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Humidification During Non-Invasive Ventilation

By Richard Branson, MS, RRT, FAARC

Non-invasive ventilation (NIV) for acute exacerbations of chronic obstructive pulmonary disease (COPD) has been shown to reduce both morbidity and mortality in this population when compared with endotracheal intubation. NIV may also be used in a host of other diseases including cardiogenic pulmonary edema, post-extubation hypoxemia, and chronic ventilatory failure associated with muscular weakness. Ancillary therapy (e.g. aerosol therapy, antibiotics, fluid management, and secretion clearance) also plays an important role in successful NIV. Humidification during NIV is poorly understood and there are no current standards or recommendations in this area. This is an issue ripe for further investigation, as humidification could play an important role in the success of NIV. Patient comfort, secretion removal, and the efficiency of ventilation may all be affected by the adequacy of humidification. In this article, registered respiratory therapist, Richard Branson, discusses current knowledge and recent evidence with regard to humidification within the NIV setting.

Panel Discussion: Humidification in Non-invasive Ventilation: Clinical Practice Today.

Moderator: *Richard Branson, MS, RRT, FAARC*

Panelists: *Carl Haas, MLS, RRT, FAARC*
François Lellouche, MD
Antonio Esquinas, MD
David Wheeler, RRT, FAARC

In a panel discussion moderated by Mr. Branson, four experts discuss issues concerning the use of humidification in non-invasive ventilation (NIV). Questions addressed include whether short-term humidification during NIV can be used in the emergency room, issues to consider when using an artificial nose during NIV, pros and cons of using a heat and moisture exchanger or a heated humidifier during NIV, potential physiological irregularities that can arise during NIV without humidification, and assessment of success. A short case presentation is also discussed.

Humidification During Non-Invasive Ventilation

By Richard Branson, MS, RRT, FAARC

Non-invasive ventilation (NIV) for acute exacerbations of chronic obstructive pulmonary disease (COPD) has been shown to reduce both morbidity and mortality in this population when compared with endotracheal intubation.[1-3] NIV may also be used in a host of other diseases including cardiogenic pulmonary edema, post-extubation hypoxemia, and chronic ventilatory failure associated with muscular weakness. Ancillary therapy (e.g. aerosol therapy, antibiotics, fluid management, and secretion clearance) also plays an important role in successful NIV.[4] Humidification during NIV is poorly understood and there are no current standards or recommendations in this area.[5] This is an issue ripe for further investigation, as humidification could play an important role in the success of NIV. Patient comfort, secretion removal, and the efficiency of ventilation may all be affected by the adequacy of humidification.

Normal Humidification

The respiratory tract warms and humidifies inspired gases such that alveolar gas is at BTPS (body temperature, atmospheric pressure and saturated with water vapor).[6] The point at which gases reach 37° C and 100% relative humidity (absolute humidity of 44 mg H_2O/L) is known as the "isothermic saturation boundary" (ISB).[6-8] Humidity and temperature are constant below the ISB, while above the ISB, the airway acts as a countercurrent heat and moisture exchanger.[6] During hyperventilation or the breathing of cold, dry air, the ISB moves down the bronchial tree forcing the lower respiratory tract to aid in heat and moisture exchange.[9,10] Under room temperature conditions and a minute ventilation (VE) of 8 L/min, the respiratory tract evaporates 400 grams of water daily, and condenses 150 grams during expiration.[9-11] The normal daily respiratory evaporative heat loss is 250 kcal, 65 to 70 kcal of which are recovered during expiration.[12,13]

> A harbinger of successful NIV is improved patient comfort as work of breathing is reduced.

Heat and moisture exchange intensifies while breathing cool, dry air and increasing VE. NIV can be considered a unique condition of breathing cool, dry gases at high VE. When NIV is supplied via a critical care ventilator, delivered gases are anhydrous from wall air and oxygen. Devices that use a blower to provide room air have a slightly higher water vapor content. However, the leak compensation of many NIV devices creates high flows resulting in further heat and moisture loss.[14] During NIV, patients breathe primarily via the oral route which is less efficient from a heat and moisture standpoint than nasal breathing.[12,13] Dry mouth is the most common complaint of patients using NIV.[15]

Humidification during NIV

A harbinger of successful NIV is improved patient comfort as work of breathing is reduced. This is commonly identified as reduced accessory muscle use and decreased respiratory rate. Oxygen saturation may also increase as dyspnea is relieved.[1,3,4] Comfort involves not only relief of respiratory distress, but also the application of the interface. Mask fit is a critical component of patient comfort during NIV.

Humidification can also affect patient comfort and as a consequence, tolerance of NIV. Nava et al compared compliance with long-term NIV, airway symptoms, side-effects and number of severe acute pulmonary exacerbations requiring hospitalization in 16 patients.[16] Patients suffered chronic hypercapnia and received either heated humidification or an HME for 6 months in a cross-over fashion. The investigators followed side effects of NIV as well as a patient-reported score of the severity of each side effect. They demonstrated improved comfort with the heated humidifier.

Lellouche and co-workers evaluated humidification during NIV in normal volunteers comparing no humidity to one of 2 humidification devices (heated humidification or HME).[17] Two ventilators were used: a turbine powered device delivering ambient air and an ICU ventilator delivering medical grade air and oxygen. Normal volunteers breathed without humidity, with heated humidification, and with an HME at normal (10 L/min) and elevated VE (21 L/min) with and without mask leaks. Delivered humidity with each technique was measured and subjects rated comfort based on mucosal dryness. The investigators found that, without humidification, an absolute humidity of 5 mg H_2O/L was delivered. The HME provided 30 mg H_2O/L but this fell to 20 H_2O/L in the presence of a leak. The heated humidifier provided 30 mg H_2O/L even in the face of mask leak. Comfort scores were similar for humidity ranging from 15-30 mg H_2O/L. However in the absence of humidity, comfort scores fell in half.

At this low level of humidity volunteers reported severe discomfort related to mouth dryness.

These are compelling data in light of the experiences with long-term, home nasal ventilation where two-thirds of patients report upper airway drying and discomfort.[18-21] Hospitalized patients are more likely to have elevated VE, to be febrile, to be dehydrated, to receive oxygen, and to have large mask leaks. There is little doubt that inadequate humidification during NIV results in patient discomfort. Because patient comfort is so critical to the success of NIV, the improved comfort associated with humidification may facilitate NIV success.

Effect on Airways Resistance

Cooling of the airway causes moisture loss, drying of the mucosa and results in increased airway resistance. Richards et al found that 40% of patients on nasal CPAP reported dry nose and throat and sore throat during treatment.[22] Mouth leak and the resulting unidirectional gas flow is the most likely cause of these adverse effects. Using normal volunteers, they found that during CPAP with a mouth leak, nasal airway resistance increased 3-fold. The addition of a heated humidifier ameliorated this increase in airway resistance, but a cool pass-over humidifier had no effect.[22]

Tuggey and colleagues studied the effect of mouth leak during nasal NIV on VT, nasal resistance and comfort.[23] At a mouth leak of 40 L/min, nasal resistance increased resulting in a slight (12%) reduction in expired VT during pressure-targeted NIV. Heated humidification prevented both the change in nasal resistance and fall in VT. Comfort was greater using heated humidification, which also reduced the increased discomfort that followed a period of mouth leak. Fischer found that nasal CPAP without humidification resulted in significant decreases in nasal humidity, a key factor in the development of

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increased nasal resistance.[24]

The magnitude of leaks observed during NIV are unique. Because the normal respiratory tract operates as a countercurrent heat and moisture exchanger, when gas flow becomes unidirectional, there is no chance to reclaim moisture. This also explains the reduction in efficacy of an HME when used with NIV. During NIV the volume traversing the HME during inspiration may be three times the volume expired.

Secretion Retention & Removal

Secretion management during mechanical ventilation is a standard of care.[25] During NIV, preservation of the patients innate cough mechanism is one of the significant advantages of NIV.

The efficiency of heated humidifiers during NIV are adversely affected by the type of ventilator, increased FIO_2, and leaks around the mask or through the mouth during nasal ventilation.[26-28] Given the high flow, low humidity, and complications of unidirectional flow associated with NIV, plus 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.

Esquinas and co-workers conducted an international survey to define humidification practices during NIV and association with outcomes.[29] Data from 15 hospitals encompassing 1635 patients were analyzed for adverse events and failures. They reported that patients who failed NIV, were classified as difficult intubations in 5.4% (88/1625) of cases. In this group of patients who failed NIV, failure to use humidification was the most important factor in predicting difficult intubation. Difficult intubation is related to mucosal drying and secretion retention, rendering the airway friable, inelastic and littered with dried secretions. The presence of thick mucus in the oropharynx and fragile, dry mucosa clearly create a difficult environment for endotracheal tube placement.

Success of NIV

NIV results in improvements in outcomes of patients with COPD. Successful NIV requires appropriate patient selection, interfaces, ventilators, and

Table 1. **Factors which must be considered when choosing a humidification device for non-invasive ventilation.**

Patient Issues	Device Issues
• Comfort • Airway resistance • Deadspace of mask and humidification device • Reduced tidal volume • Increased work of breathing • Secretion retention • Failure requiring intubation • Difficult intubation	• Minute ventilation • Inspired oxygen concentration (the higher the FIO2 the lower the humidity) • Mask leak • Mouth leak with nasal ventilation • Ventilator driving system (some devices, e.g., turbines, heat gas during compression to as high as 110 °F) • Type of ventilator (ICU ventilators typically use anhydrous medical air and oxygen vs. NIV devices which entrain room air).

endpoints. Patient comfort is both a goal of NIV and predictor of NIV success. The role of humidification in the success of NIV has not been adequately studied. Table 1 lists the factors related to humidification which impact NIV therapy. Adequate humidification during NIV improves patient tolerance, patient comfort, and enhances airway function and secretion removal. Humidification during NIV deserves further study.

Cost versus Benefit of Humidification during NIV

There is no doubt that an NIV circuit without either an HME or heated humidifier is cheaper and easier to manage. However, to date, there have been no studies comparing the cost benefit of humidity during NIV. In short term cases, such as cardiogenic pulmonary edema, where the duration of NIV is related to successful medical management, humidification might be avoided. The use of an HME is a further complicating factor as the added dead space and resistance, coupled with the negative impact of leaks on HME output warrant close inspection. While HME's might be used short term, the reduced humidity may be tolerated, but the additional work of breathing might not be.[28,30]

Summary

The evidence surrounding the role of humidification in NIV success is mostly circumstantial. Yet, there are clearly physiologic changes associated with low humidity on airways resistance and, most importantly, patient comfort. Both the type of humidifier and the type of ventilator can impact delivered humidity. Leaks, the most challenging aspect of NIV application alter triggering, cycling, and delivered humidity as well. Continued exploration into these mechanisms to further define the 'best' humidification system for NIV is warranted.

There is no doubt that an NIV circuit without either an HME or heated humidifier is cheaper and easier to manage. However, to date, there have been no studies comparing the cost benefit of humidity during NIV.

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Humidification in Non-invasive Ventilation. *Panel Discussion*

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Do you normally use humidication during short-term, noninvasive ventilation (NIV) in the emergency department (ED)? If so, which method do you use and why?

Lellouche: In most situations, I use humidification, even for short term NIV. In the ED it may be difficult to predict the total duration of NIV requirement. NIV is sometimes required for very short durations (e.g. a few hours for cardiac pulmonary edema) or up to several days. Considering that comfort may have an impact on NIV outcome[1] and the fact that NIV is associated with a high incidence of mouth dryness[2], the gas should be humidified. However, this has not been definitively demonstrated and the optimal level of humidification is not clear at this point.

(HME) or heat and moisture exchanger/filter (HMEF) as the first-line choice to humidify gases during NIV. The question of cost comes first, considering that a very short session may be sufficient for the patients. Indeed, it would be inappropriate to use an heated humidification (HH) kit for few hours, considering the cost. No proof exists for the superiority of HH in comparison with an HME as a first-line humidification strategy.

Haas: Our general practice is to use either an ICU ventilator in NIV mode with humidity, or a turbine bilevel device without humidity. In the ED, most therapists prefer the bilevel device, such as the Respironics Vision®, because patients seem to better tolerate the flows and it compensates for leaks, which helps with patient comfort and produces fewer alarms. We do not routinely add humidity unless the patient complains of dryness, or their secretions are noted to be more viscous and difficult to clear.

Outside of the home environment, little has been reported on the need for supplemental humidity and there are no written humidity guidelines for NIV. In fact, a recent survey of 272 European hospitals reports that for patients with acute hypercarbic respiratory failure, no humidification was used in ~48% of the cases. For patients with cardiogenic pulmonary edema, it was not used in ~67% of the cases.[3] These rates reflect all areas of hospital care, not just the ED.

We have not focused on humidity with NIV in the ED because the duration of NIV before moving the patient out of the ED is relatively short and patients are generally so sick that they usually don't complain of dryness. For the occasional bronchodilator delivered via NIV, the low humidity level may actually enhance drug delivery too.

Esquinas: We use an HH in the ED because hygrometric determining factors are not well known, and there are no randomized clinical trials.[4] Also, there is a higher level of stability and final value of inhaled absolute humidity (AH). Pathophysiologically, there is a high or superior (>50%) range of fraction of inspired oxygen (FiO_2), and leak levels.[5,6] We also use it for patients who exhibit tachypnea, a high peak inhaled flow and minute volume, mouth breathing, high airway nasal resistance, which lead to a higher risk of difficult orotracheal intubation, and in patients who are hypoxemic.

Wheeler: Generally our ED takes steps to assess the patient's needs and facilitate patient throughput in an expedited fashion. This practice model guides the patient based on their individual therapeutic requirements and acuity towards their respective anatomic silo for care. This process rarely takes longer than 23 hours, therefore, the ED does not use a humidification device for NIV.

What should be considered when using an "artificial nose" during noninvasive ventilation?

Haas: HMEs can effectively humidify and warm inspired air for most cases when the upper airway is bypassed. Concerns raised about HMEs during invasive ventilation include added dead space and increased resistance. Both issues are relevant when considering an HME with NIV. Jaber et al. randomized 24 patients with acute respiratory failure to a HME or a heated humidifier during NIV.[7] After 20 minutes with one device, patients crossed over to the other. Compared to a heated humidifier, the HME

was associated with a higher $PaCO_2$ level (40.8 vs 43.4 mm Hg) in spite of a higher minute ventilation (13.2 vs 14.8 L/min). The effect was more pronounced in patients with a lower tidal volume and/or a $PaCO_2$ above 45 mm Hg. Lellouche and colleagues found similar results in their randomized crossover study of 9 patients with hypercapnic respiratory failure.[8] Compared to the group treated with heated humidity, the HME group had a higher minute ventilation (12.8 vs 15.8 L/min) with a similar $PaCO_2$ (57 vs 60 mm Hg) and increased work of breathing. The added HME dead space can be overcome with higher pressure support levels, which may unfortunately also lead to an increased level of mask leaks and reduced tolerance of NIV in certain individuals.

There are a few additional factors to consider when using HMEs with NIV. When a significant mask leak exists, the patient expires less heat and moisture back into the HME, thereby reducing its efficiency. Position of the leak port on bilevel ventilators is also a factor. If the port is in the circuit the HME may work fine but if the leak port is in the face mask, similar to an interface, less gas will be expired back into the HME. Lastly, if inhaled medicated aerosol therapy is desired, either the HME should be taken out of the circuit during therapy, or the patient taken off NIV to receive therapy.

Lellouche: The first parameter to consider is the humidification performance, and an efficient HME should be prioritized (above 28 mg H_2O/L).[9] Even if there is no clear recommendation concerning the level of humidification, the highest performing HME should be preferred, considering that there will be a loss of moisture related to leaks.[10] Also, as leaks are almost inevitable during NIV, the issue of filtration becomes secondary. Indeed, in the case of leaks there will be a potentially high number of viruses or other microorganisms disseminated in the air around the patient

I would answer this question with the comment that recent evidence strongly suggests that the use of an HME greatly increases the work of breathing when utilized as an adjunct to NIV.

through the leaks. Thus, it is not appropriate to focus on the filtration performances of these devices. The dead space in the HME may also be an issue. Indeed, during assisted ventilation, increased instrumental dead space reduces alveolar ventilation, leading to increased $PaCO_2$ and subsequent increased respiratory drive. This additional respiratory load leads to increased work of breathing. It is likely that the impact of dead space is more important if the tidal volume is low and if the respiratory rate is high. However, we showed in a multicentre RCT comparing HH with HME (75 mL of volume) that this did not impact on the rate of intubation, even in the subgroup of hypercapnic patients.[11] Only if very high $PaCO_2$ is the main reason for delivering NIV, the HME dead space should be considered to improve CO_2 removal, although this was not definitely demonstrated.

Esquinas When HME is used, several key factors should be taken into account. With regards to the patient, one should be able to maintain the endogenous AH. It is vital that the selected interface can prevent leaks because this would represent a loss of exhaled AH not captured by the HME.[7,12] High inhaled flows and tidal volume could worsen the level of internal resistance. With regard to the mechanical ventilator, it should be able to generate a peak inhaled flow and sensitivity which is adequate to compensate for the extra increase of the HME's internal resistance. There should be a low status of inhaled AH (i.e. hypoxemic) and an exhale orifice should be included in the respiratory circuit. Alarm signals for loss of inhaled AH should be maximized. One should be able to identify signals of respiratory tract trapping due to an increase of resistance, (flow curve, lengthening of the exhalation period, tachypnea, descent of the current exhaled volume and patient-ventilator lack of synchrony. Gas exchange and enviromental factors (e.g. low external temperature) are also important.

Wheeler: I would answer this question with the comment that recent evidence strongly suggests that the use of an HME greatly increases the work of breathing when utilized as an adjunct to NIV. As Dr. Lellouche noted, Jaber and colleagues demonstrated that HME use was associated with significantly higher $PaCO_2$ as well as an increased minute ventilation and mouth occlusion pressure, while Lellouche and his team showed that in hypercapnic patients the inspiratory effort was significantly higher with HME use. In this very fragile patient population, minute alveolar ventilation exacted a greater work of breathing when an HME was used with NIV.

One must consider that the primary clinical intentions of NIV are to increase alveolar ventilation and to reduce respiratory muscle work. Recent evidence demonstrates that the use of an HME actually works in opposition to theses stated clinical goals. Certainly, one must question the clinical efficacy and or utility of an HME given the unique flow variations, propensity for leaks and unidirectional flow inherent with NIV. Additionally, the case might be made that

the increased iatrogenic deadspace, resistance and amplified work of breathing imposed by the HME argue strongly for its exclusion from any prudent clinical application of NIV.

What are a few of the major issues that argue both for and against the use of a heat and moisture exchanger or a heated humidifier in noninvasive ventilation?

Haas: Normal room air is typically conditioned to a temperature of ~22 C°, with a relative humidity (RH) of 50% and AH of 9 mg H_2O/L. During normal breathing, the upper airway conditions the gas so it is warmed to a fully saturated 29-32 C° as it enters the trachea. A humidification goal for NIV should be to condition the air to at least a level similar to normal ambient levels. It has been suggested that delivery of >15 mg H_2O/L improves comfort during NIV so that seems like a reasonable target.

Dr. Lellouche's study helps one appreciate the humidity level delivered by various NIV devices and settings.[9] When no humidity was added, an ICU ventilator delivered only 5 mg H_2O/L, while a turbine bilevel device delivered 13 mg H_2O/L with minimal FiO_2 and less humidity as FiO_2 increased. Both HME and the heated humidifier had comparable performance (25-30 mg H_2O/L) with no mask leak, but the HME performance decreased with leaks (15 mg H_2O/L) while the heated humidifier was minimally affected.

Regarding the HME, I think the issues mentioned earlier (i.e. dead space, increased resistance, inefficiency with leaks, thick secretions, challenges delivering inhaled medications) argue against it. The ability to potentially provide adequate humidity, reduce supply cost and reduce maintenance effort might argue for its use.

As for heated humidifiers, the factors against their use include increased equipment cost and increased monitoring of the patient to ensure adequate but not excessive heat and humidity. Factors favoring heated humidifiers include no additional dead space and better CO_2 clearance, minimal increased work of breathing, increased ability to effectively deliver aerosolized medications, and ability to adequately humidify in most conditions.

The main advantages of a heated humidifier are the absence of additional dead space and the good humidification performances (when used in optimal conditions) that are not

Lellouche: The main advantages of an HME are their low cost and ease of use. Performances are probably sufficient for recent HMEs (mainly mixed hygroscopic and hydrophobic). The main issue with these devices is the impact of leaks on humidification performances. It is not clear how HMEs perform with NIV ventilators (mandatory leaks). Another issue is the additional dead space which may be a problem in patients with high work of breathing or high $PaCO_2$ associated with encephalopathy.

The main advantages of a heated humidifier are the absence of additional dead space and the good humidification performances (when used in optimal conditions) that are not influenced by leaks. The main issue with this device is the cost. Also, we showed that when the inlet temperature is high in the humidification chamber, the delivered inspiratory humidity of HH is low. This problem is even more marked with NIV settings as the temperature gradient between the inlet and outlet humidification chamber is lower in comparison with settings for intubated patients (recommended outlet temperature being 31°C for NIV settings and 37°C in intubated patients).

Esquinas: With regard to HH, the inhaled AH provided for most physical conditions that might reduce it is higher and more stable. They also have low resistance built into their design, which makes them technically ideal for the following clinical situations (alone or in combination): (1) Symptomatic and previous discomfort history, (2) Hypercapnic acute respiratory failure (ARF) (COPD, asthma), (3) Hypoxemic ARF, with a range of (FiO_2) ≥ 50% and/or applications during more than 48 hours (pneumonia, acute respiratory distress syndrome), (4) Leaks: The loss of inhaled AH around the face mask should be taken into account, together with the loss associated to the exhale orifice; both are constant in NIV, and might cause the final inhaled AH to be less-than-optimal when leaks are important,[13] (5) Ventilation pattern: high peak inhaled flow and tidal volume,[14] (6) Profuse bronchial secretions,[15] (7) Difficult airways (Mallanpatti III, IV score). HH should be not used with an inappropriate interface (e.g. helmet interface). Also, HH is contraindicated in several situations, such when there is a high high risk of infection via aerosols from healthcare staff, poor control of the external room temperature (condensation), or if the patient is hyperthermic.

Wheeler: A recent paper by Branson and Gentile addressed in a rigorous and thorough fashion this very question.[16] Again, I think the discreet practitioner would avoid the utilization of an HME in NIV as the iatrogenic work of breath-

ing is too high and the efficacy of the HME is overly problematic in the NIV environment. However, the use of heated humidity in the clinical application of NIV bears some consideration and discussion.

Heated humidification may have a significant part in the successful clinical course of NIV for a number of reasons. HH has been shown to enhance both patient comfort and compliance. Obviously, if a patient is compliant with and participates in their prescribed therapy the opportunity for a successful outcome increases. This aspect of HH as it relates to NIV is highly subjective and patient context specific. I would argue in favor of any adjunct to NIV that enhances patient compliance as this is the lynchpin to a favorable clinical outcome.

In an interesting study, Tuggey and colleagues considered mouth leak during nasal NIV and described increased nasal resistance and decreased tidal volumes that were attenuated with the application of heated humidification.[17] Also of note a paper by Esquinas and colleagues determined that in patients who failed NIV and required endotracheal intubation the absence of heated humidification was a primary factor in predicting a difficult airway.[4]

Heated humidification of inspired gas has a demonstrated role in the maintenance of normal secretion viscosity, normal airway tone and the prevention of inspissated secretions. However, the fundamental nature of NIV flow velocity profiles renders traditional assumptions of either the clinical necessity or efficacy of humidity protocols suspect. We must assess the clinical effect of heated humidity in the context of the individual patient and their therapeutic needs. In a very real sense the clinical schematic for both NIV and heated humidity may vary within the same institution depending on patient response and therapeutic intent. In cases where patients report an increase in comfort and compliance then heated humidification is an indispensable therapeutic adjunct.

You have a patient with an acute exacerbation of COPD who is expected to need ventilation for 48 hours. What is your recommendation for humidification if the patient is to be treated with (1) an ICU ventilator, or (2) a noninvasive (non-life support) ventilator. In each case, what factors would lead you make this recommendation?

Haas: Patients with acute COPD have inflamed airways leading to increased airway edema, bronchospasm, and increased sputum production, so it seems prudent to humidify the NIV system, particularly if they require it for more than 24 hours. These patients generally have increased work of breathing with a rapid shallow breathing pattern and an increased dead space ratio. Hypercarbia with acidemia is their primary reason for NIV so we should be mindful of adding additional dead space with an HME. This patient will need inhaled medication therapy and may not tolerate coming off the NIV system to receive metered dose inhaler (MDI) or nebulizer therapy. If I were adding humidity, I'd recommend using a heated humidifier set to 30-32 C°, unless the patient complains that it is too warm or feels suffocating. Having said this, we do not routinely add humidity on these patients unless they require it for more than 24 hours. Our pulmonologists claim to not appreciate any lack of humidity related issues when intubating these patents who are failing NIV. Possibly it is because we take most patients off NIV to provide nebulizer therapy.

Lellouche: With an ICU ventilator using only dry medical gases for air and oxygen, I recommend humidification to avoid very dry gases which can lead to mouth dryness after few respirations. The first-line strategy would be to use a properly performing HME with or without filtration properties. If the clinical condition of the patients is deteriorating, mainly due to high $PaCO_2$, the reduction of the dead space using an HH may be an option for a short period. However, this trial with an HH should not unduly delay the intubation if it is required. With an ICU turbine ventilator using dry oxygen and ambient air, no humidification may be acceptable if (1) ambient air is not dry (no air conditioning), and (2) FiO_2 is low (<50%). Most of the time however, humidification should be used. HME is probably sufficient in this situation.

With a specific NIV ventilator using medical dry oxygen but ambient air, no humidification may be sufficient if (1) ambient air is not dry (no air conditioning), or (2) FiO_2 or oxygen flow is low (<50% or <5L/min). Most of the time, humidification should be used. With inevitable leaks in single limb NIV ventilators, heated humidifiers (with or without heated wire) are the most evaluated devices. They provide acceptable humidification even in the presence of leaks.[10,18,19] There is no data with HME in this setting.

Esquinas: Currently there are no differences regarding the type of ventilator (i.e. ICU vs noninvasive, non-life support ventilator). The use of a ventilator depends on equipment, experience, and area (Emergency, Intensive Care, Ward, etc).

In the case presented, if we choose an ICU ventilator, HH will be initially applied according to pathophysiological factors. On a physical level, the use of HME may result in an increase of resistance in work of breathing, particularly in exhalation. HH with less additional internal resistance should be considered. From a technical point of view, ICU ventilators generate an inferior level of basal inhaled AH compared to noninvasive (non-life support) ventilators.
Situations supporting the use of a non-

invasive (non-life support) ventilator include: (1) Acute exacerbations of COPD in emergency areas (BiPAPs), advanced age and comorbidities (e.g. bronchitis), and home oxygen therapy. Internal resistance is lower, and there is less risk of exhalation being affected. The following precautions should be taken into account: (a) High IPAP levels increase demands for a higher AH, particularly during acute exacerbation stages. In this situation, an early use of HH is justified. Accuracy in terms of regulating the final AH will be determined by a servo-control mechanism, according to the flow and temperature measured at the interface. This allows a fast adaptation to variable flows, volumes and/or leaks, an aspect which cannot be technically compensated by HME.[18,20] An exhale orifice or valve included in the distal section of the respiratory circuit with a single respiratory circuit is another source of inhaled AH loss; a disadvantage compared to an ICU ventilator with a double respiratory circuit.

Wheeler: I would be reticent to predict a timetable for the therapeutic application of NIV in most clinical scenarios. I trust that we all have encountered patients who recover in an astonishing fashion as well as the "routine" patient that decompensates in contrast to their clinical assessment.

In this patient population the use of NIV will usually manifest either success or failure within the first few hours. Should the patient respond, in an assessment based manner, the 48 hour timetable is reasonable and representative of a frequent clinical presentation.
Indeed, the clinical application of NIV has been demonstrated to have a great deal of utility in patients with acute hypercapnic exacerbations of COPD. The humidity question was discussed at a recent International Consensus Conference in Intensive Care and they noted that inadequate humidification may contribute to patient distress and NIV failure.[21]

Reduced levels of inspired humidity have been demonstrated to cause cessation of ciliary function, increased viscosity of mucus and inflammation of the airway mucosa.

I discussed earlier my reasons for the exclusion of an HME in NIV and in this particular clinical case the very real potential for an increased work of breathing, attendant increased minute ventilation, $PaCO_2$ and a commensurate decrease in pH disqualify the HME from any cogent discussion.
Nearly 80% of the time an ICU ventilator platform is employed for NIV. The reasons for this overwhelming utilization are largely tied to bedside clinician comfort, unit culture, unit availability and patient setting.[22] The primary concerns when examining NIV humidification with an ICU platform are the necessary use of pipeline or, (rarely), cylinder gas which is dry in the extreme. One recent paper noted that absent a humidification device, an ICU ventilator delivered inspiratory gas with a humidity as low as 5 mg H_2O/L. This alarmingly low level of humidification was inversely related to both minute ventilation and leak rate however it is a genuine cause for clinical concern. One must also consider the fact that typically, during NIV, these patients are mouth breathers and experience much greater inspiratory flows than under normal conditions both of which will increase the potential for extreme drying of secretions.

Given the above stated considerations, I would recommend a protocol for NIV with an ICU platform that allows for a period of patient assessment and evaluation sans humidification. Should the patient be assessed to have improved or stabilized due to the NIV therapy then the therapist should incorporate a heated humidification device into the patient circuit. The heated humidity will increase both patient comfort and compliance whilst potentially avoiding an increase in airways resistance secondary to airway drying.
In those cases where a turbine driven unit is used one must be aware of the fact that delivered humidity, (at FiO_2 = .21), will be co-attendant with ambient humidity. In one study of the use of a turbine ventilator the delivered gas had a water content of 13.0 ± 1.6 mg H_2O/L and was not influenced by leaks. This level of humidification may be adequate to satisfy patient care concerns. In this scenario I would recommend a context specific patient protocol.

What are some of the physiologic derangements that can be seen during noninvasive ventilation without humidification?

Haas: Most of what we know about the effects of inadequate humidification are from studies of patients where the upper airway was bypassed with an artificial airway or laryngectomy. Reduced levels of inspired humidity have been demonstrated to cause cessation of ciliary function, increased viscosity of mucus and inflammation of the airway mucosa. Fortunately, if the damage is not sustained, it can be reversed. Some suggest that mucosal dysfunction may occur in the lower airways unless the inspired gas is conditioned to BTPS (body temperature pressure saturated). An animal model demonstrated that inspired gas at 30 C° or even 34 C° at 100% RH was

insufficient to prevent epithelial damage, which occurred during a 6-hour exposure.[23] Regarding NIV, there was an abstract describing difficult intubation in patients failing NIV[6] and another case of a patient on unhumidified NIV for 6 days developing a life threatening mucus plug/blood clot.[15] Other than these isolated reports, there appears to be little in the literature on the actual effects of low inspired humidity during NIV. This is not to suggest that it is not a problem, but rather that we do not know the magnitude and true clinical significance.

Lellouche: Most patients complain about mouth dryness during NIV. This complication happens within few minutes after exposure to dry gases. In some cases, this may be a cause of major discomfort and NIV failure. Even if this is not demonstrated, it is likely that the first experience with the mask may negatively influence tolerance during the hospital stay. Another issue is the impact of dry gases on bronchial hyperreactivity. This feature is frequently encountered in many patients receiving NIV, such as those with COPD exacerbation[24] and cardiopulmonary edema[25], even if the bronchospasm is not clinically obvious. There is an abundant literature of patients with respiratory disease showing a negative impact of dry gases on bronchial hypereactivity. In some studies, dry gas is equivalent to metacholine for detecting hyperreactivity.[26] It was also demonstrated in healthy subjects that the absence of humidification could increase nasal resistance.[27] Finally, as Dr. Esquinas notes below, it was recently shown that poor humidification may be associated with difficult intubation.

Esquinas: Lack of AH entails severe functional consequences at all levels of the respiratory system. A level of inhaled AH without humidification (close to 5 mg H_2O/L) has been measured, and it is known that levels <15 mg H_2O/L are associated with lack of tolerability in NIV.[6] The range of functional complications depends upon the level of low AH and its duration. Studies have shown increased nasal resistance[28], early cilia dysfunction in the airways, metaplasic changes and accumulation of bronchial secretions, low pulmonary compliance and hypoxemia.

Wheeler: Again I would recommend highly the recent paper by Branson and Gentile which contains an excellent summative hierarchy of the disadvantages of a humidity deficit.[16] Inspissated secretions, mucus plugging, ciliary dyskinesis and epithelial desquamation are potentially life threatening and very destructive sequelae of treatment. Moreover, a dry airway has the greater potential for increased resistance and is notably more difficult to intubate.

This inventory of morbidities is of real concern and is exacerbated by time and humidity deficit. I think any informed clinician would argue for the vigilant assessment of airway wellbeing and integrity on a continuing basis. Perhaps that is the greater point; a reasonable clinician must always practice in an assessment based, evidence-driven fashion.[29]

How can you tell if humidification is adequate during noninvasive ventilation?

Haas: During invasive ventilation, visual inspection of the condensation in the flex-tube at the patient connection has been shown to correlate with adequate humidification.[30] But with NIV, we do not need to deliver as much humidity to the upper airway, because the upper airway still functions as an air conditioner. It has been recommended, if using an active humidification system, the heat be adjusted until condensation appears, then adjusted down a bit to minimize condensation.

Lellouche: The best clinical marker is probably the patient comfort and mouth dryness. Condensation in the mask or in a flex tube may also be a marker. However, this has not been evaluated and may not been as accurate during NIV. If an HME is used, leaks should be monitored. Large leaks should be avoided to limit the loss of humidity.

Esquinas: In everyday practice, hygrometric measurements cannot be taken and we can only apply data from studies conducted under stable and controlled conditions. Therefore, monitoring of optimal humidification can only be conducted under clinical supervision. Some physical and clinical factors might interfere with observation. Therefore, we can differentiate various definitions for an optimal humidification strategy: (1) Resolution of symptoms (dryness, discomfort, lack of tolerability, compliance), (2) Improvement of bronchial clearance, (3) Gas exchange improvement, and (4) Mechanical ventilation (flow, volume).[31]

Wheeler: I would begin with a regular examination of the patient. The initial evaluation might be a brief interview to determine what subjective signs or symptoms the patient is experiencing. The most frequently reported complaint about NIV is dry mouth. Obviously this would prompt a more thorough inspection of the mouth and nose in an attempt to greater quantify the level of dryness. The drying of the eyes is all too frequently reported. Increased use of accessory muscles, stridor, wheezing, dry cough, epistaxis and "crackles" may also be indicative of a humidity deficit.

The reasonably up-to-date therapist must be able to assess their patient, create a plan of care and then execute that plan in a timely fashion. Decisions concerning humidification issues must be made with the patient's best interest in mind. Comfort and subsequent patient compliance are issues of concern when utilizing NIV. In most cases humidi-

fication decisions will be made in the unique context of the individual we are treating in the moment.[32]

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Questions

1. The negative impact of dry gases on bronchial hypereactivity is associated with:
- a. increase nasal resistance
- b. difficult intubation
- c. cessation of ciliary function
- d. all of the above

2. During nasal ventilation a mouth leak results in unidirectional flow and a decrease in airway resistance.
- a. True
- b. False

3. Normal heat and humidification of the respiratory tract does not lose moisture under normal conditions.
- a. True
- b. False

4. The isothermic saturation boundary does not change with changes in inspired humidity.
- a. True
- b. False

5. The main advantages of heated humidification are:
- a. absence of additional dead space
- b. Improved humidification performance
- c. Low cost
- d. A and B only

6. The use of an HME increases deadspace and requires an increase in respiratory rate and or tidal volume to maintain the same $PaCO_2$.
- a. True
- b. False

7. NIV failure is often associated with excessive secretion production.
- a. True
- b. False

8. NIV has been shown to reduce hospital mortality in COPD patients ?
- a. True
- b. False

9. The best indicator of adequate humidification during NIV is:
- a. condensation in the flex-tube at the patient connection
- b. patient comfort
- c. Decreased use of accessory muscles
- d. hygrometric measurements

10. The use of an HME during hypercarbic respiratory failure and NIV should be tried initially?
- a. True
- b. False

11. The use of the HME always increases the work of breathing.
- a. True
- b. False

12. Delivered humidity falls with higher minute ventilation, higher FIO_2, and greater leak.
- a. True
- b. False

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   Strongly Agree 1 2 3 4 5 6 Strongly Disagree

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   Strongly Agree 1 2 3 4 5 6 Strongly Disagree

Objectives

Upon completion of the course, the reader was able to:

1. Describe the effects of humidification during NIV on nasal resistance.

   Strongly Agree 1 2 3 4 5 6 Strongly Disagree
2. List the positive and negative aspects of providing humidity during NIV vs. not providing humidity.

   Strongly Agree 1 2 3 4 5 6 Strongly Disagree
3. Compare and contrast humidity via and HME versus heated humidification.

   Strongly Agree 1 2 3 4 5 6 Strongly Disagree
4. Please indicate your agreement with the following statement. "The content of this course was presented without bias of any product or drug."

   Strongly Agree 1 2 3 4 5 6 Strongly Disagree

Answers

1	☐☐☐☐	9	☐☐☐☐
2	☐☐	10	☐☐
3	☐☐	11	☐☐
4	☐☐	12	☐☐
5	☐☐☐☐	13	
6	☐☐	14	
7	☐☐	15	
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