Boletín Médico del
Hospital Infantil de México

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RESEARCH ARTICLE

Analysis of predictors of response to high-flow oxygen nasal cannula therapy in a pediatric intensive care unit

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Abstract

Background: *Bronchiolitis is one of the most frequent reasons for admission to pediatric intensive care units. Medical treatment is primarily supportive. The usefulness of high-flow oxygen (HFO) nasal cannula in these patients has been described. This study evaluated the clinical and analytical variables of patients admitted to our Pediatric Intensive Care Unit (PICU) for initiation or continuation of HFO for respiratory distress and to identify any variable that may be a predictor of success or failure of this technique.* **Methods:** *We conducted a retrospective observational study that included infants aged < 24 months admitted to our PICU due to bronchiolitis between January 2015 and March 2019 for HFO.* **Results:** *We analyzed the characteristics between responders (n = 112) and non-responders (n = 37). No statistically significant differences were observed between groups regarding sex, age, weight, comorbidities, nasopharyngeal aspirate result, hours of evolution, and respiratory and heart rate. However, a pCO_2 ≥ 75 mmHg (p = 0.043) and a SCORE of bronchiolitis severity (p = 0.032) were predictors of HFNC failure.* **Conclusions:** *The pCO_2 level and SCORE of bronchiolitis severity are predictors of this respiratory support modality.*

Keywords: *High-flow oxygen nasal cannula. Bronchiolitis. Non-invasive respiratory support. Pediatric Intensive Care Unit (PICU).*

Análisis de factores predictores de respuesta a la oxigenoterapia de alto flujo en una unidad de cuidados intensivos pediátricos

Resumen

Introducción: *La bronquiolitis es uno de los motivos más frecuentes de ingreso en las Unidades de Cuidados Intensivos Pediátricos (UCIP); el tratamiento médico es básicamente de soporte. Se ha descrito la utilidad de la oxigenoterapia de alto flujo (OAF) en estos pacientes. El objetivo de este estudio fue evaluar algunas variables clínicas y analíticas de los pacientes que ingresan en nuestra UCIP para inicio o continuación de OAF ante cuadros de dificultad respiratoria e identificar cualquier variable que pueda ser factor predictor del éxito o fracaso de esta técnica.* **Métodos:** *Se realizó un estudio retrospectivo observacional, incluyendo lactantes menores de 24 meses ingresados en la UCIP entre enero de 2015 y marzo de 2019 para OAF ante cuadros de bronquiolitis.* **Resultados:** *Se analizaron las características entre el grupo de respondedores (n = 112) y no respondedores (n = 37). No se observaron diferencias estadísticamente significativas en cuanto al sexo,*

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Date of reception: 06-11-2021
Date of acceptance: 15-02-2022
DOI: 10.24875/BMHIM.21000218

Available online: 31-08-2022
Bol Med Hosp Infant Mex. 2022;79(4):222-227
www.bmhim.com

edad, peso, comorbilidades, resultado del aspirado naso-faríngeo, horas de evolución, frecuencia respiratoria, frecuencia cardiaca entre ambos grupos. Sin embargo, una pCO_2 ≥75 mmHg (p = 0.043) y un SCORE de gravedad de la bronquiolitis mayor (p = 0.032) fueron factores predictores de fracaso de la OAF. **Conclusiones:** *El nivel de pCO_2 y el SCORE de gravedad de la bronquiolitis son factores predictores de esta modalidad de soporte respiratorio.*

Palabras clave: *Oxigenoterapia de alto flujo. Bronquiolitis. Soporte respiratorio no invasivo. Unidad de Cuidados Intensivos Pediátricos (UCIP).*

Introduction

Acute bronchiolitis is the first episode of respiratory distress with wheezing or decreased alveolar air entry caused by inflammation of the lower airway in infants under two years of age. It is usually preceded by a catarrhal presentation of the upper airways with rhinitis, cough, or fever[1-4]. Its diagnosis is essentially clinical[2,5,6]. Bronchiolitis is a pathology affecting the lower respiratory tract, usually of viral etiology[2,7]. Although most cases are self-limited and can be managed at home, bronchiolitis is the leading cause of hospital admission in infants during the winter months[1,2,8]. Between 1-5% of patients require hospital admission, and 5-15% need respiratory support in a Pediatric Intensive Care Unit (PICU). Acute bronchiolitis is the most frequent infectious cause of hospitalization in infants with no underlying chronic disease[1,7,9,10].

Treatment options are limited as the available evidence does not support the routine use of bronchodilators, anticholinergics, inhaled or systemic corticosteroids, antiviral drugs, or antibiotics. Respiratory support remains the mainstay of treatment due to the lack of effective medications to treat this pathology[2,10-13].

In recent years, high-flow oxygen (HFO) therapy with nasal cannula has been described as a valuable and safe alternative to conventional oxygen therapy to treat these patients[2,8,14,15]. It has been observed that its use reduces the need for invasive and non-invasive respiratory support to treat respiratory distress[12,16-20]. In addition, it could provide adequate comfort with fewer side effects[21-24]. However, as it has not been established in which patients its success may be more likely, it is not known who would be suitable candidates for its application[2,10,24,25].

On this basis, the main objective of this study was to characterize the patients with bronchiolitis in whom HFO is used in our PICU. As secondary objectives, we sought to evaluate the effectiveness of HFO in these patients and the response rate and to analyze possible variables associated with a greater probability of success or failure that could serve as predictors for the management of these patients.

Methods

We conducted a cross-sectional, retrospective, observational study on infants < 24 months (including patients < 28 days) admitted to the Pediatric Intensive Care Unit of the Hospital Universitario Miguel Servet de Zaragoza for respiratory distress between January 2015 and March 2019. We included patients admitted for respiratory distress in the presence of bronchiolitis. We excluded those patients who were already receiving intensive respiratory support (invasive or non-invasive mechanical ventilation) at the time of admission to the unit.

Microsoft Excel and SPSS (Statistical Package for the Social Sciences) for Windows were used to create the database and analyze the data.

The descriptive results were expressed as the arithmetic mean, median, and standard deviation. The Kolmogorov-Smirnov test was used to analyze the distribution of quantitative variables since the sample size was > 30 patients. The variables were considered to follow a normal distribution when a *p*-value > 0.05 was obtained.

HFO success was established when patients did not require intensification of respiratory support and HFO failure in cases where non-invasive or invasive mechanical ventilation was needed. The validated SCORE Wood-Downes-Ferrés bronchiolitis severity scale was applied to all patients to standardize the severity assessment.

For the contrast of hypotheses between two qualitative variables, we applied the χ^2 test. To compare quantitative variables related to the success or failure of the HFO, we used the Student's t-test for variables with a normal distribution or the Mann-Whitney's U test for those variables that did not follow a normal distribution.

To compare two or more quantitative variables, we applied ANOVA if the quantitative variable followed a normal distribution or the Kruskal-Wallis test in the opposite case.

For linear correlation between quantitative variables with normal distribution, Pearson's correlation was

applied, and for correlation between qualitative variables with no normal distribution, Spearman's correlation was used.

The limit of statistical significance accepted for the analysis was 95%. A statistically significant difference was considered when the *p*-value < 0.05.

For the present study, we followed the protocols established by the hospital for access to medical record data, publication of patient data, and divulgation among the scientific community, always respecting patient privacy.

Results

We included 149 patients who received HFO as the first respiratory support therapy on admission (or continued with its application if they had started such treatment in their hospital of origin). The mean age at admission was 4.58 months ± 6.41 (median 2 months), and 60.4% were male and 39.6% female. Clinical variables before the onset of HFO are shown in Table 1.

In 112 patients (75.2%), an adequate response to HFO was observed and did not require escalation to other respiratory support modalities. In 37 patients (24.8%), HFO failed, and escalation or change to another respiratory support modality was necessary.

No statistically significant differences were found in sex, age (in months), age group, and weight between patients who responded adequately to HFO and those in whom this measure failed. There were also no differences in terms of the history of prematurity, respiratory pathology, bronchopulmonary dysplasia, neurological pathology, or cardiac pathology between the responder and non-responder groups. Similarly, no statistically significant differences were found between the two groups in the nasopharyngeal aspirate virus results (Table 2).

Regarding clinical variables before initiating oxygen therapy (respiratory rate and heart rate), it was observed that the group of HFO responders showed lower heart and respiratory rates at admission than the group of non-responders. However, these differences were not statistically significant (Table 3). Regarding gasometry variables, higher pCO_2 levels were found in HFO non-responders than responders (Table 3). However, these differences were not significant (p = 0.083). Given this tendency, we analyzed whether there was a pCO_2 level at which HFO failure could be predicted. We found that a baseline pCO_2 level ≥ 75 mmHg was a predictor of HFO therapy failure (p = 0.043). The SCORE for bronchiolitis severity was significantly higher in the group in which HFO failed than the group in which it was effective (p = 0.032). The SCORE for bronchiolitis severity could also be a predictor of HFO therapy failure (Table 3).

Discussion

Acute bronchiolitis in infants is the leading cause of hospital admission in the winter months, and up to 5-15% of them require admission to a PICU[1,2,7,8].

Recently, HFO with nasal cannula has been described as a valuable and safe alternative to conventional oxygen therapy for treating patients with acute respiratory distress[14]. Multiple studies have concluded the efficacy and adequate clinical response of patients after initiating this respiratory support system[2,11,21-23]. In addition, other reports support this system in an inpatient ward or pediatric emergency room due to the good results obtained and the reduced need for admission to an Intensive Care Unit[8,11,26].

Due to the increased use of HFO in infants with bronchiolitis, research has been conducted to determine which demographic, clinical, or analytical characteristics of the patients could select or predict a greater probability of success when using this respiratory support. It has been described that pCO_2 levels, pH, respiratory rate, and heart rate[14,22,27-29] before initiating HFO therapy may be related to its success or failure.

Here, we analyzed a sample of 149 patients. Most of them were infants < 6 months of age who were admitted to initiating HFO for respiratory failure. In this population, the success rate of HFO was 75%, with 15 patients requiring invasive mechanical ventilation for nonresponse. Other studies have reported a similar response rate (between 60-90%, depending on the source)[3,12,17].

When analyzing patient characteristics, no statistically significant differences were observed between the responder and non-responder groups regarding sex, age (in months), weight, history of prematurity, bronchopulmonary dysplasia, respiratory disease, neurological disease, or cardiac disease. Other studies that also analyzed these differences between responders and non-responders to HFO have reported similar results[14,22,27-29].

Lower heart rate and respiratory rate were observed in patients who responded adequately to HFO compared to non-responders. However, these differences were not significant. In contrast, statistically significant differences in respiratory rate between responders and

Table 1. Variables before starting high-flow oxygen therapy

	Mean	Median	Standard deviation	Min	Max
pCO_2 pre-HFO	58.19 mmHg	56.50 mmHg	17.82	29	123
HR pre-HFO	165 bpm	165 bpm	27	94	257
RR pre-HFO	60 Bpm	60 Bpm	14	22	98
$SatO_2$ pre-HFO	95.85%	97%	5.47	82	100
FiO_2 pre-HFO	0.39	0.35	0.173	0.21	1
SCORE	7	7	2	2	11

HR: heart rate (beats per minute); RR: respiratory rate (breaths per minute); pCO_2: partial pressure of carbon dioxide (mmHg); $SatO_2$: oxygen saturation; FiO_2: fraction of inspired oxygen; SCORE: validated Wood-Downes-Ferrés bronchiolitis severity scale.

Table 2. Distribution of variables between the group of responders vs. non-responders

	HFO success (n = 112)		HFO failure (n = 37)		*p*-value
Sex					
Male	72	64.3%	18	48.6%	0.092
Female	40	35.7%	19	51.4%	
Age (months)	4.40		4.46		0.88
Age (months)					
< 28 days	24	21.4%	8	21.6	0.395
1 – 6	62	55.4%	23	62.2%	
6 – 12	14	12.5%	2	5.4%	
12 – 18	8	7.1%	3	8.1%	
18 – 24	4	3.6%	1	2.7%	
Weight (kg)	5.29		5.16		0.58
History of prematurity					
No	78	70%	24	64.5%	0.588
Yes	34	30%	13	35.1%	
History of bronchopulmonary dysplasia					
No	103	91.7%	34	92%	0.98
Yes	9	8%	3	8.1%	
History of respiratory disease					
No	90	80.4%	30	81%	0.923
Yes	22	19.6%	7	18.9%	
History of cardiac disease					
No	87	77.7%	30	81%	0.662
Yes	25	22.3%	7	19%	
History of neurological disease					
No	98	87.5%	30	81%	0.267
Yes	14	12.5%	7	19%	
NPA					
Negative	26	23.3%	9	28.1%	0.89
Positive	86	76.7%	28	71.8%	

HFO: high-flow oxygen therapy; NPA: nasopharyngeal aspirate.

non-responders were found in other studies[22,27,28] where the respiratory frequency was higher in the group in which oxygen therapy failed. Consistent with other studies[14,22,27], no statistically significant differences were found in heart rate between the HFO responder and non-responder groups.

Differences in pCO_2 levels obtained by measuring blood gases before initiating HFO were also observed in

Table 3. Differences between clinical and blood gas variables among responders and non-responders

	HFO responders	HFO non-responders	*p*-value*
HR (bpm)	160	170	0.521
RR (BPM)	58 ± 14	63 ± 16	0.13
pCO_2 (mmHg)	56.59 ± 15.31	62.54 ± 23.04	0.083
SCORE	6	7	0.032
Hours of evolution	36	48	0.39
$SatO_2$ (%)	97	96	0.425
FiO2	0.35	0.35	0.655
$SatO_2/FiO_2$	279.3 ± 83.2	270.9 ± 82	0.597

FiO_2: fraction of inspired oxygen; HFO: high-flow oxygen therapy; HR: heart rate (beats per minute, bpm); RR: respiratory rate (breaths per minute, bpm); pCO_2: partial pressure of carbon dioxide; $SatO_2$: oxygen saturation; SCORE: validated Wood-Downes-Ferrés bronchiolitis severity scale.
The table shows the means and standard deviations for the variables that follow a normal distribution and the medians for those with a non-normal distribution. Mann-Whitney's U test (nonparametric test), Student's t test (parametric test). *p*-value < 0.05 was considered statistically significant.

this study between responder and non-responder groups. The pCO_2 levels were higher in the nonresponder group than in the responder group. In addition, moderate-severe hypercapnia with a pCO_2 level ≥ 75 mmHg was identified as a predictor of HFO failure (p = 0.043). These results are consistent with other studies[14,22,27], in which elevated pCO_2 levels were also associated with HFO failure.

When analyzing the differences between responder and non-responder groups, the SCORE for bronchiolitis severity was also significantly higher in the group of non-responders (p = 0.032).

In summary, we identified moderate-severe hypercapnia with a pCO_2 level ≥ 75 mmHg and a higher level of respiratory symptoms severity (according to the SCORE Wood-Downes-Ferrés bronchiolitis severity scale) were predictors of HFO failure in a PICU. The rest of the variables analyzed were not related to a higher probability of success or failure of HFO.

Based on these results, initial moderate-severe hypercapnia (pCO_2 level ≥ 75 mmHg) and SCORE of bronchiolitis severity according to the Wood-Downes-Ferrés rating scale are proposed as predictors of HFO failure. The presence of these factors represents a possible risk in the initial evaluation of the patient and increases the probability of requiring intensive respiratory support with non-invasive or invasive mechanical ventilation. However, these data come from a single center. Thus, given the limited sample size, further evidence is required to extrapolate these results and conclusions.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. This study involved a retrospective review of medical records, for which approval was obtained from a formally constituted review board (Institutional Review Board or Institutional Ethics Committee).

Conflicts of interest

The authors declare no conflicts of interest.

Funding

No funding.

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