

Outdoor Cold Air Versus Room Temperature Exposure for Croup Symptoms: A Randomized Controlled Trial

Johan N. Siebert, MD,^{a,b,*} Coralie Salomon, MD,^{a,*} Ilaria Taddeo, MD,^a Alain Gervaix, MD,^{a,b} Christophe Combescure, PhD,^c Laurence Lacroix, MD^{a,b}

abstract

OBJECTIVES: Croup is the most common cause of acute upper airway obstruction in children. The benefits of treating croup with steroids are well established, with an onset of effect 30 minutes after administration. We investigated whether a 30-minute exposure to outdoor cold air might improve mild to moderate croup symptoms before the onset of action of steroids.

METHODS: This open-label, single-center, randomized controlled trial, enrolled children aged 3 months to 10 years with croup and a Westley Croup Score (WCS) ≥ 2 attending a tertiary pediatric emergency department. Participants were randomized (1:1) to either a 30-minute exposure to outdoor cold ($<10^{\circ}\text{C}$) atmospheric air or to indoor ambient room air immediately after triage and administration of a single-dose oral dexamethasone. The primary endpoint was a decrease in WCS ≥ 2 points from baseline at 30 minutes. Analyses were intention to treat.

RESULTS: A total of 118 participants were randomly assigned to be exposed to outdoor cold air ($n = 59$) or indoor room temperature ($n = 59$). Twenty-nine of 59 children (49.2%) in the outdoor group and 14 of 59 (23.7%) in the indoor group showed a decrease in WCS ≥ 2 points from baseline at 30 minutes after triage (risk difference 25.4% [95% confidence interval 7.0–43.9], $P = .007$). Patients with moderate croup benefited the most from the intervention at 30 minutes (risk difference 46.1% [20.6–71.5], $P < .001$).

CONCLUSIONS: A 30-minute exposure to outdoor cold air ($<10^{\circ}\text{C}$), as an adjunct to oral dexamethasone, is beneficial for reducing the intensity of clinical symptoms in children with croup, especially when moderate.



WHAT'S KNOWN ON THIS SUBJECT: Steroids and nebulized epinephrine are effective treatments for children with moderate to severe croup. Mist, although previously used for decades, is ineffective and should not be administered. Cold air exposure is thought to be beneficial, but scientific evidence is scarce.

WHAT THIS STUDY ADDS: A first evidence of the benefits of exposure to outdoor cold air ($<10^{\circ}\text{C}$) in acute care settings in children with mild to moderate croup symptoms as an adjunct to steroids in the first 30 minutes before their onset.

To cite: Siebert JN, Salomon C, Taddeo I, et al. Outdoor Cold Air Versus Room Temperature Exposure for Croup Symptoms: A Randomized Controlled Trial. *Pediatrics*. 2023;152(3):e2023061365

^aDepartment of Pediatric Emergency Medicine, Geneva Children's Hospital, Geneva University Hospitals, Geneva, Switzerland; ^bFaculty of Medicine, University of Geneva, Geneva, Switzerland; and ^cDivision of Clinical Epidemiology, Department of Health and Community Medicine, University of Geneva and Geneva University Hospital, Geneva, Switzerland

*Contributed equally as co-first authors.

Drs Siebert and Salomon conceptualized and designed the study, collected the data, drafted the initial manuscript, prepared the figures and tables, and critically reviewed and revised the manuscript; Dr Taddeo contributed to the design, collected the data, and contributed to the critical review of the paper; Dr Gervaix critically reviewed and revised the manuscript; Dr Combescure conducted the trial analyses and contributed to the figures and tables; (Continued) Dr Lacroix was the principal investigator and the trial coordinator, conceived the study, led the

Croup, also known as acute viral laryngotracheitis or laryngotracheobronchitis, is the most common cause of acute upper airway obstruction commonly occurring in children aged 6 months to 3 years and showing varying degrees of severity.¹⁻³ Although most cases are mild, croup represents a heavy burden on health care systems accounting for 3% to 5% of annual pediatric emergency department (PED) visits and 72-hour readmissions in children aged <2 years.⁴⁻⁸ It is characterized by the abrupt onset of a distinctive, predominantly nocturnal,⁹ seal-like barking cough in children with hoarseness and inspiratory stridor of variable intensity with retractions because of subglottic airway inflammation, swelling, and partial upper airway obstruction. Symptoms may be preceded by nonspecific prodromal upper respiratory tract symptoms and low-grade fever. The mainstay of pharmaceutical treatment is a single-dose oral dexamethasone for children with croup of any severity both in outpatient and inpatient settings.^{10,11} Children with moderate to severe croup, defined by a Westley Croup Score (WCS)¹² >3, may benefit from nebulized epinephrine as an adjunct to oral dexamethasone.^{1,13}

Nonpharmacological measures have been mentioned. Mist therapy, although used for years,¹⁴ is no longer recommended because no evidence supports its effectiveness.^{11,15} Exposure to cold air is often reported beneficial in daily practice by parents, but documented evidence to support this measure lacks.¹⁶ This study compares the efficacy of a 30-minute exposure to cold, atmospheric, outdoor air versus to ambient indoor room air during seasonal peaks of croup in children with mild to moderate croup.

METHODS

Trial Design

This prospective, open-label, single-center, randomized controlled trial was conducted at a tertiary PED. The study took place during the cold days and nights from late fall to spring, when outdoor air temperature was <10°C, correlating with the highest prevalence of parainfluenza viruses, though other viruses are also responsible, to a lesser extent, for croup.^{17,18} The Geneva institutional ethics committee approved the study. The trial was registered under the Swiss National Clinical Trials Portal (#SNCTP000002514/BASEC2016-00845) and ClinicalTrials.gov (#NCT05668364).

Participants

All children aged 3 months to 10 years presenting to the PED were eligible for inclusion. Requirements for participant inclusion were: outdoor cold air temperature <10°C, WCS ≥2, and written informed consent. Exclusion criteria were history or physical examination suggesting any another diagnosis (eg, epiglottitis, diphtheria, bacterial tracheitis, foreign body aspiration,

peritonsillar or retropharyngeal abscess, laryngomalacia, vascular ring, neoplasm, or hemangioma), WCS <2, severe croup at presentation judged to need nebulized epinephrine, chronic respiratory disease (asthma excluded), airway abnormalities, known immunodeficiency, and contraindications to steroids.

Randomization and Masking

Randomization sequence was created using a Web-based software, ensuring allocation concealment, with a single, constant 1:1 allocation ratio.¹⁹ Immediately after triage, written informed consent was obtained from parents or guardians before disclosure of allocation to treatment arms and was consistent with the Declaration of Helsinki, with full information disclosure before participation in the study. The allocation group was then released to both the physician enrolling the patient and the participants, and baseline assessment was obtained. Because of the nocturnal predominance of croup symptoms, physicians were not blinded to the allocation group, because they both enrolled and assessed patients during their night-shifts. Although the intervention could not be blinded, study investigators remained unaware of the outcomes until all data were unlocked for analysis at the end of the trial. The specialist in data analysis (C.C.) was not blinded to treatment allocation.

Trial Procedures

The effect of exposure to outdoor cold air on croup symptoms was assessed with the validated WCS.^{12,20,21} Concomitant hygrometry and temperatures were recorded simultaneously (Supplemental Information). If outdoor temperature conditions were satisfying (<10°C), patients were triaged²² upon PED arrival and participation was offered. The length of time spent under exposure to outdoor cold air before PED arrival was recorded. Symptoms present at home before departure to the PED were also specified using a modified version of the Telephone Out Patient (TOP)²³ score (Supplemental Information and Supplemental Table 4). On arrival, age, sex, and weight were documented, as well as vital signs, including room-air pulse oximetry (saturation measured via pulse oximetry [SpO₂]), respiratory rate, and heart rate. Baseline WCS was calculated, ranging from 0 to 17 (Supplemental Information and Supplemental Table 5). After triage and administration of a single 0.6 mg/kg dose oral dexamethasone,¹⁰ participants were randomly assigned either to wait during 30 minutes outside the PED in sight of the triage desk exposed to outdoor cold air (intervention group), with blankets made available to patients, parents, or caregivers, or to wait inside the PED where ambient air is pulsed at 24 to 25°C (control group). At 30 minutes, participants in the intervention group reentered the PED and were immediately assessed, without further exposure to outdoor environment. In the event of an early return, time spent outside

was documented. A minimum of 15 minutes in length spent outside was considered valid for the intervention. WCS, SpO₂, and respiratory and heart rates were reassessed in both groups at 30 minutes from triage and at 60 minutes. Patients were discharged from the hospital when clinically appropriate. The need for any additional treatments was noted (nebulized epinephrine). Finally, home evaluation using the modified TOP score, the need for return visits to any medical care facility and associated reasons, and hospitalization rate within 7 days of the initial PED visit were recorded by a standardized telephone interview with parents or caregivers on day 7.

Outcomes

The primary outcome was the proportion of participants showing clinical improvement defined as a decrease in WCS ≥ 2 points from baseline at 30 minutes. A decrease in WCS of 1 point from baseline is already thought to be a clinically relevant change.¹⁰ In children with croup, a single dose of oral dexamethasone has been shown to provide benefit from 30 minutes after administration,²⁴ thus allowing to assess the effect of cold air in the meantime.

Secondary outcomes measures included changes in WCS from baseline at 60 minutes, differences in SpO₂ on room air by pulse oximetry, and respiratory and heart rates from baseline, at 30 and 60 minutes. Parent or patient perception of any adverse events related to exposure to outdoor cold air was also a secondary outcome. The need (and reasons) for an initially discharged patient to reattend any medical care or to be subsequently admitted for worsening or ongoing symptoms within 7 days was recorded. At follow-up interviews, parents or guardians were also asked to provide the residual presence of croup symptoms using the outpatient score derived from the TOP score.

Statistical Analysis

No study had previously evaluated the effect of exposure to cold air on croup symptoms. We estimated that 50% of participants exposed to outdoor cold air versus 20% of participants in the control group would show clinical improvement. Assuming that 20% of participants exposed to outdoor cold air could quit the intervention earlier because of discomfort, with a similar improvement rate than the control group, we expected a proportion of improvement in the exposed group of 44% (ie, $0.8 \times 50 + 0.2 \times 20$). Hence, a sample of 56 participants per group provided 80% power to detect an absolute difference of at least 24% in proportion of participants with clinical improvement at 30 minutes between study groups, with a 2-sided $\alpha = .05$. To prevent a potential loss of power because of misspecification of assumptions, the counts were increased to 59 participants per group.

Participants' characteristics at triage were described by means and SDs, or by counts and percentages. The primary analysis was performed on an intention-to-treat basis. A per-protocol analysis including only participants in the intervention arm truly exposed to the intervention (ie, patients exposed to a temperature $< 10^{\circ}\text{C}$ for at least 15 min) was also performed for verification.

The primary outcome was compared between both arms with a χ^2 test. The intervention's effect was assessed with the absolute risk difference. The odds ratio was reported with a 95% confidence interval (CI). The mean change in WCS at 30 min from triage was compared between both groups with a student's *t* test. The mean differences between both arms were reported with 95% CIs. Subgroup analyses were also conducted according to severity at presentation corresponding to WCS category at triage (mild, moderate). Similar analyses were conducted for WCS at 30 and 60 minutes. The modified TOP score was compared between both groups using a Mann-Whitney's test because of large asymmetry in the distributions. All statistical tests were 2-sided with a 5% significance level. Analyses were performed with R software v4.0.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

From November 1, 2016, to May 31, 2021, of 3602 patients presenting with croup to the PED, 1505 were assessed for eligibility, of whom 118 children were randomly assigned to either outdoor cold air ($n = 59$) or indoor room temperature ($n = 59$), with no dropouts (Fig 1). Mean age was 32 months (SD 25), 36 (31%) participants were female, and 82 (69%) were male. After randomization, 1 patient assigned to the intervention group mistakenly remained seated in the waiting room. All other 58 patients assigned to the intervention group were exposed to outdoor cold air for a mean of 30.1 minutes (95% CI 28.5–31.7). A total of 108 of 118 children completed follow-up at 7 days ($n = 52$ outdoor cold air group; $n = 56$ indoor room temperature group). Baseline characteristics were comparable in the 2 groups (Table 1). On average, the difference between outdoor and indoor temperatures was 20°C and the difference for humidity 38%.

The number of patients showing a reduction of at least 2 points in WCS at 30 minutes after triage was significantly higher in patients allocated to the outdoor cold air exposure group compared with patients who remained at indoor room temperature (Table 2, Fig 2, and Supplemental Fig 3). Mean reductions in WCS by study group and croup severity on an intention-to-treat or per-protocol analysis are presented in Supplemental Table 6. Patients with moderate croup benefited the most from the intervention. When patients improved, WCS at 30 minutes was reduced by 2 to 3 points most frequently. More patients showed a reduction of 2 points from their

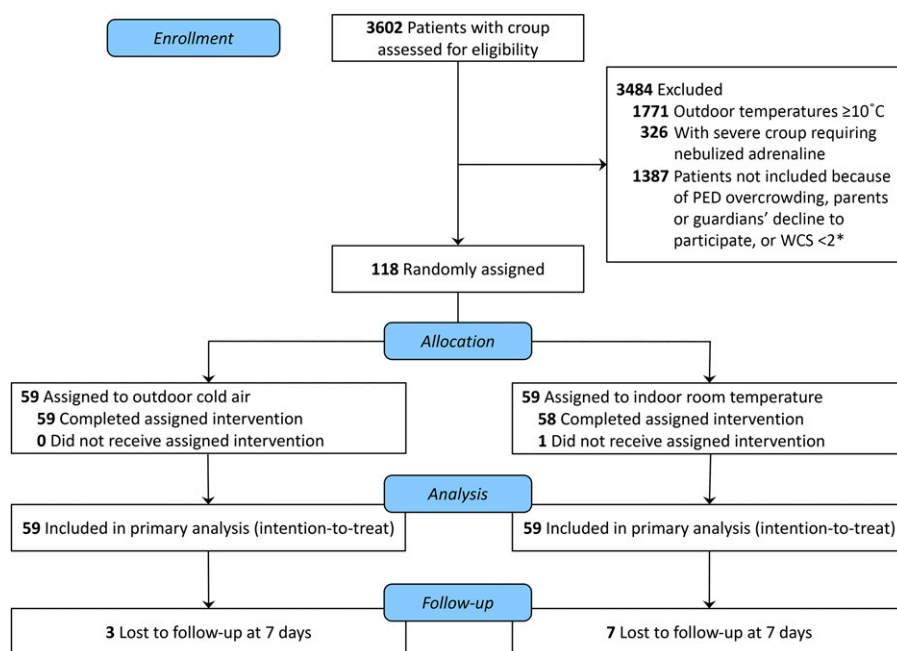


FIGURE 1

Consolidated Standards of Reporting Trials diagram. *In the context of PED overcrowding, nurses were not systematically available for patient inclusions. Although only few patients declined to participate, data concerning these patients and those with $\text{WCS} < 2$ were not possible to obtain from triage nurses and rotating staff on a 24-hour basis.

baseline WCS in the intervention group (19 of 59, 32.2%) than in the control group (12 of 59, 20.3%) (Supplemental Fig 3). The same pattern was observed for a reduction of 3 points in WCS : 8 of 59 (13.6%) in the intervention group and 2 of 59 (3.4%) in the control group.

At 60 minutes, the effect of the intervention was no longer different between the 2 groups. On a per-protocol analysis, 1 participant was missing after they had mistakenly remained inside, but similar results were observed (Supplemental Table 7). Concerning vital signs, only pulse oximetry showed a difference between the 2 groups, with a higher mean value at 30 and 60 minutes in the group exposed to cold outdoor air. However, with a mean value remaining above 98% in both groups under an inspired oxygen fraction of 21%, this difference is not clinically relevant (Table 2).

Table 3 shows the distribution of patients by TOP-derived score at home immediately before departure for the PED, at triage, and at 7 days of the visit, by study group. At home and at triage, the number of patients showing a score of 3 was slightly larger in the group exposed to outdoor cold air than in the control group. Thirty-five of the 68 children (17 of 36 [47.2%] in the intervention group and 18 of 32 [56.3%] in the control group) with a TOP-derived score of 3 at home showed a decrease of 1 unit or more at presentation. By day 7, the number of children with no persisting symptoms was slightly higher in the intervention group. Symptoms had completely resolved in 44.2% of children in the intervention group and 32.1% of

children in the control group. The total score at day 7 was not different between study groups ($P = .28$). Return visits and hospitalization rates are reported in Table 3. Only 1 patient in the control group required hospitalization for gastroenteritis within a week of the initial visit. No adverse event was reported related to the intervention.

DISCUSSION

This single-center, open-label, randomized clinical trial provides a first clinical evidence that a 30-minute exposure to outdoor cold air ($< 10^{\circ}\text{C}$) is beneficial for reducing the severity of croup symptoms in children, particularly if moderate. Considering that oral dexamethasone shows a therapeutic effect after a 30 minute-delay,^{10,24} this nonpharmacological additional measure, easy to perform by parents and guardians, could be an initial measure to offer.

To our knowledge, cold air exposure as a therapeutic adjunct for viral croup has not been supported by published data to date. Faraji-Goodarzi et al compared the effect of cold drinks versus dexamethasone, and their combined effect on children with croup.²⁵ The authors concluded that cold drinks had less therapeutic effect than dexamethasone alone and than combined measures, presumably because of the topical site of action of cold. It is likely that the contact of cold drinks with the esophageal mucosa, which is somewhat distant from that of the laryngeal wall, differs from the direct effect of inhaled cold air on the airway. This may explain the

Characteristics	Participants	
	Outdoor Cold Air (<i>n</i> = 59)	Indoor Room Temperature (<i>n</i> = 99)
Age, mo	30.9 (24.6) [4–117]	33.2 (25.9) [7–96]
Sex		
Female	14 (23.7)	22 (37.3)
Male	45 (76.3)	37 (62.7)
Weight, kg	14.2 (6.6)	14.3 (4.9)
Body temperature, °C	37.6 (0.9)	37.4 (1.0)
Heart rate at triage, beats per min	138 (20)	137 (26)
Respiratory rate at triage, breaths per min	31 (8)	30 (8)
Missing data	1	0
Pulse oximetry at triage, %	98.1 (2.2)	98.4 (1.6)
Missing data	1	0
Outdoor temperature, °C	5.3 (2.9) [−0.8 to 9.9]	5.3 (3.0) [−2.6 to 9.8]
Indoor temperature, °C	25.3 (0.5) [24.0–26.7]	25.2 (0.4) [24.5–26.3]
Outdoor hygrometry, %	68.1 (14.5) [38.0–98.0]	69.2 (15.9) [39.0–98.0]
Indoor hygrometry, %	30.7 (12.5) [25.0–77.0]	30.2 (8.1) [11.0–52.0]
Missing data ^a	43	37
Cold exposure before triage, min	9.5 (8.7)	8.2 (9.4)
Cold exposure after triage, min	30.1 (6.0)	0.5 (3.9)
WCS at triage, mean (SD) [95% CI]	2.83 (0.99) [2.57–3.09]	2.71 (0.85) [2.49–2.93]
Mild (0–2)	29 (49.2)	30 (50.8)
0	0 (0)	0 (0)
1	0 (0)	0 (0)
2	29 (49.2)	30 (50.8)
Moderate (3–5)	30 (50.8)	29 (49.2)
3	16 (27.1)	18 (30.5)
4	9 (15.3)	9 (15.3)
5	5 (8.5)	2 (3.4)
Severe (6–11)	0 (0)	0 (0)
6	0 (0)	0 (0)
Past medical history		
Croup	16 (27.1)	20 (33.9)
Wheezing disorders ^b	14 (23.7)	12 (20.3)
Previous intubation	0	0

Data are *n* (%) or mean (SD) [range] unless otherwise stated. Percentages may not total 100 because of rounding.
^a Indoor hygrometry values noted “LL” (low) by the weather station were not coded and considered as missing.
^b Bronchiolitis, viral bronchitis, or asthma.

difference in our study results. Although exposure to cold air has been shown to cause inflammation of the lower respiratory tract and to trigger bronchial hyper-responsiveness, bronchoconstriction, and asthma,²⁶ the effects of cold air at the laryngeal level are more uncertain. In experimental models of adult animals, the presence of cold-sensitive receptors has been demonstrated in the upper airway.^{27,28} Stimulation of these receptors by cooling has been shown to both mediate ventilatory depression and increase upper airway dilator muscle activity,^{29–33} thus reducing laryngeal and supraglottic upper airway resistance. Temperature changes at these levels may play a role in controlling upper airway patency. This effect is abolished by laryngeal anesthesia³¹ or transection of the superior laryngeal nerves,^{29,30,32,34,35}

indicating a partial reflex origin.³⁶ Another mechanism that could explain the decrease in upper airway resistance could be related to a reduction in laryngeal mucosal blood flow induced by vasoconstriction under the effect of cold air. This could result in a reduction in mucosal thickness and an increase in luminal cross-sectional area favoring better ventilation.^{29,37} In young animals, the effect of cold air on reducing upper airway resistance has also been demonstrated.^{33,36,38} Whether similar physiologic effects participate in the reduction of upper airway resistance in humans, and particularly in children with croup, remains unknown but may be hypothesized. The larynx in humans is also a densely innervated organ with cold-sensitive receptors.³⁹

The question of the effect of inhaled air humidity, which averaged 68% for children exposed to outdoor

TABLE 2 Changes in Westley Group Score and Clinical Parameters From Triage (Baseline) to 30 and 60 Minutes

Variables	Outdoor Cold Air	Indoor Room Temperature	Odds Ratio	Risk Difference	P
	(n = 59)	(n = 59)	(95% CI)	(95% CI)	
Decrease in WCS					
Mild WCS					
≥2-point drop at 30 min	10 of 29 (34.5)	9 of 30 (30.0)	1.2 (0.4–3.7)	4.5 (–22.7 to 31.7)	.93
≥2-point drop at 60 min	13 of 29 (44.8)	16 of 29 (55.2)	0.7 (0.2–1.9)	–10.3 (–39.4 to 18.7)	.60
Moderate WCS					
≥2-point drop at 30 min	19 of 30 (63.3)	5 of 29 (17.2)	8.3 (2.5–28.0)	46.1 (20.6–71.5)	<.001
≥2-point drop at 60 min	24 of 30 (80.0)	21 of 27 (77.8)	1.1 (0.3–4.1)	2.2 (–21.2–25.7)	>.99
All patients					
≥2-point drop at 30 min	29 of 59 (49.2)	14 of 59 (23.7)	3.1 (1.4–6.8)	25.4 (7.0–43.9)	.007
≥2-point drop at 60 min	37 of 59 (62.7)	37 of 56 (66.1)	0.9 (0.4–1.9)	–3.3 (–22.6–15.9)	.86
Clinical parameters					
Respiratory rate ^a					
At triage	31.4 (7.7)	30.3 (8.0)	N/A	N/A	.38
At 30 min	29.2 (7.0)	29.2 (7.6)	N/A	N/A	.78
At 60 min	27.9 (6.4)	28.7 (7.9)	N/A	N/A	.60
Pulse oximetry ^b					
At triage	98.1 (2.2)	98.4 (1.6)	N/A	N/A	.60
At 30 min	98.8 (1.3)	98.2 (1.6)	N/A	N/A	.027
At 60 min	99.1 (1.1)	98.3 (1.6)	N/A	N/A	.002
Heart rate ^c					
At triage	138.4 (19.8)	137.4 (25.8)	N/A	N/A	.99
At 30 min	133.2 (20.9)	135.9 (25.4)	N/A	N/A	.29
At 60 min	129.7 (17.9)	127.0 (21.6)	N/A	N/A	.89

Data are n/N or mean (SD) unless otherwise stated. N/A, not applicable.

^a In breaths per minute.

^b In percentage.

^c In beats per minute.

humidity and 30% in the indoor group, may be raised. The literature shows that it is unlikely that humidity plays any role. A Cochrane review showed that humidified air, generated by various unnatural humidification mechanisms, was not superior to nonhumidified air or low-humidity air in reducing symptom severity in children with moderate

to severe croup after 30 to 60 minutes.¹⁵ Scolnik et al even showed that 100% humidity using optimally sized water particles to reach areas of the respiratory tract beyond the oropharynx failed to result in greater improvement compared with 40% inspired humidity or humidity through humidifiers in children with moderate to severe croup.⁴⁰ In an animal

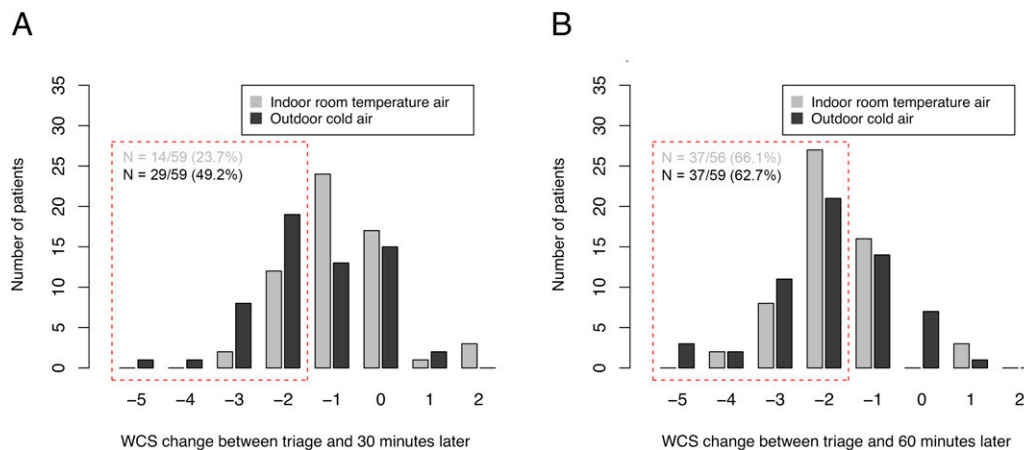


FIGURE 2

Joint distribution (number of patients) according to WCS change between triage and (A) 30 or (B) 60 minutes for patients exposed either to outdoor cold air or indoor room temperature. The red box denotes patients for whom the WCS decreased by at least 2 points.

TABLE 3 Evolution of Croup Symptoms by Study Group

TOP-Derived Score ^a	Outdoor Cold Air			Indoor Room Temperature		
	At Home	At PED	At D 7	At Home	At PED	At D 7
	(N = 59)	(N = 59)	(N = 52)	(N = 59)	(N = 59)	(N = 56)
0	0 (0.0)	2 (3.4)	23 (44.2)	0 (0.0)	0 (0.0)	18 (32.1)
1	2 (3.4)	7 (11.9)	27 (51.9)	2 (3.4)	10 (16.9)	37 (66.1)
2	21 (35.6)	26 (44.1)	2 (3.8)	25 (42.4)	32 (54.2)	1 (1.8)
3	36 (61.0)	24 (40.7)	0 (0.0)	32 (54.2)	17 (28.8)	0 (0.0)
Missing data	0	0	7	0	0	3
Mean (SD)	2.58 (0.56)	2.22 (0.79)	0.60 (0.57)	2.51 (0.57)	2.12 (0.67)	0.70 (0.50)
Return visits	N/A	N/A	20 (38.4) ^b	N/A	N/A	20 (35.7) ^c
Hospitalization	N/A	N/A	0 (0.0)	N/A	N/A	1 (1.8) ^d

Data are n/N (%). N/A, not applicable.

^a The score is displayed as an additive total score, that is, adding the first item (stridor) ranging from 0 (no stridor) to 2 (stridor at rest or when quiet), to the second item (cough) ranging from 0 (no cough) to 1 (barking cough).

^b Five, croup (including 1 asthma); 9, upper respiratory tract infection without residual croup; 1, media otitis; 1, bronchiolitis.

^c Seven, croup; 9, upper respiratory tract infection without residual croup; 3, media otitis; 24-month routine checkup.

^d Hospitalized for gastroenteritis.

models of croup, data have demonstrated that dry air (either warm or cold) produced greater reduction in airway resistance than cold moist air, whereas warm moist air produced no change.⁴¹ And the maximum effect of cold, dry air on reducing the dogs' laryngeal resistance occurred within the first 30 minutes of therapy, after which virtually no further changes were noted.

In our study, the number of patients showing significant clinical improvement in symptoms (reduction ≥ 2 points from the initial WCS) or even symptom resolution at 60 minutes was identical between the 2 groups. Many reasons can explain this finding. First, the beneficial physical effect of cold air ceased when exposure was discontinued after 30 minutes. Second, after 60 minutes, the beneficial effects of dexamethasone administered at triage may have already partially relieved symptoms. Third, it is possible that cold air exposure might only accelerate the improvement in symptoms in exposed patients, but that the course would be spontaneously favorable in most cases. This would be comparable to the effect of nebulized epinephrine, which was associated with WCS improvement 30 minutes after it is administered, but with no persisting effect 2 and 6 hours later.¹³ Our findings suggest that the benefits of cold air exposure already begin on the way to the health care facility when exposed to outdoor temperatures, as often reported by parents.

No statistically significant difference was observed between groups in heart and respiratory rates at 30 and 60 minutes. This is probably because of the high variability of these parameters in a pediatric population showing various age ranges and to the little influence of mild to moderate croup on these parameters, unlike obstructive pathologies such as asthma. Pulse oximetry, whose standard values do not vary according to the age, seemed to be improved by exposure to cold air. However, the difference found in mean oxygen saturation is not clinically significant.

Pulse oximetry has not been demonstrated sensitive enough for assessing the severity of viral croup,¹⁶ but it is useful if the tracheo-bronchial airway is involved (ie, prolonged expiration and expiratory wheezing) or in case of ventilation-perfusion mismatch. Frequent evaluation of mental status, work of breathing, and chest air entry remain the most accurate tool for recognizing worsening croup.¹

We failed to show any statistically significant difference in residual symptoms between the 2 study groups at 7 days. Also, there was no difference in reattendance rates between the 2 groups, which are similar to those extracted from dexamethasone studies.⁴²

Finally, although only few parents related sensation of cold while waiting outside, no other side effects were observed.

Our study has limitations. First, it is difficult to assess the effect of possible confounding distraction in both groups, and patients with croup show fewer symptoms when they are not agitated. Second, the study was an open-label trial. For practical reasons linked to limited resources in health care providers at night when croup symptoms peak, the allocation group could not be blinded, making possible a bias in the clinical assessment by the physician in charge to occur. The use of a recognized and validated score limits this risk. Several studies have evaluated the interobserver reproducibility of the WCS and shown good interobserver agreement rates.⁴⁰ In addition, the absence of difference at 60 minutes may indicate objectivity in measuring WCS.

CONCLUSIONS

This randomized controlled trial supports the benefits of exposure to outdoor cold air on croup symptoms in children with mild to moderate croup in the first 30 minutes before the onset of action of steroids. More studies are needed to

assess the efficacy of cold air exposure. Perspectives include reinforcing these findings using digital auscultation coupled with blinding of the clinical assessment.

ACKNOWLEDGMENTS

We thank the triage nurses and pediatric emergency physicians for their contributions to the trial by enrolling the study participants.

ABBREVIATIONS

CI: confidence interval
PED: pediatric emergency department
SpO₂: saturation measured via pulse oximetry
TOP: Telephone Out Patient
WCS: Westley Croup Score

design, oversaw the study coordination, and critically reviewed and revised the final manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

This study is registered at Swiss National Clinical Trials Portal, #SNCTP000002514/BASEC2016-00845, <https://www.kofam.ch/en/snctp-portal/searching-for-a-clinical-trial/study/40689>, August 8, 2016, and ClinicalTrials.gov, #NCT05668364, <https://clinicaltrials.gov/ct2/show/NCT05668364>, December 29, 2022. Individual participant data that underlie the results reported in this study, after deidentification (text, tables, figures, and appendices), will be made available. The study protocol will also be made available. The data can be accessed by contacting Johan N. Siebert, MD, at Johan.Siebert@hcuge.ch, beginning 6 months and ending 10 years after article(s) publication. Data will be made available for a specified research purpose to qualified external researchers whose proposed use of the data has been approved by their institutional review board. Those requesting data also must have a signed data access agreement, and the request proposal must include a statistician.

DOI: <https://doi.org/10.1542/peds.2023-061365>

Accepted for publication May 23, 2023

Address correspondence to Johan N. Siebert, MD, Department of Pediatric Emergency Medicine, Geneva Children's Hospital, Geneva University Hospitals, 1211 Geneva, Switzerland. E-mail: Johan.Siebert@hcuge.ch

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2023 by the American Academy of Pediatrics

FUNDING: No external funding.

CONFLICT OF INTEREST DISCLOSURES: The authors have indicated they have no conflicts of interest relevant to this article to disclose.

REFERENCES

1. Cherry JD. Clinical practice. Croup. *N Engl J Med*. 2008;358(4):384–391
2. Bjornson CL, Johnson DW. Croup. *Lancet*. 2008;371(9609):329–339
3. Kivekäs I, Rautiainen M. Epiglottitis, acute laryngitis, and croup. In: Durand ML, Deschler DG, eds. *Infections of the Ears, Nose, Throat, and Sinuses*. Cham, Switzerland: Springer International Publishing AG; 2018:247–255
4. Hanna J, Brauer PR, Morse E, Berson E, Mehra S. Epidemiological analysis of croup in the emergency department using two national data sets. *Int J Pediatr Otorhinolaryngol*. 2019;126:109641
5. Weinberg GA, Hall CB, Iwane MK, et al. New Vaccine Surveillance Network. Parainfluenza virus infection of young children: estimates of the population-based burden of hospitalization. *J Pediatr*. 2009;154(5):694–699
6. Henrickson KJ, Kuhn SM, Savatski LL. Epidemiology and cost of infection with human parainfluenza virus types 1 and 2 in young children. *Clin Infect Dis*. 1994;18(5):770–779
7. Smith DK, McDermott AJ, Sullivan JF. Croup: diagnosis and Management. *Am Fam Physician*. 2018;97(9):575–580
8. Tyler A, McLeod L, Beaty B, et al. Variation in inpatient croup management and outcomes. *Pediatrics*. 2017;139(4):e20163582
9. Walsh PS, Lipshaw MJ. Diurnal variation in frequency and severity of croup in the emergency department. [Published online ahead of print September 22, 2022] *Hosp Pediatr*. 2022. 10.1542/hpeds.2022-006682
10. Gates A, Gates M, Vandermeer B, et al. Glucocorticoids for croup in children. *Cochrane Database Syst Rev*. 2018;8(8):CD001955
11. Johnson DW. *Croup*. *BMJ Clin Evid*. 2014;0321
12. Westley CR, Cotton EK, Brooks JG. Nebulized racemic epinephrine by IPPB for the treatment of croup: a double-blind study. *Am J Dis Child*. 1978;132(5):484–487
13. Bjornson C, Russell K, Vandermeer B, Klassen TP, Johnson DW. Nebulized epinephrine for croup in children. *Cochrane Database Syst Rev*. 2013;(10):CD006619
14. 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(9):873–879
15. Moore M, Little P. Humidified air inhalation for treating croup. *Cochrane Database Syst Rev*. 2006;(3):CD002870
16. Petrocheilou A, Tanou K, Kalampouka E, Malakasioti G, Giannios C, Kaditis AG. Viral croup: diagnosis and a treatment algorithm. *Pediatr Pulmonol*. 2014;49(5):421–429

17. Bjornson CL, Johnson DW. Croup in children. *CMAJ*. 2013;185(15):1317–1323
18. Brewster RC, Parsons C, Laird-Gion J, et al. COVID-19-associated croup in children. *Pediatrics*. 2022;149(6):e2022056492
19. Sealed envelope. Archived by WebArchive.org. Available at: <https://web.archive.org/web/20230112160930/https://sealedenvelope.com/>. www.sealedenvelope.com. Accessed January 12, 2023
20. Klassen T, Rowe P. The croup score as an evaluative instrument in clinical trials. *Arch Pediatr Adolesc Med*. 1995;149:60
21. Ausejo M, Saenz A, Pham B, et al. The effectiveness of glucocorticoids in treating croup: meta-analysis. *BMJ*. 1999;319(7210):595–600
22. Beveridge R. Canadian Association of Emergency Physicians. CAEP issues. The Canadian Triage and Acuity Scale: a new and critical element in health care reform. *J Emerg Med*. 1998;16(3):507–511
23. Bjornson CL, Williamson J, Johnson DW. Telephone Out Patient Score: the derivation and validation of a telephone follow-up assessment tool for use in clinical research in children with croup. *Pediatr Emerg Care*. 2016;32(5):290–297
24. Dobrovoljac M, Geelhoed GC. How fast does oral dexamethasone work in mild to moderately severe croup? A randomized double-blinded clinical trial. *Emerg Med Australas*. 2012;24(1):79–85
25. Faraji-Goodarzi M, Taei N, Mohammadi-Kamalvand M. Comparison of the effect of cold drink and dexamethasone, and their combined effect on children with croup. *Drug Res (Stuttg)*. 2018;68(4):185–188
26. D'Amato M, Molino A, Calabrese G, Cecchi L, Annesi-Maesano I, D'Amato G. The impact of cold on the respiratory tract and its consequences to respiratory health. *Clin Transl Allergy*. 2018;8:20
27. Sant'Ambrogio G, Mathew OP, Sant'Ambrogio FB. Characteristics of laryngeal cold receptors. *Respir Physiol*. 1988;71(3):287–297
28. Sant'Ambrogio G, Mathew OP, Sant'Ambrogio FB, Fisher JT. Laryngeal cold receptors. *Respir Physiol*. 1985;59(1):35–44
29. O'Halloran KD, Curran AK, Bradford A. Ventilatory and upper-airway resistance responses to upper-airway cooling and CO₂ in anaesthetized rats. *Pflugers Arch*. 1994;429(2):262–266
30. O'Halloran KD, Curran AK, Bradford A. Effect of upper airway cooling and CO₂ on diaphragm and genioid muscle activity in the rat. *Eur Respir J*. 1996;9(11):2323–2327
31. Orani GP, Anderson JW, Sant'Ambrogio G, Sant'Ambrogio FB. Upper airway cooling and l-menthol reduce ventilation in the guinea pig. *J Appl Physiol* (1985). 1991;70(5):2080–2086
32. Ukabam CU, Knuth SL, Bartlett D Jr. Phrenic and hypoglossal neural responses to cold airflow in the upper airway. *Respir Physiol*. 1992;87(2):157–164
33. Mathew OP, Anderson JW, Orani GP, Sant'Ambrogio FB, Sant'Ambrogio G. Cooling mediates the ventilatory depression associated with airflow through the larynx. *Respir Physiol*. 1990;82(3):359–367
34. Jammes Y, Barthelemy P, Delpierre S. Respiratory effects of cold air breathing in anesthetized cats. *Respir Physiol*. 1983;54(1):41–54
35. Mathew OP, Sant'Ambrogio FB, Sant'Ambrogio G. Effects of cooling on laryngeal reflexes in the dog. *Respir Physiol*. 1986;66(1):61–70
36. Curran AK, O'Halloran KD, Bradford A. Upper airway cooling reduces upper airway resistance in anaesthetized young guinea-pigs. *Eur Respir J*. 1998;11(6):1257–1262
37. Wasicko MJ, Hutt DA, Parisi RA, Neubauer JA, Mezrich R, Edelman NH. The role of vascular tone in the control of upper airway collapsibility. *Am Rev Respir Dis*. 1990;141(6):1569–1577
38. Curran AK, O'Halloran KD, Bradford A. Effects of superior laryngeal nerve section on ventilation in neonatal guinea pigs. *Respir Physiol*. 1995;101(1):23–29
39. Widdicombe J. Airway receptors. *Respir Physiol*. 2001;125(1-2):3–15
40. Scolnik D, Coates AL, Stephens D, Da Silva Z, Lavine E, Schuh S. Controlled delivery of high versus low humidity versus mist therapy for croup in emergency departments: a randomized controlled trial. *JAMA*. 2006;295(11):1274–1280
41. Wolfsdorf J, Swift DL. An animal model simulating acute infective upper airway obstruction of childhood and its use in the investigation of croup therapy. *Pediatr Res*. 1978;12(11):1062–1065
42. 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;22(8):541–544