An Analysis of the Risk Factors for the Failure of Respiratory Support With High-flow Nasal Cannula Oxygen Therapy in Children with Acute Respiratory Dysfunction:a case-control study

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Abstract

Background:

Different causes of acute respiratory insufficiency threaten the lives of pediatric patients, while High-flow nasal cannula oxygen therapy (HFNC) is a new type of non-invasive respiratory support technique that widely used in pediatric intensive care units (PICUs);however, improper use of HFNC is likely to bring adverse consequences to critically ill children.Our objective in this study was to identify the risk factors for the failure of HFNC, that can guide clinicians during managing of HFNC treatment correctly.

Methods:

Divided the patients into different categories: HFNC success group (237 patients), a 48 h failure group (112 patients), a 24 h failure group (84 patients), and a 2 h failure group (24 patients). The clinical indexes and the change trend in HFNC before and after treatment were dynamically observed in 67 pediatric patients. Risk factors for HFNC failure were determined using multivariate logistic regression analysis.

Results:

PRISM III score >4 points and $\text{PaCO}_2 >43$ mmHg were risk factors for 48 h failure (OR were 4.064, 4.516, $P<0.05$); $\text{PaCO}_2 >43$ mmHg was risk factors for 24 h failure (OR was 3.152, $P<0.05$); PRISM III score >6.5 points and $\text{PaCO}_2/\text{PaO}_2$ ratio >0.67 were risk factors for 2 h failure (OR were 27.977, 64.366, $P<0.05$) and the risk of HFNC failure increased more than 5 times when the oxygenation index decreased by >28% after 2 h of HFNC treatment, and the invasive mechanical ventilation time was statistically longer in the patients that upgraded from HFNC to invasive respiratory support than that of patients who received invasive respiratory support directly($P<0.05$).

Conclusions:

The PRISM III score, PaCO_2 and $\text{PaCO}_2/\text{PaO}_2$ ratio were risk factors for HFNC failure. Totally the shorter the failure time, the higher the values of the risk factors were, and the higher the failure risk of HFNC was. The change trend in oxygenation index before and after HFNC is a warning factor for early HFNC failure. And early HFNC failure might lead to prolonged invasive mechanical ventilation.

Introduction

Different causes of acute respiratory insufficiency threaten the lives of pediatric patients, therefore, respiratory support via oxygen therapy has been widely used in pediatric intensive care units (PICUs). Many studies have shown that the complications of invasive respiratory support, such as ventilator-induced lung injury (VILI), might increase the fatality rate of pediatric patients^[1]. In the past few years, non-invasive respiratory support has become an important means of ventilation support in the early

stages of emergencies involving respiratory insufficiency diseases. High-flow nasal cannula oxygen therapy (HFNC) is a new type of non-invasive respiratory support technique that is not only easy to manipulate, well tolerated, and has a low risk of nasal mucosa and septum injury but also avoids invasive ventilation complications such as VILI. HFNC has been widely used in PICUs. Some surveys showed that 77% of hospitals in the United States, and 63% of medical units in Australia and New Zealand use HFNC^[2]. Studies have found that HFNC can reduce the use of endotracheal intubation for invasive mechanical ventilation^[3], but a retrospective study by Taha DK et al in 2016 found that if infants with very low birth weight received HFNC, respiratory support failure could increase death or the risk of bronchial pulmonary dysplasia (BPD), increase the incidence of respiratory system disorders, and extend the length of hospital stay^[4]. At present, there is no unified guidance or standard for the selection of respiratory support modes for critically ill children. Improper use of HFNC is likely to bring adverse consequences to critically ill children, which is worth studying. In this paper, we analysed clinical data from pediatric patients who underwent HFNC treatment by comparing various clinical indexes from the HFNC success group to those from the 48 h failure group, 24 h failure group and 2 h failure group and the change trend of clinical indexes before and after treatment to identify risk factors for HFNC failure and sum up our experience for improving use of HFNC.

Materials And Method

Study Object

We prospectively analysed the clinical data of 377 pediatric patients with acute respiratory insufficiency who received respiratory support synchronously directly after admission in the PICU of the West China Second Universally Hospital of Sichuan University from March 2017 to February 2019. A total of 237 patients who did not need upgrade respiratory support and successfully weaned from HFNC were classified as the HFNC success group. The remaining 140 patients need upgrade respiratory support during hospitalization. According to the time to upgrade respiratory support of these 140 patients (see Fig. 1), 80% of these patients had upgraded respiratory support within 48 h, 60% had it within 24 h, and 17% had it within 2 h. Because of the complicated circumstances influencing the failure of HFNC after 48 h, it is hard to confirm whether failure was caused by inappropriate choice to initial respiratory support, and this study is aimed to explore the risk factors for HFNC as the initial treatment; hence, the failure cases after 48 h were not included in this study. The earlier HFNC failed, the less possibility there was of failure caused by disease progression; therefore, we divided the 112 patients that used HFNC and required to upgrade respiratory support within 48 h into a 48 h failure group (112 patients), a 24 h failure group (84 patients), and a 2 h failure group (24 patients) according to the failure time and performed further analyses. We also dynamically observed clinical indicators before and after 2 h of HFNC in 67 patients included in the study from January to February 2019 to distinguish the risk factors for failure to HFNC. Because new residents always change their shifts into PICU in the 1st half of a month, 349 patients were still divided into the 1st half of a month group (174 patients) and the 2nd half of a month group (175 patients) according to their date of hospitalization, which HFNC failure rate were compared in

order to identify whether the failure was caused by the inexperience of residents. 20 patients among the 112 patients in 48 h failure group were upgraded to non-invasive bilevel positive airway pressure (BIPAP); after that, their condition was alleviated, and they successfully weaned from non-invasive respiratory support. The remaining 92 patients were upgraded to invasive respiratory support and classified into the group that changed from HFNC to invasive respiratory support. Then we compared them with 129 patients synchronously admitted to the PICU and directly received invasive respiratory support in terms of invasive mechanical ventilation time, PICU stay time, hospitalization expenses and hospital mortality to explore the consequences of HFNC failure (see Fig. 2).

Inclusion Criteria^[5–7]

The definition of acute respiratory insufficiency was as follows: lack of consciousness or restlessness, cough, fatigue, increased heart rate, polypnea (infants < 2 months, respiratory rate ≥ 60 times/min; 2–12 months, respiratory rate ≥ 50 times/min; 1–5 years, respiratory rate ≥ 40 times/min; ≥ 5 years, respiratory rate ≥ 30 times/min), mouth cyanosis, positive for the three concave signs during inspiration or auxiliary respiratory muscles participating in respiratory movement, accompanied by blood gas analysis without oxygen inhalation $\text{PaO}_2 < 8.0$ kPa (60 mmHg) and/or $\text{PaCO}_2 > 6.67$ kPa (50 mmHg), or oxygenation index ($\text{PaO}_2/\text{FiO}_2$) ≤ 300 in oxygen inhalation. All the patients requested all-out rescue efforts, and no one has given up for economic reasons.

1.3 Exclusion Criteria^[8]: ☐Respiratory support had been used outside the hospital, ☐post-surgery pediatric patients, ☐HFNC intolerance, ☐incomplete HFNC support parameter record.

1.4 Definition of HFNC Failure

The criteria for HFNC failure were as follows^[9]: HFNC failure was defined as in the presence of disturbance of consciousness, dysphoria, dyspnoea, blood oxygen saturation that would not remain above 90% or carbon dioxide retention that could not be improved within 2 h, 24 h or 48 h of undergoing HFNC (with an oxygen concentration $\geq 60\%$, oxygen flow ≥ 2 L/kg.min, and a maximum no more than 40 L/min) which required to upgrade the respiratory support mode to BIPAP or invasive respiratory support therapy.

1.5 Statistical Analysis

SPSS 22.0 statistical software was used for the statistical analysis. Measurement data that had a normal distribution were expressed as the mean $\pm$ standard deviation ($\bar{X} \pm s$), and two independent sample t tests were used for comparisons between groups. Measurement data that did not have a normal distribution were expressed as the median (four-digit interval) [P_{50} (P_{25} , P_{75})], and comparisons between groups were conducted with Mann-Whitney U tests. Enumeration data were expressed as percentages (%). Chi-square tests, Pearson chi-square tests or Fisher's exact probabilistic tests were used for intergroup comparisons. Significant indexes were analysed by multivariate logistic regression analysis to determine the risk factors, and $P < 0.05$ was considered statistically significant.

Results

2.1 General Condition

The initial parameters for the HFNC success group included the following: fraction of inspired oxygen (FiO_2) 30–100%; and flow 2–3 L/kg.min. The initial parameters for the HFNC failure groups were as follows: fraction of inspired oxygen (FiO_2) 40–100%; and flow 2–3 L/kg.min. The inhaled gas temperature of each group was 37 °C, and the oxygen was inhaled for 24 h without interruption. The parameters were adjusted according to the blood gas analysis results, and the arterial partial oxygen pressure (PaO_2) was maintained at 60–80 mmHg (8.0–10.67 kPa), the arterial partial carbon dioxide pressure (PaCO_2) was maintained at 40–50 mmHg (5.33–6.67 kPa), and the percutaneous oxygen saturation (SpO_2) was maintained above 90%.

2.2 Comparisons between the HFNC success group and the HFNC failure groups to analyze the risk factors for HFNC failure

2.2.1 HFNC 48 h failure risk factor analysis

(1) Comparisons of General Clinical Data

349 patients with acute respiratory insufficiency suffered from severe pneumonia 155 cases(44.4%), Sepsis 59 cases(16.9%), Shock 34 cases(9.7%), Multiple organ dysfunction syndrome 31 cases(8.9%), Intracranial hypertension syndrome 38 cases(10.9%), Bronchopulmonary dysplasia(BPD) with pulmonary infection 26 cases(7.4%), Acute respiratory distress syndrome 3 cases(0.9%), or Chemotherapy-induced myelosuppression with infection 2 cases(0.6%) and Pneumorrhagia 1 case(0.3%), and the distributions of disease types were no significant differences between the HFNC success group and the 48 h failure group($P>0.05$). There also were no significant differences in age, sex or weight between the two groups ($P>0.05$), as shown in Table 1.

Table 1

Comparisons between the high-flow nasal cannula oxygen therapy Success Group and the 48 h Failure Group

Group	No.	Age [$P_{50}(P_{25}, P_{75})$, month]	Male/Female (patients)	Weight [$P_{50}(P_{25}, P_{75})$, kg]
HFNC success group	237	6(2, 18)	132/105	7.00(4.95, 10.60)
48 h failure group	112	7(2,48)	50/62	7.30(4.33,15.60)
$U(x)^2$ value		-0.870	(3.724)	-0.148
P value		0.384	0.054	0.883
(2) Common clinical indexes and blood gas analysis affecting the respiratory support mode				
The clinical indexes and blood gas analysis results of the two groups of patients are shown in Table 2. The GCS score, pH value and oxygenation index of the HFNC 48 h failure group were lower than those of the success group, and the PRISM III score, PCT, PaCO ₂ and PaCO ₂ /PaO ₂ ratio were higher than those of the success group. The differences between the two groups were statistically significant ($P < 0.05$). However, there was no significant difference in SpO ₂ , CRP, LAC or PaO ₂ between the two groups ($P > 0.05$).				

Table 2

Comparison of the Clinical Indexes and the blood gas analysis between the high-flow nasal cannula oxygen therapy Success Group and the 48 h Failure Group

	HFNC success group (n = 237)	48 h failure group (n = 112)	Uvalue	P value
SpO ₂ [P ₅₀ (P ₂₅ , P ₇₅), %]	95.00 (90.00, 97.00)	93.00 (88.25, 97.00)	-1.832	0.067
GCS score [P ₅₀ (P ₂₅ , P ₇₅),point]	13.00 (13.00, 14.00)	13.00 (11.00, 14.00)	-4.139	0.000*
PRISM III score [P ₅₀ (P ₂₅ , P ₇₅),point]	1.00 (0.00, 3.00)	4.00 (1.00, 8.00)	-7.875	0.000*
CRP [P ₅₀ (P ₂₅ , P ₇₅), mg/L]	4.60 (1.00, 24.85)	9.00 (2.00, 45.00)	-1.732	0.083
PCT [P ₅₀ (P ₂₅ , P ₇₅), ng/mL]	0.35 (0.15, 1.51)	0.63 (0.21, 3.87)	-2.577	0.010*
LAC [P ₅₀ (P ₂₅ , P ₇₅), mmol/L]	1.70 (1.30, 2.60)	1.80 (1.31, 3.18)	-0.940	0.347
pH [P ₅₀ (P ₂₅ , P ₇₅)]	7.40 (7.36, 7.43)	7.36 (7.31, 7.43)	-3.332	0.001*
Oxygen index [P ₅₀ (P ₂₅ , P ₇₅)]	215.20 (169.00, 268.51)	150.37 (118.72, 216.34)	-6.232	0.000*
PaO ₂ [P ₅₀ (P ₂₅ , P ₇₅), mmHg]	81.70 (66.80, 99.85)	74.10 (60.79, 100.68)	-1.650	0.099
PaCO ₂ [P ₅₀ (P ₂₅ , P ₇₅),mmHg]	38.70 (33.35, 45.25)	43.40 (32.50, 54.43)	-2.246	0.025*

Note: SpO₂ = oxygen saturation, GCS score = Glasgow Coma Scale, PRISM III score = pediatric risk of mortality, CRP = C- reactive protein, PCT = procalcitonin, LAC = blood lactate, pH = pondus hydrogenii, Oxygenation index = ratio of PaO₂ and FiO₂, PaO₂ = partial pressure of oxygen, PaCO₂ = partial pressure of carbon dioxide, PaCO₂/PaO₂ = ratio of partial pressure of carbon dioxide to partial pressure of oxygen.

	HFNC success group (n = 237)	48 h failure group (n = 112)	Uvalue	P value
PaCO ₂ /PaO ₂	0.48	0.58	-3.159	0.002*
[P ₅₀ (P ₂₅ , P ₇₅)]	(0.38, 0.62)	(0.37, 0.75)		
Note: SpO ₂ = oxygen saturation, GCS score = Glasgow Coma Scale, PRISM III score = pediatric risk of mortality, CRP = C- reactive protein, PCT = procalcitonin, LAC = blood lactate, pH = pondus hydrogenii, Oxygenation index = ratio of PaO ₂ and FiO ₂ , PaO ₂ = partial pressure of oxygen, PaCO ₂ = partial pressure of carbon dioxide, PaCO ₂ /PaO ₂ = ratio of partial pressure of carbon dioxide to partial pressure of oxygen.				

(3) Multi-factor Logistic Analysis Results (shown in additional file 1)

The PRISM III score (OR = 4.064, 95% CI = 1.989–8.302) and PaCO₂ (OR = 4.516, 95% CI = 2.272–8.976) were risk factors for 48 h failure.

2.2.2 HFNC 24 h failure and 2 h failure risk factor analysis (shown in additional file 2)

The analysis results for the HFNC 24 h failure group were almost identical to those for the preceding 48 h, except that the CRP level in the 24 h failure group was also found to be higher than that in the HFNC success group ($P < 0.05$). After multivariate logistic regression analysis, PCT (OR = 2.794, 95% CI = 1.390 ~ 5.614) and PaCO₂ (OR = 3.152, 95% CI = 1.480 ~ 6.713) were risk factors for HFNC 24 h failure.

The analysis results for the HFNC 2 h failure group were roughly the same as those for the preceding 48 h and 24 h. The PRISM III score, CRP and PaCO₂/PaO₂ ratio in the 2 h failure group were all higher than those in the success group ($P < 0.05$). The PRISM III score (OR = 27.977, 95% CI = 3.693–211.961) and PaCO₂/PaO₂ ratio (OR = 64.366, 95% CI = 7.320–566.008) were risk factors for HFNC 2 h failure.

2.3 The Prediction Function of the Change Trend in Clinical Indexes before and after HFNC Treatment for Early Failure of HFNC

2.3.1 Zhang's research suggests that^[9] evaluation of the effectiveness of non-invasive respiratory support therapy 1–2 h after initial treatment plays an important role in subsequent treatment decisions.

Therefore, this study dynamically observed the before-and-after data of 67 patients who suffered acute respiratory insufficiency and received HFNC, among which 55 therapies were successful and 12 failed. There were no significant difference in age, sex or weight between the two groups ($P > 0.05$) (shown in additional file 3). The PEWS scores of the success group before and after HFNC treatment were lower than those of the failed groups, while the oxygen saturation index and oxygenation index were higher than those of the failed groups. PaO₂ after 2 h of HFNC treatment in the success group was higher than that in the failed groups, but the PaCO₂/PaO₂ ratio in the success group was lower than that in the failed

groups. For these data, there were statistically significant differences between the two groups ($P < 0.05$). There was no significant difference in heart rate, respiration, GCS score or PaCO_2 between the two groups before and after HFNC treatment ($P > 0.05$). The range of decrease in PEWS scores for the success group was greater than that for the failed groups, while the changes in pH value, oxygen saturation index and oxygenation index before and after HFNC treatment showed an upward trend in the success group and a downward trend in the failed group. The comparison had statistically significant differences ($P < 0.05$) (see additional table).

2.3.2 Multi-factor Logistic Analysis Results (shown in additional file 4)

The Δ oxygenation index% (OR = 5.875, 95% CI = 1.512 ~ 22.830) was a warning factor for early HFNC failure.

2.4 HFNC Failure Analysis with Respect to Residents (shown in additional file 5)

The rotation of residents into the PICU is usually carried out in the 1st half of the month, we compared HFNC failure rate between the 1st half and the 2nd half of each month in order to identify whether the failure was caused by the inexperience of residents, but there was no significant difference ($P > 0.05$).

2.5 Analysis of Failed Outcomes for HFNC (shown in additional file 5)

Although there were no significant differences in the PICU stay time, hospitalization cost and in-hospital mortality, the patients that upgraded from HFNC to invasive respiratory support has a longer invasive mechanical ventilation time than that of patients who received invasive respiratory support directly ($P < 0.05$).

Discussion

Respiratory support technology is the main means of treating children with critical and severe conditions. Because invasive respiratory support has been noticed to have many disadvantages, such as the presence of ventilator-induced lung injury (VILI), in recent years, more attention has been paid to non-invasive respiratory support, which could alleviate the pain of endotracheal intubation and reduce complications. However, studies have confirmed that the failure of non-invasive respiratory support is related to an increase in intubation rate and mortality^[10]. Therefore, if the focus is only on non-invasive respiratory support, invasive respiratory support via endotracheal intubation may be delayed, accompanied with poor prognosis for patients. As a new type of non-invasive ventilation oxygen therapy device, high-flow nasal cannula oxygen therapy (HFNC) is even more comfortable than traditional non-invasive mechanical ventilation (NIV), with a lower incidence of complications such as head shaping, nasal injury, pneumothorax, and abdominal distension^[11-12]. Several clinical studies have shown that HFNC has achieved good clinical effects in the treatment of respiratory diseases, such as respiratory

failure, respiratory distress syndrome (RDS), sleep paroxysmal apnoea symptoms, and reduced the rate of endotracheal intubation in children^[13–15]. The study by Wing et al^[16] also found that early HFNC used in children with acute respiratory insufficiency would reduce their possibility of endotracheal intubation and invasive mechanical ventilation. However, there is no uniform standard for HFNC indications and contraindications in pediatric applications, and there are few reports on its related risks. Furthermore, the study by Gaunt et al^[17–18] found that if the patient's condition did not improve within 48 h after HFNC, the respiratory support mode should be upgraded; otherwise, it led to further deterioration in respiratory function and increased mortality. Therefore, we suspected that the failure to HFNC in critically ill children would also have adverse consequences.

Considering that the earlier the failure time was, the lower the possibility was that failure was caused by disease progression, we compared the HFNC success group with the 48 h failure group, 24 h failure group and 2 h failure group, and the results were almost consistent. Among the 349 pediatric patients who were included in this study, the GCS score, PRISM III score, pH value, PaCO₂/PaO₂ ratio and oxygenation index were significantly different between the HFNC success and failure groups ($P < 0.05$). By multivariate logistic regression analysis, PRISM III score and PaCO₂/PaO₂ ratio were considered as risk factors for HFNC failure.

Neither PCT nor the CRP, which suggested inflammatory reactions exist, were significantly different in the 48 h failure group or 2 h failure group compared with success group, but their differences between the 24 h failure group and the success group were statistically significant ($P < 0.05$). Multivariate logistic regression showed that when PCT > 0.67 ng/ml, the risk of HFNC failure within 24 h increased by more than 2 times. Normally when PCT and CRP were significantly increased, inflammation or organ damage was often more severe in pediatric patients. Therefore, PCT and CRP are supposed to be a risk factor for HFNC failure. Further study is needed to expand the sample size and conduct hierarchical analysis for the inconsistent results. At same time when PCT or CRP significantly increase, HFNC as a support treatment should be closely monitored.

The pediatric risk of mortality (PRISM III) is currently the most widely used as pediatric critical assessment tool worldwide, which was positively correlated with organ failure^[19]. This study found that the PRISM III score was higher in each failure group than in the success group ($P < 0.05$). Multivariate logistic regression showed that when the PRISM III score was > 4 points, the risk of HFNC failure within 48 h was over 4 times higher, while a PRISM III score > 6.5 points was associated with an over 27 times higher risk of HFNC failure within 2 h. The higher the score, the higher the risk of failure was. Therefore, for critically ill children, especially those with PRISM III scores > 6.5 points, HFNC should be closely monitored. Because PRISM III score involves 14 physiological parameters and 23 parameter ranges^[20], such as blood gas, blood sugar, electrolytes, liver and kidney function, and coagulation function, it would take longer time to get than some warning scores for example PEWS score, which limits the value of PRISM III to early predict and need more research to find more valuable scoring system.

HFNC can provide not only a constant oxygen concentration but also a certain positive end-expiratory pressure in the airway with high-flow gas, thus improving oxygenation^[21]. PaO_2 is an index of respiratory function, while PaCO_2 is a better index to pulmonary ventilation function^[22]. Therefore, the $\text{PaCO}_2/\text{PaO}_2$ ratio could indicate pulmonary ventilation and diffusion function. In this study, it was found that the difference of PaCO_2 between the 24 h or 48 h failure group and success group was statistically significant ($P < 0.05$), while $\text{PaCO}_2/\text{PaO}_2$ ratio was statistically different between all the failure groups and the success group ($P < 0.05$). Moreover, the higher PaCO_2 and the $\text{PaCO}_2/\text{PaO}_2$ ratio, the shorter failure time is. Multivariate logistic regression showed that when $\text{PaCO}_2 \geq 43$ mmHg, the risk of HFNC failure within 24 h and 48 h was over 3 times and 4 times higher, respectively. When the ratio of $\text{PaCO}_2/\text{PaO}_2$ was ≥ 0.67 , the risk of HFNC failure within 2 h was over 64 times higher. Therefore, for pediatric patients with abnormal ventilation, HFNC should be carefully selected. More research on how to combine PaCO_2 and the $\text{PaCO}_2/\text{PaO}_2$ ratio to judge the failure risk of HFNC is needed.

Expert guidelines for clinical practice with non-invasive positive pressure ventilation^[9] indicated that evaluation about the effectiveness of non-invasive respiratory support therapy after 2 h initial treatment played an important role in subsequent treatment decisions; therefore, in this study, we found that the decline in PEWS scores for the success group was significantly greater than that for the failed groups. Furthermore, the changes in pH value, oxygen saturation index and oxygenation index before and after HFNC showed an upward trend in the success group and a downward trend in the failed group ($P < 0.05$). Multivariate logistic regression analysis found that when the oxygenation index decreased by $> 28\%$ after 2 h of HFNC treatment, the risk of early HFNC failure increased by more than 5 times. Given that, the change trend of the oxygenation index was a warning for early HFNC failure, if which showed a decreasing trend after 2 h treatment with HFNC, there was a high possibility of failure to HFNC and close monitoring was required, and the respiratory support mode should be upgraded in time to avoid further deterioration of respiratory function.

To further analyse the possibility of increased HFNC failure due to improper choice about respiratory support modes by inexperienced physicians, we compared the HFNC failure rates between the 1st half and the 2nd half of each month and found that there was no significant difference ($P > 0.05$), which means no reason to attributes the failure to inexperienced new residents, suggesting that the current training and working modes were reasonable.

The PICU stay time, hospitalization cost and in-hospital mortality were greater in the group that respiratory support upgraded from HFNC to invasive than the group that was synchronously admitted to the PICU and directly received invasive respiratory support, but not statistically different, while the invasive mechanical ventilation time was statistically longer ($P < 0.05$). The failure of HFNC in critically ill children had adverse consequences, which at minimum, might prolong the invasive mechanical ventilation time.

Limitations

Our study has several limitations. First, the sample size might not be large enough to determine the consistency of the predictors of HFNC failure, and studies with larger sample size are needed. Moreover, further studies should address the changes occurring in the parameters and their associations during the course of the HFNC treatment. Second, the instantaneous evaluation was not taken into account in the initial study design that some parameters, such as PEWS score, was failed to be included; however, the comparison of before and after HFNC treatment found that PEWS score was very valuable, a larger scale prospective study is therefore needed to validate a more valuable scoring system in judging the failure risk of HFNC. An effective and simple scoring tools that prognostically assess the risk of HFNC failure in pediatric patients should remain a priority.

Conclusions

HFNC is an effective treatment for critically ill children, but its indications need to be strictly controlled. The PRISM III score, PaCO_2 and $\text{PaCO}_2/\text{PaO}_2$ ratio were risk factors for HFNC failure. When the PRISM III score > 6.5 points and the $\text{PaCO}_2/\text{PaO}_2$ ratio > 0.67 , HFNC as a support treatment should be selected carefully. And the change trend in the oxygenation index before and after HFNC is a warning factor for early HFNC failure too. Early HFNC failure might lead to prolonged invasive mechanical ventilation. Therefore, in these conditions the choice of HFNC respiratory support should be made cautious.

Abbreviations

BPD:Bronchial pulmonary dysplasia;BIPAP:Bilevel positive airway pressure;CRP:C-reactive protein; FiO_2 :Fraction of inspired oxygen;GCS:Glasgow Coma Scale;HFNC:High-flow nasal cannula oxygen therapy;LAC:Blood lactate;NIV:Non-invasive mechanical ventilation; PaO_2 :arterial partial oxygen pressure; PaCO_2 :arterial partial carbon dioxide pressure; PCT:Procalcitonin;pH:Pondus hydrogenii;PEWS:Pediatric Early Warning Signs;PICUS:Pediatric intensive care units;PRISM:Pediatric risk of mortality;RDS:Respiratory distress syndrome; SpO_2 :Oxygen saturation;VILI:Ventilator-induced lung injury.

Declarations

1. Ethical approval and consent to participate:

The study was performed according to the Multi-center study for the early diagnosis and treatment of critically ill children (medical research 2016 ethical approval from medical ethics committee of West China Second Universal Hospital of Sichuan University) (No. 026).Informed consent was obtained from all individual participants included in the study.

2. Consent for publication

The authors hereby declare that the article is original and that its contents have not been published in full or in part. We also would like to declare that the manuscript has been read and approved by all authors.

3. Availability of data and materials

The datasets analyzed during the current study available from the corresponding author on reasonable request.

4. Competing Interest

All authors declare that they have no conflicts of interests.

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6. Authors' contributions

Liu jie had primary responsibility for protocol development,patient screening,enrollment,outcome assessment,preliminary data analysis and writing the manuscript.Dr LI De-yuan and Drs LUO Li-li participated in the development of the protocol and analytical framework for the study and contributed to the writing of the manuscript.Dr LIU Zhong-qiang contributed in the same ways as Dr LI De-yuan and Drs LUO Li-li and was responsible for patient screening.LI Xiao-qing coordinated data acquisition and contributed to the interpretationof data.Drs QIAO Li-na supervised the design and execution of the study,performed the final data analyses and contributed to the writing of the manuscript.All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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8. Authors' information

Not applicable.

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Figures

Figure 1

Analysis of the HFNC Failure Constituent Ratio

Figure 1

Analysis of the HFNC Failure Constituent Ratio

Figure 2

Patient Classification

Figure 2

Patient Classification

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