Is Humidification Always Necessary During Noninvasive Ventilation in the Hospital?

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Noninvasive ventilation (NIV) is a standard of care for the treatment of exacerbation of chronic obstructive pulmonary disease, to prevent intubation and reduce morbidity and mortality. The need for humidification of NIV gas is controversial. Some unique aspects of NIV conspire to alter the delivered humidity and airway function. In the presence of air leaks, unidirectional air flow dries the airways and increases airway resistance. Patient comfort is also a critical issue, as tolerance of NIV is often tied to patient comfort. This paper provides the arguments for and against routine humidification during NIV in the hospital setting. Data from clinical research demonstrate the effects of delivered humidification on relevant physiologic variables. The impact of humidification on NIV success/failure remains speculative. *Key words: mechanical ventilation; noninvasive ventilation; NIV; humidification; chronic obstructive pulmonary disease*. [Respir Care 2010;55(2):209–216. © 2010 Daedalus Enterprises]

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Introduction

Noninvasive ventilation (NIV) for the treatment of exacerbation of chronic obstructive pulmonary disease (COPD) to prevent endotracheal intubation reduces morbidity and mortality.[1-3] Ancillary therapies, including bronchodilator, fluid management, and secretion clearance, are part of a successful NIV program.[4] The appropriate application of humidification during NIV, however, is poorly understood and not uniformly accomplished.[5] This issue requires further study, as humidification may play an important role in the success of NIV, because it relates to secretion removal and patient comfort.

We will address the points of contention regarding humidification during NIV, discuss the available evidence, and, where evidence is lacking, provide our opinions on best practice, based on our experience. Data supporting both sides of the argument will be presented, with a final consensus as a goal.

Normal Humidification

The respiratory tract heats and humidifies inspired gas so the gas entering the alveoli is warmed to body temperature and fully saturated with water vapor. This condition is commonly referred to as body temperature, atmospheric pressure, and saturated with water vapor (BTPS).[6] During normal breathing through an intact upper airway, inspired gas entering the trachea is warmed to 29–32°C and is fully saturated with water vapor. In the mid-trachea, temperature and absolute humidity reach approximately 34°C and absolute humidity is 34–38 mg H_2O/L.[7-9] The point at which the gas reaches 37°C and 100% relative humidity (which corresponds to an absolute humidity of 44 mg H_2O/L) is known as the "isothermic saturation boundary,"[6] which is located below the carina during quiet breathing, in the third to fifth generation of the bronchial tree.[6,8] Humidity and temperature are constant below the isothermic saturation boundary, while above the isothermic saturation boundary the airway acts as a counter-current heat-and-moisture exchanger.[6] Heat and moisture exchange continues as long as there is a thermal and moisture difference between the gas and the airway mucosa: the greater the difference, the greater the transfer of heat and water. During hyperventilation or when cold, dry air enters the trachea; the isothermic saturation boundary moves further down the bronchial tree, pressing the lower respiratory tract into assisting with heat and moisture exchange.[10,11] Expiratory gas is cooled when traversing the airway above the isothermic saturation boundary, resulting in water condensation. However, the upper airway recovers only a part of the added inspiratory heat and moisture. During normal breathing, the temperature of expired air ranges from 32°C to 34°C at 100% relative humidity.

Under normal conditions for room air (temperature 22°C, relative humidity 50%, ambient humidity 9 mg H_2O/L) and with a minute ventilation ($\dot{V}_E$) of approximately 8 L/min, the respiratory tract evaporates about 400 g of water during inspiration each day, and approximately 150 g of water condenses during expiration, so the daily water need for respiratory humidification is about 250 g.[9,10]

Humidification of inspired gas is typically provided by evaporation of water from tracheobronchial secretions. The latent heat of vaporization is the heat that must be added to a liquid to change its state to vapor at a given temperature (or the amount of heat released when vapor condenses to a liquid).[11] The latent heat of vaporization of water is approximately 540 kcal/kg. As liquid water evaporates, sensible heat in the liquid is converted to latent heat in the vapor leaving the liquid, and the temperature of the remaining liquid falls. Evaporation cools the airway. The more water evaporating from the airway surface, the greater the airway temperature drop in that airway surface area.[12] However, in the airway this cooling effect is partially compensated for by heat and water provided by the bronchial blood flow. In a normal adult the daily respiratory evaporative heat loss is approximately 250 kcal, 65–70 kcal of which are recovered by condensation during expiration.[12,13]

The intensity of heat and moisture exchange increases with breathing dry and cold air, and with increasing $\dot{V}_E$. When ventilation is provided via face mask instead of via endotracheal tube, the inspired gas is heated and humidified by the upper airways. NIV is a special circumstance of the patient breathing a high $\dot{V}_E$ of cool, dry gas. When NIV is supplied via an intensive-care ventilator, the gas is typically anhydrous wall air and/or oxygen. Devices that use room air provide a slightly higher humidity. The leak compensation of many NIV devices creates high flow throughout the respiratory cycle, which also contributes to respiratory heat and moisture loss.[14] During NIV, patients often breathe mainly via the oral route, which is less efficient than nasal breathing. Dry mouth is one of the most frequently reported adverse effects of NIV.

Humidification During Invasive Ventilation

Humidification during invasive mechanical ventilation is a standard of care.[15,16] Delivery of cool, anhydrous gas from institutional compressed air and liquid oxygen systems to a patient with an instrumented airway, bypassing the normal mechanisms of heat and humidification, has dire consequences, including alterations in tracheobronchial structure and function, inspissated secretions, mucus plugging of airways, endotracheal-tube occlusion, ciliary dyskinesis, and epithelial desquamation.[17-21]

There is agreement among clinicians that heating and humidifying inspired gas during invasive ventilation are required. The 2 general approaches for supplying heat and humidification are (1) "active" (heated humidifier that utilizes an external power source and water supply), and (2) "passive" (heat-and-moisture exchanger [HME], which recycles the patient's own heat and humidity).

However, the amount of heat and moisture that should be delivered, and the device used, remain an area of debate. Clinical decision making on humidification requires an understanding of the patient's pathophysiology and the available equipment. Clearly, device selection must be based on the patient's lung disease, ventilator settings, intended duration of use, and other factors (eg, presence of leaks, body temperature). Recent changes in the practice of mechanical ventilation, particularly the use of small tidal volume (V_T) (4–6 mL/kg predicted body weight) also impact the choice of humidifier.[21,22]

Though heat and humidification of inspired gas is a clear standard of care in invasive ventilation, there are no agreed upon goals, so it is no surprise that standards for humidification during NIV remain controversial.

Pro: Humidification Is Needed During Noninvasive Ventilation

NIV encompasses a myriad of therapies, from continuous positive airway pressure (CPAP) for sleep apnea at home and for cardiogenic pulmonary edema in pre-hospital care, to high levels of ventilatory support in the hospital. Extensive literature demonstrates the benefits of humidification to improve comfort and tolerance of nasal CPAP for sleep apnea.[23-39] However, our debate concerns humidification during NIV for COPD exacerbation in the hospital.

Patient Comfort

Successful NIV is predicted by improved patient comfort, because the work of breathing is reduced. This is most noticeable as decrease in accessory muscle use and respiratory rate. Oxygen saturation may increase, and dyspnea is relieved.[1,3,4] Mask fit and leak around the mask also impact patient comfort.[3]

Humidification can also affect patient comfort and, therefore, NIV tolerance. In 16 patients with chronic hypercapnia, Nava et al compared patient adherence to long-term NIV, airway symptoms, adverse effects, and number of severe pulmonary exacerbations that required hospitalization. In a randomized, crossover fashion, all the patients used heated humidification for 6 months, and an HME for 6 months. The investigators followed adverse effects of NIV and patient-reported severity scores for each adverse effect. They found fewer adverse effects with heated humidification (Table 1), including fewer sinus infections and pneumonias, although that difference was not statistically significant. Hospitalizations for exacerbations were twice as frequent in the HME group, although the incidence was low in both groups and not significantly different.[31] The study used 2 types of humidification and found better comfort with the heated humidifier. Comparison to no humidification would probably lead to even more disparate findings.

Table 1. Adverse Effects With Heated Humidifier and Heat-and-Moisture Exchanger*

Symptoms	Baseline (%)	Heated Humidifier (%)	HME (%)
Dry nose	21	28	42
Runny nose	7	14	14
Postural drip	0	0	7
Nasal congestion	21	21	28
Epistaxis	0	0	0
Reduced sense of smell	7	28	28
Sinus infection	14	36	50
Dry throat	7	7	14
Sore throat	7	7	7
Cough	43	36	43

* Percent of patients who reported these adverse effects before (baseline) and during 6 months of using heated humidifier and 6 months of using heat-and-moisture exchanger (HME).
(Data from Reference 31.)

Lellouche and co-workers recently evaluated humidification during NIV in normal volunteers. They compared no humidification to heated humidification and HME.[32] They used 2 different ventilators: one with a turbine that delivers room air, and one intensive-care ventilator that uses compressed air and oxygen inputs, and altered inspired oxygen settings. The normal volunteers breathed on CPAP without humidification, with heated humidification, and with HME, at normal (10 L/min) and elevated (21 L/min) $\dot{V}_E$, and with and without leaks around the mask. The delivered humidity was measured, and the subjects rated their comfort with a mucosal dryness 0–10 scale. No humidification delivered an absolute humidity of around 5 mg H_2O/L. The HME provided nearly 30 mg H_2O/L, but that value fell 30% in the presence of mask leak. The heated humidifier provided 30 mg H_2O/L regardless of mask leak. Interestingly, the comfort scores were similar for humidity ranges from 15 to 30 mg H_2O/L, but with no humidification (5 mg H_2O/L) the comfort scores were half of those with HME or heated humidifier. With no humidification the volunteers reported severe discomfort related to mouth dryness. The observation period was only 1 hour, and the discomfort associated with longer periods of unhumidified NIV would probably be magnified.

These data are compelling in light of the experience with long-term nasal ventilation at home, where two thirds of patients report upper airway drying and discomfort. Hospitalized patients are more likely to have elevated $\dot{V}_E$,

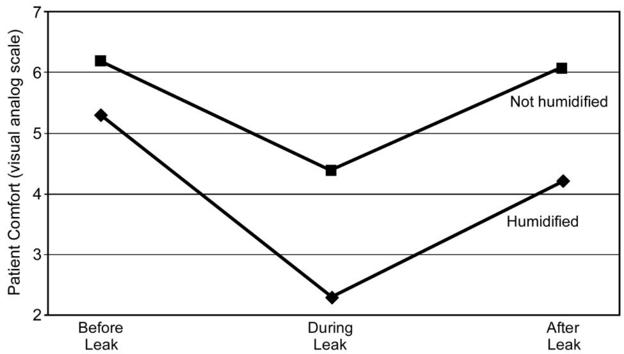

Fig. 1. Patient comfort before, during, and after air leak, with and without humidification during noninvasive ventilation. (From data in Reference 39.)

fever, and dehydration, and more likely to receive oxygen and to have large mask leaks, which all contribute to upper airway dryness and discomfort. There is little doubt that failure to humidify gas, even during short-term NIV, results in patient discomfort. As patient comfort is important to NIV success, humidification probably improves NIV success (Fig. 1).

Airways Resistance

The cooling of airway mucosa results in heat and moisture loss and drying, which increases airway resistance. Richards and colleagues found that 40% of patients on nasal CPAP reported dry nose and throat and sore throat during therapy, probably due to mouth leak and the resulting unidirectional gas flow.[37] With normal volunteers, Richards and colleagues found that during CPAP with a mouth leak, nasal airway resistance increased by a factor of three, but heated humidification ameliorated that increase in airway resistance. A cool pass-over humidifier did not reduce nasal airway resistance.[37]

Tuggey and colleagues studied the effect of mouth leak during nasal NIV on V_T, nasal resistance, and comfort.[38] Following a mouth leak of approximately 40 L/min, they found increased nasal resistance, which resulted in a small (12%) but significant reduction in expired V_T during pressure-targeted NIV. Heated humidification attenuated both the nasal-resistance and V_T changes. Comfort was greater with heated humidification, which also reduced the increased discomfort that followed a period of mouth leak. The short duration of observation (5 min) suggests that patients admitted to the hospital requiring NIV will have even greater alterations in resistance. The leak in this study (40 L/min) was similar to the leaks seen during in-hospital NIV.[38]

Fischer et al found that nasal CPAP without humidification significantly decreased nasal humidity, which is a key factor in the development of increased nasal resistance.[39]

The issue of mask leak is critical and unique to NIV. The normal respiratory tract operates as a counter-current HME. When gas flow becomes unidirectional, all the moisture is lost because there is no chance to reclaim moisture. This also explains the reduced efficacy of an HME during NIV.

Secretion Retention and Removal

Secretion management in the ventilated patient is accomplished with various common and exotic techniques.[40] Preservation of the patient's innate cough mechanism is one of the many advantages of NIV over endotracheal intubation. However, nasotracheal suctioning is more traumatic than suctioning via the endotracheal tube. In the intubated patient the secretion-management techniques are suctioning and humidification.

The efficiency of heated humidification during NIV can be adversely affected by the type of ventilator, elevated fraction of inspired oxygen (F_{IO_2}), and leak around the mask or through the mouth during nasal NIV.[41-43] Given the high flow, low humidity, and complications of unidirectional flow associated with NIV, and the ever present leaks, drying of the respiratory mucosa and secretions is inevitable. While this remains a critical issue for NIV, it has not been often studied. In a recent presentation at the meeting of the American Thoracic Society, Esquinas and colleagues introduced some insight into this problem.[44] They conducted an international survey to determine humidification practices and the relationship of those practices to untoward outcomes. Data from 15 hospitals and 1,635 patients were analyzed. They found that in patients who failed NIV, difficult intubation was encountered in 88 (5.4%), and in that group, failure to use humidification was the leading factor in predicting difficult intubation. Approximately half of the difficult-intubation patients had never received humidification during NIV. Forty-seven percent of the patients used a heated-wire-circuit humidifier, and 15% used pass-over humidifiers. Forty percent of the hospitals reported no protocols for humidification during NIV.

The most likely cause of difficult intubation is mucosal drying and secretion retention. The presence of thick mucus in the oropharynx, and fragile, dry mucosa clearly create a difficult environment for endotracheal tube placement.

Success of Noninvasive Ventilation

NIV represents one of the great paradigm shifts in mechanical ventilation over the last decade. The data on outcome improvements in patients with COPD exacerbation

Table 2. Factors Related to Humidification During Noninvasive Ventilation

Patient Issues	
	Comfort
	Airway resistance
	Reduced tidal volume
	Increased work of breathing
	Dead space
	Secretion retention
	Failure of therapy
	Difficult intubation
Device Issues	
	Minute ventilation
	Fraction of inspired oxygen
	Mask leak
	Mouth leak during nasal noninvasive ventilation
	Ventilator driving system

are compelling. Successful NIV includes the appropriate selection of the patient, the NIV interface, the ventilator, and the variables chosen to identify NIV success/failure. Patient comfort is both a goal of NIV therapy and predictor of NIV success. Early time commitment while establishing NIV also pays dividends in patient tolerance and NIV success.

The role of humidification in NIV success has been underappreciated. Table 2 lists the factors related to humidification that impact NIV therapy. Humidification improves patient comfort and therefore tolerance, and enhances airway function and secretion removal. This is one area of NIV that deserves further study in the near future.

Con: Humidification Is Not Needed During Noninvasive Ventilation

The success of NIV in avoiding endotracheal intubation in patients with COPD and congestive heart failure is indisputable.[1-3] Numerous clinical randomized controlled trials and meta-analyses have concluded that, compared to standard care, NIV reduces dyspnea and respiratory distress, improves gas exchange, reduces the need for intubation by up to 50%, and decreases mortality.[45-48] However, evidence is lacking to support the routine use of active humidification during NIV. Similar to the debate about HME versus active humidification in invasive ventilation, there is no published recommendation or guideline concerning the type of humidification that should be provided during NIV for acute respiratory failure.

Clinical trials that have examined various humidification methods in intubated patients cannot be extrapolated to NIV applications. Without supplemental humidification the gas may be dryer when an intensive-care ventilator is used. But, in contrast with an intubated patient, the upper airways are not bypassed during NIV. Additionally, no studies of humidification during NIV have measured quantifiable clinical outcomes, so the question of whether humidification during NIV affects outcome remains unanswered. However, this lack of data for any association between supplemental humidification and NIV failure and tolerance does not indicate that patient comfort is not influenced by the absence of humidification. Important questions remain regarding how much humidification is required during NIV, and if it affects clinical outcomes.

Long-Term Versus Short-Term Noninvasive Ventilation

The clinical application of NIV in the acute setting typically serves a single purpose: to avoid endotracheal intubation. Numerous randomized controlled clinical trials have described successful use of NIV to accomplish that goal.[45-49] The amount of time patients remained on NIV was variable, but only a few clinical trials mention the use of humidification, instead focusing on the patient interface and positive-pressure devices/parameters. Also of note is that the patients who failed NIV and required intubation usually did so within 12 hours. A systematic review by Ram and colleagues[49] included 8 studies and found that, compared to usual care, NIV was associated with greater improvements in pH (weighted mean difference 0.03, 95% CI 0.02 to 0.04), P_{aCO_2} (weighted mean difference −0.40 mm Hg, 95% CI −0.78 to −0.03), and respiratory rate (weighted mean difference −3.08 breaths/min, 95% CI −4.26 to −1.89) after 1 hour of treatment. The major finding was that patients responded to NIV within 1 hour, which indicates that humidification is not required for patients who require NIV for only a short period.

In theory it appears logical to humidify gas delivered via NIV. However, NIV has traditionally been delivered with just ambient air, and questions remain as to who will benefit from NIV humidification. During NIV, humidification takes place in the upper airways. Typically, NIV is used in patients with hypoxia, hypercarbia, and resulting respiratory acidosis. It is unclear if any of these gas-exchange impairments would benefit from supplemental humidification during NIV. It is possible that humidified gas simply makes NIV more tolerable when the face and upper airways come in contact with humidified gas. Physiological humidification mechanisms are not bypassed during NIV, as compared to during invasive ventilation via an artificial airway. It may be useful to add supplemental humidification in patients who have thick, retained, or tenacious secretions, or if nasal dryness/congestion interferes with NIV patient adherence and/or tolerance. Patient discomfort could occur from inspiration of dry gas, but to what extent this discomfort may lead to NIV failure is unknown. Clinical studies are needed to determine the benefits of humidifying NIV gas.

Ambient Air Supplies Enough Humidity for Short-Term Noninvasive Ventilation

Heated humidification is most often used during mechanical ventilation via an artificial airway. There is general agreement that 30 mg H_2O/L is the theoretical minimum humidity to ensure adequate gas conditioning during invasive ventilation,[44] However, it is not known if 30 mg H_2O/L is also required for NIV, during which the upper airways heat and humidify the inspired gas. Data provided by Lellouche et al suggest that the minimum absolute humidity required during NIV is 15 mg H_2O/L.[43] Admittedly, there is a dramatic reduction in absolute humidity, down to 5 mg H_2O/L, during NIV without humidification.[44] Is that low humidity relevant for short-term NIV, when the threshold for improvements is measured at 1, 2, 4, or 12 hours? To date there are no published data to assist clinicians in addressing this issue.

Cost Versus Benefit of Humidification During Noninvasive Ventilation

The majority of clinical trials that have measured outcomes of NIV have concentrated on NIV failure, defined by intubation, intensive care unit stay, hospital stay, and mortality. Other measurements assessed have been comfort, adherence, and tolerance. Cost considerations enter into the conversation with all medical procedures, and NIV is no exception. With no decisive evidence providing guidance, the question is whether the potential benefits of humidification outweigh the cost. Studies of NIV financial costs have evaluated numerous factors, including personnel, training, capital equipment, and other costs.[50-52] Two recent surveys of academic medical center emergency departments and Veterans Affairs hospitals discussed technical aspects of NIV, such as NIV interfaces and devices, but failed to address humidification.[53,54] The additional equipment required for NIV humidification (humidifier, sterile water, heating chamber, specialized circuit) adds considerably to the procedural costs.

Evidence Is Strong to Eliminate the Heat-and-Moisture Exchanger From the Noninvasive Ventilation Circuit

It is rare to place an HME into an NIV circuit. The first concern is the large amount of dead space added by the HME. Additionally, the gas flow associated with NIV is mostly unidirectional, due to inherent leaks in the gas delivery path. Thus, the amount of heat and moisture that can be exchanged is dramatically decreased. Despite the physiologic concerns about greater dead space and low efficiency with an HME, 2 studies evaluated the physiologic effects of HME versus heated humidification.[43,55] The results demonstrated that HME increases the work of breathing and may decrease patient adherence to therapy and ultimately cause NIV failure. The greater dead space with an HME may create an intolerable situation because of flow resistance and work of breathing. It is important to remember that an HME can affect ventilator triggering, and caution needs to be exercised.

Summary

Controversy continues concerning whether supplemental humidification is routinely required during NIV in the acute-care setting. Gas law principles and clinical experience suggest humidification may be added as warranted by patient comfort and duration of NIV. Evidence is lacking to support the routine use of active humidification during NIV. Few data have been reported in the field of NIV regarding humidification devices.

Should humidification be used with all patients receiving NIV? Currently, information is not available to answer that question. Only a properly designed randomized controlled clinical trial comparing outcomes of NIV patients receiving humidification versus ambient air will answer the question. Potential clinical variables to measure include improvements in gas exchange, intubation rate, and subjective improvement in patient symptoms while using humidified versus ambient gas. The answer will assist in the development of future consensus statements and practice guidelines.

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Discussion

Gay: Mike, I admire your tenacity in trying to support the con argument. I'm a little surprised that you didn't try to use the relatively low infection rate associated with humidification. Regardless, I think you have to give credence to the CPAP literature, with the evidence review[1] that shows compelling data that humidification increases patient adherence to and tolerance of CPAP, to the extent that even CMS [Centers for Medicare and Medicaid Services] pays for it, and there is not a single device being produced now that doesn't have built in humidification.

1. Gay P, Weaver T, Loube D, Iber C; Positive Airway Pressure Task Force; Standards of Practice Committee; American Academy of Sleep Medicine. Evaluation of positive airway pressure treatment for sleep related breathing disorders in adults. Sleep 2006;29(3):381-401.

MacIntyre: Might that be a short-term versus long-term phenomenon?

Gay: It could be, and I accept that argument, because in most of the NIV studies the patients were only on NIV for hours. To the extent that you probably can't show a great difference between those who do and do not get humidification in a randomized controlled trial, it doesn't necessarily say that it wouldn't be a reasonable thing to do, given the lack of problematic situations that you get in by using heated humidity. I will raise my hand already to say, "Yes, we use it on everybody."

Börg:* Many French studies have been shown—and now the French require us, from an industry standpoint, to provide humidifiers to long-term NIV patients. There is no way you could get away with *not* doing it.

Gentile: I agree that it must be provided during long-term NIV. I know several people who wear CPAP at night, and they say humidification is essential. But in *all* patients, especially short-term patients coming through the emergency department, I don't think it's worth it.

Branson: Three hours total NIV, or 3 hours in the emergency department?

* Ulf Börg, Covidien, Boulder, Colorado.

Gentile: Three hours total.

Branson: Sounds like you're noninvasively ventilating people who don't need NIV.

Gentile: We're just good. We've been doing it a long time. There were several that were outliers, but either they got better or they got intubated.

Branson: This issue has taken on renewed importance for me. Some of our new attendings will have patients on NIV on 60% oxygen and PEEP of 10 cm H_2O, and they're on NIV for 12 to 18 hours, and I'm begging them to intubate, but they keep trying to convince me that NIV is going to work. And in some of these patients who haven't gotten humidification, when we're trying to intubate them, the first thing we encounter is a big clot of mucus in the back of the throat, so you can't even see the vocal cords. I think the answer is, the higher the F_{IO_2}, the sicker the patient; the higher the pressure, the more you have to use a humidifier during NIV.

Gentile: I totally agree. Hey, I didn't pick the con side of this debate.