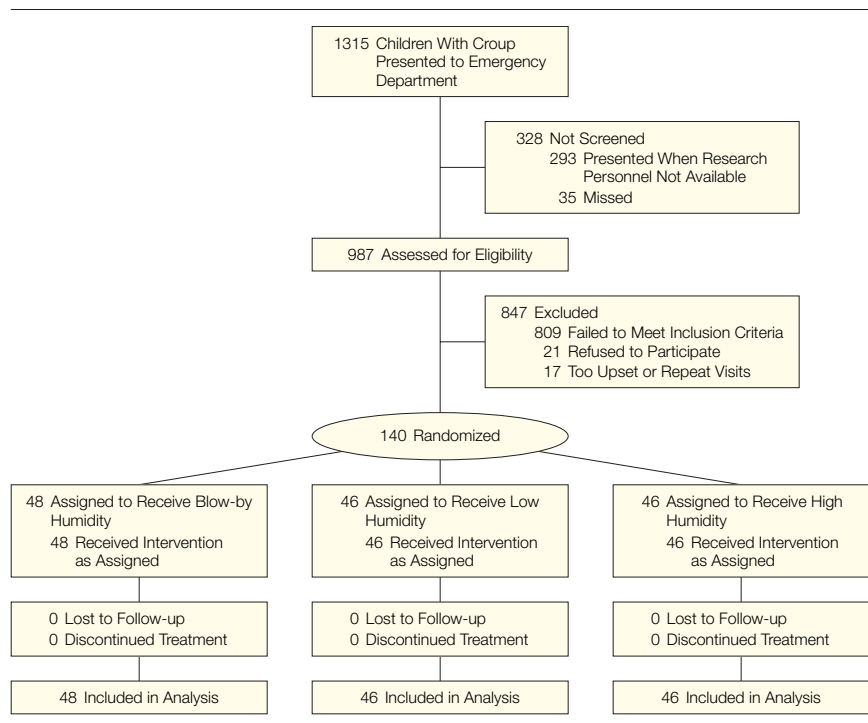
During the study period, 1315 patients with a diagnosis of croup presented to the ED (FIGURE). Of these, 987 were screened. Eight hundred twenty-six were excluded: 281 patients had a croup score 1 or less on arrival, 357 reached a croup score of 1 or 0 after the 30-minute prestudy resting period, 69 had comorbidities, 24 had received dexamethasone, 30 had nebulized epinephrine prior to arrival, 34 were judged to need immediate therapy, 6 were outside the age limits of the study, 10 had been in the study before, 7 remained too upset to obtain an accurate score, and 8 were unable to participate because of language limitations. Twenty-one families refused participation. A total of 140 children were

randomly assigned to experimental therapy: 48 to the blow-by, 46 to the low-humidity, and 46 to the high-humidity groups. All of the randomized patients completed the trial and were included in the analysis. Their baseline characteristics were comparable (TABLE 1). Nine patients were older than 72 months, and they were equally divided among the 3 groups. Two patients, in different groups, weighed more than 47 kg.

Westley Croup Score

The overall difference in the score changes over time between the 3 groups was not statistically significant ($P = .13$). Likewise, the differences in the changes in the scores from time 0 to either 30 minutes or 60 minutes were minimal and neither clinically nor statistically significant (TABLE 2). No child worsened during the study period. We did not find a significant interaction between the main treatment effect and patients' age, sex, baseline croup score, duration of symptoms, or time of presentation.

Figure. Flow Diagram of Study



Other Outcomes

There was no significant difference in changes in respiratory rate, heart rate, or oxygen saturation at 30 or 60 minutes in the 3 groups. Table 2 shows the changes in croup score at 30 and 60 minutes and in the other parameters at

60 minutes. Proportions of excellent responders or of patients with croup score of 0 at the end of the study and proportions of patients seeking further medical care, being hospitalized, or receiving pharmacotherapy after the study were not different among the groups

(TABLE 3). No study patient required corticosteroids, epinephrine, or any additional intervention during the study period.

COMMENT

Our trial shows that, in children with moderate to severe croup, 100% humidity, even when delivered in water-particle size designed to deposit in the larynx, does not result in greater clinical improvement than either controlled delivery of 40% humidity (optimally delivered placebo) or humidity delivered using the blow-by method (commonly used placebo). Likewise, the differences in all secondary outcomes between the groups were both clinically and statistically insignificant. The 95% CIs for the comparisons in the score are narrow and the up-

Table 1. Baseline Characteristics of the Study Patients

Characteristics	Blow-by Group (n = 48)	Low-Humidity Group (n = 46)	High-Humidity Group (n = 46)
Age, mean (SD), mo	26.8 (20.7)	25.3 (23.2)	23.9 (16.7)
Male sex, No. (%)	34 (71)	28 (61)	35 (76)
Previous history, No. (%)			
Croup	11 (22)	13 (28)	12 (27)
Emergency department visits for croup	12 (25)	13 (29)	8 (17)
Admission(s) for croup	0	2 (4)	2 (4)
Asthma or wheezing	2 (4)	6 (13)	4 (9)
Duration of symptoms, mean (SD), min	27 (23)	31 (33)	24 (22)
Temperature, mean (SD), °C	37.8 (1.3)	38.0 (1.1)	37.9 (1.2)

Table 2. Changes in Westley Croup Score From Baseline to 30 and 60 Minutes and in Clinical Parameters From Baseline to 60 Minutes

	Mean (SD) at Baseline			Change, Mean (SD)			Mean Predicted Difference (95% Confidence Interval)*		
	Blow-by Humidity Group (n = 48)	Low-Humidity Group (n = 46)	High-Humidity Group (n = 46)	Blow-by Humidity Group (n = 48)	Low-Humidity Group (n = 46)	High-Humidity Group (n = 46)	Blow-by vs Low Humidity	Low vs High Humidity	High vs Blow-by Humidity
Westley score									
0 min	3.17 (0.76)	2.95 (0.97)	3.00 (0.87)						
30 min	2.36 (1.13)	2.27 (1.55)	2.49 (1.49)	0.74 (1.18)	0.70 (1.3)	0.53 (1.2)	0.03 (−0.72 to 0.66)†	0.16 (−0.86 to 0.53)†	0.19 (−0.87 to 0.49)†
60 min	2.23 (1.40)	2.0 (1.46)	1.93 (1.40)	0.89 (1.42)	0.98 (1.22)	1.09 (1.11)	0.05 (−0.63 to 0.74)†	0.09 (−0.61 to 0.79)†	0.14 (−0.54 to 0.83)†
Heart rate, beats/min									
0 min	133 (20)	142 (19)	143 (23)						
60 min	130 (19)	135 (28)	135 (21)	2.5 (12.6)	7.1 (30.3)	9.9 (17.5)	4.2 (−7.0 to 15.3)	2.4 (−8.7 to 13.5)	6.6 (−4.4 to 17.6)
Respiratory rate, breaths/min									
0 min	31 (7)	31 (10)	35 (9)						
60 min	30 (7)	30 (6)	30 (9)	0.6 (5.6)	1.8 (7.0)	4.0 (5.5)	0.9 (−2.6 to 4.5)	2.4 (−1.1 to 6.0)	3.4 (−0.1 to 6.9)
Oxygen saturation, %									
0 min	98.3 (1)	98.3 (1.1)	98.2 (1.4)						
60 min	98.4 (1.4)	98.5 (1.4)	97.8 (2.2)	0.09 (1.38)	0.13 (1.5)	0.41 (2.07)	0.03 (−0.91 to 0.85)	0.49 (−0.42 to 1.39)	0.46 (−0.41 to 1.33)

*The fact that all the differences of the changes include 0, there were no statistically significant differences.

†The fact that the lower and upper limits of the 95% confidence intervals are not greater than 1, decided a priori to represent a clinically significant change, indicates that there were no clinically significant differences in Westley croup scores.

Table 3. Clinical Outcomes After the Study

	No. (%)			Comparison, OR (95% CI)		
	Blow-by Group (n = 48)	Low-Humidity Group (n = 46)	High-Humidity Group (n = 46)	Blow-by vs Low Humidity	Low vs High Humidity	High vs Blow-by Humidity
Hospitalization	1 (2.1)	2 (4.3)	0	0.47 (0.01 to 9.36)
Excellent responders	14 (29.2)	12 (26.1)	18 (39.1)	1.17 (0.43 to 4.2)	0.55 (0.2 to 1.45)	0.64 (0.25 to 1.65)
Westley score 0 at end of study	9 (18.8)	6 (14.0)	8 (18.6)	1.54 (0.44 to 5.76)	0.71 (0.19 to 2.6)	1.1 (0.34 to 3.64)
Dexamethasone after study	43 (91.5)	39 (86.7)	38 (82.6)	1.54 (0.38 to 6.68)	1.17 (0.33 to 4.21)	1.81 (0.47 to 7.62)
Epinephrine after study	4 (8.3)	4 (8.7)	4 (8.7)	0.95 (0.17 to 5.48)	1.00 (0.17 to 5.75)	0.95 (0.17 to 5.48)
Returned for medical care	9 (19)	16 (35)	9 (20)	0.43 (0.15 to 1.22)	2.19 (0.77 to 6.44)	0.95 (0.3 to 3.0)

Abbreviations: CI, confidence interval; OR, odds ratio. Ellipses indicate that the OR cannot be calculated.

per CI limit does not approach the target clinical difference of 1 point, which adds to the strength of the trial. This lack of benefit occurred despite using optimum water-particle size and controlling for temperature, total gas flow, and oxygen concentration. Our study results should be generalizable to other pediatric and general EDs since we provide a mix of primary care to patients living in the downtown core near the hospital and secondary and tertiary care to patients from neighboring hospitals. Patients sick enough to have been transferred from other hospitals would not have met our inclusion criteria.

Mist has been used as croup therapy since the 19th century.³³ Further developments included the use of croup tents,³³ which are now rarely used due to their anxiety provoking effect, worsening airway obstruction, and problems with accurate monitoring.^{1,34} Instead, humidity is usually delivered via flexible tubing. This blow-by method is still widely used, despite recent evidence suggesting its lack of efficacy.²⁰

Humidification therapy with droplets suspended in the inhaled gas is not without problems. Its use has led to hot water scalds,^{9,35} pulmonary changes and impairment of the mucociliary elevator,³² bronchospasm in children prone to wheezing,³⁶ and hyponatremia in newborns.³⁷ These harmful effects underscore the need to establish whether humidification therapy has important enough positive effects in croup treatment to justify its ongoing use. Humidity may actually have been found useful because of other factors associated with its use such as the comfort of being close to parents or the low temperature³⁸ used for delivery in certain humidification devices.

Four studies have evaluated humidification therapy.^{19,20,39,40} In a study of 16 children Bouchier et al³⁹ found no difference between the treatments with a croup tent vs room air, mostly likely due to large-water particle size produced by the tent apparatus. Lenney et al⁴⁰ studied 5 children with croup receiving

nebulized water, with no improvement. However, all children were given xylometazoline, a vasoconstrictor, to ensure nasal patency and were given chloral hydrate for sedation, and the results are not generalizable to the ED. Jamshidi et al¹⁹ evaluated 46 children with mild to moderate croup receiving humidified air vs no therapy. The treated group achieved greater improvement than the controls. However, the evaluators were not blinded and measurement bias was thus possible. Neto et al²⁰ carried out a randomized, single-blind comparison of humidity using the blow-by method vs no therapy on 71 children with moderate croup, detecting no difference. In the blow-by technique, patients entrain room air and the amount of inspired humidity is comparable with that of room air.

This study is limited in not being double-blinded, but for practical reasons it could only be single-blinded. Importantly, the nurses measuring the outcomes were blinded to the intervention, so measurement bias is unlikely. Because the participating children were very young and the improvements in the score in the 3 groups were virtually the same, it is unlikely that patients' knowledge of the intervention influenced the outcome. A control group receiving no therapy was not considered ethical because many perceive the blow-by method to be the standard of care. The results of our study may not be generalizable to children with either mild or more severe croup presenting to the ED because most of our patients were of moderate severity. Croup symptoms resolved in 36% of screened patients within half an hour of presentation, showing that many mild cases resolve spontaneously without the need for any treatment. Children with severe croup are often treated with epinephrine and steroids without the delay entailed by humidity treatment. In addition, the results may not apply to children whose croup symptoms are treated at home with humidity delivered by humidifier, vaporizers, or exposure to outdoor humid climate. The relatively wide age range of patients

could have led to the inclusion of a few patients whose disease had a different mechanism or etiology compared with younger croup patients, but the number of such patients was low and the average age in each study group was approximately 25 months.

The main reason for respiratory distress in children presenting to EDs with croup is inflammatory edema in the subglottic region. This pathology may be severe enough to require anti-inflammatory pharmacotherapy, with or without vasoconstricting agents, for clinical relief⁸ and is unlikely to be affected by humidification therapy. Our results suggest that the use of humidity in children with croup seen in EDs is not warranted.

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Study concept and design: Scolnik, Coates, Stephens, Da Silva, Lavine, Schuh.

Acquisition of data: Scolnik.

Analysis and interpretation of data: Scolnik, Stephens, Schuh.

Drafting of the manuscript: Scolnik, Coates, Schuh, Lavine.

Critical revision of the manuscript for important intellectual content: Scolnik, Coates, Stephens, Da Silva, Lavine, Schuh.

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REFERENCES

1. Rosekrans JA. Viral croup: current diagnosis and treatment. *Mayo Clin Proc.* 1998;73:1102-1107.
2. Denny FW, Murphy TF, Clyde WA Jr, Collier AM, Henderson FW. Croup: an 11-year study in a pediatric practice. *Pediatrics.* 1983;71:871-876.
3. Johnson DW, Jacobson S, Edney PC, Hadfield P, Mundy ME, Schuh S. A comparison of nebulized budesonide, intramuscular dexamethasone, and placebo

- for moderately severe croup. *N Engl J Med*. 1998;339:498-503.
4. Klassen TP, Feldman ME, Watters LK, Sutcliffe T, Rowe PC. Nebulized budesonide for children with mild-to-moderate croup. *N Engl J Med*. 1994;331:285-289.
 5. Ausejo M, Saenz A, Pham B, et al. The effectiveness of glucocorticoids in treating croup: meta-analysis. *BMJ*. 1999;319:595-600.
 6. Kairys SW, Olmstead EM, O'Connor GT. Steroid treatment of laryngotracheitis: a meta-analysis of the evidence from randomized trials. *Pediatrics*. 1989;83:683-693.
 7. Tibballs J, Shann FA, Landau LI. Placebo-controlled trial of prednisolone in children intubated for croup. *Lancet*. 1992;340:745-748.
 8. Bjornson CL, Klassen TP, Williamson J, et al. A randomized trial of a single dose of oral dexamethasone for mild croup. *N Engl J Med*. 2004;351:1306-1313.
 9. Grealley P, Cheng K, Tanner MS, Field DJ. Children with croup presenting with scalds. *BMJ*. 1990;301:113.
 10. Henry R. Moist air in the treatment of laryngotracheitis. *Arch Dis Child*. 1983;58:577.
 11. Couriel JM. Management of croup. *Arch Dis Child*. 1988;63:1305-1308.
 12. Skolnik NS. Treatment of croup: a critical review. *AJDC*. 1989;143:1045-1049.
 13. Dulfano MJ, Adler K, Wooten K. Physical properties of sputum, IV: effects of 100 per cent humidity and water mist. *Am Rev Respir Dis*. 1973;107:130-132.
 14. Sasaki CT, Suzuki M. The respiratory mechanism of aerosol inhalation in the treatment of partial airway obstruction. *Pediatrics*. 1977;59:689-694.
 15. Ophir D, Elad Y. Effects of steam inhalation on nasal patency and nasal symptoms in patients with the common cold. *Am J Otolaryngol*. 1987;8:149-153.
 16. Szilagyi PG. Humidifiers and other symptomatic therapy for children with respiratory tract infections. *Pediatr Infect Dis J*. 1991;10:478-479.
 17. Westley CR, Cotton EK, Brooks JG. Nebulized racemic epinephrine by IPPB for the treatment of croup—a double blind study. *AJDC*. 1978;132:484-487.
 18. Kristjansson S, Berg-Kelly K, Winso E. Inhalation of racemic adrenaline in the treatment of mild and moderately severe croup: clinical symptom score and oxygen saturation measurements for evaluation of treatment effects. *Acta Paediatr*. 1994;83:1156-1160.
 19. Jamshidi PB, Kemp JS, Peter JR, et al. The effect of humidified air in mild to moderate croup: evaluation using croup scores and respiratory inductance plethysmography [abstract]. *Acad Emerg Med*. 2001;8:417.
 20. Neto GM, Kentab O, Klassen TP, Osmond MH. A randomized controlled trial of mist in the acute treatment of moderate croup. *Acad Emerg Med*. 2002;9:873-879.
 21. O'Callaghan C, Barry PW. The science of nebulized drug delivery. *Thorax*. 1997;52(suppl 2):S31-S44.
 22. Rudolph G, Kobrich R, Stahlhofen W. Modelling and algebraic formulation of regional aerosol deposition in man. *J Aerosol Sci*. 1990;21(suppl 1):S306-S406.
 23. Smith CM, Anderson SD. Inhalation provocation tests using nonisotonic aerosols. *J Allergy Clin Immunol*. 1989;84:781-790.
 24. Mochizuki H, Shimizu T, Maeda S, Tokuyama K, Morikawa A, Kuroume T. Relationship between ultrasonically nebulized distilled water-induced bronchoconstriction and acetic acid-induced cough in asthmatic children. *J Allergy Clin Immunol*. 1995;96:193-199.
 25. Klassen T, Rowe P. The croup score as an evaluative instrument in clinical trials. *Arch Pediatr Adolesc Med*. 1995;149:60.
 26. Iliff A, Lee VA. Pulse rate, respiratory rate, and body temperature of children between two months and eighteen years of age. *Child Dev*. 1952;23:237-245.
 27. Stick S. Measurements during tidal breathing. In: Stocks J, Sly PD, Tepper RS, Morgan WJ, eds. *Infant Respiratory Function Testing*. Toronto, Ontario: Wiley-Liss; 1996:117-138.
 28. Yeh HC, Phalen RF, Raabe OG. Factors influencing the deposition of inhaled particles. *Environ Health Perspect*. 1976;15:147-152.
 29. Kwong WTJ, Ho SL, Coates AL. Comparison of nebulized particle size distribution with Malvern laser diffraction analyzer versus Andersen cascade impactor and low-flow Marple personal cascade impactor. *J Aerosol Med*. 2000;13:303-314.
 30. Hinds WC. *Particle Size Statistics. Aerosol Technology: Properties, Behavior, and Measurements of Airborne Particles*. Toronto, Ontario: John Wiley & Sons; 1982:69-103.
 31. Klassen TP, Craig WR, Moher D, et al. Nebulized budesonide and oral dexamethasone for treatment of croup: a randomized controlled trial. *JAMA*. 1998;279:1629-1632.
 32. Johnson DW, Schuh S, Koren G, Jaffe DM. Out-patient treatment of croup with nebulized dexamethasone. *Arch Pediatr Adolesc Med*. 1996;150:349-355.
 33. Kaditis AG, Wald ER. Viral croup: current diagnosis and treatment. *Pediatr Infect Dis J*. 1998;17:827-834.
 34. Avery ME, Galina M, Nachman R. Mist therapy. *Pediatrics*. 1967;39:160-165.
 35. Asher MI. Infections of the upper respiratory tract. In: Taussig LM, Landau LI, eds. *Pediatric Respiratory Medicine*. St Louis, Mo: Mosby; 1999:530-547.
 36. Rodriguez GE, Branch LB, Cotton EK. The use of humidity in asthmatic children. *J Allergy Clin Immunol*. 1975;56:133-140.
 37. Tamer MA, Modell JH, Rieffel CN. Hyponatremia secondary to ultrasonic aerosol therapy in the newborn infant. *J Pediatr*. 1970;77:1051-1054.
 38. Folland DS. Treatment of croup: sending home an improved child and relieved parent. *Postgrad Med*. 1997;101:271-278.
 39. Bourchier D, Dawson KP, Fergusson DM. Humidification in viral croup: a controlled trial. *Aust Paediatr J*. 1984;20:289-291.
 40. Lenney W, Milner AD. Treatment of acute viral croup. *Arch Dis Child*. 1978;53:704-706.