Original Article Analysis of therapeutic effects on type II respiratory failure and impact on blood gas changes: high-flow nasal oxygen therapy vs. non-invasive positive pressure ventilation

Yongping Liu^{1*}, Ning Liu^{2*}, Ying Li³, Lixiu Nie⁴, Lin Li⁴

¹Department of Internal Medicine, Xi'an International Medical Center Hospital, No. 777 Xitai Road, Chang'an District, Xi'an 710000, Shaanxi, China; ²Department of Cardiovascular Medicine, Urumqi Friendship Hospital, No. 558 Shengli Road, Tianshan District, Urumqi 830049, The Xinjiang Uygur Autonomous Region, China; ³Department of General Medicine, Xi'an International Medical Center Hospital, No. 777 Xitai Road, Chang'an District, Xi'an 710000, Shaanxi, China; ⁴Department of Respiratory and Critical Care Medicine, The Second People's Hospital of Lanzhou City, No. 388 Jingyuan Road, Chengguan District, Lanzhou 730046, Gansu, China. *Equal contributors.

Received November 7, 2023; Accepted January 17, 2024; Epub February 15, 2024; Published February 28, 2024

Abstract: Objective: To evaluate the efficacy of high-flow nasal oxygen therapy (HFNO) vs. non-invasive positive pressure ventilation (NIPPV) in type II respiratory failure, and analyze their impact on blood gas parameters. Methods: A retrospective analysis of 110 cases of type II respiratory failure treated from April 2021 to March 2023 categorized patients into control (NIPPV, n=50) and observation (HFNO, n=60) groups. Both groups received comprehensive nursing interventions. Treatment outcomes, respiratory and hemodynamic parameters, blood gas parameters, and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores were compared before and 48 hours after treatment. Additionally, the complication rates and independent risk factors affecting prognosis were analyzed. Results: The observation group exhibited superior treatment efficacy compared to the control group (P=0.001). Both groups showed significant improvements in APACHE II scores and respiratory, hemodynamic, and blood gas parameters after treatment (P<0.001), with the observation group experiencing more pronounced improvements (P<0.001). The observation group also had a lower incidence of complications than the control group (P=0.013). Logistic regression identified PaC0₂ and treatment protocol as independent risk factors affecting adverse outcomes (P<0.05). Conclusion: HFNO demonstrates superior therapeutic efficacy in type II respiratory failure, significantly improving blood gas parameters with a high level of safety, supporting its clinical applicability.

Keywords: High-flow nasal oxygen therapy, non-invasive positive pressure ventilation, type II respiratory failure, therapeutic effects, blood gas parameters

Introduction

Acute respiratory failure is a multifaceted syndrome resulting from severe impairment of pulmonary ventilation and/or gas exchange attributed to diverse underlying factors [1]. Patients manifesting concurrent carbon dioxide retention are classified as type II respiratory failure, commonly denoted as hypercapnic respiratory failure [2]. Diagnostic criteria for type II respiratory failure include an arterial oxygen partial pressure (PaO₂) below 60 mmHg and an arterial carbon dioxide partial pressure (PaCO₂) exceeding 50 mmHg. This disease is characterized by a rapid onset, swift progression, and a notably high mortality rate, significantly impacting patient survival [3, 4]. Consequently, prompt and efficacious interventions are imperative in the management of type II acute respiratory failure, with the goal of alleviating clinical symptoms and reducing mortality.

Non-invasive ventilation is presently the predominant method in clinical practice to assist ventilation in patients with such condition. Nevertheless, it has certain limitations [5], including challenges, such as the absence of airway control, restricted ventilation pressure, complexities in sustaining an airtight airway, insufficient airway humidification and drainage, inadequate monitoring devices, the potential risk of aspiration, facial pressure injuries resulting from respiratory masks, and patient anxiety [6]. Consequently, the quest for novel ventilation assistance methods has emerged as a substantial challenge in clinical practice for the management of these patients.

In recent years, advancements in medical technology have led to the gradual incorporation of high-flow nasal oxygen (HFNO) in the management of acute respiratory failure. HFNO, a technique delivering humidified and heated oxygen through nasal cannulas, ensures a consistent oxygen concentration and enhances respiratory function in patients [7, 8]. Globally, HFNO has become a prevalent ventilation method in clinical practice [9]. While HFNO is gaining traction in China, comprehensive efficacy assessment data in patients remain relatively limited.

The primary aim of this study is to observe the therapeutic effects of HFNO and non-invasive positive pressure ventilation (NIPPV) in patients with type II respiratory failure and to assess their impact on blood gas parameters, so as to provide further insights into treatment options for type II respiratory failure.

Materials and methods

Clinical data

A retrospective analysis was conducted on 110 patients with type II respiratory failure treated at Xi'an International Medical Center Hospital between April 2021 and March 2023. Patients were stratified into two groups based on treatment plans: the control group (n=50) received NIPPV, and the observation group (n=60) received HFNO. Inclusion criteria: (1) Patients who met relevant diagnostic criteria for type II respiratory failure [2]; (2) Patients with good compliance and clear consciousness; (3) Patients with complete clinical data; (4) Patients who received NIPPV or HFNO with post-treatment outcome assessment. Exclusion criteria: (1) Patients with coagulation disorders; (2) Patients with significant organ dysfunction (e.g., liver or kidney impairment); (3) Patients with severe infectious diseases or immunodeficiency; (4) Pregnant or lactating women; (5) Patients with contraindications to the treatment regimens. This study obtained approval from ethics committee of Xi'an International Medical Center Hospital and adheres to the principles of the Helsinki Declaration. The research flow chart is shown in **Figure 1**.

Treatment methods

Upon admission, all patients received standard treatment for their underlying primary diseases, coupled with mucolysis, anti-infective, and bronchodilator therapies. In the control group, patients underwent non-invasive ventilation utilizing the MAQUET SERVO-S ventilator from Shanghai Pumow Medical Equipment Co., Ltd. The ventilator operated in synchronized/timed mode, delivering positive pressure ventilation through an oronasal mask. Initial parameters were set as follows: expiratory pressure of 4-6 cmH₂O (1 cmH₂O = 0.098 kPa), inhaled oxygen concentration of 30-50%, respiratory rate of 14-18 breaths/min, expiratory pressure of 10-12 cmH_oO, inspiratory-to-expiratory ratio of 1:(1.5-2), and pressure rise time of 0.5-1.0 seconds.

The patients in the observation group received HFNO using the Maismart HUMID-BM device (manufactured by Shenyang Maismart Medical Technology Co., Ltd.). The initial temperature setting was 34-37°C, and the inhaled oxygen concentration and flow rate were determined following the parameters in the control group. The inhaled oxygen concentration was continuously adjusted to maintain SpO, at or above 92%. If the patient's respiratory status remained stable, the oxygen flow rate was reduced to 20 L/min, and simultaneously, the inhaled oxygen concentration was adjusted to 26-30%. Oxygen was delivered via nasal cannula to maintain SpO, at or above 92% for a minimum of 12 hours.

Primary observation indicators

(1) Assessment of treatment efficacy: The treatment efficacy was evaluated and compared between the two groups. Patients were categorized into the following groups based on their response to treatment: markedly effective (significant alleviation of respiratory failure symptoms with all vital signs recovered to normal), effective (symptomatic relief with vital signs



Figure 1. Research flow chart.

showing improvement), and ineffective (patient's condition showed no improvement, persisted in progression, or even resulted in fatality despite the treatment). The overall response rate was calculated as the sum of marked improvement and improvement cases divided by the total number of cases, multiplied by 100%. (2) Arterial blood gas analysis: Arterial blood samples (5 mL) were collected from patients before and 48 hours after treatment. Arterial blood gas parameters, including PaO_2 , $PaCO_2$, and pH value, were measured using an automated blood gas analyzer.

Secondary observation indicators

(1) Vital signs: The respiratory rate, heart rate, and mean arterial pressure (MAP) were evaluated and compared before and 48 hours after treatment in both groups. (2) Acute Physiology and Chronic Health Evaluation II (APACHE II) score [10]: Within 24 hours of admission and 72 hours post-treatment, the APACHE II score was assessed, and the acute physiological and chronic health status of patients were compared. A higher score indicates a more severe condition and a higher predicted mortality. (3) Complications: Incidence of complications during the treatment period was recorded. Complications included gastric distension, nasal bleeding, aspiration, and facial pressure injuries. (4) Prognostic analysis: Patients were divided into a good prognosis group and a poor prognosis group based on whether they experienced treatment failure or death. Logistic regression analysis was used to identify independent risk factors affecting patient prognosis.

Statistical analysis

Excel tables were used to collect data from the hospital case database. SPSS 20.0 software and GraphPad Prism 8 software were employed for data processing, analysis, and visualization. Descriptive statistics for continuous data were presented as mean \pm SD. Between-group comparisons were conducted using independent samples t-tests, while within-group comparisons using paired t-tests. Categorical data were expressed as percentages (%) and processed using the chi-square test. A significant level was set at P<0.05.

Variable	Observation group n=60	Control group n=50	X ²	Р	
Gender			0.011	0.917	
Male	33 (55.00)	27 (54.00)			
Female	27 (45.00)	23 (46.00)			
Age (years)			0.005	0.944	
≥52	32 (53.33)	27 (54.00)			
<52	28 (46.67)	23 (46.00)			
Body mass index (kg/m²)			0.642	0.423	
≥23	29 (48.33)	28 (56.00)			
<23	31 (51.67)	22 (44.00)			
Smoking history			0.185	0.667	
Yes	36 (60.00)	32 (64.00)			
No	24 (40.00)	18 (36.00)			
Hypertension			0.019	0.889	
Yes	28 (46.67)	24 (48.00)			
No	32 (53.33)	26 (52.00)			
Range of disease course (d)	8.35±1.13	8.27±0.86	0.999	0.000	
APACHE II	16.4±0.58	16.32±0.59	0.715	0.476	

Table 1. Comparison of general data

APACHE II, Acute Physiology and Chronic Health Evaluation II.

Table 2. Comparison	of treatment efficacy between	the two groups [n (%)]
---------------------	-------------------------------	------------------------

Efficacy	Observation group n=60	Control group n=50	X ²	Р
Markedly effective	42 (70.00)	27 (54.00)	0.070	0.791
Effective	16 (26.67)	11 (22.00)		
Ineffective	2 (3.33)	12 (24.00)		
Overall response rate	58 (96.67)	38 (76.00)	10.49	0.001

Results

Comparison of general data

There were no significant differences between the two groups in terms of gender, age, body mass index, and other baseline characteristics (P>0.05), as shown in **Table 1**.

Comparison of clinical efficacy

The overall response rate in the observation group was 96.67%, which was significantly higher than 76.00% in the control group, with a statistically significant difference (P=0.001). See **Table 2** for more details.

Comparison of vital signs

Before treatment, there was no statistically significant difference in the respiratory rate, heart rate, and MAP between the two groups (P>0.05). However, 48 hours after treatment, both groups showed a significant reduction in respiratory rate and heart rate, and a notable increase in MAP. Importantly, the improvements in the observation group were more pronounced compared to those in the control group (P<0.001). See **Figure 2**.

Comparison of blood gas parameters

Before treatment, there was no statistically significant difference in the PaO_2 , $PaCO_2$, and pH values between the two groups (P>0.05). After treatment, the $PaCO_2$ of the two groups were lower, and the PaO_2 and pH values were higher than those before treatment in both groups, with statistical significance (P<0.001). Moreover, the improvements in the observation group were more significant than those in the control group (P<0.001). See **Figure 3**.

Analysis of the therapeutic effect of type II respiratory failure



Comparison of APACHE II scores

Before treatment, there was no statistically significant difference in the APACHE II scores between the two groups (P>0.05). After treatment, the APACHE II scores were significantly reduced in the two groups, but the reduction in the observation group was more obvious than that in the control group (P<0.001). See **Figure 4**.

Comparison of the incidence of adverse reactions

The incidence rate of adverse reactions in the observation group was 8.33%, which was significantly lower than 26.00% in the control group, and the difference was statistically significant (P=0.013). See **Table 3**.

Analysis of factors affecting patient prognosis

Based on patients' outcomes, they were divided into a group with a good prognosis (80

cases) and a group with a poor prognosis (40 cases). Univariant analysis revealed that age, $PaCO_2$, and treatment program were factors affecting patient prognosis (**Table 4**). Subsequently, logistic regression analysis identified $PaCO_2$ and the treatment plan as independent risk factors for adverse patient outcomes (**Table 5**, P<0.001).

Discussion

Studies have demonstrated that the onset of type II respiratory failure not only induces respiratory dysfunction, impacting blood gas analysis parameters, but also exacerbates local inflammatory responses due to ineffective secretion clearance. This leads to the persistent accumulation of endogenous pulmonary secretions, resulting in local atelectasis and an increased risk of deteriorating lung function [11, 12]. Hence, a key clinical challenge is how to effectively address type II respiratory failure, enhance respiratory function, regulate blood

Analysis of the therapeutic effect of type II respiratory failure



Figure 4. Comparison of APACHE II scores between the two groups before and after treatment. * indicates P<0.05. APACHE II, Acute Physiology and Chronic Health Evaluation II.

gas analysis parameters, and facilitate the recovery of pulmonary function in patients.

eral advantages. It allows oxygen humidifica-

patient cooperation but is associated with

potential complications, such as gastrointesti-

nal distention. Clinical reports also suggest

that it is associated with an increased risk of anxiety and depression [14]. HFNO, a relatively recent auxiliary ventilation method, offers sev-

Adverse reactions	Observation group n=60	Control group n=50	X ²	Ρ
Bloating	2 (2.17)	3 (7.5)	0.447	0.504
Nasal bleeding	2 (4.38)	3 (7.5)	0.447	0.504
Aspiration	1	6 (10.00)	4.887	0.027
Facial pressure injury	0	1 (2.5)	1.211	0.271
Overall incidence of adverse reactions	5 (8.33)	13 (26.00)	6.220	0.013

Table 3.	Comparison	of adverse	reaction rates
10.010 01	oompanoon	01 00100	10000101110000

Factor	Good prognosis group (n=75)	Poor prognosis group (n=35)	t/X²	Ρ
Gender			0.140	0.709
Male (n=60)	40 (53.33)	20 (57.14)		
Female (n=50)	35 (46.67)	15 (42.86)		
Age (years)			6.535	0.011
≥52 (n=59)	34 (45.33)	25 (71.43)		
<52 (n=51)	41 (54.67)	10 (28.57)		
Body mass index (kg/m²)			1.376	0.241
≥23 kg/m² (n=57)	36 (48.00)	21 (60.00)		
<23 kg/m² (n=53)	39 (52.00)	14 (40.00)		
Smoking history			0.330	0.566
Yes (n=68)	45 (60.00)	23 (65.71)		
No (n=42)	30 (40.00)	12 (34.29)		
PaCO ₂	8.03±0.77	9.61±0.82	9.215	<0.001
Hypertension			0.401	0.526
Yes (n=52)	37 (49.33)	15 (42.86)		
No (n=58)	38 (50.67)	20 (57.14)		
Treatment programs			33.56	< 0.001
Non-invasive positive pressure ventilation therapy (n=50)	20 (26.67)	30 (85.71)		
Nasal high flow oxygen therapy (n=60)	55 (73.33)	5 (14.29)		

PaCO₂, arterial carbon dioxide partial pressure.

Table 5. Multivariate analysis

Variable	B S	° E	Wald	Р	RR -	95% C.I.	
		5.E.				Lower limit	Upper limit
PaCO ₂	0.231	0.072	2.982	0.033	1.083	1.461	1.263
Treatment programs	0.514	0.093	2.964	0.015	1.637	1.318	1.973

PaCO₂, arterial carbon dioxide partial pressure.

tion and heating for patient comfort, significantly improving respiratory mucociliary function and facilitating mucus clearance [15]. Moreover, it permits adjustments in inspiratory flow rates based on the patient's oxygen saturation levels, meeting the body's oxygenation needs. Additionally, it aids in clearing physiological dead space in the respiratory system, promoting carbon dioxide removal and rapidly improving hypercapnia [16]. Our study revealed that the treatment outcomes in the observation group were significantly superior to those in the control group. Although both groups showed effective improvements in blood gasrelated parameters compared to their baseline values, the observation group demonstrated more pronounced enhancements compared to the control group. This suggests that, in addressing hypercapnia, HFNO outperforms NIPPV.

For an extended period, NIPPV has been widely utilized in treating hypoxemic respiratory failure due to its numerous advantages. This technique non-invasively delivers oxygen and highflow gas into a patient's airway to assist in improving ventilation. By providing an adequate oxygen concentration, NIPPV enhances the ciliary clearance function of the airway mucosa, efficiently removing airway secretions. This contributes to adjusting the patient's blood gas parameters and restoring respiratory function [17, 18]. However, NIPPV often involves longer treatment durations and primarily focuses on oxygen supply, with less attention to maintaining oxygen concentration, gas humidity, and temperature, potentially affecting treatment efficacy. In contrast, HFNO is another non-invasive ventilation method, comprising a heated circuit, air blender, and humidifier. This approach subjects the delivered gas to physical heating and humidification before providing it to the patient. While delivering oxygen, this method also supplies gas with humidity and temperature closely resembling those of the human body, facilitating airway humidification, secretion thinning, and clearance. This not only aids in improving inflammatory responses and hypercapnia, but also enhances patient comfort, effectively reducing the incidence of complications and providing substantial benefits for promoting lung function recovery [19, 20].

After comparing adverse reaction rates between the two patient groups, we identified a significantly lower incidence of adverse reactions in the observation group compared to that of the control group, as anticipated. Subsequently, to delve into patient prognosis, we conducted an analysis of factors contributing to unfavorable outcomes. Existing research highlights high PaCO, as an independent risk factor for treatment failure in respiratory failure patients [21]. Our multifactorial logistic regression analysis results underscore high PaCO, and treatment plan selection as independent risk factors for poor patient outcomes. This suggests that controlling blood gas-related parameters during treatment and adjusting treatment plans can mitigate the risk of treatment failure. A prior investigation [22] reported that intolerance resulted in a treatment failure rate of up to 29% in the NIPPV group, while the failure rate in the HFNO group was only 4%, consistent with our observational findings.

In summary, HFNO has a good therapeutic effect on type II respiratory failure, and can significantly improve the patient's blood gas parameters and lung function, with a high safety profile, thereby worthy of clinical promotion. However, this study has certain limitations, such as a relatively small sample size. Although the results remain internally consistent, further validation is warranted. Additionally, the study did not perform subgroup analysis on patients with type II respiratory failure due to different etiologies. Therefore, whether there are efficacy differences of HFNO among patients with type II respiratory failure caused by different etiologies requires further in-depth analysis in subsequent studies.

Disclosure of conflict of interest

None.

Address correspondence to: Lin Li, Department of Respiratory and Critical Care Medicine, The Second People's Hospital of Lanzhou City, No. 388 Jingyuan Road, Chengguan District, Lanzhou 730046, Gansu, China. E-mail: Lilin730046@163.com

References

- Shi T and Feng L. Blood biomarkers associated with acute type II respiratory failure in COPD: a meta-analysis. Clin Respir J 2022; 16: 75-83.
- [2] Xu Z, Zhu L, Zhan J and Liu L. The efficacy and safety of high-flow nasal cannula therapy in patients with COPD and type II respiratory failure: a meta-analysis and systematic review. Eur J Med Res 2021; 26: 122.
- [3] Liu W, Zhu M, Xia L, Yang X, Huang P, Sun Y, Shen Y and Ma J. Transnasal high-flow oxygen therapy versus noninvasive positive pressure ventilation in the treatment of COPD with type II respiratory failure: a meta-analysis. Comput Math Methods Med 2022; 2022: 3835545.
- [4] Wada M, Nagata A, Kawashima A and Kagawa K. An autopsy case of TAFRO syndrome with type II respiratory failure. Am J Case Rep 2020; 21: e926721.
- [5] Osadnik CR, Tee VS, Carson-Chahhoud KV, Picot J, Wedzicha JA and Smith BJ. Noninvasive ventilation for the management of acute hypercapnic respiratory failure due to

exacerbation of chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2017; 7: CD004104.

- [6] Luo F, Annane D, Orlikowski D, He L, Yang M, Zhou M and Liu GJ. Invasive versus non-invasive ventilation for acute respiratory failure in neuromuscular disease and chest wall disorders. Cochrane Database Syst Rev 2017; 12: CD008380.
- [7] Nishimura M. High-flow nasal cannula oxygen therapy in adults: physiological benefits, indication, clinical benefits, and adverse effects. Respir Care 2016; 61: 529-541.
- [8] Ospina-Tascon GA, Calderon-Tapia LE, Garcia AF, Zarama V, Gomez-Alvarez F, Alvarez-Saa T, Pardo-Otalvaro S, Bautista-Rincon DF, Vargas MP, Aldana-Diaz JL, Marulanda A, Gutierrez A, Varon J, Gomez M, Ochoa ME, Escobar E, Umana M, Diez J, Tobon GJ, Albornoz LL, Celemin Florez CA, Ruiz GO, Caceres EL, Reyes LF, Damiani LP and Cavalcanti AB; HiFLo-Covid Investigators. Effect of high-flow oxygen therapy vs conventional oxygen therapy on invasive mechanical ventilation and clinical recovery in patients with severe COVID-19: a randomized clinical trial. JAMA 2021; 326: 2161-2171.
- [9] Zielinska A, Jassem-Bobowicz JM and Kwiatkowska J. Oxygen therapy with high-flow nasal cannulas in children with acute bronchiolitis. Anaesthesiol Intensive Ther 2019; 51: 51-55.
- [10] Shang X and Wang Y. Comparison of outcomes of high-flow nasal cannula and noninvasive positive-pressure ventilation in patients with hypoxemia and various APACHE II scores after extubation. Ther Adv Respir Dis 2021; 15: 17534666211004235.
- [11] Aoki T, Wada M, Kawashima A, Hirakawa K, Nagata A and Kagawa K. Tocilizumab-resistant TAFRO syndrome complicated by type II respiratory failure. Intern Med 2017; 56: 3249-3254.
- [12] Gan Q, Tang D, Yan Q, Chen J, Xu Y, Xue W, Xiao L, Zheng F, Xu H, Fu Y and Dai Y. Differential expression study of lysine crotonylation and proteome for chronic obstructive pulmonary disease combined with type II respiratory failure. Can Respir J 2021; 2021: 6652297.
- [13] Teng W, Chen H, Shi S, Wang Y and Cheng K. Effect of bilevel continuous positive airway pressure for patients with type II respiratory failure due to acute exacerbation of COPD: a protocol for systematic review and meta-analysis. Medicine (Baltimore) 2021; 100: e24016.

- [14] He J, Luo W, Mei Y, Xu Y and Ding S. Nalmefene combined noninvasive positive-pressure ventilation in Chinese patients with chronic obstructive pulmonary disease coupled with type II respiratory failure: a meta-analysis. Medicine (Baltimore) 2023; 102: e34624.
- [15] Yildiz F. The efficacy of lung volume reduction coil treatment in patients with severe chronic obstructive pulmonary disease (COPD) type II respiratory failure. Int J Chron Obstruct Pulmon Dis 2020; 15: 479-486.
- [16] Li XW, Liu LN, Wang F and Wang XD. Emergency treatment and diagnosis of Pompe disease with chronic type II respiratory failure: a case report. Asian J Surg 2022; 45: 1020-1021.
- [17] Sakuraya M, Okano H, Masuyama T, Kimata S and Hokari S. Efficacy of non-invasive and invasive respiratory management strategies in adult patients with acute hypoxaemic respiratory failure: a systematic review and network meta-analysis. Crit Care 2021; 25: 414.
- [18] Hannan LM, Dominelli GS, Chen YW, Darlene Reid W and Road J. Systematic review of noninvasive positive pressure ventilation for chronic respiratory failure. Respir Med 2014; 108: 229-243.
- [19] Lemyre B, Davis PG, De Paoli AG and Kirpalani H. Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for preterm neonates after extubation. Cochrane Database Syst Rev 2017; 2: CD003212.
- [20] Carpenter CR and Steel PAD. In severe COVID-19, high-flow vs. conventional oxygen therapy reduced intubation and time to clinical recovery at 28 d. Ann Intern Med 2022; 175: JC38.
- [21] Storgaard LH, Hockey HU, Laursen BS and Weinreich UM. Long-term effects of oxygenenriched high-flow nasal cannula treatment in COPD patients with chronic hypoxemic respiratory failure. Int J Chron Obstruct Pulmon Dis 2018; 13: 1195-1205.
- [22] Doshi P, Whittle JS, Bublewicz M, Kearney J, Ashe T, Graham R, Salazar S, Ellis TW Jr, Maynard D, Dennis R, Tillotson A, Hill M, Granado M, Gordon N, Dunlap C, Spivey S and Miller TL. High-velocity nasal insufflation in the treatment of respiratory failure: a randomized clinical trial. Ann Emerg Med 2018; 72: 73-83, e75.