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High-flow oxygen therapy in immunocompromised patients with acute respiratory failure: A review and meta-analysis☆,☆☆

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ABSTRACT

Purpose: Acute respiratory failure remains a common hazardous complication in immunocompromised patients and is associated with increased mortality rates when endotracheal intubation is need. We aimed to evaluate the effect of high-flow nasal cannula oxygen therapy (HFNC) compared with other oxygen technique for this patient population.
Methods: We searched Cochrane library, Embase, PubMed databases before Aug. 15, 2017 for eligible articles. A meta-analysis was performed for measuring short-term mortality (defined as ICU, hospital or 28-days mortality) and intubation rate as the primary outcomes, and length of stay in ICU as the secondary outcome.
Results: We included seven studies involving 667 patients. Use of HFNC was significantly association with a reduction in short-term mortality (RR 0.66; 95% CI, 0.52 to 0.84, $p = 0.0007$) and intubation rate (RR 0.76, 95% CI 0.64 to 0.90; $p = 0.002$). In addition, HFNC did not significant increase length of stay in ICU (MD 0.15 days; 95% CI, −2.08 to 2.39; $p = 0.89$).
Conclusions: The results of current meta-analysis suggest that use of HFNC significantly improve outcomes of acute respiratory failure in immunocompromised patients. Owing to the quality of the included studies, further adequately powered randomized controlled trials are needed to confirm our results.

1. Introduction

With the advance in organ transplantations, bone marrow and chemotherapy, the number of immunocompromised patients have increased over the past decades [1,2]. However, these patients are at high risk of many life-threatening complications, especially acute respiratory failure (ARF) [3,4]. Once these patients evolve into ARF, they often need mechanical ventilation and admission to intensive care unit (ICU). Unfortunately, invasive mechanical ventilation under such situation is associated with a significant increase in mortality rate that ranges between 40% and 90% [3,5]. Therefore, non-invasive respiratory support techniques are still the most common application in such patient population.

The 2011 Canadian guidelines made a weak recommendation (grade 2B) favoring the use of non-invasive ventilation (NIV) in immunocompromised patients with ARF [1]. However, the above recommendation is based on only two early small randomized controlled trials (RCTs) [6,7] and respiratory support techniques for patients with ARF has rapidly developed over the past two decades. Recently, a large RCT enrolling 374 immunocompromised patients showed that NIV strategy showed no significant benefit on outcomes compared with standard oxygen therapy [8]. In this RCT, high-flow nasal cannula (HFNC) was also used in both groups. Of note, HFNC was used more often in oxygen group than NIV group (44% vs. 31%, $p = 0.01$) and the overall mortality rate of this RCT was lower than previous reported. Therefore, one might easily associate the use of HFNC with their result of mortality, which showed no difference in both groups (27% vs. 24%, $p = 0.47$) but was lower than that of other studies (25.7% versus 40–90%) [3,5].

HFNC is a new technique that may deliver up to 100% humidified oxygen at high flow rate. The advantages of HFNC include high fraction of inspired oxygen to improve oxygenation, generation of flow-dependent positive end-expiratory pressure (2 to 5 cm H_2O) to improve alveolar recruitment, enhanced wash out of nasopharyngeal dead space and more comfort to patients requiring oxygen therapy [9]. Many studies have shown that, compared with conventional oxygen therapy, HFNC

Abbreviations: ARF, acute respiratory failure; CIs, confidence intervals; HFNC, high-flow nasal cannula; ICU, intensive care unit; IQR, interquartile range; MD, mean differences; NIV, noninvasive ventilation; RCTs, randomized controlled trials; RR, risk ratio; SD, standard deviations.

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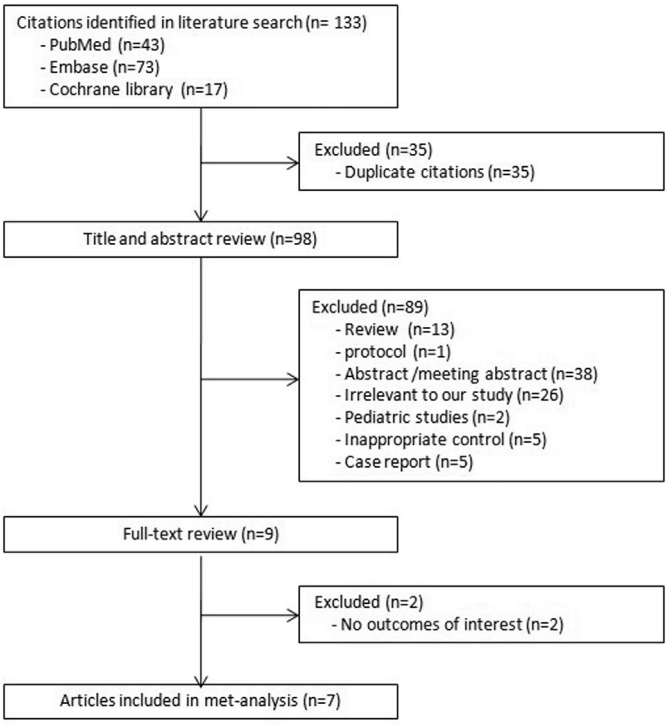

Fig. 1. Selection process for studies included in the meta-analysis.

in immunocompetent patients with ARF could improve respiratory parameters, comfort and patient tolerance, decreased intubation rate and mortality [10-12]. Therefore, whether HFNC can bring similar benefits in immunocompromised patients with ARF has been attracting more and more attentions. Recently, several studies on this topic have been published and some of these studies have a modest sample size, while the conclusions are inconsistent [13-15].

Therefore, with the aid of increased power of meta-analytic techniques, we aimed to perform a systematic review and meta-analysis of all available studies to address the hypothesis that comparing with other respiratory support techniques, use of HFNC in immunocompromised patients with ARF is more effective for reduction of short-term mortality, intubation rate, and ICU length of stay.

2. Methods

2.1. Search strategy and selection criteria

This systematic review and meta-analysis was conducted in accordance with the PRISMA guidance. We searched Cochrane library, Embase, PubMed databases before Aug. 15, 2017 to identify potentially relevant studies. Search terms included: "high-flow nasal cannula oxygen", "HFNC", "nasal high flow", "humidified high-flow nasal cannula", "hematologic," "hematological," "transplant," "tumor," "cancer," "immunosuppression," "immunosuppressed," and "immunocompromised". Our research was limited to humans without language and study design restriction. Reference lists of relative articles were also reviewed. Studies were included if they met the following criteria: (1) immunocompromised adult patients with ARF; (2) use of HFNC compared with control strategy; (3) studies included should report at least one of the predefined outcomes: mortality, intubation rate, and length of stay in ICU. We excluded studies enrolling patients <18 years old, and studies without a control group.

2.2. Data extraction and quality assessment

Two reviewers (H-BH and J-MP) independently extracted data from included studies, such as the name of first author, year of publication, country, sample size, study design, setting, treatment algorithms of intervention and control groups, severity of illness, as well as all predefined outcomes.

The above two independent reviewers (H-BH and J-MP) evaluated the quality of included studies. To assess the possible risk of bias for RCTs, we used the risk of bias tool recommended by the Cochrane Collaboration, which assigned a value of high, unclear, low to the following items: sequence generation; allocation concealment; blinding; incomplete outcome data; selective outcome reporting; and other sources of bias [16]. To assess the possible risk of bias for case-control or cohort study, we adopted the Newcastle-Ottawa scale, which focused on three categories: selection, comparability, and exposure or outcome with each being awarded a maximum of nine stars on items [17].

2.3. Outcomes and statistical analysis

The primary outcomes were short-term mortality and intubation rate. We defined short-term mortality as ICU or hospital or 28-day mortality. If a study reported all of these outcome measures, the longest

Table 1
Characteristics of the included studies in current review and met-analysis.

Study	Year	Study design	Setting	Underlying conditions	Patient characteristics (HFNC/control)					Algorithm		Primary outcome
					Patient number	Age, (years)	Disease severity	RR/min	PO_2:FiO_2	Intervention group	Control group	
Tu et al.	2017	Retrospective	ICU	Renal transplant	20/18	47/47	APACHE II 20 (4)/19 (4)	32/30	150/148	HFNC	NIV	Need for intubation
Coudroy et al.	2016	Retrospective	ICU	Mixed	60/55	45/44	SAPS II 46 (13)/42 (11)	29/30	149/141	HFNC	NIV	28-Days mortality
Frat et al.	2016	Post-hoc analysis	ICU	Mixed	26/30	62/63	SAPS II 29 (11)/30 (17)	32/32	138/155	HFNC	COT	Need for intubation
Lemiale et al.	2016	Post-hoc analysis	ICU	Mixed	90/90	64/63	SOFA 4 (2–6)/3 (2–6)	28/25	—	HFNC	COT	28-Days mortality
Lemiale et al.	2015	RCT	ICU	Mixed	52/48	50/49	SAPS II 42 (30–52)/38 (32–47)	26/27	128/100	HFNC	COT	Need for IMV or NIV
Mokart et al.	2015	Retrospective	ICU	Cancer	69/69	56/59	SAPS II 47 (37–55)/42 (38–59)	—	128/116	HFNC + NIV	COT + NIV	28-Days mortality
Roca et al.	2015	Retrospective	ICU	Lung transplant	22/18	56/53.5	APACHE II 21 (18–25)/20 (19–25)	28/20	—	HFNC	COT	Need for IMV and mortality

Data are expressed as median (interquartile range), or mean (standard deviation); APACHE, acute physiology and chronic health evaluation; HFNC, high flow nasal cannula oxygen; ICU, intensive care unit; IMV, invasive mechanical ventilation; NIV, non-invasive ventilation; COT, conventional oxygen therapy; RR, respiratory rate; SAPS, simplified acute physiologic score; SOFA, sequential organ failure assessment score.