Original Article

A comparison of two interventions for HHHFNC in preterm infants weighing 1,000 to 1,500 g in the recovery period of newborn RDS

Alireza Sadeghnia, Zohre Badiei, Hassan Talakesh

Department of Pediatrics, Beheshti Hospital, Isfahan University of Medical Sciences, Isfahan, Iran

Abstract

Background: Nasal cannula, beside administering low-flow therapy, showed the capability for the administration of continuous positive airway pressure (CPAP) through high-flow nasal cannula (HFNC). Meeting specific physical criteria of 100% relative humidity (RH) and temperature of 37°C are the basic interventional requirements to administer oxygen for the newborns through a nasal cannula. Recently, two systems, MR850 and PMH7000, received the Food and Drug Administration (FDA) approval to administer heated, humidified HFNC (HHHFNC). These systems are evaluated in this study based on their humidifying and heating capabilities.

Materials and Methods: This study was done as an RCT on newborns weighing 1,000 to 1,500 g recovering from respiratory distress syndrome (RDS) while nCPAP was administered at CDP = 4 cmH_2O, Fio_2<30%. Patients were randomized to two groups of 35 receiving HHHFNC after treatment with nCPAP, with one group using MR850 humidifier and the other PMH7000. The patients were compared according to the duration of HHHFNC administration, repeated need for nCPAP respiratory support, the need for invasive ventilation, apnea, chronic lung disease (CLD), nasal trauma, RH, and temperature of the gases.

Results: The average time of support with HHHNFC did not show any significant difference in the two groups. There was no significant difference between the groups in the need for nCPAP, invasive ventilation, apnea, nasal trauma, and CLD. The difference in the levels of average temperature and humidity was significant (*P* value <0.001).

Conclusion: Although the records of temperature and RH in the PMH7000 system was lower than the records from the MR850 system, no clinical priority was observed for respiratory support with HHHNFC in the two systems.

Key Words: HHHFNC, MR850, PMH7000, respiratory distress syndrome

Address for correspondence:
Dr. Alireza Sadeghnia, Beheshti Hospital, Isfahan University of Medical Sciences, Isfahan, Iran. E-mail: sadeghnia@med.mui.ac.ir
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INTRODUCTION

Diseases related to prematurity were the cause of death for 17% of overall newborns in the United States in 2003, whereas respiratory distress syndrome (RDS) and bronchopulmonary dysplasia (BPD) are the most common among the diseases resulting in death in this group of newborns. Despite the increasing number of

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cases treated with corticosteroids before birth and the administration of surfactants aiming to reduce RDS, the incidence of BPD in very-low-birth-weight (VLBW) newborns showed no significant change during the last decade. Although in the pathogenesis of BPD, genetic inheritance is responsible for the half of the affiliations, other important factors such as chorioamnionitis, hyperoxia, pulmonary edema, nosocomial infection, and respiratory management–induced injury are considered major influencing factors.[1]

At the moment, establishing a continuous positive pressure (CPAP) through the airways of an RDS-affiliated newborn together with the administration of surfactant is the cobblestone and the most common intervention for these newborns, especially the ones with extremely low birth weight (ELBW).[2-4] Nasal cannula, which was first used to administer supplemental oxygen (low-flow therapy) on a large scale, also showed the capability for the administration of CPAP through high-flow nasal cannula (HFNC) as it developed. Needless to say, apart from meeting specific physical criteria, a relative humidity (RH) of 100% and a temperature of 37°C are the basic requirements of this intervention.[5]

The application of HHHFNC in the neonatal intensive care unit has developed significantly during the last decade due to the fact that not only is this system capable of providing a specific percentage of the respiratory oxygen, but it can also administer noninvasive respiratory support of constant-flow CPAP without the need for any further equipment.[6]

When the respiratory disease is accompanied by increasing respiratory work, supportive mechanisms of HHHFNC are specifically categorized as follows:

- Dead space ventilation in the nasopharyngeal space: High-flow therapy (HFT) may eventually enhance alveolar ventilation by decreasing the dead space through establishing washout in the nasopharyngeal space by gas insufflations (GI), which in turn increases the minute ventilation.
- A decrease in respiratory work: This is the result of providing some level of splinting in the nasopharynx, which has a significant ability of compliance. When HFT produces GIs beyond demand flow in the nasopharynx, it avoids the retraction of the nasopharynx wall in inspiration and with the lowering of resistance in this space, the respiratory work also decreases in inspiration. Moreover, in expiration, the expiratory flows face resistance in the nsaopharynx (due to the jet caused by the nasal cannula), and are redirected to the oropharynx, which eventually decreases the expiratory work because of the occurrence of the Coanda effect in the behavior of the gas.
- Providing the maximum humidity and temperature: To establish optimal gas exchange with the consumption of energy, the airways increase the temperature and RH of the inhaled gases to 37°C and 100%, respectively, while the HFT systems block the waste of energy in the airways by establishing these conditions and eventually improving the mechanics of the lungs.

It should be noted that the similar effects of CPAP on respiratory management are also considered in the description of HFT effects.[7]

The most vital characteristic of HFT is establishing maximum optimal heating and humidifying for inhaled gases, due to the fact that the ability of the airways, which normally increase the temperature of the gas to 37°C and RH to 95-100% in the second and third subsegmental divisions, is dramatically limited and if these criteria are not met, loss of humidity in the airway epithelium, bleeding, inflammation, infection, surfactant degradation, and finally alveolar collapse are inevitable. In 2004, the Food and Drug Administration (FDA) approved a kind of HFT system called Vapotherm 2000i (Vapotherm Inc., Stevensville, MD, USA) which is designed on the basis of semipermeability membranes that are arranged compressively in a kind of cartridge. Sterilized water is pumped into the cartridge while heated, and gas is also pumped with a high pressure into the compressed membranes of the cartridge, and the gas which is extracted from the cartridge enters the airways of the newborn.[8]

MATERIALS AND METHODS

This study was done as a prospective randomized clinical trial on newborns with a weight of 1,000 to 1,500 g as they were recovering from RDS in the neonatal intensive care unit of Beheshti Hospital affiliated to Esfahan Medical University from September 2011 to August 2012.

Newborns receiving surfactants due to affiliation with RDS and whose oxygen saturation was equal or more than 90% under nasal CPAP (nCPAP) with continuous distending pressure (CDP) = 4 cmH_2O and fraction of inspired oxygen (FiO_2) <30% during the last four hours and those who still needed oxygen supplement after disconnection from nCPAP were included in the study; the exclusion criteria for this study was if there was a congenital malformation, prenatal asphyxia apgar score of 0 to 3 at min 5, or umbilical cord pH less than 7, and bicarbonate level of the umbilical cord was reported to be less than 12), or nasal mucosa erythema.[9,10]

The newborns were randomly put in one of the two groups of MR850 or PMH7000 after they were eligible to be disconnected from nCPAP, and HHHFNC respiratory support was administered for them. Speculum inspection was done on the nasal mucosa and written consent was received from the parents before any newborn was included in this study.

- For the MR850 group newborns, first, appropriate nasal cannula was provided with a diameter not more than 50% of the nostril of the newborn.[11] Then, the nasal cannula was attached to the specific circuit and was linked to the chamber exit while the entrance of the chamber was adjusted by the blender through a pressure manifold. The humidifying system was attached to the circuit through a heater wire and temperature probes and the system was set to invasive status.
- For the newborns in the 7000PMH group, the same procedure was applied except for the humidifying system for which the RH and the temperature were set to 100% and 37°C, respectively, at the end of the circuit, and also the temperature of the heater was set to 37°, whereas the temperature of the end probe was set to 40°C.
- The nasal cannula was BC2425-BC3790 (Fisher & Paykel Healthcare, Auckland, New Zealand).
- The circuit was RT329 (Fisher & Paykel Healthcare, Auckland, New Zealand)

The heating and humidifying capability of the system was tested every six hours with a psychrometer (Dri-Eaz, GE); during intervals, the hygrometer probe was exposed to dry oxygen flow to get a humidity percentage of 0%.[12]

- The gas flow through the circuit was estimated by the following formula[8]:
  Flow (L/min) = 0.92 + [0.68 × W (Kg)]
- The nostril was checked on a daily basis (by speculum and ophthalmoscope) and the following categorization was used to describe the level of injury of the nasal mucosa in each nostril:
  - Degree 1 (edema and erythema)
  - Degree 2 (edema and erythema together with mucosa thickening)
  - Degree 3 (nostril obstruction by mucosa thickening and edema)
  - Degree 4 (bleeding)

  The total of each nostril score was used to determine the degree of injury.[10]
- During the treatment if the need for FiO_2 to maintain the oxygen saturation above 90% was increased to more than 30% (and continued for more than four hours), capillary gasometry was obtained on the newborn and nCPAP was administered. In the case of any of the following criteria, the newborn was treated by invasive ventilation:
  - The inability to maintain oxygen saturation in the range of 90 to 95% in the right hand while CDP = 8 cmH_2O and $Fio_2 \leq 75\%$.[13]
  - CBG gasometric criteria representing respiratory insufficiency (pH <7.2 and PCO_2 >65 mmHg).[9]
  - Occurrence of apnea more than three times in an hour which needed stimulation or ventilation with manual resuscitator.[9]
- If the newborn could maintain the oxygen saturation level more than 90% for four hours without the need for supplemental oxygen (tolerated Fio_2 equal to 21%), he would be disconnected from HFT respiratory support.
- If the newborn needed supplemental oxygen after the 28th day of birth, he would be diagnosed as affiliated with CLD.

RESULTS

The demographic characteristics are listed in Table 1. Using *t*-test, the mean of gestational age, age of afterbirth, and the weight at birth showed no significant difference between the two groups. (*P* value >0.05).

Mean and standard deviation of gas humidity and heat in the circuit for a period of 48 hours are shown in Table 2. Variance analysis frequency test shows that

Table 1: Demographic characteristics of the neonates in the two groups of MR850 and PMH7000

Variant	Scale	MR850	PMH7000	*P* value
Gestational age	Week	29.73±2.07	29.13±1.3	0.18
Weight	Gram	1193.3±117.3	1204.7±104.9	0.7
Postbirth age	Day	4.69±3.2	4.61±5.84	0.95
Sex	Male	16 (53%)	14 (46.7%)	0.61
	Female	14 (46.7%)	16 (53%)	

Table 2: Distribution of demographic variants in the two groups of MR850 and PMH7000

Parameter	Relative humidity (%)		Temperature (°C)	
Hours	MR850	PMH7000	MR850	PMH7000
6	93.28±9.02	100±0	38.85±2.24	36.09±2.3
12	88.6±8.51	99.61±1.17	37.71±1.48	35.58±1.67
18	93.93±9	99.21±2.37	38.83±1.43	35.14±1.89
24	94.91±9.18	100±0	38.94±2.15	35.93±2
30	91.17±9.68	100±0	37.92±1.85	36.34±2.3
36	87.11±8.35	100±0	39.17±1.46	35.12±1.32
42	91.33±8.09	99.96±0.13	38.41±1.28	35.28±2.01
48	92.43±8.45	99.18±1.67	38.56±1.73	35.72±2.06
P value		<0.001		<0.001

the mean of changes in humidity and heat showed a significant difference between the two groups during the study (*P* value <0.001). Figures 1 and 2 represent the trend for gas humidity and temperature in both groups.

Table 3 shows the nasal mucosa injury in the left and right nostrils in both groups. Fisher's exact test showed that there was no significant difference in the severity of the mucosa injury between the two groups (*P* value >0.05).

In Figure 3, the two groups are compared based on the incidence of complications. Three cases of apnea and one case of the need for invasive mechanical ventilation were observed in both groups (*P* value = 1). The need for a second administration of nCPAP in the MR850 group and PMH7000 group was three cases to one case, respectively, which when tested by Fisher's exact test, showed no significant difference (*P* value = 0.61) between the two groups. Among the 60 patients in both groups, seven cases were reported to have CLD, of which five cases were in the MR850 group and the two others were observed in the PMH7000 group; however, the difference between the two groups was not significant according to Fisher's exact test (*P* value = 0.42).

The mean and confidence interval of the duration of treatment for both groups are shown in Figure 4 (at 25%, 50%, and 75%). The mean of the duration of treatment in the MR850 and PMH7000 groups are 5.3 ± 1.5 and 3.4 ± 1.3 days, respectively. The *t*-test showed no significant difference between the two groups (*P* value =0.36).

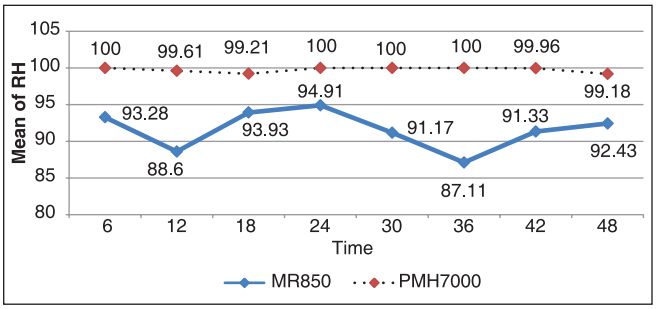

Figure 1: Humidity trend in the two groups of MR850 and PMH7000

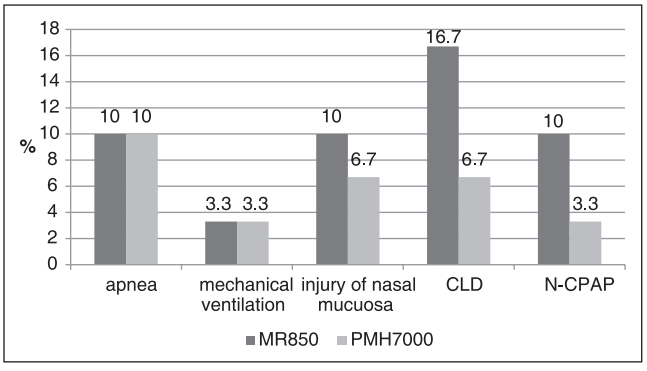

Figure 3: Percentage of complication incidence of the patients in the two groups of MR850 and PMH7000

DISCUSSION

There are a limited number of comparative studies focused on the theme of capabilities of HFT systems in the field of neonatology, and the available studies focus mainly on the Vapotherm 2000i systems. Although a few studies have been done on the application of the

Table 3: Distribution of incidence for the severity of nasal injury in patients in both groups of MR850 and PMH7000

Nostril	Severity of injury	MR850	PMH7000	*P* value
Left	None	26 (86.7%)	28 (93.3%)	0.55
	Mild	2 (6.7%)	0 (0%)	
	Moderate	2 (6.7%)	2 (6.7%)	
	Severe	0 (0%)	0 (0%)	
Right	None	26 (86.7%)	28 (93.3%)	0.8
	Mild	2 (6.7%)	1 (3.3%)	
	Moderate	1 (3.3%)	1 (3.3%)	
	Severe	1 (3.3%)	0 (0%)	

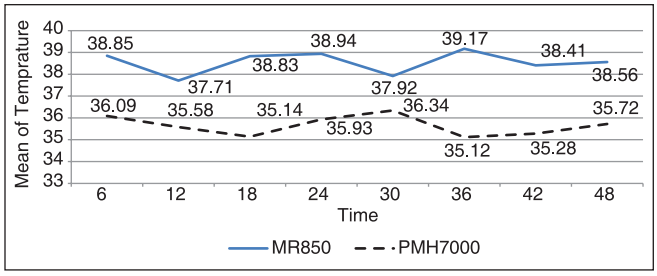

Figure 2: Gas temperature trend in the two groups of MR850 and PMH7000

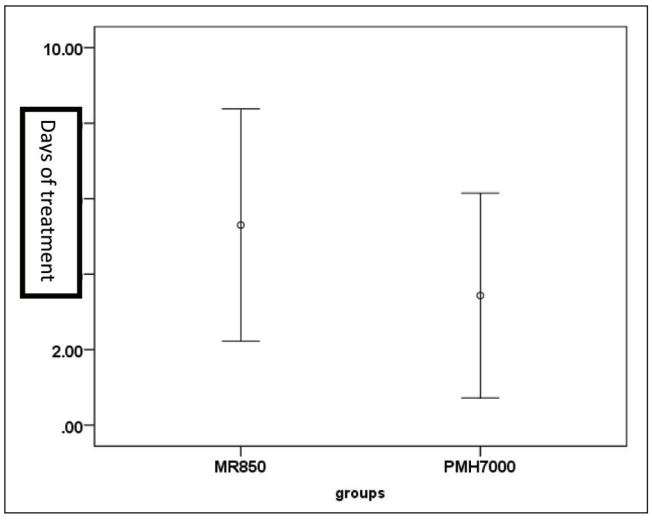

Figure 4: The mean and confidence interval of the duration of treatment in the two groups of MR850 and PMH7000

MR850 system, no study has been found to challenge the PMH7000 humidification system.

In a study done in 2005 in the neonatal intensive care unit of the McKay-Dee hospital, Woodhead *et al*. included 30 newborns who met the criteria of extubation. The newborns in the first group (n = 15) were treated with Vapotherm 2000i respiratory support for the first 24 hours, whereas the newborns in the second group (n = 15) were treated with nasal cannula (standard high flow/SHF) as respiratory intervention. During the next 24 hours, the respiratory intervention method for the treatment of the newborns was exchanged between the two groups. This study significantly revealed that when the newborns were treated with Vapotherm 2000i system, their respiratory work was reduced, and the nasal mucosa had a more normal condition; however, respiratory rate and incidence of reintubation after the establishment of Vapotherm 2000i system showed a statically insignificant decrease compared to SHF.[10]

In a study done by Waugh *et al.,* two systems of HFT, Vapotherm 2000i and Salter Labs, were evaluated based on the humidity level and the temperature of the flow at 5, 10, and 15 L per minute. In the Salter Labs system, the humidifying mechanism is designed based on bubble humidification and active humidification is not applied. The capabilities of the two systems were tested with a digital thermo hygrometer (Mannix, Lynbrook, New York), and the results showed that at a flow of 5 L per minute, the RH for Vapotherm 2000i was 99.9% and the same criterion for the Salter Labs system was estimated to be 78.7%, whereas the temperature for the Vapotherm 2000i system was 36.5 ± 0.1°C and the same for the Salter Labs system was estimated 23 ± 0.2°C. For higher flows, the capabilities of the Salter Labs system decreased dramatically, whereas the Vapotherm 2000i system maintained the temperature of 37.1 ± 0.3°C and RH of 99.9% even at a flow of 40 L per minute.[14] This study revealed that the capabilities of the MR850 and PMH7000 systems in humidifying and heating the inhalation gas were more than the those of the Salter Labs system; however, these systems did not turn out to exceed the high capabilities of the Vapotherm 2000i system.

In another study by Walsh *et al*., RH was evaluated with a digital thermo hygrometer (Omega Engineering, Stamford, CT) in both humidifier systems, that is, Vapotherm 2000i and MR850 (produced by Fisher & Paykel) for the flows of 1 to 8 L per minute, whereas temperature and humidity environment were 22°C and 12%, respectively. The MR850 humidification system is designed based on active humidification. In this study, RH was estimated as an average of 95.75% for MR850 and 98.75% for Vapotherm 2000i which showed a statistically significant difference by the *t*-test (*P* value = 0.015). In a parallel study done by the same group at flows of 15 to 35 L per minute, Aquanox (Smiths Medical, Kent, UK) and Vapotherm 2000i humidification systems were compared and the resulting RH was 98.5 and 98%, respectively, which showed no statistically significant difference between the groups (*P* value = 0.667).[15]

According to technical characteristics, it was noted that the average temperature in the MR850 system was equal to 38.54 ± 1.13°C, whereas the average temperature in the PMH7000 system was estimated to be 36.53 ± 1.93°C. This difference was not only statistically significant, but it also justified the significant and noticeable difference in the average RH in both systems (RH was equal to 91.59 ± 8.77% in the MR850 system compared to 99.74 ± 0.66% in the PMH7000 system).

Although the need to administer invasive mechanical ventilation, nCPAP, and incidence of CLD decreased in the PMH7000 system, the difference was not statistically significant. The nasal trauma showed to be reduced in the PMH7000 group as well, but the difference was not significant. Now the question is whether we can achieve HFT with a nasal cannula in lower temperatures in which RH of 100% is more easily achieved.

There seems to be a need for more comprehensive clinical trials to answer the question raised in this study.

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