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Letters

Non-invasive ventilation in hypoxemic respiratory failure a systematic review: *ex nihilo nihil fit*

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None

To the Editor,

We read with interest the study by David-Joao, et al. [1] on the role of non-invasive ventilation in acute hypoxemic respiratory failure (AHRF). The authors perform a systematic review and a meta-analysis of randomized controlled trials (RCT's) comparing NIV with standard care (oxygen therapy). The authors identified nine studies that described the utility of NIV in AHRF. However, the systematic review lacks a few important RCT's that compare NIV with oxygen therapy in AHRF. This is probably due to the search terms and the strategy used by the authors that might have resulted in missing these important studies.

A cursory search of our personal files identified five major studies, which were clearly missed by David-Joao et al. (Table 1). Four studies compared NIV with oxygen therapy in acute hypoxemic respiratory failure and the landmark 3CPO trial studied role of NIV in acute cardiogenic pulmonary edema [2-6]. In a study including subjects with solid organ transplant with ahrf, 40 subjects were randomized to NIV or oxygen therapy [2]. The intubation rate in the NIV arm was 20% compared to 70% in the oxygen therapy arm. In another study, NIV could avoid intubation in 62.5% vs. 56% in the oxygen therapy arm [3]. Two more studies also showed a significant reduction in the chances of intubation in the NIV arm compared to the oxygen therapy arm [4,5]. The 3CPO trial compared standard oxygen therapy with either NIV or continuous positive airway pressure (CPAP) [6]. More than one-thousand subjects were included in this RCT and the authors did not find any difference in either the intubation rates or the 7 day mortality between the study groups [6].

In conclusion, it is important to design the search strategy before performing a systematic review of the literature. Use of restrictive strategy is appealing as it reduces the time to perform a systematic review, however it can occasionally cause omission of important literature. It would be interesting to see if reanalysis after including these missing studies by David-Joao, et al. would yield different results.

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Table 1
Randomized trials describing the use of NIV in acute hypoxemic respiratory failure.

Author/Year	No. of patients	Methods	Inclusion criteria	Intubation rate in NIV	Intubation rate in control arm	ICU mortality in NIV arm	ICU mortality in control arm
Antonelli et al. [2] 2000	40	NIV vs. oxygen therapy	Solid organ transplant	4/20	14/20	4/20	10/20
Delclaux et al. [3] 2000	81	NIV vs oxygen therapy	Mild-to-moderate ARDS	15/40	18/41	9/40	9/41
Gray et al. [6] 2008	1069	CPAP vs NIV vs oxygen therapy	Acute cardiogenic pulmonary edema	20/702	10/367	67/702	36/367
Squadrone et al. [4] 2009	40	CPAP vs. oxygen therapy	Hematological malignancy (post chemotherapyor BMT) with mild-to-moderate ARDS	2/20	16/20	3/20	15/20
Zhan et al. [5] 2012	40	NIV vs. oxygen therapy	Mild-to-moderate ARDS	1/21	7/19	1/21	5/19

ARDS: acute respiratory distress syndrome; BMT: bone marrow transplant; CPAP: continuous positive airway pressure; ICU: intensive care unit; NIV: non-invasive ventilation; PSV: pressure support ventilation.

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Noninvasive ventilation in acute hypoxemic respiratory failure: A systematic review and meta-analysis. Response to letter

To the Editor,

We agree with Sehgal et al. that it is important to design a comprehensive search strategy for several important database in order performing a systematic review of the literature. It is also crucial to followa predefined selection criteria for including primary studies. Therefore cursory searches can be misleading without a proper protocol and a clear research question. Our systematic review was conducted according to the PRISMA [1]. After working in pairs of independent reviewers and consulting a third independent reviewer whenever consensus was not reached we presented the final nine studies that met our selection criteria. Sehgal et al. mentioned five studies that were potentially missed by our systematic review that aimed to analyze available evidence of noninvasive ventilation (Bi-level positive airway pressure- BiPAP modality) in hypoxemic acute respiratory failure, excluding chronic obstructive pulmonary disease as mentioned in our abstract [2]. The studies mentioned by Sehgal et al. did not meet our inclusion criteria and the reasons are described below.

Gray et al. published a very important trial for the use of NIV in acute pulmonary edema [3]. This trial was considered in our analysis however all three groups included patients with significant hypercapnia. Also, in the inclusion criteria, there is no mention for hypoxia (only tachypnea and pH < 7,35), also showed in their Table 1, in the pO2 parameters. According to our predefined protocol, we looked at studies reporting hypoxia as a major inclusion criteria [2]. That is also the reason why this study [3] was excluded from our systematic review.

After reading Delclaux et al. [4] and Squadrone et al. [5] it is clear from the abstract that the noninvasive ventilation modality chosen was not CPAP and rather BiPAP. As we mentioned early in our review, studies that reported only CPAP were excluded from our analysis.

Antonelli et al. [6] and Zhan et al. [7] showed positive results in reduction of mortality and intubation by performing a study that compares NIV with oxygen therapy delivered by Venturi mask in hypoxemic patients after solid organ transplantation and acute lung injury, respectively. Our independent reviewers agreed that in both studies the population was heterogeneous, describing pneumonia, pulmonary edema, acute respiratory distress syndrome, pulmonary embolism, trauma as causes of acute respiratory failure.

We believe that due to space restriction, the lack of detailed description of our inclusion criteria lead to misinterpretation of our research question and we appreciate the methodological discussion.

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