Randomized double-blind trial of the effects of humidified compared with nonhumidified low flow oxygen therapy on the symptoms of patients

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OBJECTIVE: To determine the effects of humidified versus nonhumidified low flow oxygen therapy on the subjective symptoms of patients.
METHODS: Randomized double-blind clinical trial conducted in a tertiary care university teaching hospital. The sample included medical and surgical in-patients receiving oxygen therapy who met criteria including medical stability, no overt cognitive impairment, English comprehension, voluntary participation and attending physician agreement. Humidified subjects numbered 96 and nonhumidified subjects were 95. The intervention was humidified or nonhumidified oxygen administration using two flowmeters covered by an opaque bag. Patients receiving oxygen therapy longer than three days (first period) were crossed to the alternate treatment (second period) and followed for three more days.
RESULTS: Mean symptom scores for nasal dryness were low (mild) for both groups; however, humidification group scores were significantly lower (P=0.018) in the first period than the nonhumidification scores. A corresponding increase in the incidence of nosebleeds was not statistically significant between groups nor were there statistically significant differences between groups for other symptoms/problems. The prevailing trend was decreased incidence of dry mouth, dry throat, headache and chest discomfort during the study.
CONCLUSIONS: Although this sample was large enough to expose statistically significant group differences in nasal dryness, the difference was not judged to be clinically significant. The predominant trend was a decrease in symptom scores over time with either treatment. In this group of patients, humidified oxygen does not appear to alleviate subjective symptoms.

Key Words: *Humidification, Oxygen, Patient symptoms*

Essai randomisé à double insu comparant les effets d'une oxygénothérapie à faible débit et humidifiée avec les effets d'une oxygénothérapie non humidifiée sur les symptômes des patients

OBJECTIF : Déterminer les effets d'une oxygénothérapie à faible débit et humidifiée par rapport à une oxygénothérapie à

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faible débit non humidifiée sur les symptômes subjectifs des patients.
MÉTHODES : Essai clinique randomisé à double insu mené dans un hôpital universitaire de soins tertiaires. L'échantillon comprenait des patients sous oxygénothérapie et hospitalisés dans les services de médecine et de chirurgie, répondant à certains critères notamment un état médical stable, aucun signe d'atteinte cognitive, la compréhension de l'anglais, la participation volontaire et l'accord du médecin traitant. Quatre-vingt-seize patients ont reçu de l'oxygène humidifié et 95 patients de l'oxygène non humidifié. L'intervention consistait à administrer de l'oxygène humidifié ou non humidifié à l'aide de deux débitmètres recouverts d'un sac opaque. Les patients soumis à une oxygénothérapie excédant trois jours (première période) ont ensuite reçu l'autre traitement (deuxième période) et ont été suivis pendant trois jours supplémentaires.
RÉSULTATS : Les scores moyens des symptômes pour la sécheresse nasale étaient faibles (légers) pour les deux groupes ; cependant, les scores du groupe recevant une humidification étaient nettement plus faibles (P=0.018) dans la première période que les scores obtenus sans humidification. Une augmentation correspondante de l'incidence des saignements de nez n'était pas significative sur le plan statistique entre les deux groupes. Il n'y avait pas non plus de diffférences significatives entre les groupes pour les autres symptômes. La tendance dominante était une diminution de l'incidence de la sécheresse de la bouche et de la gorge, des maux de tête et de l'oppression thoracique pendant l'étude.
CONCLUSIONS : Si l'échantillon était suffisamment important pour mettre en évidence des différences entre les groupes, significatives sur le plan statistique pour la sécheresse nasale, cette différence n'a pas été jugée importante sur le plan clinique. La tendance dominante était une diminution des scores des symptômes dans le temps avec l'un ou l'autre traitement. Dans ce groupe de patients, l'oxygène humidifié ne semble pas soulager les symptômes subjectifs.

Humidified oxygen is widely prescribed in hospitals across North America, presumably to alleviate symptoms and improve the comfort of nonintubated patients (1). There appears to be little, if any, scientific basis for this practice, which has continued for at least the past three decades. However, most North American hospitals have accepted its use as routine practice because of the clinical opinions of expert practitioners.

Humidification of supplemental oxygen is achieved by bubbling the gas through sterile water before it reaches the patient. Because of concern about the possible contamination of humidification systems, they are purchased sealed, and most are changed every seven to 30 days. The overall cost of these systems may approximate $40,000 per year for moderately large hospitals. In addition, used humidification bottles represent a source of biomedical waste.

Previous researchers have questioned the use of tap versus sterile water with oxygen humidification as well as the optimal frequency of changing systems based on contamination rates (2,3). The impact of humidification on patients' symptoms also has been investigated with high and low flow oxygen administration. Campbell et al (1) questioned whether humidification was necessary for patients receiving oxygen at the rate of 5 L/min or more, and Estey (4) studied 34 patients who received either dry or humidified oxygen therapy of 4 L/min or less. No differences were found in either study in the subjective complaints of patients receiving humidified versus nonhumidified oxygen, and it was concluded that routine humidification of oxygen by nasal cannula could not be justified for nonintubated patients receiving high or low flow oxygen. However, limitations in both study designs included small sample sizes, quasi-randomization and/or a nonblinded method for oxygen administration. Despite the scarcity of evidence regarding the effectiveness of humidification as a therapeutic intervention, some experts believe that, for patients with chronic chest disease and superimposed infection, supplemental humidity may help defective clearance mechanisms, and its use is well established for intubated patients receiving dry anesthetic gases (5).

The purpose of this study was to determine the clinical effects of humidified versus nonhumidified low flow oxygen administration on the subjective symptoms of patients.

PATIENTS AND METHODS

A randomized double-blind experimental study design was used. The independent variable was the method of low flow oxygen administration. The treatment group received nonhumidified oxygen whereas the control group received humidified oxygen according to standard hospital practice. Dependent variables included symptoms of dry nose, dry mouth, dry throat, headache, chest discomfort and other possible problems (nosebleed, cough, phlegm).

Sample: Potential subjects were patients admitted to one tertiary care university teaching hospital who were prescribed low flow oxygen therapy by nasal prongs or mask. Selection criterion was the predicted administration of supplemental oxygen therapy of 4 L/min or less for each patient for two or more days. Subjects were to be included if they were medically stable, lacked evidence of cognitive impairment, were able to give informed consent, comprehended English and their attending physician agreed with their participation. When oxygen therapy was ordered, potential subjects who met inclusion criteria were provided with verbal and written explanations about the purpose of the study and extent of participation before their informed voluntary consent was requested. Randomization of each subject to group was based on computer generated tables. The study was approved by the hospital and university research and ethics committees.

Procedure: Only the respiratory therapist commencing the oxygen administration knew of the patient's random assignment to group. Patients received oxygen using two flowmeters attached to a duplex outlet. Only one flowmeter was attached to a humidification bottle so that randomization to either treatment was possible. The entire apparatus was covered by an opaque bag to blind patients and caregivers to the method of oxygen administration. Patients who received oxygen therapy for longer than three days (first period) were crossed over

TABLE 1
Demographic characteristics

Variable	Nonhumidification Number (%)	Humidification Number (%)
Sex		
Female	57 (45)	53 (48)
Male	69 (54)	58 (52)
Prior home oxygen	17 (13)	21 (19)
Remained in study		
Day 0 (baseline)*	126 (100)	111 (100)
1	95 (75)	96 (86)
2	70 (56)	74 (67)
3†	52 (41)	54 (49)
4	36 (29)	40 (36)
5	28 (22)	33 (30)
6	21 (17)	24 (22)

**Despite inclusion criteria requiring medical stability and that oxygen therapy be anticipated to last for two or more days, patient attrition (n=93) occurred from baseline (day 0) to day 2 for the following reasons: oxygen therapy discontinued (n=55); patient discharged (n=16); patient withdrew (n=11); medical instability (n=5); changes in patient location (n=4); patient death (n=2) †Further patient attrition (n=99) occurred from day 2 to day 6 because oxygen therapy was discontinued (n=56); patient was discharged (n=31); patient withdrew (n=5); medical instability (n=2); or changes in patient location (n=5)*

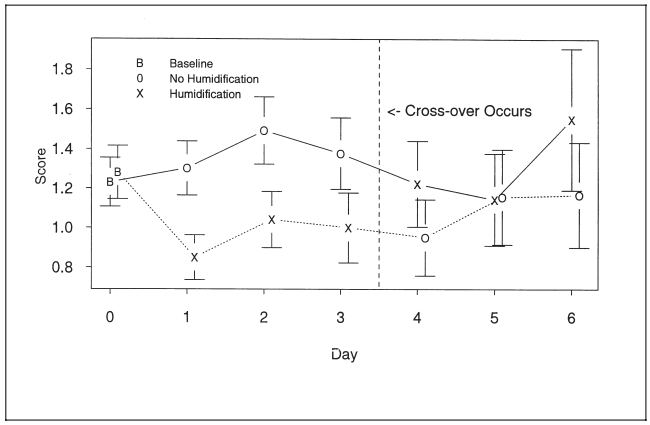

Figure 1) *Mean symptom scores for nasal dryness by day. Randomization groups are connected by lines. Treatment administered is denoted by 'X' for humidification, and by '0' for nonhumidification. Scores: 0 = no discomfort; 1 = mild discomfort; 2 = some discomfort; 3 = moderate discomfort; 4 = worst possible discomfort*

to the alternate treatment (second period) and were followed for a maximum of six days.

The questionnaire used for data collection was based in part on information described by Campbell et al (1) and on the clinical expertise of the co-investigators. After being critiqued by university-based experts in medicine, nursing and educational psychology, the questionnaire was pilot tested and revised. Questionnaires were administered at the time subjects commenced oxygen therapy (day 0 – baseline data) and daily thereafter. Subjects were asked about five possible symptoms – dry nasal passage, dry mouth, dry throat, headache and chest discomfort – and they rated each symptom according to a five-item Likert scale. Possible responses ranged from asymptomatic to severely symptomatic. Patients also were asked forced choice (Yes/No) questions about the existence of epistaxis, cough and phlegm.

Statistical methods: Symptom scores over the two treatment periods were studied using linear mixed effects models (6) to allow for the repeated measures per patients. Explanatory variables included appropriate baseline values as well as terms for treatment, days on treatment, period and interactions involving treatment. A similar approach was taken to analyze dichotomous outcomes, based on the generalized estimating equation approach (7). Model reduction was based on likelihood ratio and Wald type tests. Treatment effects were assessed using the asymptotic normal distributions of the associated estimates.

RESULTS

Subjects: In total 1576 nonintubated patients ordered to receive low flow supplemental oxygen were evaluated for study. Of these, 1182 did not meet inclusion criteria; 237 of the remaining 394 eligible patients became voluntary subjects after receiving information about the study. There were 157 patient refusals, with reasons stated as follows: not interested (n=63); unwell (n=40); preferred humidity (n=37); unable to comprehend concept (n=6); and miscellaneous (n=11). Most of the patients who refused had respiratory (n=77), gastrointestinal (n=30) or circulatory (n=24) disorders. The final sample included 150 medical and 87 surgical patients from seven patient care units. Data were gathered over 10 months including autumn, winter and spring.

Characteristics between groups were compared for age, sex and administration of home oxygen before hospital admission (Table 1). Mean age was 61.9 years and 62.7 years for the nonhumidification and humidification groups, respectively. No significant differences in demographic characteristics were found between groups.

Of the 16 patients who withdrew, six stated a sense of increased dryness as the reason. Four others were unwell ("too tired", etc), two became confused, two were "not interested", one preferred dry oxygen and one had miscellaneous reasons.

Symptom and problem scores: The primary symptom of interest was nasal dryness. Mean symptom scores for nasal dryness (Figure 1) indicate a statistically significant decrease (P=0.018) in dryness symptoms in the humidification group relative to the nonhumidification group in the first period. This difference is characterized by a slight, insignificant increase in symptoms in the nonhumidified group compared with a significant decrease (P=0.002) in the humidified arm from baseline to day 1. The same pattern difference did not occur in the second period after treatment crossover, as evidenced by a statistically significant period-treatment interaction (P=0.043) (Figure 1).

A second measure of interest was nosebleed. Results (Figure 2) indicate a corresponding increase in the incidence of nosebleeds in the nonhumidified compared with the humidified groups, peaking at day 2, which did not, however, attain statistical significance (P=0.093).

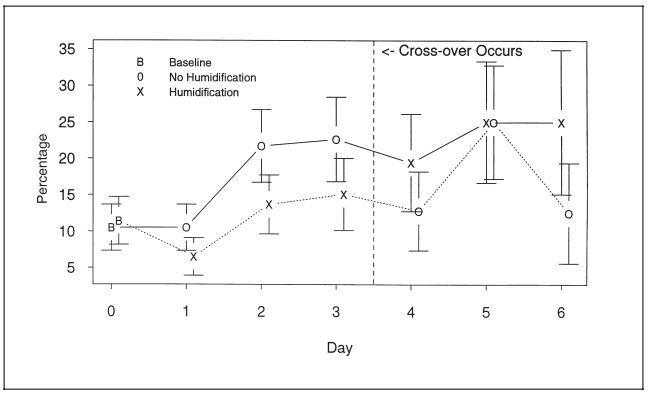

Figure 2) *Prevalence of nosebleed (%) by day. Randomization groups are connected by lines. Treatment administered is denoted by 'X' for humidification, and by '0' for nonhumidification*

There were no statistically significant differences between treatments for the four other symptoms. The prevailing trend in both groups was towards decreased incidence of dry mouth and dry throat, and in headache and chest discomfort over the study (Table 2). In particular, mouth dryness (P=0.01), headache (P<0.0001) and chest discomfort (P=0.0001) showed marked decreases from baseline to the first day. Thereafter, the general trends over the study were downward and statistically significant, except for the symptom of headache.

DISCUSSION

Based on a pilot project, it was anticipated that a larger number of subjects would receive oxygen therapy for at least three days. However, oxygen therapy for a shorter time period (ie, 24 h or less) and decreasing lengths of stay resulted in high attrition rates, particularly noticeable with surgical patients. Campbell et al (1) also observed comparatively short term oxygen administration for subjects in their study and reported that only 17 of 185 patients received supplemental nasal oxygen of 5 L/min for four days or more. Short term humidified oxygen therapy for acute care patients is a frequent occurrence that has important cost implications, given the amount of funding currently allocated by medium and large hospitals to purchase humidification bottles for oxygen administration. For the study hospital of approximately 500 beds, this amounted to more than $40,000 per year.

All symptoms except dry nose improved over time whether oxygen therapy was humidified or not. Because subject effects were accounted for in the analysis, these patterns can not be attributed to progressive attrition in symptom-prone patients during the study. Patients' most frequent complaints at the level of "some" or greater discomfort were relative to dry mouth, cough and phlegm. Humidification did not appear to have an obvious clinical advantage in alleviating these symptoms.

The original suspicion that a lack of humidity might affect patient comfort by increasing the occurrence of dry nose was supported by the statistically significant difference between groups for dry nose. However, because the mean scores between groups representing patients' perceptions of their symptom severity were in the mild range, this difference is not clinically relevant.

TABLE 2
Incidence (per patient day) of symptoms (symptom score = 2) or problems (presence of nosebleed, cough, phlegm) in first period*

	Nonhumidified		Humidified	
	Day 0†	Days 1-3	Day 0	Days 1-3
Dry nose (%)	41.5	40.9	40.9	29.1
Dry mouth (%)	60.6	53.0	63.4	50.2
Dry throat (%)	48.9	42.8	38.7	36.2
Headache (%)	19.1	11.7	26.9	16.4
Chest discomfort (%)	44.7	22.9	34.4	23.6
Nosebleed (%)	10.6	17.3	10.8	10.8
Cough (%)	76.6	80.4	86.0	78.4
Phlegm (%)	59.6	56.3	69.9	63.8

**Scores for dry nose, dry mouth, dry throat, headache and chest discomfort: 0 = no discomfort; 1 = mild discomfort; 2 = some discomfort; 3 = moderate discomfort; 4 = severe discomfort. Scale for nosebleed, cough, phlegm: yes or no. †Day 0 is baseline day*

The lack of clinical relevance for the severity of dry nose with nonhumidified oxygen and the improvement reported by patients over three days with other symptoms/problems whether oxygen therapy was humidified or not suggests guidelines for clinicians. We recommend nonhumidification for short term low flow oxygen therapy (ie, up to three days). However, when oxygen therapy is ordered, patients should be assessed individually for their propensity for dry nose and nosebleed and, based on this assessment, clinicians may elect to order humidified oxygen for individual patients.

Findings from this study do not support continuation of routine humidification with low flow oxygen therapy on the basis of improved patient comfort and presumed improvement in their subjective symptoms because most symptoms/problems were not alleviated by oxygen humidification. Some may argue that further research is needed to address other possible effects achieved with humidified oxygen administration before established therapies are jettisoned. For example, investigations have been suggested to determine the effect of humidified oxygen on the rate of recovery for patients with chest disease (5), on its effect on asthmatics and on its relationship to patient outcomes (eg, length of stay and infection rates). Others would question the need for additional evidence to continue a therapy with unproven benefit. We recognize that further studies would allow comparison of the effects of humidified and nonhumidified oxygen therapy on the symptoms of patients in similar diagnostic categories according to severity of illness. Although replication of this study with a larger sample would confirm or refute present study findings, larger studies are difficult to justify based on anticipated cost savings. Consequently, we recommend that patient outcomes be monitored with routine short term nonhumidified oxygen therapy, especially for possible adverse occurrences such as dry nose and nosebleed. Findings from this study contribute new informa-

tion compared with previously published studies of less rigorous design. The sample size of the present study was sufficient to achieve statistical significance and is larger than that of other studies focused on oxygen humidification reported in the literature. The large number of subjects who did not meet inclusion criteria and who were discontinued after enrolment was unfortunate, yet reflects current patterns of delivering oxygen therapy in hospital.

Changing hospital policy to accept nonhumidification as the standard method for delivering low flow oxygen therapy has potential benefits, including the possibility of decreasing the patient's risks of developing nosocomial pneumonia, reducing expenditures for oxygen therapy and eliminating one source of biomedical waste. The findings and recommendations make a significant contribution at a critical time in the evolution of evidence-based care and a focus on patient outcomes.

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BOOKS

Comprehensive human physiology: From cellular mechanisms to integration, volumes 1 and 2. Rainer Gregor, Uwe Windhorst (1996). Springer-Verlag New York Inc, 333 Meadowlands Parkway, Secaucus, New Jersey USA 07094. 2528 pages; ISBN 3-54058109-X; US$129.00.

The editors have assembled 106 experts in their respective fields of physiology to write a textbook to provide not only basic concepts but also the most recent developments in physiology. The basic aim was not to provide yet another introductory text, but to compile current knowledge for a more advanced readership.

The test is divided into two volumes: one devoted primarily to cellular physiology and aspects of neuroscience and the second to the organ systems and reproduction. With this format, the text uses the concept that the integrative physiological processes can be understood best from the basis of cellular and molecular biology, biochemistry and biophysics.

All the chapters are well illustrated with both figures and tables. They all have excellent up-to-date reference lists, making it convenient for a reader to gather further information on specific topics.

Although the editors have directed the text to a more advanced readership, the text appears to be more a reference book for those wishing to review specific areas of interest. Because of the amount of information provided (two large volumes, 126 chapters), the text is not very well suited to graduate or medical students. In addition, the specialty chapters are not the level of review articles such as those that are published in peer-reviewed journals. This work would be excellent for those who have been away from the field and need to review it at a more advanced level than appears in basic texts.

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