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Humidified air inhalation for treating croup: a systematic review and meta-analysis

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Background. Croup (laryngotracheobronchitis) is a common cause of upper airway obstruction in children. Treatment with humidified air was previously widely used and is still commonly recommended as home treatment.

Objective. To assess the efficacy of humidified air in the treatment of croup.

Design. Systematic review and meta-analysis.

Data sources. We searched the Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE.

Review methods. We included randomized controlled trials with or without blinding. All studies treating children with a clinical diagnosis of croup with warm or cool humidified air delivered by steam or humidified tent whether inpatients, attenders at the Emergency Department or in the community were eligible.

Main results. Three studies in emergency settings provided data on 135 patients with moderate croup for the main outcome (croup score). The combined results from 20 to 60 minutes in the three studies marginally favoured the treatment group with a weighted standardized mean difference of –0.14 (95% confidence interval = –0.75 to 0.47). No outcomes were significantly different between the groups.

Conclusions. The croup score of children managed in an emergency setting with mild to moderate croup probably does not improve greatly with inhalation of humidified air. There is insufficient evidence to exclude either a small beneficial or a harmful effect.

Keywords. Cochrane, emergency medicine, meta-analysis, paediatrics, respiratory medicine.

Background

Croup (laryngotracheobronchitis) is a common cause of upper airway obstruction in children with a peak incidence of 60 per 1000 child years in those aged between 1 and 2 years.[1] It is characterized by hoarseness, a barking cough and inspiratory stridor. These symptoms are thought to occur as a result of oedema of the larynx and trachea which have been triggered by a recent viral infection. Para influenza virus type 1 is the agent most commonly identified in cases of croup. It occurs most commonly between the ages of 3 months to 6 years and the incidence is highest between 1 and 2 years of age.[2] Severe cases are admitted to hospital for observation with reported admission rates between 1% and 15%.[2,3] A seasonal variation in hospitalization rates has been noted and hospitalization rates are higher in boys and in those aged less than 1 year.[4] Treatment with inhaled or oral steroids is established as an effective treatment in outpatient and hospital settings.[5] Since the advent of this effective treatment, a steady reduction in hospital admissions has been reported and the observed reduction has been attributed to the adoption of outpatient steroid treatment.[4] Croup nevertheless, can be a severe condition and prior to the introduction of steroid treatment intubation was required in 2% of hospitalized children.[6] Although mortality rates are low there are still occasional case reports of deaths following rapid unexpected deterioration.[7]

Traditional treatment of croup has included the use of humidified air either using warm moist air at home

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or a cool mist in hospital. Warm moist air has been in use since the 19th century and is continued to be advocated at home as it is readily available either by moving the child to a bathroom and running a hot bath or shower or by boiling a kettle in the room. Cool mists have been used in the hospital setting as the production of a humidified atmosphere can be more safely delivered. A variety of methods have been described using a perspex cot or mist tent or using a mist stick.[8–10] Theoretically cool humidified air will result in mucosal cooling and a reduction in oedema together with a reduction in the viscosity of secretions.[11] There are, however, two concerns regarding the theoretical benefits of traditional humidity. Firstly that the particle size generated by 'blow by' humidifiers is not optimal for deposition in the larynx.[12] Secondly that in an animal experiment with experimentally induced laryngeal oedema, warm dry and cool dry air produced the greatest reduction in airway resistance, whereas warm moist air produced no change.[13]

In some countries, the use of humidified air in hospital settings has been abandoned without adverse effect[9] however its use continues in some European countries [14]and in a recent North American study, no control group for moist air was used because humidification remains the standard treatment for croup.[12] The advice to use steam treatment at home is also still widespread in primary care settings and some review articles continue to cite humidified air as a potential treatment strategy.[11,15] None of the identified reviews, however, were based on a systematic search of the literature, including unpublished research. This review aims to systematically search for and combine evidence from all randomized controlled trials relating to humidified air treatment of croup in order to inform current practice.

Objectives

The objective of this review is to examine the effect of humidified air in the treatment of croup, with particular attention on the relief of symptoms, the prevention of admission or the prevention in deterioration.

The most widely used outcome in studies on croup is the Westley croup score (Box 1) or a variation of this.[16] While being easily measurable with good interrater reliability and agreeing well with global assessment of severity[17] changes in a score may not be valued highly by parents. We chose also to include other measures likely to concern parents [admission rates, duration of symptoms, number of visits to the Emergency Department (ED) and time lost from school].

Methods

The criteria for considering studies for this review were as follows:

- Types of studies

Randomized controlled trials with or without blinding.

- Types of participants

All studies treating children with a clinical diagnosis of croup whether inpatients, attenders at the ED or in the community.

- Types of interventions

Warm or cool humidified air delivered by steam or humidified tent. We are not aware of any plausible placebo treatment. Humidified air was compared with no treatment.

- Types of outcome measures

1. Mortality (if any)
2. Admission to hospital
3. Ventilation/intensive care treatment
4. Symptom severity or symptom scores
5. Duration of symptoms or inpatient treatment
6. Number of visits to the ED or for other medical attention (excluding routine visits) concerning croup in the week following treatment
7. Time lost from school

It was planned to separately record the outcomes for the week following treatment.

Search strategy
All references in the identified trials were checked and trial authors contacted to identify any additional published or unpublished data. There were no language restrictions. Search strategy can be found in the supplementary material online.

Study identification
From this list of references, both authors independently selected studies as being potentially relevant based on a review of titles and, when available, the abstracts. The potentially relevant studies were retrieved as full manuscripts. All potentially relevant studies were reviewed independently by both authors. Discrepancies were resolved through discussion. The authors decided which trials fitted the inclusion criteria and graded their methodological quality. Any disagreement was resolved by discussion between the authors. Trial authors were contacted for clarification where necessary.

Methodological quality
The methodological quality of the included trials was assessed with particular emphasis on the allocation

concealment, which was ranked using the Cochrane approach. Grade A: adequate concealment, Grade B: uncertain, Grade C: clearly inadequate concealment. Where there was uncertainty trial authors were contacted for clarification. The methodological quality of studies was also documented using the following criteria: baseline comparison of experimental groups, explicit diagnostic criteria, completeness of follow-up and blind outcome assessment.

Data extraction

Data were extracted using a structured form that captured patient status (inpatient or outpatient) and intervention and control characteristics, such as type of humidity and method of administration. Additionally, data were collected on the primary outcome measures: change from baseline clinical croup scores; return visits and/or (re)admissions; length of stay in hospital or accident and emergency (hours); patient improvement (yes or no) and the use of additional interventions such as epinephrine, supplemental glucocorticoids, intubation or antibiotic treatment. Data extraction was performed by both authors then entered by one author. The trial authors were contacted to provide missing data where possible. Data entry was checked by the second author.

A weighted treatment effect (using random effects) was calculated across trials using the Cochrane statistical package, Review Manager version 4.2. The results are expressed as odds ratio (OR) and 95% confidence interval (CI), risk difference with 95% CI for dichotomous outcomes and weighted mean difference (WMD) and 95% CI for continuous outcomes.

Only three studies were included in the review. No sensible subgroup analyses could be performed.

Description of studies

We identified three studies suitable for inclusion (Table 1). Bourchier *et al.* (1984)[18] is widely cited. In this study, 16 consecutive inpatients with croup (age range 0.4–4.5 years) were allocated using a random process not described to one of two groups. Treatment consisted of either using air alone or treatment with humidified air provided in a perspex cot. Humidified air was provided directly to the covered cot kept at a temperature of 21–23°C with a relative humidity of 87–95%. There was no allocation concealment for the assessors. Detailed outcome measures were provided for up to 12 hours following treatment. No long-term data were provided. No statistical differences were found between the outcome measures (croup score, pulse rate, respiratory rate, oxygen saturation or global impression).

Neto *et al.* (2002)[19] enrolled children between the ages of 3 months to 6 years with moderate croup

TABLE 1 *Characteristics of included studies*

Study	Methods	Participants	Interventions	Outcomes	Notes	Allocation concealment
Bourchier *et al.* (1984)[18]	Randomized controlled trial	16 consecutive admissions to paediatric ward (9 males) age 0.4–4.5 years.	Humidified air in perspex covered cot versus room air. Humidified cot air at 87–95% and temperature 21–23°C.	Westley symptom score	Data 0, 1, 2, 3, 4, 5, 6, 12 hours. Oxygen saturation only available at 2 hourly intervals for 12 hours. Hourly intervals.	D
Jamshidi *et al.* (2001)[20]	Randomized controlled trial	58 children aged 3 to –6 years (39 male) with clinical diagnosis of croup with score 1 to 8. Excluded if score > 8 or oxygen saturation < 93%. Excluded if prior treatment with humidified air budesonide or epinephrine. Outcome data on 48 only.	Humidified cool air delivery by 'mist tube'	Respiratory induced plethysmography (RIP) modified Taussig croup score pulse oxygen saturation	Data at baseline and 20 minutes. Investigator calculated RIP score blind to interventions. Other outcomes not blind. Computer generated random number tables but no description of allocation concealment.	C
Neto *et al.* (2002)[19]	Randomized controlled trial	71 children 3 months to 6 years presenting to ED with clinical diagnosis of croup and croup score of 2 or more. Excluded if oxygen saturation < 92% or if asthmatic and wheezing.	Humidified cool oxygen delivered using 'mist stick' by parents. Control held in semi-recumbent position in room air for 20 minutes All received oral dexamethasone. Inhaled epinephrine/budesonide at discretion of treating physician.	Westley symptom score. Oxygen saturation, pulse rate, respiratory rate, global score, length of stay, admission.	Data at 30-minute intervals for 2 hours. Treatment in separate room. Research assistant and physician blind to treatment allocation.	A

presenting at an ED. Children with a low Westley score less than 2 or low oxygen saturation were excluded. A total of 71 children entered the study and were randomized to receive moisturized air delivered by a mist stick or room air. All children initially received a dose of oral dexamethasone (0.6 mg/kg) and other treatments were allowed according to clinician choice. Both nebulized steroids and epinephrine were used in 25 subjects, unequally distributed between the randomized groups (mist 16 and no mist 10). A separate analysis excluding subjects given additional treatment was performed by the authors, which failed to alter the results. Nor was there any difference in baseline characteristics or in response to treatment in those given additional treatments (information supplied by trial author). All subjects were included in our analysis. Measures of symptom severity were made at 30, 60, 90 and 120 minutes following treatment and the assessors were blinded to the treatment group. All patients improved over time with no significant differences between any outcome measure at any assessment time.

Jamshidi *et al.* (2001)[20] recruited children aged 3 months to 6 years attending a university children's hospital ED. Children were included only if no prior treatment had been given and with moderate symptoms (modified croup scores of 1 to 8, and oxygen saturation higher than 93%) and were randomized to receive humidified air from a mist tube or room air. The main outcome of the study was resistance inductance plethysmography. This is a technique to objectively quantify the ribcage and abdominal movements. The purpose is to measure the asynchronous motion between the two manifested as chest retraction, which is included as an ordinal variable in croup scoring systems. Plethysmography was undertaken by a technician blinded to treatment allocation but croup score and other measures were not blinded. Data were provided only on the children completing successful plethysmography—48 from 58 children entering the study. Measures of croup severity, pulse respiratory rate and oxygen saturation were reported from baseline and after 20 minutes. Croup scores improved significantly in the mist group and not in the control group. This study has been published in abstract form and further details for the review were obtained directly from the trial authors.

Box 1: *Components of the Westley croup score*

Stridor

[0 no stridor; 1 stridor audible with the stethoscope at rest; 2 stridor audible without stethoscope]

Retraction of intercostals and subcostal regions

[0 none; 1 mild; 2 moderate; 3 severe]

Air entry into lungs

[0 normal; 1 decreased; 2 severely decreased]

Cyanosis

[0 none; 4 cyanosis with agitation; 5 cyanosis at rest]

Consciousness

[0 normal; 5 altered]

One high quality study[12] was identified but not included. This study included randomized treatments of 140 children with croup to one of three groups; standard humidified oxygen (blow by) compared to 40% or 100% humidity with a particle size appropriate for deposition in the larynx. The trial authors argued that traditional humidification has uncontrolled particle size which may limit therapeutic effect and that particles reaching the lower airway may induce bronchospasm. Their control group of traditional humidification meant we were unable to include it in our review where the traditional humidification is regarded as the active treatment. This study failed to show any differential benefit between traditional humidification or the more theoretically correct treatments.

All other identified papers were not trials and did not involve randomized allocation of children to different treatment groups[8,21–25] (Supplementary Table 2).

Methological quality of included studies

Both authors independently assessed the quality of the included studies. Minor differences between the authors were agreed upon after discussion. The results are summarized in Supplementary Table 3.

Results

The search strategy was first run in August 2003 and repeated in November 2004 and January 2006. No new studies were identified from the subsequent searches. Mortality data were not explicitly reported in any study but it is unlikely that there were fatalities.

Bourchier *et al.* (1984)[18] studied only inpatients and thus could not be included in analysis of admissions. Combined results from Jamshidi *et al.* (2001)[20] and Neto *et al.* (2002)[19] gave a Peto OR 3.09; 95% CI = 0.71–13.47 in favour of admission with active treatment (mist) (Fig. 1). No patient was reported as needing intensive care treatment in any study.

Symptom severity was reported in all three studies at different time points (all times in minutes). Bourchier *et al.* (1984)[18] at time 0, 60, 120, 180, 240, 300, 360 and 720. Neto *et al.* (2002)[19] at 0 30, 60, 90 and 120. Jamshidi *et al.* (2001)[20] at 0 and 20.

For the main analysis, in order to maximize numbers available for the review, data from Bourchier *et al.* (1984)[18] 60 minutes, Neto *et al.* (2002)[19] 60

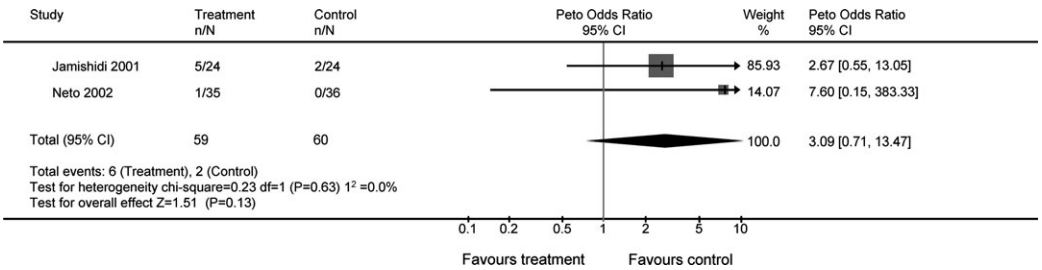

FIGURE 1 *ORs for admission: humidified air versus no treatment*

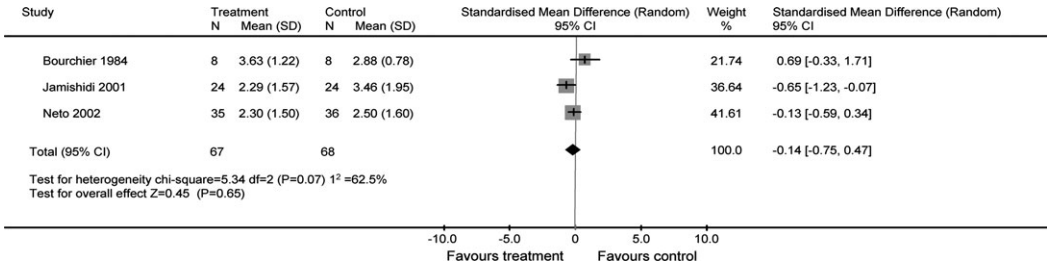

FIGURE 2 *Clinical score at 20–60 minutes combined: humidified air versus no treatment*

minutes and Jamshidi *et al.* (2001)[20] 20 minutes were combined. All studies used a clinical scoring scale based on the Westley scale. Jamshidi used a modified scale and thus scores were compared using standardized mean difference. The combined results from 20 to 60 minutes in the three studies favoured the treatment group but failed to reach significance, WMD –0.14; 95% CI = –0.75 to 0.47 (Fig. 2). Additional analyses were completed using combined data at 20–30 minutes[19,20] and data from time point 60 and 120 minutes.[18,19] Data from 20 to 30 minutes favoured mist therapy –0.40 (–0.82 to 0.02) although it should be noted that this includes the unblinded assessment from Jamshidi *et al.* (2001). Assessment data at 60 minutes favoured no treatment 0.2 (–0.64 to 1.05). Data quality at 120 minutes suffers since those with scores of less than 2 were discharged in the Neto study, thus reducing numbers available for analysis but revealed no differences between the groups.

It was not possible to ascertain for any study, duration of symptoms or inpatient stays, number of subsequent visits to the ED or need for medical attention in the week following treatment or time lost from school.

Other measures of symptom severity included in the studies were pulse respiratory rate and oxygen saturation. There was no detectable influence of the intervention on pulse –0.18 (–8.02 to 7.65) (WMD) or respiratory rate –0.55 (–3.20 to 2.09) (WMD). Oxygen saturation favoured treatment but failed to reach significance 0.41(–0.26 to 1.09) analysed using the standard mean difference as different measures of oxygen saturation were used.

Discussion

Despite the widespread use of humidified air in both primary and secondary care settings, only three relevant trials were identified; two in EDs and one in inpatients. Two of the studies[19,20] compared cool humidified air with no treatment, while the third[18] compared warmed humidified air fed into a perspex cot with no treatment. There were no trials in primary care settings and none involving warm mist delivered more directly to infants. We were unable to provide evidence of any therapeutic benefit from the routine use of humidified air for the treatment of moderate croup in the settings studied. The combined results from all three studies favoured mist therapy, however the CIs around the effect on the croup score include the possibility of a small harmful effect (+0.47 SD) or a benefit as large as –0.75 SD (equivalent to one point on the Westley scale).

We opted to perform a meta-analysis by combining the results of all three studies in order to have the maximum power to elicit any effect. However, these results must be interpreted with caution since it is questionable whether it is valid to (i) combine results from different time points since croup may spontaneously recover in this time frame (20–60 minutes), (ii) combine results from different types of humidity (warm and cool air) or (iii) combine results from different settings (one inpatient and two ED). When the studies were combined at more closely matching time points the trend favoured humidified air at 20–30 minutes and control at 60 minutes. Moreover, the trend in admissions favoured control although none of these

results reached statistical significance and this variation may reflect the play of chance. Two of the studies were methodologically weak[18,20] while the more rigorous Neto study[19] included initial treatment of all children with oral dexamethasone probably limiting the potential for improvement. It is questionable therefore whether there is sufficiently robust evidence to rule in or rule out any beneficial effect of humidified air.

The main outcome reported the Westley score or variations upon this score. In mild to moderate croup, the score is likely to be insensitive to change: children with cyanosis or altered consciousness which contribute most points in the score are only likely to be in the severe group who were excluded, so only three variables in the croup score are likely to change (air entry, stridor and retractions) with a very small range of 0–7. Nevertheless, trials of nebulized steroids in children with mild to moderate croup (i.e. a similar group) and using this score have demonstrated significant benefit.[17,26] However, the effect size of a 2-point change in the score[17] is approximately double the maximum benefit, consistent with our results, so it is unclear if the score is sensitive to the smaller change likely to occur with humidified air. It is not clear whether an improvement of 1 on the Westley scale the maximum potential benefit consistent with our results would be regarded as clinically significant.

Glucocorticoid treatment has been convincingly demonstrated to be associated with an improvement in the Westley score at 6 hours with a WMD of –1.2 (95% CI = –1.6 to –0.8) and at 12 hours –1.9 (–2.4 to –1.3).[5] Glucocorticoid treatment is beneficial in mild croup and led to significantly earlier discharge from the ED and lower admission rates in the week following treatment.[17] In contrast it appears that treatment with[12] humidified air might lead to an increased risk of admission, albeit with wide CIs.

It is possible that the particle size obtained by standard methods of humidification may not reach the site of inflammation (larynx). However, one more recent high quality study comparing standard humidification with humidification with particle size of potential theoretical benefit also failed to show any improvement in symptom scores.[12]

Although use of humidity at home is currently often recommended following telephone consultation, we have no data regarding the use of warm humidified air in the home or other community environment. Not only are there theoretical disadvantages of warm humidified air[13] there is also the potential of harm through scalding which has been reported in the literature.[27] On the other hand, it is also plausible that positive advice on action may help to calm an anxious situation.

There may be theoretical reasons for recommending taking a child into cool dry air rather than warm moist air and given the potential for harm from scalding a further trial in the primary care setting might be warranted if only to provide clear evidence against continued use of warm-air humidification. Cool humidified air carries a low risk and particular attention should be paid in future research to admission rates. With the limited potential for variation at the mild end of the range of the Westley score, it would be prudent to develop more sensitive measures of improvement for instance by developing new measures based on parental rating of the severity of the main symptoms of croup.

Conclusion

We have been unable to find evidence that the croup score of children managed in an emergency setting with mild to moderate croup improves substantially with inhalation of humidified air. There is no evidence to guide treatment in primary care. In the ED, however, there is clear benefit from the administration of nebulized or oral steroids and there is no justifiable reason to continue to offer standard humidification as a mainstay of treatment.

Supplementary Data

Search Strategy and Supplementary Tables 2 and 3 are available at *Family Practice* online (http://fampra.oxfordjournlas.org/).

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Contributors: MM and PL jointly developed the protocol. Data extraction was performed by MM and checked by PL.

Declaration

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