



## LETTER TO THE EDITOR

### Prognostic impact of high flow nasal cannula compared to noninvasive positive-pressure ventilation in the treatment of acute pulmonary edema



### Impacto prognóstico da cânula nasal de alto fluxo em comparação com a ventilação por pressão positiva não invasiva no tratamento de edema agudo de pulmão

Dear Editor,

The use of non-invasive mechanical ventilation (NIMV) reduces the rate of intubation and mortality in patients with acute pulmonary edema (APE).<sup>1</sup> High flow nasal cannula oxygen (HFNC) may offer an alternative to ventilatory support in patients with APE<sup>2,3</sup> with theoretical advantages related to patient adaptation, comfort and less of a need for staff training to achieve optimal therapy. However, clinical efficacy and safety of HFNC compared to NIMV in APE is not well established.

We performed a prospective, observational study between November 2018 and January 2020. Forty-seven patients with criteria of non-hypercapnic APE were classified into two groups according to the initial therapy: Continuous positive airway pressure (CPAP)/NIPPV versus HFNC. The selected ventilatory therapy was at the discretion of the treating clinician and patients with cardiogenic shock, hemodynamic instability, hypercapnic respiratory failure (partial pressure of carbon dioxide >45 mmHg) were excluded. The device used for NIMV ventilation was a V V60® (Philips, Respironics Inc, MA, USA), whereas for HFNC therapy an Airvo™ 2 (Fisher & Paykel Healthcare, East Tamaki, New Zealand) was used. Primary composite endpoint was death or need for orotracheal intubation within 30 days after admission. The secondary endpoints were length of

hospital stay, admission to the critical care unit and composite of orotracheal intubation/change of therapy secondary to respiratory worsening.

The mean age was 68.8±13.1 years, 83% male. Twenty-eight (59.6%) patients received HFNC and 19 (40.4%) NIPPV-CPAP as initial treatment for APE. De novo acute heart failure (HF) was the initial presentation in 76.6% and 61.7% was secondary to acute coronary syndrome. Disease severity at admission was similar in both groups (Table 1). In patients treated with HFNC, initial flow was 44.3±22.7 L/min and 37°C. In the case of CPAP treatment, the initial pressure was 7±2 cmH2O and in NIPPV patients, the inspiratory pressure was 14±4 and expiratory 6±2 cmH2O.

There was no significant difference in 30-day mortality or combined objective of death/intubation in HFNC vs. NIMV (21.5 vs. 15.8 p=0.72) and (37.0 vs. 21.1% p=0.24). However the failure of therapy, defined as the combined objective of intubation or change of therapy due to respiratory worsening, was more frequent in the HFNC group (40.7 vs. 15.8 p=0.07). In-hospital or coronary care unit long stay was no different between both groups (Table 2).

In this study, HFNC was not associated with increased 30-day mortality in patients with non-hypercapnic APE, but was associated with non-significant increase in treatment failure secondary to respiratory worsening. These findings could be explained for several reasons related to the physiological effects of positive end-expiratory pressure (PEEP) over compliance, alveolar recruitment, decrease of left ventricular afterload and right ventricular preload.<sup>4,5</sup> Although HFNC seems to have an impact on RV preload, PEEP is often inconsistent, depending on the flow delivered and patient collaboration. This effect could explain that despite the good results in hypoxemic respiratory failure of other causes,<sup>5</sup> it has no benefit in APE.<sup>6</sup> Although the use of HFNC possibly does not provide benefits in the treatment of APE over NIMV, it could have better results in decompensated HF over conventional oxygen<sup>2,3,6</sup> or in weaning from NIMV therapy. Randomized studies are needed.

**Table 1** Baseline characteristics of the patients according to the modality of noninvasive ventilation therapy.

Characteristic	Global population n=47	CPAP/NIPPV n=19	HFNC n=28	p value
Age (years)	68.6±16.49	70.42±11.56	67±14.74	0.451
Male gender (%)	83.0	78.9	85.7	0.697
Diabetes (%)	46.8	68.4	32.1	0.014
Hypertension (%)	76.0	89.5	67.9	0.159
COPD (%)	12.8	21.1	7.1	0.204
OSAS (%)	4.3	5.3	3.6	0.999
Previous cardiac surgery (%)	19.1	21.1	17.9	0.999
Ischemic heart disease (%)	34.0	36.8	32.1	0.739
Chronic kidney failure (%)	14.9	21.4	10.7	0.417
Valvular heart disease (%)	36.2	36.8	35.7	0.937
AF (%)	12.8	15.8	10.7	0.674
<b>Admission characteristics</b>				
Pulse rate (beats/min)	97.8±16.5	103.1±27.7	94.2±25.5	0.269
Systolic BP mmHg	120±30.4	125.3±37.04	117.5±25.31	0.391
Diastolic BP mmHg	71.04±16.6	75.1±20.6	68.2±12.87	0.164
Respiratory rate (breaths/min)	28.6±4.3	28.4±5.7	27.74±3.23	0.843
Peripheral oxygen saturation %	89.7±5.7	89.6±5.6	89.8±5.1	0.935
Apache II score	15.16±6.41	15.34±5.31	15.05±7.11	0.889
<b>Etiology of heart failure</b>				
ACS (%)	12 (61.7)	17 (63.2)	60.7	0.866
STEMI (%)	42.4	42.1	3.1	0.847
NSTEMI (%)	19.3	21.1	17.9	0.999
Syntax score	21.0±10.6	20.04±12.2	21.71±9.5	0.687
Valve disease (%)	4 (8.5)	1 (5.3)	3 (10.7)	0.638
Arrhythmia (%)	3 (6.4)	2 (7.1)	1 (5.3)	0.946
Hypertensive crisis (%)	3 (6.4)	1 (3.6)	2 (10.5)	0.557
Chronic HF (%)	11(23.4)	5 (26.3)	6 (21.4)	0.737
Aortic dissection (%)	1 (2,1)	0.0	1 (3.6)	0.999
LVEF	37.4±11.3	33.8±9.7	39.9±11.9	0.074
<b>Treatment in first 24 hours</b>				
Furosemide (%)	42 (95.5)	19(100.0)	26(92.0)	0.498
Mean dose 24 hours (mg)	168.4±136.3	136.84±82.3	193.5±164.7	0.100
Hydric balance first 24 hours (L)	-2.9±2.3	-1.8±1.5	-2.2±2.1	0.498
Nitroglycerin (%)	23(52.3)	9(47.4)	14(56.0)	0.570
Mean dose 24 hours mg/kg/min	37.3±60.5	51.2±90	27±23	0.953
Thiazides (%)	5 (11.4)	2 (10.5)	3 (12.0)	0.999
CRRT (%)	3 (6.8)	1 (5.3)	2 (8.0)	0.999

ACS: acute coronary syndrome; AF: atrial fibrillation; BP: blood pressure, CCRT: continuous renal replacement therapy; COPD: chronic obstructive pulmonary disease; CPAP: continuous positive airway pressure; HF: heart failure; HFNC: high flow nasal cannula; LVEF: left ventricular ejection fraction. MCS: mechanical circulatory support, NIPPV: noninvasive positive-pressure ventilation; OSAS: obstructive sleep apnea syndrome, STEMI: ST elevation myocardial infarction. NSTEMI: non ST elevation myocardial infarction.

**Table 2** Primary and secondary ends point comparing noninvasive positive-pressure ventilation and high flow nasal cannula.

Variable	Overall (n=47)	CPAP/NIPPV n=19	HFNC n=28	p value
Death at 30 days (%)	19.1	15.8	21.5	0.72
Respiratory infection after 48 hours of admission (%)	15.2	26.3	7.4	0.10
Intubation at 30 days (%)	23.9	15.8	29.6	0.32
Death or intubation 30 days (%)	30.4	21.1	37.0	0.24
Intubation or change therapy for worsening RD (%)	30.4	40.7	15.8	0.07
Length hospital stay (days)	11.8±10.9	12.06±9.6	11.7±11.8	0.65
Length critical care unit stay (days)	5.87±6.8	6.9±7.2	5.1±6.5	0.24

CPAP: continuous positive airway pressure; HFNC: high flow nasal cannula; RD: respiratory distress; NIPPV: noninvasive positive-pressure ventilation.

## Conflicts of interest

None declared.

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