Heated Humidifier versus Heat-and-Moisture Exchanger During Positive Pressure Ventilation With a T-Piece Resuscitator in Rabbits

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BACKGROUND: There are many proven benefits of the use of conditioned gases in mechanically ventilated patients. In spite of this, its use in the delivery room is limited, perhaps because of known difficulties with heated humidifiers (HH); moreover, there is no evidence regarding the use of heat-and-moisture exchangers (HME) in a delivery room setting. We sought to asess the airway's absolute humidity level using three diferents strategies: HH, HME and unconditioned gases. METHODS: We conducted an experimental study in 12 intubated rabbits ventilated with a T-piece resuscitator. Absolute humidity levels in inspired gases were measured at baseline and at 5, 10, 15, and 20 min while using HH, HME, or no conditioning method (ie, unconditioned). The animals were initially randomized to one of the 3 interventions, and each animal underwent the other methods with at least 24 h between each test. RESULTS: There were no differences in vital signs at baseline or at the end of the procedures. Mean absolute humidity at the end of the tests was 38.2 ± 1.7 g/m^3 for HH, 28.9 ± 4.7 g/m^3 for HME, and 13.9 ± 5.1 g/m^3 for unconditioned gas (P = .003). CONCLUSIONS: During ventilation with a T-piece resuscitator, the absolute humidity was the highest with HH. The absolute humidity with HME was lower, but it was still significantly more than that with unconditioned gas. Therefore, the use of a T-piece resuscitator with HME could be a good alternative to HH given that positive-pressure ventilation is used ideally for short periods of time in the delivery room. *Key words: gas conditioning; respiratory support; delivery room; newborn resuscitation; humidification.* [Respir Care 2020;65(9):1295–1300. © 2020 Daedalus Enterprises]

Introduction

The administration of cold and dry gases directly into the lower respiratory tract can cause lung damage.[1-4] Mechanically ventilated neonates are particularly sensitive to lung injury. Furthermore, the use of unconditioned inspired gases has been associated with an increased severity of bronchopulmonary dysplasia.[5-7]

The respiratory loss of water and heat can cause hypothermia in neonates, and it has been reported that the use of active humidification associated with a T-piece resuscitator during initial stabilization of premature infants decreases the incidence of hypothermia on admission to the neonatal ICU.[8-10] Admission hypothermia is an independent risk factor for mortality in preterm infants and neonatal morbidities.[11-13]

However, cold and dry gases are still used in many delivery rooms for the resuscitation of newborn patients.[14] The

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heated humidifier (HH) system, which is the only device proposed for the delivery room, takes approximately 9 min to reach full operative functionality, which makes it inadequate for emergency situations.[15] In addition, the HH requires a power source; if the neonatal ICU and the delivery room are far apart, absolute humidity levels would decrease during transport.

The heat-and-moisture exchanger (HME) could be a practical alternative to HH. Although there are studies that have tested the use of HME devices in mechanically ventilated neonatal and pediatric subjects, there is no evidence to date of the use of these devices associated with a T-piece resuscitator.[16-18] Because HME devices require adequate humidification and temperature of the exhaled gases, it is difficult to evaluate the system in an in vitro model. An experimental model in animals was used as the initial stage for the evaluation of the system.

The objective of this study was to compare the absolute humidity levels in the airway of ventilated rabbits using a T-piece resuscitation device with active humidity (ie, HH), a passive system (ie, HME), or no conditioning at all.

QUICK LOOK

Current knowledge

The administration of cold and dry gases directly into the lower respiratory tract can cause lung damage in neonates. The use of active humidification via a heated humidifier associated with a T-piece resuscitator during initial stabilization of premature infants decreases the incidence of hypothermia on admission to the neonatal ICU.

What this paper contributes to our knowledge

In an animal model of ventilation with T-piece resuscitator, the absolute humidity obtained with the active humidification system was higher and within the recommended range. Although lower values of absolute humidity were obtained with the heat-and-moisture exchange system, these values were higher than without conditioning. Results of this study support the recommendation to discontinue the use of nonconditioned gases in the delivery room.

Methods

Study Design and Procedures

This randomized controlled study in animals was performed in December 2017 at the Institute of Basic Sciences and Experimental Medicine of the Hospital Italiano de Buenos Aires, Argentina. The research protocol was approved by both the Experimental Research Committee and the Ethics Committee of Research Protocols of the Hospital Italiano de Buenos Aires (Protocol E/131). The experiments were performed in adherence to the Canadian Council on Animal Care Guidelines on the Use of Laboratory Animals.

Adult New Zealand rabbits were anesthetized and intubated with neonatal endotracheal tubes size 3 and 3.5 mm internal diameter with and without balloon, without cutting the tube (Rusch, Teleflex, Wayne, Pennsylvania). The endotracheal tube size was determined by the veterinarian at the time of endotracheal intubation, and the same endotracheal tube size was used in each test for each animal. In all cases, animals were treated with intramuscular injections of 2 mg/kg midazolam and 10 mg/kg ketamine. Then we placed a venous access for induction with 5 mg/kg propofol. Once the endotracheal intubation was performed, the anesthetic plane was maintained with an infusion of 1% propofol at a dose of 15 mg/kg/h, which could be titrated to keep the animals in a deep anesthetic plane throughout the duration of the tests. Continuous monitoring of vital signs was performed with a multiparameter monitor, including rectal temperature, heart rate, breathing frequency, and oxygen saturation. The tests were performed on a radiant warmer set at a constant level. A neonatal T-piece resuscitator (NeoPuff, Fisher & Paykel, Auckland, New Zealand) was connected to a compressed air/oxygen blender with gas flow set at 10 L/min for all tests. The 3 options for interventions were HME (Humid-Vent Mini, Teleflex), active HH (MR850, Fisher & Paykel), and no device (Fig. 1). The HH was turned on in advance to achieve a full warm-up for each test.

After intubation, adequate ventilation parameters were used for adult New Zealand rabbits, as indicated by the veterinary team. Starting settings were peak inspiratory pressure 15 cm H_2O, PEEP 4 cm H_2O, and breathing frequency 50 breaths/min. A metronome was used to ensure consistency in the breathing frequency.[19] The animals were in a deep anesthetic plane during the tests, so all breaths were delivered actively through the T-piece resuscitator. Each test lasted 20 min. The initial parameters could be modified according to oxygen saturation and heart rate. During the tests, the relative humidity and temperature at the level of the endotracheal tube were recorded with a thermo-hygrometer (Testo 605-H1, Lenzkirch, Germany), and absolute humidity was calculated. These values were measured at the beginning of the test (ie, baseline) and then every 5 min up to 20 min, with 5 measurements per test. The thermo-hygrometer was placed on the edge of the radiant warmer, wrapped in thick plastic tubing to avoid receiving radiant energy. At the end of the test, sedation was suspended, and the animals were returned to the animal facility. Three tests were performed for each animal, one test for each arm of the study, with at least 24 h between each test.

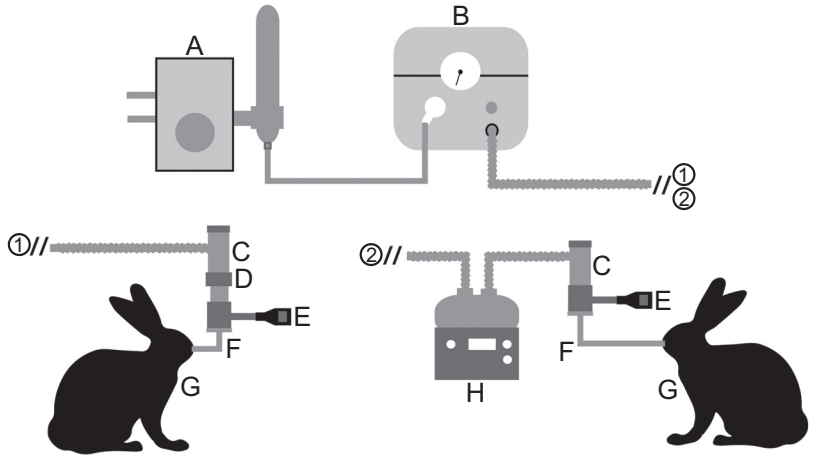

Fig. 1. Schematic picture of the circuits with heat-and-moisture exchanger (1) and heated humidifier (2). A: gas blender and flow meter; B: Neopuff infant T-piece resuscitator; C: T-piece; D: heat-and-moisture exchanger; E: thermo-hygrometer; F: endotracheal tube; G: rabbit; H: heated humidifier. The figure is not drawn to scale.

Each animal was identified and the order in which the tests were carried out was randomized using permuted blocks (ie, blocks of 4 or 6 opaque and sealed envelopes). Because the use of cold and dry gases could cause lung damage, randomization was limited to HH or HME, and the test without gas conditioning was performed last for each rabbit.

Study Outcomes

The primary outcome was the absolute humidity value measured at the beginning and every 5 min until the end of the test. Secondary outcomes variables included incidence of hypothermia (ie, rectal temperature $< 38.5°C$) and differences in oxygen saturation (S_{pO_2}), ventilator pressures, F_{IO_2}, and heart rate between the beginning and the end of each procedure.

Measurements

Temperature values of the exhaled air and relative humidity were assessed with a thermo-hygrometer. Absolute humidity was calculated from those values and registered at 0, 5, 10, 15, and 20 min of each test. Hypothermia was defined as rectal temperature $< 38.5°C$. Differences (Δ) in S_{pO_2}, peak inspiratory pressure, F_{IO_2}, and heart rate between the beginning and end of each procedure were recorded and compared.

Data Analysis

Continuous variables are expressed as mean (SD) or median (interquartile range [IQR]) according to their distribution and analyzed using the Shapiro-Wilk normality test. Differences among the means were analyzed using analysis of variance, and the Bonferroni test was performed for pairwise comparison between group means. For non-normal data distribution, the Kruskal-Wallis test was used. Absolute and relative frequencies were used to report categorical variables. Differences were calculated using chi-square test. Statistical analyses were performed using Stata Software 13 (StataCorp, College Station, Texas). Results with P values $< .05$ were considered statistically significant. Because there were no previous data to suggest the effect size, a sample size was not calculated for this research study. It was estimated that 12 rabbits were an adequate sample.

Results

A total of 36 tests were performed. The mean weight of the rabbits was 3,180 ± 400 g. One test from the HME arm was excluded from analysis due to a large leakage from the endotracheal tube, which could have altered the measurements. The absolute humidity values were different in the 3 arms at every measured time point. Mean absolute humidity values at the end of the tests were statistically different between the 3 studied arms: 38.2 ± 1.7 g/m^3 for HH, 28.9 ± 4.7 g/m^3 for HME, and 13.9 ± 5.1 g/m^3 without conditioning ($P = .003$) (Fig. 2). The mean temperature in the airway was 34.3°C (IQR 33–34.8) with HH, 31.4°C (IQR 30–33) with HME, and 28.7°C (IQR 27.8–29.7) without conditioning ($P < .001$). Seven episodes of hypothermia were recorded: 3 episodes with HH, 2 with HME, and 2 with unconditioned gases. All of the episodes happened at the beginning of the test. There were no significant differences between the starting temperature and the ending temperature, for any of the arms of the study (Δ temperature). There were no significant differences in ambient temperature for any of the 3 arms: HH 25 ± 1.2°C, HME 24.7 ± 1.0°C, and no device

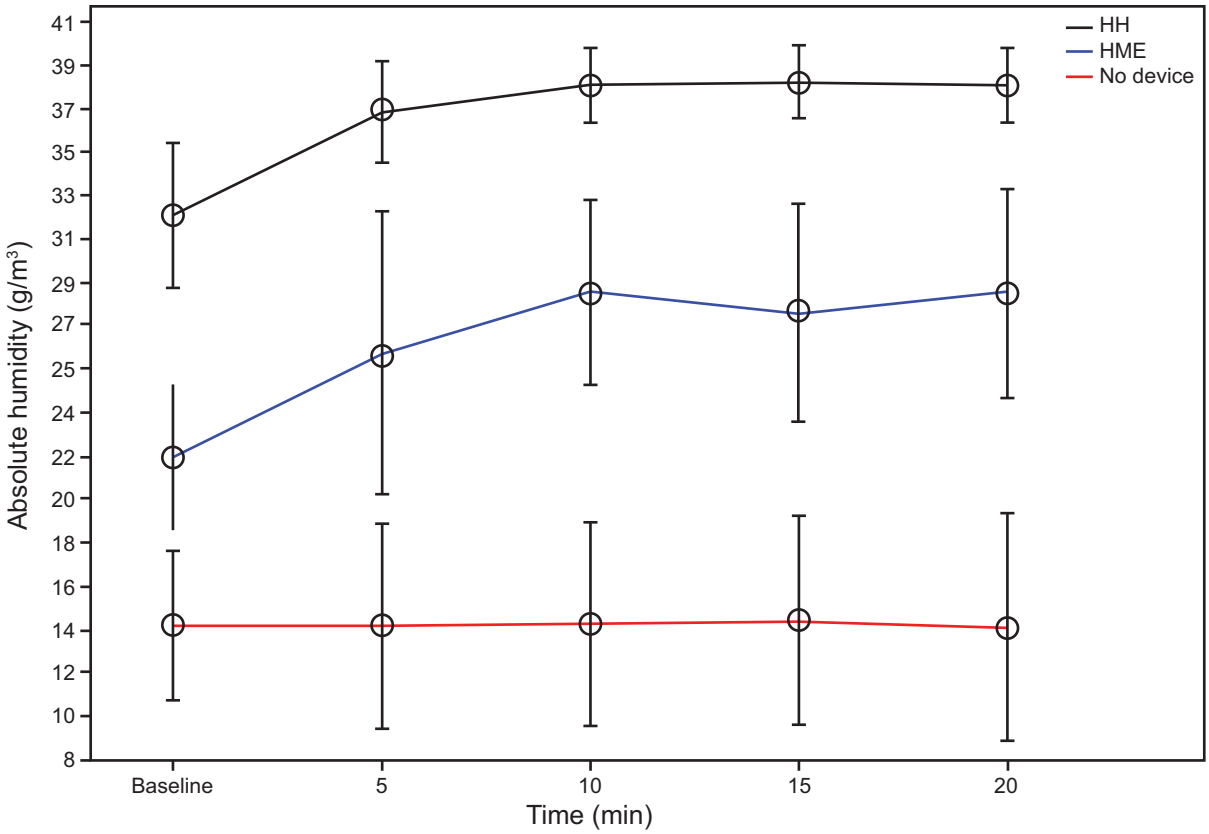

Fig. 2. Mean and SD of absolute humidity as a function of time, according to the device used. HH = heated humidifier; HME = heat-and-moisture exchanger. Analysis of variance: Baseline $P = .01$; 5 minutes $P = .01$; 10 minutes $P = .01$; 15 minutes $P = .006$; 20 minutes $P = .003$.

24.2 ± 1.2°C ($P = .86$). There were no significant differences neither in the vital signs recorded, nor in respiratory support at the beginning or at the end of the procedures (Table 1).

Discussion

The absolute humidity measured using HH was not only higher but also adequate, according to recommended values for invasive ventilation. The use of HME resulted in lower values of absolute humidity compared to HH, but these values were significantly higher than those obtained in the tests without conditioning. These results could be reasonably interpreted as expected. However, to our knowledge, there are no published studies evaluating the use of HME devices for T-piece resuscitator ventilation.

A few studies have evaluated the absolute humidity obtained with the use of HME compared with HH in mechanically ventilated neonatal subjects. Fassassi et al[16] compared the absolute humidity levels obtained with HH and HME, reporting similar results, although their HME absolute humidity values were somewhat higher than those obtained in our study. Schiffmann et al[18] found no difference in the use of the 2 methods of humidification in 40 neonates and infants who needed mechanical ventilation. Luchetti et al[17] compared 2 HME systems in mechanically ventilated children under 10 kg and reported values similar to ours. Chikata et al[20] evaluated the effect of expiratory leakage in HME systems in an artificial lung model and reported absolute humidity values that were within the range of those observed in our study. Finally, Owen et al[15] evaluated the use of an HH associated with a T-piece resuscitator, with higher absolute humidity values than those observed in our study. The variable values of absolute humidity obtained in all of these studies could be explained by the different measurement methods used, clinical conditions, ventilation methods, and the mixture of gases used. In all of these studies, the absolute humidity values obtained with HME devices were lower than or similar to those obtained with HH. However, the levels of absolute humidity were close to 30 mg/L, which is the minimum value recommended by the American Association for Respiratory Care.[21]

Despite lower absolute humidity values with HME devices, a recent systematic review of studies including both adult and pediatric subjects did not find significant differences in clinical outcomes.[22]

Table 1. Vital Signs and Respiratory Support at the Beginning and at the End of the Procedures

	Heated Humidifier	Heat-and-Moisture Exchanger	Unconditioned	*P*
Baseline				
Rectal temperature, °C	38.9 (1.0)	39.2 (0.7)	39.2 (0.7)	.31
Heart rate, beats/min	222 (47)	220 (37)	230 (45)	.77
S_{pO_2}, %	94 (90–99)	98 (94–100)	96 (92–99)	.41
PIP, cm H_2O	14 (1.4)	14 (1.6)	15.5 (1.4)	.80
F_{IO_2}	35 (21–60)	30.5 (21–50)	23 (21–32.5)	.60
Difference: End − Baseline				
Δ Rectal temperature, °C	0.3 (0.3)	0.3 (0.3)	0.1 (0.3)	.94
Δ Heart rate, beats/min	−15 (44)	−17 (38)	−30 (22)	.14
Δ S_{pO_2}, %	2.5 (−2 to 7)	−1 (−2 to 5)	1 (−3 to 4)	.63
Δ PIP, cm H_2O	0 (−0.3 to 1)	0 (−0.6 to 2)	−0.5 (−2 to 0.5)	.21
Δ F_{IO_2}	0 (−15 to 5)	−9.5 (−29 to 0)	0 (−6.5 to 0)	.34

Data are presented as mean (SD) or median (interquartile range).
PIP = peak inspiratory pressure

According to some published studies, one of the main limitations when using HME is increased endotracheal tube leaks of exhaled gases, which results in decreased effectiveness.[20,23] In this study, we observed absolute humidity values below recommended values in a few rabbits, which improved when the airway was repositioned and the peritube leakage was reduced. Because respiratory function monitoring was not available for the study, the magnitude of the leakage could not be measured.

The efficiency of the HME device depends on the exhaled air temperature, so it is possible that the absolute humidity values are lower in hypothermic neonates. However, in the few HME-ventilated rabbits that experienced hypothermia, the obtained absolute humidity values were similar to the ones found in normothermic rabbits. Because all the hypothermia episodes were at the beginning of the test, they could not be related to the method of airway humidification, but rather to the ambient temperature and the anesthetic induction. It is important to mention that the experimental design of our study is different from real-life situations in a delivery room. Human neonates have no fur coat and are born wet. Although it is true that the animals were dry and warm, rabbits are particularly prone to develop hypothermia due to peripheral vasodilatation when under deep anesthesia. The latter was reflected in the fact that 7 animals had episodes of hypothermia. We evaluated these systems in a model in which the animals did not breathe spontaneously, so it may not reflect the way in which all newborns are ventilated.

One known issue with HME systems is the increased dead space, which can prevent adequate ventilation and can lead to unacceptably high CO_2 levels. It has been reported that spontaneously breathing patients increase their breathing frequency to keep adequate minute ventilation, whereas paralyzed patients rely on ventilator parameters and may have some degree of hypercapnia.[24] In our study, we did not analyze blood gases, so we cannot speculate about this issue, which may be important in actual clinical scenarios in neonates.

Both HH and HME devices achieved absolute humidity values above the minimum recommended by the American Association for Respiratory Care for each type of device; however, these results have to be considered carefully because the standards were developed for the adult population.[21,25,26] As expected, with unconditioned gases, the recommended minimum humidity values were not reached at any time.

Randomized trials have indicated that gas conditioning in the delivery room using HH results in lower incidence of hypothermia in preterm infants on neonatal ICU admission. However, it has been stated that, considering the lack of effect on major outcomes and the cost of the equipment, the use of HH in the delivery room should be further evaluated before it is recommended for clinical practice.[8-10,27] While awaiting more studies in neonates, alternative ways to provide adequate absolute humidity levels are being considered. Because the HME can be used immediately with no previous preparation, it could be particularly useful during emergency deliveries, when there is no time to prepare or set up more complicated equipment. Premature babies present a different kind of challenge: they have lower tidal volumes and high risk for CO_2 retention and hypothermia. When there is a nonemergency premature delivery, the optimal gas-conditioning device could be prepared and preheated in advance.

Conclusions

In an animal model of ventilation with a T-piece resuscitator, the absolute humidity obtained with the active humidification system (ie, heated humidifier) was higher and within the recommended range for mechanical ventilation.

Although lower values of absolute humidity were obtained with the heat-and-moisture exchange system, these values were higher than those observed in the tests without conditioning, and its use in the delivery room could be a feasible alternative, especially for brief periods of time. Human studies are needed to evaluate whether the difference between the 2 methods is clinically important. The absolute humidity levels obtained when using unconditioned gases were well below the recommended values, and its use should be discouraged. Our study adds to this recommendation.

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