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Feasibility of high-flow nasal cannula oxygen therapy for acute respiratory failure in patients with hematologic malignancies: A retrospective single-center study

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ABSTRACT

Purpose: This study investigated the feasibility of high-flow nasal cannula (HFNC) oxygen therapy for acute respiratory failure in adult patients with hematologic malignancies.
Materials and methods: We identified 45 acute respiratory failure patients with hematologic malignancies who received HFNC therapy between March 2012 and June 2014 at Seoul St Mary's Hospital. Their medical records were reviewed retrospectively to identify useful prognostic factors for successful treatment.
Results: Of the 45 patients, 15 (33.3%) successfully recovered, and 30 were changed to invasive ventilation due to failed HFNC treatment. The etiologies of acute respiratory failure were bacterial pneumonia (57.8%), *Pneumocystis jirovecii* pneumonia (17.8%), pulmonary edema (8.9%), and bronchiolitis obliterans organizing pneumonia (8.9%). The overall mortality rate was 62.2%. The HFNC treatment success rate was significantly different between the survivors and nonsurvivors. To evaluate risk factors for HFNC treatment failure, differences between the HFNC treatment success and failure groups were compared. There were no significant differences in the severity of underlying medical conditions. The percentage of bacterial pneumonia was significantly higher in the HFNC treatment failure group compared with the success group (73.3% vs 26.7%; $P = .004$).
Conclusions: High-flow nasal cannula offers an interesting alternative to invasive ventilation in acute respiratory failure patients with hematologic malignancies. However, attention must be paid to the appropriate choice of HFNC settings such as oxygen flow.

1. Introduction

Respiratory failure, the leading cause of intensive care unit (ICU) admission, has a high mortality rate in patients with hematologic malignancies [1]. Several studies have demonstrated that invasive ventilation (IV) is associated with increased mortality, whereas early noninvasive ventilation (NIV) has improved the clinical outcome [2-4]. A prospective randomized study that compared NIV to conventional oxygen therapy found that avoiding IV lowered the rate of ICU deaths and serious complications such as ventilator-associated pneumonia and septic shock [4]. This finding could be due to the immunocompromised state of patients with hematologic malignancies because IV could cause more opportunistic infections associated with tracheal intubation.

Recently, the prognosis of patients with hematologic malignancies has improved with the development of treatment methods [5]. A high-flow nasal cannula (HFNC) combined with a heated humidification system can deliver up to 100% at a maximum flow of 60 L/min of gas via a cannula or nasal prongs [6,7]. Given its physiologic benefits, including positive expiratory pressure effects, alveolar recruitment, and increased comfort and tolerance compared to conventional facial masks, HFNCs have been widely used in pediatric patients [8,9]. In adult patients with acute respiratory failure, a pilot prospective monocentric study [10] and prospective observational study [11] showed that HFNC use significantly improved both the clinical and biological parameters in patients. However, until now, data from adult patients with hematologic malignancies have been lacking.

This study investigated the feasibility of HFNC use in patients with hematologic malignancies for the treatment of acute respiratory failure by comparing the clinical characteristics between treatment failure and success groups and identifying prognostic factors associated with treatment failure.

2. Materials and methods

2.1. Data collection and patients

More than 450 hematopoietic stem cell transplants are performed annually at Seoul St Mary's Hospital (Seoul, Republic of Korea), and a

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total of 6801 patients visited between March 2012 and June 2014. We identified 1424 adult patients older than 15 years with hematologic malignancies who received oxygen therapy at this hospital during the study period. Among the 1424 patients, 1138 (79.9%) improved with conventional oxygen therapy such as nasal prong or face mask, 234 (16.4%) were changed to IV, and 52 (3.7%) were treated with HFNC. The decision to initiate HFNC therapy was based on the clinical judgment of the intensive care specialist who assessed the patients' clinical parameters. Seven patients with an HFNC who died in do-not-intubate status were excluded, leaving 45 patients for retrospective review (Figure). High-flow nasal cannula therapy was delivered using the Fisher & Paykel Optiflow system, with an MR850 respiratory humidifier and an MR290 chamber; RT202 heated delivery tubing; and OPT842, OPT844, or OPT846 bore nasal cannulae (Fisher & Paykel Healthcare, Auckland, New Zealand). Therapy was titered at a fraction of inspired oxygen (FIO_2) sufficient to maintain the arterial O_2 saturation level at greater than 90% and a flow of up to 45 to 50 L/min, according to the specific clinical situation. Patients were identified from a medical record review. The Institutional Review Board of Seoul St Mary's Hospital approved the study and waived the requirement for informed consent.

The following variables were analyzed: age, sex, hematologic diagnosis and disease status, prior hematologic treatment, underlying lung condition, reason for acute respiratory failure, result of an arterial blood gas analysis, alveolar partial pressure of oxygen PaO_2/FIO_2 ratio at the time of HFNC use, initial settings for HFNC therapy (flow and FIO_2), duration of HFNC therapy, laboratory values, length of hospital stay, and inhospital mortality. Based on these data, we calculated the Acute Physiology and Chronic Health Evaluation (APACHE) II score for each patient on the day that HFNC therapy was started.

Patients were monitored and switched to IV if they exhibited altered consciousness, seizures, exacerbation of respiratory failure on HFNC therapy, hemodynamic instability, or intolerance to the HFNC interface based on the clinical judgment of the intensivist. During HFNC oxygen supplementation, patients who successfully tapered to a face mask or nasal prongs were classified as the treatment success group, whereas those who required IV were the treatment failure group.

Disease status was based on available medical records and the most recent bone marrow biopsy data. Complete remission was defined as less than 5% blast cells in marrow aspirates in patients with leukemia, the disappearance of peripheral and deep lymphadenopathy and other malignant foci in patients with lymphoma, and the disappearance of monoclonal immunoglobulins in blood and urine and less than 5% plasma cells in bone marrow aspirates in patients with myeloma.

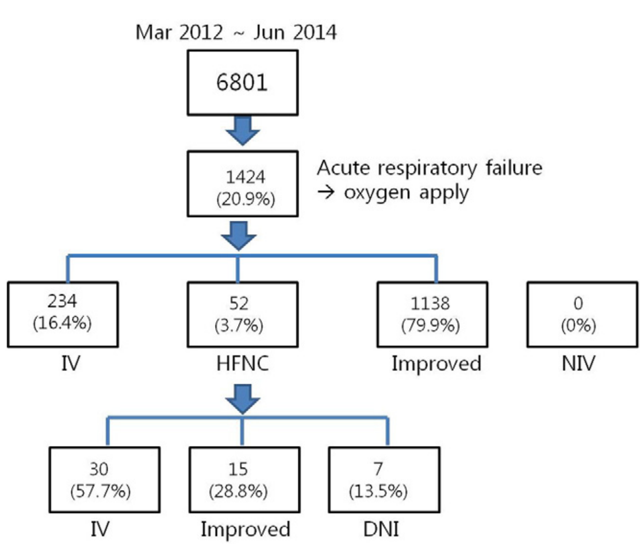

Figure. Flow chart of the 6801 patients who visited our BMT center during the study period.

Neutropenia was defined as an absolute neutrophil count less than 500 cells/mm^3.

2.2. Statistical analysis

All results are expressed as the mean ± SEM for continuous variables and proportions for categorical variables. Analyses of the differences between survivors and nonsurvivors and between the treatment success and failure groups were performed using the Mann-Whitney *U* test for continuous variables and the χ^2 test or Fisher exact test for categorical variables. Odds ratios and their 95% confidence intervals (CIs) were computed. All tests were 2 sided, and $P < .05$ was considered statistically significant. All statistical analyses were performed using the SPSS software program (version 18.0.0 for Windows; SPSS, Inc, Chicago, IL).

3. Results

The general characteristics of the patients are shown in Table 1. The mean patient age was 49.6 ± 2.0 years, and 75.6% of the patients were male. The most common underlying hematologic diseases were acute myeloid leukemia (AML) (46.7%), myelodysplastic syndrome (13.3%), and lymphoma (11.1%). At the time of HFNC treatment, 33 patients (73.3%) had active disease, and 12 (26.7%) were in complete remission. In total, 21 patients (46.7%) underwent bone marrow transplantation (BMT), and 22 (48.9%) received systemic chemotherapy 30 days before HFNC therapy. Furthermore, 19 patients (42.2%) were neutropenic, and 12 (26.7%) were taking immunosuppressants due to chronic graft versus host disease or for graft versus host disease prophylaxis after BMT. Of 45 patients, 44 (97.8%) were admitted to the ICU for a mean of 12.3 ± 1.3 days. The mean length of hospital stay was 28.5 ± 2.8 days, and the overall mortality rate was 62.2%.

The clinical characteristics of acute respiratory failure are shown in Table 2. The most common etiology was bacterial pneumonia in 26 patients (57.8%); the others were *Pneumocystis jirovecii* pneumonia in 8 (17.8%), pulmonary edema in 4 (8.9%), bronchiolitis obliterans organizing pneumonia in 4 (8.9%), and pulmonary hemorrhage in 3 (6.7%). At the time of starting HFNC therapy, the mean APACHE II score was 17.4 ± 0.6. The mean PaO_2/FiO_2 ratio was 99.9 ± 6.5, and the alveolar partial pressure of carbon dioxide ($PaCO_2$) was 34.4 ± 1.5 mm Hg. The mean initial HFNC settings were a flow of

Table 1
Characteristics of 45 patients with hematologic malignancies

Demographics	
Age (y)	49.6 ± 2.0
Male, n (%)	34 (75.6)
Underlying hematologic disease, n (%)	
AML	21 (46.7)
Myelodysplastic syndrome	6 (13.3)
Lymphoma	5 (11.1)
Acute lymphoblastic leukemia	4 (8.9)
Aplastic anemia	3 (6.7)
Multiple myeloma	2 (4.4)
Hemophagocytic lymphohistiocytosis	2 (4.4)
Chronic myelogenous leukemia	1 (2.2)
Autoimmune hemolytic anemia	1 (2.2)
Status of hematologic disease, n (%)	
Active status	33 (73.3)
Complete remission	12 (26.7)
Relapsed malignancy	11 (24.4)
Prior treatment, n (%)	
Post-BMT	21 (46.2)
Systemic chemotherapy in last 30 d	22 (48.9)
Use of immunosuppressant agent	12 (26.7)
Neutropenia	19 (42.2)
Length of ICU stay (d)	12.3 ± 1.3
Length of hospital stay (d)	28.5 ± 2.8
Mortality, n (%)	28 (62.2)

Continuous variables are reported as mean ± SEM.