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RESEARCH ARTICLE

High-flow nasal cannula and non-invasive mechanical ventilation in pediatric asthma exacerbation: two-year prospective observational study in intensive care

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Abstract

Background: *Asthma is a common cause of admission to the pediatric intensive care unit (PICU). We described and analyzed the therapies applied to children admitted to a tertiary PICU because of asthma. Later, we evaluated high-flow nasal cannula (HFNC) use in these patients and compared their evolution and complications with those who received non-invasive ventilation.* **Methods:** *We conducted a prospective observational study (October 2017-October 2019). Collected data: epidemiological, clinical, respiratory support therapy needed, complementary tests, and PICU and hospital stay. Patients were divided into three groups: (1) only HFNC; (2) HFNC and non-invasive mechanical ventilation (NIMV); and (3) only NIMV.* **Results:** *Seventy-six patients were included (39 female). The median age was 2 years and 1 month. The median pulmonary score was 5. The median PICU stay was 3 days, and the hospital stay was 6 days. Children with HNFC only (56/76) had fewer PICU days (p = 0.025) and did not require NIMV (6/76). Children with HFNC had a higher oxygen saturation/fraction of inspired oxygen ratio ratio (p = 0.025) and lower PCO_2 (p = 0.032). In the group receiving both therapies (14/76), NIMV was used first in all cases. No epidemiologic or clinical differences were found among groups.* **Conclusion:** *HFNC was a safe approach that did not increase the number of PICU or hospital days. On admission, normal initial blood gases and the absence of high oxygen requirements were useful in selecting responders to HFNC. Further randomized and multicenter clinical trials are needed to verify these data.*

Keywords: *Asthma. Pediatric critical care. Children. High-flow nasal cannula. Non-invasive ventilation.*

Cánula nasal de alto flujo y ventilación no invasiva en asma pediátrico grave: estudio observacional prospectivo de dos años de duración en cuidados intensivos

Resumen

Introducción: *El asma es una causa frecuente de ingreso en la unidad de cuidados intensivos pediátricos (UCIP). En este, cuadro el uso de cánula nasal de alto flujo (CNAF) se ha visto extendido. En este trabajo se describe el tratamiento global en la UCIP ante el ingreso por asma en un hospital monográfico pediátrico y se evalúa la respuesta al uso de la CNAF, comparando la evolución de los pacientes con aquellos que recibieron ventilación no invasiva (VNI).* **Métodos:** *Se llevó a cabo un estudio observacional prospectivo (de octubre del 2017 a octubre del 2019). Se describieron epidemiología, clínica, tratamiento y soporte respiratorio. Para la comparación se crearon tres grupos de pacientes: 1) solo CNAF; 2) CNAF y VNI; y 3) solo VNI.*

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Resultados: *Se incluyeron 76 pacientes. La mediana de edad fue de dos años y un mes; la mediana de índice pulmonar fue 5. La mediana de ingreso en UCIP fue de tres días y de ingreso hospitalario, seis días. Los niños con solo CNAF (56/76) mostraron menos días de UCIP (p = 0.025) y no requirieron VNI (6/76). También mostraron mayor $SatO_2/FiO_2$ (saturación de oxígeno/fracción de oxígeno inspirado) (p = 0.025) y menor nivel de PCO_2 (presión parcial de CO_2) (p = 0.032). La VNI se utilizó primero siempre en el grupo que recibió ambas modalidades (14/76). No se encontraron diferencias epidemiológicas o clínicas entre grupos.* **Conclusiones:** *En nuestra serie, el uso de CNAF no aumentó los días de ingreso en la UCIP ni de hospital. Tampoco requirió cambio a VNI. Al ingreso, una gasometría normal y bajo requerimiento de oxígeno permitieron seleccionar a los pacientes respondedores. Se necesitan más ensayos multicéntricos clínicos aleatorizados para verificar estos datos.*

Palabras clave: *Asma. Cuidados críticos pediátricos. Niños. Cánula nasal de alto flujo. Ventilación no invasiva.*

Introduction

Asthma is a common cause of admission to the pediatric intensive care unit (PICU). In addition to pharmacological therapies, respiratory support by non-invasive mechanical ventilation (NIMV) has been the classical approach to help these patients. In recent years, this approach has been complemented and replaced by a high-flow nasal cannula (HFNC)[1]. Both respiratory supports are used to avoid mechanical ventilation (MV), which is helpful but associated with complications[2].

The use of HFNC in children has increased. Certainly, its simplicity and comfort have influenced its implementation[3,4]. Thus, its use has been described in neonatal units[5,6], emergency rooms[7-9], hospital wards[5,10,11], transport[12], or intensive care units[13-15]. Additionally, HFNC has been defined as safe for managing bronchiolitis[16,17] or asthma[1,14,15,18].

However, using HFNC in these different clinical settings is not always supported by consistent clinical evidence[8,19]. In addition, there is concern that HFNC may delay the initiation of other ventilatory strategies with proven efficacy[7]. In asthma, for example, there are doubts about how HFNC might delay NIMV[10,13]. This potential risk should be addressed in children with severe asthma[20].

Therefore, in this short prospective observational monocentric study, we described and analyzed the therapies applied to children admitted to a tertiary PICU due to asthma. Later, we evaluated the use of HFNC in these patients and compared their evolution and complications with those who received non-invasive ventilation.

Methods

Design

We conducted an observational, prospective, longitudinal study in a tertiary PICU (from October 2017 to October 2019). The study was approved by the hospital ethics committee. Data were collected from clinical records following the principles of the Declaration of Helsinki. The parents or caregivers of each patient were informed about the study and were included after obtaining their consent. In addition, patient data were anonymized after discharge.

Inclusion criteria

Patients who met the following criteria were included in the study:

- < 18 years of age.
- Patients with asthma, defined as an acute episode of increased work of breathing with wheezing and prolonged expiratory phase in a previously healthy child or with similar previous episodes.
- Patients admitted to the PICU due to failure to respond to optimized asthma therapies in the Pediatric Emergency Department/Pediatric Unit.
- No major comorbidities or pre-existing conditions other than asthma.
- No criteria for acute bronchiolitis. On physical examination, acute bronchiolitis was defined as the onset of wheezing before 24 months in patients with a viral lower respiratory tract infection and no other explanation for the wheezing.

Study groups

- After the observation period, four groups were created based on their respiratory support: (1) “only HFNC”; (2) “NIMV and HFNC”; (3) “only NIMV”; and (4) Children on MV to evaluate HFNC and compare it against other therapies.

Respiratory support

The respiratory support used was not standardized or randomized. Physicians decided which therapy to use based on their clinical judgment.

- NIMV: bi-level positive airway pressure (BiPAP) Vision V60® (Respironics Philips) with a full-face or oronasal mask. Modalities: continuous positive airway pressure (CPAP) and BiPAP. CPAP was initially set at 5-6 cm H_2O. For BiPAP, inspiratory positive airway pressure was initially set at 8-10 cm H_2O, and end-positive airway pressure was set at 5-6 cm H_2O. Inspiratory and expiratory pressures were titrated in 2 cm H_2O increments based on tidal volume, continuous pulse oximetry, work of breathing, respiratory rate, and subject-ventilator synchrony. The fraction of inspired oxygen (FiO_2) was titrated to maintain SpO_2 > 92%.
- High flow nasal cannula (HFNC): Fisher-Paykel High Flow Nasal Cannula® and Vapotherm® were used. A cannula of a suitable size, an appropriate circuit, a humidifier, and air or oxygen were used. Cannula size was selected based on the subject's weight, and flow rates were initiated at 0.5-1 L/kg/min. The FiO_2 was titrated to maintain a SpO_2 > 92%.

Data

- Demographic characteristics (age in months and sex).
- Clinical data: respiratory rate on admission, presence and characteristics of wheezing, pulmonary score, oxygen saturation ($SatO_2$)/FiO_2 ratio, venous blood gas values on admission (pH, partial pressure of carbon dioxide, HCO_3), pharmacological treatment received (bronchodilators, corticosteroids, antibiotic therapy, magnesium sulfate), type and days of ventilatory support, length of stay in the PICU, and total hospital stay. The attending physician selected pharmacologic treatment based on his or her expertise and the clinical protocols of the PICU.

Statistical analysis

Data analysis was performed with the SPSS® statistical package (version 21.0; IBM Company®, New York, United States). The homogeneity of the demographic variables and other clinical parameters were analyzed at the beginning of the study (having a non-normal distribution) and compared between groups. Descriptions were made using the median and interquartile range, and for the qualitative variables, absolute frequency and relative frequency. The Kruskal–Wallis test for quantitative variables and Fisher's exact test for dichotomous variables were used to analyze the characteristics of the three treatment groups.

Results

Eighty-six children were initially recruited (Fig. 1). Finally, 76 patients were included in the study, of whom 39 were female; the median age of the study population was 25 months (4-160). The median length of hospital stay was 6 days (1-23). On admission to the PICU, the SaO_2/FiO_2 ratio was 195 (90-384), the pulmonary score was 5 (1-8), and the respiratory rate was 40 (20-68). Regarding the gasometer variables, we observed that children had a PCO_2 of 36.15 (15.2-86), a HCO_3- of 21.7 (13.5-40) with a pH of 7.37 (7.13-7.49) on admission to the PICU. Sixty-nine children received intravenous steroids prior to PICU admission. These data are described globally and based on each respiratory support received in table 1. There were no children in the MV group. None of the patients who received HFNC as initial therapy required NIMV. There were no deaths.

Comparisons based on respiratory support

In our series, 52/76 children underwent a chest X-ray. In addition, 33/76 received antibiotics, 13/76 received magnesium sulfate, and 19/76 received a continuous dose of albuterol. Table 2 shows the comparison between the respiratory groups. Children requiring only HFNC required less routine chest radiography, antibiotic therapy, continuous albuterol, and magnesium sulfate.

The median number of PICU days was lower in the only-HFNC group compared to other types of ventilatory support (Table 3, p = 0.025). Furthermore, $SatO_2/FiO_2$ was lower in the only-NIMV group and higher in the only-HFNC group (Table 3, p = 0.026). PCO_2 was higher in the only-NIMV group (Table 3, p = 0.032).

Discussion

In this study, we observed that HFNC was the most frequently used respiratory support in children admitted to the PICU for asthma. Furthermore, children requiring only HFNC had less pharmacological therapy and shorter PICU and hospital stays. The presence of low $SatO_2/FiO_2$ and elevated PCO_2 on admission was associated with using NIMV.

HFNC delivers a warm and humidified airflow with a variable oxygen fraction (between 0.21 and 1) and a flow between 2 L and 60 L[21]. Theoretically, HFNC reduces oropharyngeal dead space, decreases CO_2 rebreathing, improves mucociliary clearance[22], and

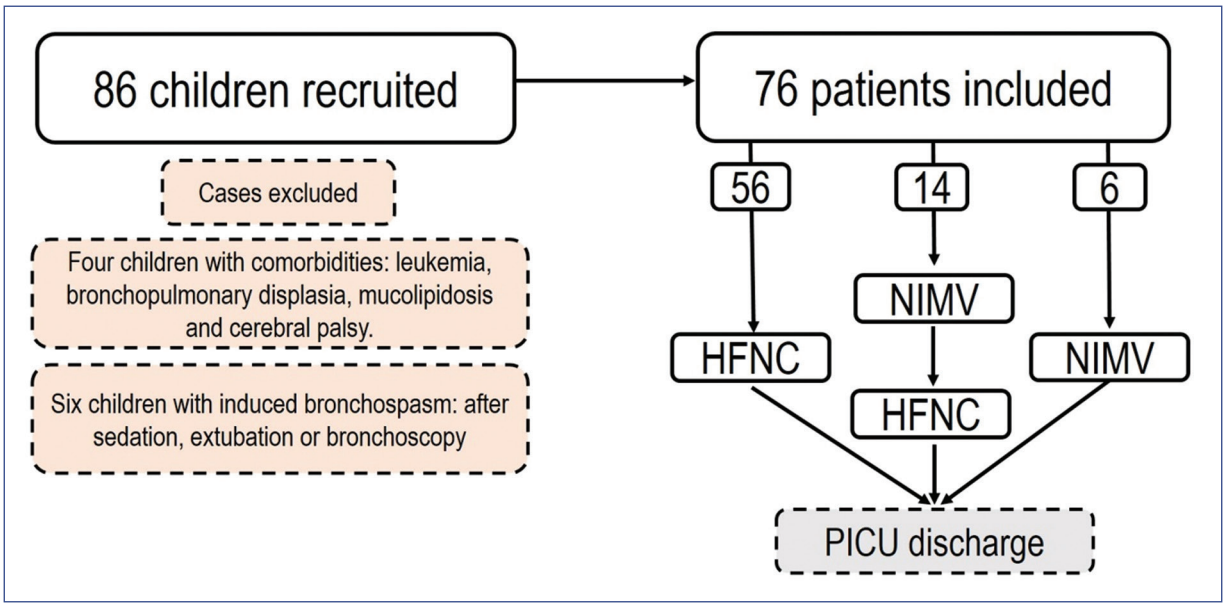

Figure 1. Flowchart of patient inclusion and exclusion.
HFNC: high flow nasal cannula; NIMV: non-invasive mechanical ventilation; PICU: pediatric intensive care unit.

Table 1. Treatments of children admitted to a tertiary PICU due to asthma

Variables analyzed	Total	Only HFNC (n = 56)	HFNC + NIMV (n = 14)	Only NIMV (n = 6)	p-value
Female	39/76 (51%)	26/56 (46%)	9/14 (64%)	4/6 (66%)	0.6
Age (months)	25 (4-160)	29 (4-143)	12.5 (4-164)	14 (5-26)	0.1
Hospital stay (days)	6 (1-24)	5 (2-24)	11 (1-12)	14 (3-22)	0.09
$SatO_2/FiO_2$ ratio	195 (90-384)	204 (97-384)	185 (92-333)	101 (90-271)	0.02
PCO_2	36.15 (15.2-86)	35 (15.7-67)	43.5 (32.8-86)	45.6 (28.1-51)	0.032
Pulmonary score	5 (1-8)	5 (1-7)	5 (3-8)	5 (2-7)	0.53
pH	7.37 (7.13-7.49)	7.37 (7.13-7.49)	7.38 (7.15-7.47)	7.41 (7.29-7.49)	0.6
HCO_3	21.7 (13.5-40)	20.7 (13.5-40)	21.7 (17.9-32.4)	24.6 (21.7-28.9)	0.11
Respiratory rate	40 (20-68)	39 (20-68)	43 (24-68)	52 (29-62)	0.06
Intravenous steroids	69/76 (90%)	50/56 (89%)	14/14 (100%)	5/6 (83%)	0.38

HFNC: high flow nasal cannula; NIMV: non-invasive mechanical ventilation; $SatO_2/FiO_2$: oxygen saturation/fraction of inspired oxygen ratio; PCO_2: partial pressure of carbon dioxide.

generates an airway positive pressure of up to 6 cm H_2O. The interest in using HFNC as respiratory support stems from these properties and increased patient comfort[17,23]. In addition, it does not require breathing synchronization and requires less nursing care (compared to a NIMV device). This constant flow may also facilitate nasopharyngeal air renewal, which would improve CO_2 washout and oxygenation[11].

As mentioned above, asthma is one of the leading causes of PICU admission. In our series, we included a similar number of males and females, with a median age of almost 2 years. This age is younger than that described in other studies and may limit the external validity of our work[14,15]. Although we applied strict exclusion criteria, preschool children inclusion may have introduced a bias. We probably also included

Table 2. Complementary tests according to each type of respiratory support

Respiratory support	Chest X-ray		Empiric antibiotics		Magnesium sulphate		Continuous albuterol	
	Yes	No	Yes	No	Yes	No	Yes	No
Only HFNC	34/56 (60%)	21/56 (40%)	21/56 (37%)	35/56 (63%)	7/56 (12%)	49/56 (88%)	10/56 (18%)	46/56 (82%)
HFNC + NIMV	14 (100%)	0	9/14 (64%)	5/14 (35%)	6/14 (43%)	8/14 (57%)	9/14 (64%)	5/14 (35%)
NIMV	4/6 (66%)	2/6 (33%)	3/6 (50%)	3/6 (50%)	0	6 (100%)	0	6 (100%)
Total	52/76 (68%)	24/76 (30%)	33/76 (44%)	43/76 (56%)	13/76 (17%)	63/76 (83%)	19/76 (25%)	57/76 (75%)
p-value	0.007		0.001		0.02		0.001	

HFNC: high-flow nasal cannula; NIMV: non-invasive mechanical ventilation.

Table 3. Progression and severity variables (median and range)

Respiratory support	PICU days	SaO_2/FiO_2 ratio	pCO_2
HFNC	3 (1-8)	204 (97-384)	35 (15.7-67)
HFNC + NIMV	5 (1-9)	185 (92-333)	43.5 (32.8-86)
NIMV	3.5 (1-10)	101 (90-271)	45.6 (28.1-51)
p-value	0.025	0.026	0.032

HFNC: high flow nasal cannula; NIMV: non-invasive mechanical ventilation; $SatO_2/FiO_2$: oxygen saturation/fraction of inspired oxygen ratio; PICU: pediatric intensive care unit.

cases of bronchospasm, more representative of infectious bronchial hyperreactivity than asthma.

As it is known, the evidence on the utility of HFNC as an optimal respiratory support in severe asthma is scarce[1,13,20]. Ramnarayan et al. conducted a pilot study to evaluate it through a multicenter and randomized clinical trial. They found that switching from HFNC to NIMV was frequent[15]. Similarly, an observational study of 42 asthmatic children by Pilar et al. concluded that initial support with HFNC was not optimal and that NIMV support was delayed. As mentioned above, HFNC was the most frequently used respiratory support[14]. In addition, we did not observe any treatment failures or increased PICU or hospital admission days in those who received HFNC as first respiratory support. These findings are in contrast to what has been published previously and should be considered with caution[15].

Given the design of our study, it is difficult to define objective data to understand and explain why the transition from HFNC to NIMV was unnecessary. We observed that patients receiving HFNC showed higher $SatO_2/FiO_2$ values and lower CO_2 levels, probably indicating a better situation on admission to the PICU for these children[20]. Furthermore, the decision to initiate one type of ventilatory support over another was not randomized but left to the clinician's judgment. It appears that $SatO_2/FiO_2$ and CO_2 levels significantly influenced the choice of NIMV as treatment. In addition, children receiving NIMV required more chest X-rays, empirical antibiotic therapy, magnesium sulfate, and continuous nebulized albuterol. Overall, these aspects would provide insight into the higher clinical severity in the NIMV group[1].

Finally, as noted above, the use of HFNC remains controversial because it is still being determined whether it can prolong hospital stays and delay other types of assistance while being cost-effective for the healthcare system. In our series, there was no delay in other types of care. In addition, we observed that patients who received HFNC had a shorter PICU stay and a significantly shorter hospital stay. Although these observations cannot be considered a direct effect of HFNC use, they are of interest because they objectively demonstrate that, at least in our center, patients requiring HFNC for severe asthma are discharged promptly without excessive impact on resource utilization.

This study has several limitations. As mentioned above, physician expertise led to selecting children who could be treated with HFNC with a low risk of treatment failure. Therefore, our results may be difficult to generalize. In addition, we included children < 2 years of age. We tried to exclude cases of acute bronchiolitis, but we assume this cohort may not represent critical asthma patients. Finally, the different pharmacological treatments used were not evaluated; their indications and impact on clinical evolution and respiratory support effectiveness should be evaluated in future studies.

In conclusion, HFNC was a safe approach for children admitted to the PICU for asthma. Those patients who received HFNC as primary respiratory support did not require escalation to NIMV. The absence of blood gas changes on admission to the PICU and the absence of high oxygen requirements may help to select good responders to HFNC. However, external validation of our results is complex. Data from other centers are needed to verify our observations.

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. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author has this document.

Conflicts of interest

The authors declare no conflicts of interest.

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References

1. Gates RM, Haynes KE, Rehder KJ, Zimmerman KO, Rotta AT, Miller AG. High-flow nasal cannula in pediatric critical asthma. Respir Care. 2021;66:1240-6.
2. Bratton SL, Newth CJ, Zuppa AF, Moler FW, Meert KL, Berg RA, et al. Critical care for pediatric asthma: wide care variability and challenges for study. Pediatr Crit Care Med. 2012;13:407-14.
3. Baudin F, Gagnon S, Crulli B, Proulx F, Jouvet P, Emeriaud G. Modalities and complications associated with the use of high-flow nasal cannula: experience in a pediatric ICU. Respir Care. 2016;61:1305-10.
4. Testa G, Iodice F, Ricci Z, Vitale V, De Razza F, Haiberger R, et al. Comparative evaluation of high-flow nasal cannula and conventional oxygen therapy in paediatric cardiac surgical patients: a randomized controlled trial. Interact Cardiovasc Thorac Surg. 2014;19:456-61.
5. Ojha S, Gridley E, Dorling J. Use of heated humidified high-flow nasal cannula oxygen in neonates: a UK wide survey. Acta Paediatr. 2013;102:249-53.
6. Wilkinson D, Andersen C, O'Donnell CP, De Paoli AG, Manley BJ. High flow nasal cannula for respiratory support in preterm infants. Cochrane Database Syst Rev. 2016;2:CD006405.
7. Long E, Babl FE, Duke T. Is there a role for humidified heated high-flow nasal cannula therapy in paediatric emergency departments? Emerg Med J. 2016;33:386-9.
8. Slain KN, Shein SL, Rotta AT. The use of high-flow nasal cannula in the pediatric emergency department. J Pediatr (Rio J). 2017;93 Suppl 1: 36-45.
9. Wang J, Lee KP, Chong SL, Loi M, Lee JH. High flow nasal cannula in the emergency department: indications, safety and effectiveness. Expert Rev Med Devices. 2018;15:929-35.
10. González Martínez F, González Sánchez MI, Toledo Del Castillo B, Pérez Moreno J, Medina Muñoz M, Rodríguez Jiménez C, et al. Treatment with high-flow oxygen therapy in asthma exacerbations in a paediatric hospital ward: experience from 2012 to 2016. An Pediatr (Engl Ed). 2019; 90:72-8.
11. Milési C, Boubal M, Jacquot A, Baleine J, Durand S, Odena MP, et al. High-flow nasal cannula: recommendations for daily practice in pediatrics. Ann Intensive Care. 2014;4:29.
12. Schlapbach LJ, Schaefer J, Brady AM, Mayfield S, Schibler A. High-flow nasal cannula (HFNC) support in interhospital transport of critically ill children. Intensive Care Med. 2014;40:592-9.
13. Coletti KD, Bagdure DN, Walker LK, Remy KE, Custer JW. High-flow nasal cannula utilization in pediatric critical care. Respir Care. 2017;62:1023-9.
14. Pilar J, Modesto IA, Lopez-Fernandez YM, Lopez-Macias O, Garcia-Urabayen D, Amores-Hernandez I. High-flow nasal cannula therapy versus non-invasive ventilation in children with severe acute asthma exacerbation: an observational cohort study. Med Intensiva. 2017;41:418-24.
15. Ramnarayan P, Lister P, Dominguez T, Habibi P, Edmonds N, Canter RR, et al. FIRST-line support for Assistance in Breathing in Children (FIRST-ABC): a multicentre pilot randomised controlled trial of high-flow nasal cannula therapy versus continuous positive airway pressure in paediatric critical care. Crit Care. 2018;22:144.
16. Bermúdez Barrezueta L, García Carbonell N, López Montes J, Gómez Zafra R, Marín Reina P, Herrmannova J, et al. High flow nasal cannula oxygen therapy in the treatment of acute bronchiolitis in neonates. An Pediatr (Barc). 2017;86:37-44.
17. Mayfield S, Bogossian F, O'Malley L, Schibler A. High-flow nasal cannula oxygen therapy for infants with bronchiolitis: pilot study. J Paediatr Child Health. 2014;50:373-8.
18. Mayfield S, Jauncey-Cooke J, Bogossian F. A case series of paediatric high flow nasal cannula therapy. Aust Crit Care. 2013;26:189-92.
19. Gutierrez Moreno M, Del Villar Guerra P, Medina A, Modesto IA, Castro Bournissen L, Mirás Veiga A, et al. High-flow oxygen and other noninvasive respiratory support therapies in bronchiolitis: systematic review and network meta-analyses. Pediatr Crit Care Med. 2023;24: 133-42.
20. Russi BW, Lew A, McKinley SD, Morrison JM, Sochet AA. High-flow nasal cannula and bilevel positive airway pressure for pediatric status asthmaticus: a single center, retrospective descriptive and comparative cohort study. J Asthma. 2022;59:757-64.
21. Nolasco S, Manti S, Leonardi S, Vancheri C, Spicuzza L. High-flow nasal cannula oxygen therapy: physiological mechanisms and clinical applications in children. Front Med (Lausanne). 2022;9:920549.
22. Hasani A, Chapman TH, McCool D, Smith RE, Dilworth JP, Agnew JE. Domiciliary humidification improves lung mucociliary clearance in patients with bronchiectasis. Chron Respir Dis. 2008;5:81-6.
23. Wilkinson DJ, Andersen CC, Smith K, Holberton J. Pharyngeal pressure with high-flow nasal cannulae in premature infants. J Perinatol. 2008;28:42-7.