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Safety and efficacy of high flow nasal canula in patients with mild hypercapnia

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Abstract

Context High flow nasal canula is usually used for management of acute hypoxemic failure; however, it may have a potential therapeutic benefits in hypercapnia as it can alter tidal volume, end expiratory volume, positive end expiratory pressure, and respiratory rate.

Aim Evaluate safety and efficacy of application HFNC (high flow nasal canula) for patients with mild hypercapnia.

Settings and design A prospective interventional study.

Patients and methods Over six months, thirty eight patients were enrolled, with mild hypercapnia and PH level not less 7.30 and PaCo2 not more 60 mmhg; with applying HFNC, serial checking of arterial blood gases was done. Checkpoints were at 2 h, 12 h, 24 h, and 48 h post application of HFNC. HFNC can be shifted to NIV or invasive MV at any time whenever indicated.

Results Primary pulmonary disorder was chronic obstructive pulmonary disorder in (22 patients) and (16 patients) had interstitial lung disease. For PH in overall, mean values had changed from 7.33 until reached 7.37 at 48 h post HFNC with calculation of *P* value at each checkpoint from baseline value; significant changes were recorded at 24 h and 48 h post HFNC application. A similar observation was observed for PaCO2. No significant changes were observed at any checkpoint for HCO3.

Conclusion High flow nasal canula is safe in cases with mild hypercapnia with a considerable success rate and a proven high efficacy.

Trial registration Clinicaltrials.gov/NCT05948527, Registered 14 July 2023—Retrospectively registered, https://www.clinicaltrials.gov/NCT05948527.

Keywords High flow nasal canula, Hypercapnia, COPD, ILD

Introduction

Hypercapnia refer to an elevated blood partial pressure of carbon dioxide (PaCo2) more than 45 mmHg while Type 2 respiratory failure is best defined by elevated PaCo2 more than 45 mmHg with lowered PH below 7.35 while partial pressure of oxygen is low or normal [1], best diagnosed by ABGA (arterial blood gases analysis) as it allows for evaluation of PH status, serum CO2, serum HCO3and an anion gap can be calculated to determine if acidosis either metabolic or respiratory [2], it can result from pulmonary and non-pulmonary etiologies (refer to central neurogenic, cardiogenic and others) [3], sub typed into acute and chronic based on duration and renal compensation for HCO3, also sub typed into mild, moderate, severe [4, 5]. Mild hypercapnia is noted when CO_2 partial pressure is up to 55–60 mmHg, moderate hypercapnia as $PaCO_2$ levels between the range of 60 to 70 mmHg, Levels higher than 70 mmHg are generally regarded as severe hypercapnia [6, 7]. High $paCO_2$ levels

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have been identified as an indicator of severe respiratory fatigue and impending cardiopulmonary arrest [8], hence, the need for different and efficient rapid tools for management and early correction. Traditional management of hypercapnia includes noninvasive ventilation or invasive mechanical ventilation [9], Endo-tracheal intubation (ETI) is associated with a wide range of complications, including ventilator-associated pneumonia (VAP). Every day, the intubated patient has a 1% risk of developing VAP, resulting in increased morbidity and mortality [10, 11]. NIV has a limitation due to claustrophobia and other mask-related complication [12]. High flow nasal canula (HFNC) is a relatively new oxygen system enable delivery of high flow humidified (31 to 37 °C) and heated oxygen up to 100% fio2, and a flow rate up to sixty liters per minute [13]. It allows a great flow control with many useful physiological impacts including increased tidal volume, increased end-expiratory volume, positive end-expiratory pressure (PEEP), control and reduce respiratory rate [14], and decrease upper and lower respiratory physiological dead space (accounts for one third of tidal volume) therapy increasing the washout of waste gases including carbon dioxide [15]. The high flow rates involved in high-flow nasal canula delivers volumes of air over what a patient ventilates physiologically, which increases ventilation and allows for displacement of excess CO2 [16]. HFNC therapy is usually used to manage hypoxemic respiratory failure (AHRF) without hypercapnia therapy decrease the need for invasive tracheal intubation compared to other low flow conventional oxygen therapies [17]. Several studies have reported that HFNC therapy might also be helpful in hypercapnic patients with underlying chronic lung diseases [18]. The aim of this study was to evaluate safety and efficacy of application of high flow nasal canula in cases with mild hypercapnia. The study protocol was approved by the Institutional Research Board (IRB), Mansoura University, and Proposal Code: R.22.12.1978.R1.R2.

Subjects and methods

We conducted a prospective study over 6 months (from January 2023), which included 38 patients who were hospitalized in Mansoura University chest department with mild Hypercapnia (PaCo2 range 45–60 mmhg and PH not less 7.30) of two different pulmonary disease categories (chronic obstructive pulmonary disease acute exacerbation, interstitial lung diseases). Excluded cases had age less than 18 years or pediatric group; also, patients with their mental state altered, confused, comatose, severe agitation or noncooperative were excluded. Cases with moderate or severe hypercapnia were also excluded since only few studies handled the topic of HFNC in hypercapnia; we only enrolled mild cases to build an initial experience. We also excluded cases in need for immediate invasive mechanical ventilation or cases with respiratory rate more than 35 breaths per minute. Respiratory exhaustion, fatigue, excess use of respiratory accessory muscles Shock, hemodynamic instability, post arrest cases, cases with facial trauma or severe nasal deformity, Patients with sleep breathing disorders or upper airway obstruction and patients with history of home ventilation prior admission were another factors for exclusion. Enrolled cases were supposed to full history taking and clinical evaluation, basic ABG analysis at emergency level, or at admission with basic evaluation of oxygen saturation at room air and administration of HFNC at initial flow 35 L per minute and Fio2 (fraction of inspired oxygen of 50%) with titration to reach oxygen saturation of 88–92%. The used device was Vapotherm Precision Flow Hi-VNI (Precision Flow, Vapotherm, Exeter, NH, USA). Then, there is a follow-up ABG at 2 h, 12 h, 24 h, and 48 h post application of HFNC. Also, additional ABG analysis was done whenever indicated. Continuous monitoring of mental state, respiratory rate, work of accessory muscles, hemodynamic, and other clinical parameters was applied. Decision about continual of HFNC or not was after 24 h and 48 h post application of HFNC. HFNC can be shifted to NIV or invasive MV at any time whenever indicated. HFNC use was only continued as long as PH did not drop below 7.25 or drop $\geq$ 0.2 from baseline in PH. Discontinued use was also arranged if rise of PaCo2 $\geq$ 10 mmhg more than previous analysis, increased respiratory rate $\geq$ 35bpm or any situation with clinical worsening even with less ABG deterioration. Patients were considered weanable from HFNC if they show clinical stability with spontaneous breathing with an oxygen flow $\leq$ 6 L/min via a nasal canula for $\geq$ 48 h after stopping HFNC therapy. The primary outcome was concerned about changes in ABG (PH, PaCo2, HCO3) in first 24 h after admission and the same changes 48 h after admission. Secondary outcome was concerned about need to noninvasive mechanical ventilation or invasive mechanical ventilation. Prognosis was either success or failed in cases needed noninvasive mechanical ventilation or invasive mechanical ventilation and in mortality cases. Variables of demographic, clinical, follow-up, and prognosis data were analyzed.

Statistical analysis

The demographic, clinical, and laboratory data gathered together were tabulated and statistically analyzed. The statistical analysis of data was carried out using excel and the SPSS programs statistical package for AQ8 social science, version 17. The quantitative data were described as

median (minimum–maximum). An analysis of the data was carried out to test statistically significant differences between groups. Quantitative data were presented as mean ± SD, and the Student *t*-test was used to compare two groups.

Ethics approval and consent to participate

The study protocol has been approved by the Institutional Research Board, Faculty of Medicine, Mansoura University, with the proposal code: R.22.12.1978.R1.R2. Precautions were used to protect participants' privacy as patients were given the option to participate or not; also, the study findings were exclusively used for scientific purpose. Personal data were hidden from any public use.

Results

A) Basic data before application of high flow nasal canula

Study enrolled 38 patients with mild hypercapnia; with their age mean 59.37 ± 6.68 SD, the majority were males 73.6%. Their primary pulmonary disorder was chronic obstructive pulmonary disorder in (22 patients); the rest of them (16 patients) had interstitial lung disease. Basic demographics, co-morbid disorders, and baseline parameters of overall included patients and of their two different categories are illustrated in Table 1.

The most common comorbid disorder was hypertension followed by diabetes mellitus (Table 1).

Table 2 included patients with mild hypercapnia and PH ranged (from 7.30 to7.48).

Table 1 Demographic data, comorbidities, and basic parameters

Parameter	Overall patients	Category with COPD	Category with ILD
Age (years) (mean ± SD)	59.37 ± 6.68	61.04 ± 6.13	57.06 ± 6.91
Gender *N* (%)			
• **Male**	28 (73.6%)	18 (81.8%)	10 (62.5%)
• **Female**	10 (26.4%)	4 (18.2%)	6 (37.5%)
BMI (mean ± SD)	24.6 ± 2.68	24.45 ± 3.17	24.84 ± 1.87
Smoking *N* (%)			
• **Smoker**	24 (63.2%)	20 (90.9%)	4 (25%)
Comorbidities			
• **Hypertension**	22 (57.9%)	14 (63.6%)	8 (50%)
• **Diabetes mellitus**	18 (47.4%)	12 (54.5%)	6 (37.5%)
• **Ischemic heart disease**	16 (42.1%)	10 (45.5%)	6 (37.5%)
• **Chronic liver disease**	5 (13.2%)	2 (9%)	3 (18.7%)
• **Chronic kidney disease**	5(13.2%)	4(18.2%)	1(6.3)
• **Hypothyroidism**	2(5.3%)	1(4.5%)	1(6.3%)
Basic parameters			
• **Oxygen saturation at admission (%)**	79 ± 6	78.3 ± 5.8	80 ± 6.2
• **Respiratory rate**	25 ± 2	24.9 ± 1.8	25.1 ± 2.3
• **Heart rate**	98 ± 3.4	100 ± 2.4	96 ± 4.7

Values are presented as number (%) or mean ± standard deviation

COPD Chronic obstructive pulmonary disorder, *ILD* Interstitial lung disease

Table 2 Analysis of blood gases before application of high flow nasal canula

Parameter (mean ± SD)	Overall patients	Category with COPD	Category with ILD
• **PH**	7.33 ± .043	7.32 ± .040	7.34 ± .046
• **PCO2 (mmhg)**	55.72 ± 3.24	56.81 ± 2.95	54.23 ± 3.08
• **HCO3 (meq/L)**	28.00 ± 4.15	28.18 ± 4.32	27.87 ± 4.12

PH Power of hydrogen, *PaCo2* Partial pressure of carbon dioxide, *HCO3* Bicarbonate, *COPD* Chronic obstructive pulmonary disorder, *ILD* Interstitial lung disease

B) Application of high flow nasal canula

Initial settings of HFNC are shown in Table 3.

C) Data interpretation after application of high flow nasal canula (analysis of follow-up arterial blood gases)

In Table 4, serial analysis of arterial blood gases was done (2 h, 12 h, 24 h, and 48 h) after application of high flow nasal canula. For PH, mean values had changed from 7.33 at 2 h post HFNC until it reached to 7.37 at 48 h post HFNC with calculation of *P* value at each checkpoint from baseline value; significant changes were recorded at 24 h and 48 h post HFNC application with nonsignificance observed at 2 h and 12 h checkpoints. A similar observation was observed for PaCO2. No significant changes were observed at any checkpoint for HCO3.

At 2-h checkpoint and at 12-h checkpoint, no significant changes were found in ABG parameters.

At 24-h checkpoint, significant changes in PH and Paco2 were found in category of interstitial lung disease.

At 48-h checkpoint**,** both categories showed significant changes in PH and Paco2 (Table 5).

D) Outcome and prognosis

Favorable outcome was achieved in most of cases (81.6%); results were better in ILD category but were significantly different only in days of hospital stay (*p* value: 0.04) and ICU days (*p* value: 0.04). Other outcome parameters were comparable in both disease categories without significant differences (Table 6).

Discussion

This study was concerned about use of HFNC in mild hypercapnia as a new area for indication rather than its classical indication in management of acute hypoxemic respiratory failure. The rationale was based on its potential physiological impact over tidal volume, end expiratory volume, PEEP, and respiratory rate [14, 15]. We applied our trial over cases with mild hypercapnia of two different categories of pulmonary diseases (chronic obstructive pulmonary disease and interstitial lung diseases with acute exacerbations); this was in accordance to the most related literature. In the same time window, other cases from other categories (pneumonia, pulmonary edema, etc.) were admitted, but only the small number of them was fulfilling our selection criteria, so we focused over COPD and ILD. The primary outcome was

Table 3 Initial settings of high flow nasal canula

Parameter (mean ± SD)	Overall patients	Category with COPD	Category with ILD
• **Flow (L/m)**	35 ± 4.7	35.9 ± 4.2	33.7 ± 5.3
• **Fio2 (%)**	38.7 ± 11.6	38.1 ± 8.3	39.3 ± 5.37

Fio2 (%) fraction of inspired oxygen, *COPD* chronic obstructive pulmonary disorder, *ILD* interstitial lung disease

Table 4 Analysis of follow-up arterial blood gases (overall cases)

Parameter (mean ± SD)	Time of follow-up	Overall patients	*P* value (change from baseline value)
• **PH**	After 2 h	7.33 ± 045	.401
• **PCO2 (mmhg)**	After 2 h	55.55 ± 3.31	.193
• **HCO3 (meq/L)**	After 2 h	28.05 ± 4.08	.725
• **PH**	After 12 h	7.33 ± 048	.613
• **PCO2 (mmhg)**	After 12 h	55.21 ± 5.58	.534
• **HCO3 (meq/L)**	After 12 h	27.94 ± 3.99	.696
• **PH**	After 24 h	7.34 ± .056	**.003**[a]
• **PCO2 (mmhg)**	After 24 h	52.82 ± 6.29	**.001**[a]
• **HCO3 (meq/L)**	After 24 h	28.22 ± 4.11	.189
• **PH**	After 48 h	7.37 ± .042	**.001**[a]
• **PCO2 (mmhg)**	After 48 h	48.71 ± 2.86	**.001**[a]
• **HCO3 (meq/L)**	After 48 h	28.09 ± 3.40	.831

PH Power of hydrogen, *PaCo2* Partial pressure of carbon dioxide, *HCO3* Bicarbonate

[a] Significant values

Table 5 Analysis of follow-up arterial blood gases (different disease categories)

Parameter (mean ± SD)	Time of follow-up post HFNC	Category with COPD	*P* value (from baseline value)/ COPD	Category with ILD	*P* value(change from baseline value)/ILD
PH	After 2 h	7.32 ± .041	.418	7.34 ± .050	.751
PCO2 (mmhg)	After 2 h	56.47 ± 2.99	.073	54.28 ± 3.41	.760
HCO3 (meq/L)	After 2 h	27.7 ± 4.02	0.256	27.7 ± 4.02	.211
PH	After 12 h	7.32 ± .043	.405	7.34 ± .054	.902
PCO2 (mmhg)	After 12 h	55.63 ± 4.81	.108	54.62 ± 6.62	.821
HCO3(meq/L)	After 12 h	28 ± 4.19	.467	28 ± 4.19	.088
PH	After 24 h	7.33 ± .057	.103	7.36 ± .050	**.006**[a]
PCO2 (mmhg)	After 24 h	54.57 ± 7.09	.119	50.21 ± 3.70	**.001**[a]
HCO3 (meq/L)	After 24 h	28.1 ± 4.5	.218	28.1 ± 4.5	0.21
PH	After 48 h	7.37 ± .041	**.001**[a]	7.38 ± .045	**.001**[a]
PCO2 (mmhg)	After 48 h	49.77 ± 2.55	**.001**[a]	47.35 ± 2.73	**.001**[a]
HCO3 (meq/L)	After 48 h	28.1 ± 3.8	0.532	28.1 ± 3.8	0.53

HFNC High flow nasal canula, *PH* Power of hydrogen, *PaCo2* Partial pressure of carbon dioxide, *HCO3* Bicarbonate

[a] Refer to significant values

Table 6 Outcome among studied patients

Parameter	Overall patients	Category with COPD	Category with ILD
• **Need for noninvasive ventilation** *N* (%)	6 (15.8%)	4 (18.2%)	2 (12.5%)
• **Need for invasive ventilation** *N* (%)	5 (13.2%)	3 (13.6%)	2 (12.5%)
• **HFNC success** *N* (%)	31 (81.6%)	17 (77.3%)	14 (87.5%)
• **HFNC failure** *N* (%)	7 (18.4%)	5 (22.7%)	2 (12.5%)
• **Survival** *N* (%)	34 (89.5%)	20 (90.9%)	14 (87.5%)
• **Days on HFNC** (mean ± SD)	4 (0.5–10)	4.5 (0.5–10)	4 (0.5–9)
• **ICU stay (days)** (mean ± SD)	5 (3–10)	5.5 (3–12)	4 (4–7)
• **Hospital stay (days)** (mean ± SD)	6 (4–14)	7 (4–14)	6 (5–10)

HFNC High flow nasal canula, *ICU* Intensive care unit, *COPD* Chronic obstructive pulmonary disorder, *ILD* Interstitial lung disease

concerned about measurement the efficacy for HFNC in achieving changes in ABG analysis at 24-h and 48-h checkpoints. For PH and Paco2, significant changes were recorded at 24 h and 48 h post HFNC application (proven efficacy). With subgrouping cases and regarding ABG, at 24-h checkpoint, significant changes in PH and Paco2 were found in category of interstitial lung disease, while at 48-h checkpoint, both categories showed significant changes in PH and Paco2. More larger studies are needed to prove and explain that difference; however, different pathologies may exhibit different course in response to therapeutic interventions.

On reviewing literature for similar clinical trials, Su et al. [19] studied 106 patients with mild hypercapnia ($45 < PaCO2 \leq 60$ mmHg) received HFNC, in comparison to matched group received NIV, concluded No significant difference in 48-h intubation rate between the HFNC group (the treatment group) and the NIV group (the control group) (14.2% vs. 8.5%, $p = 0.278$), but NIV was superior in other parameters (28-day intubation rate, ICU length of stay). Another study done by Nam et al. [20] applied HFNC over 42 cases with mild to moderate hypercapnia, Paco2 up to 70 mmhg, with their primary pulmonary disorders (pneumonia 23 cases (48.9%), pulmonary edema 15 cases (33.3%), COPD exacerbation 12 cases (26.7%), atelectasis 6 cases (13.3%)) and concluded that after applying HFNC, an overall decrease in PaCO2 with pH correction was seen. Most of their subjects were treated successfully; however, they documented a very early significant changes in PH and Paco2 at 1st hour checkpoint which is too early than what documented in our study; also, they grouped cases into obstructive (COPD or bronchial asthma) and nonobstructive with analysis of differences in PaCo2 changes; a significant decrease of PaCO2 was also found in the non-obstructive group, while in the obstructive group, changes were

not statistically significant. Sun et al. [21] applied HFNC with 39 cases with COPD and mild hypercapnia and concluded that the use of HFNC compared with NIV did not result in increased rates of treatment failure. Papachatzakis et al. [22] investigated HFNC with 40 cases and suggest that HFNC could be an alternative treatment of hypercapnic respiratory failure, especially when NIV is not well tolerated. Also, Yuste et al. [2] enrolled 35 patients who received HFNC, and the study demonstrated that high-flow nasal cannula therapy is effective in improving clinical and gas exchange parameters in patients with moderate hypercapnic respiratory failure, with an acceptable rate in nonresponders who required ventilatory support. A study done by Golmohamad et al. [23] demonstrated efficacy of HFNC as initial treatment option for patients presenting with mild acute hypercapnic respiratory failure, who are non-obese and do not have sleep disordered breathing. Cortegiani et al. [24] studied HFNC versus NIV as an initial ventilatory strategy in COPD with acute exacerbation with a conclusion of non-inferiority of HFNC to NIV as an initial ventilatory support in decreasing PaCO2 after 2 h of treatment in patients with mild-to-moderate acute exacerbated COPD. Also Pisani et al. [25] concluded that clinical data for application of HFNC in COPD exacerbation are increasing over time; there are still some unanswered questions regarding practical aspects of its use.

Our study is matched with most of these mentioned trials in demonstrating HFNC safety and efficacy but with slight differences that may due to different sample sizes and/or different disease categories.

Limitations

Limited number of patients and limited categories of included pulmonary diseases. Our study lacks a detailed description about type of exacerbations in included patients; however most of similar articles have the same limitation.

Conclusion

High flow nasal canula is safe in cases with mild hypercapnia with a considerable success rate and high efficacy.

Abbreviations

PaCo2	Partial pressure of carbon dioxide
ICU	Intensive care unit
NIV	Noninvasive ventilation
HFNC	High-flow nasal canula
BMI	Body mass index
CT scan	Computed tomography scan
DM	Diabetes mellitus
COPD	Chronic obstructive pulmonary disease
CKD	Chronic kidney disease
CVD	Cardiovascular diseases
CXR	Chest X-ray
ABGA	Arterial blood gases analysis
PH	Power of hydrogen
AHRF	Acute hypoxemic respiratory failure
ILD	Interstitial lung disease
PEEP	Positive end expiratory pressure
VAP	Ventilator-associated pneumonia

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Authors' contributions

Design and conception by MAI, ME, and MS; data gathering by MAI and MS; statistical analysis by ME and MS; and medical writing by MAI. The manuscript was revised by the authors. The writers reviewed the final manuscript and gave their approval.

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Availability of data and materials

The author may be contacted for reasonable requests on the datasets utilized and/or analyzed in the present study.

Declarations

Ethics approval and consent to participate

The study protocol has been approved by the Institutional Research Board, Faculty of Medicine, Mansoura University with the proposal code: R.22.12.1978.R1.R2. Precautions were used to protect participants' privacy as patients were given the option to participate or not; also, the study findings were exclusively used for scientific purpose. Personal data were hidden from any public use.

Consent for publication

Not applicable.

Competing interests

There are no conflicts of interest.

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