

Neurally-Adjusted Ventilatory Assist for Noninvasive Ventilation via a Helmet in Subjects With COPD Exacerbation: A Physiologic Study

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BACKGROUND: In patients with COPD exacerbation, noninvasive ventilation (NIV) is strongly recommended. NIV is generally delivered by using patient triggered and flow-cycled pressure support through a face mask. A specific method to generate neurally-controlled pressure support has been shown to improve comfort and patient-ventilator interaction. In addition, the helmet interface was better tolerated by patients compared with a face mask. Herein, we compared neurally-controlled pressure support through a helmet with pressure support through a face mask with respect to subject comfort, breathing pattern, gas exchange, pressurization and triggering performance, and patient-ventilator synchrony. **METHODS:** Two 30-min trials of NIV were randomly delivered to 10 subjects with COPD exacerbation redundant: (1) pressure support through a face mask with inspiratory pressure support of ≥ 8 cm H₂O to obtain a tidal volume of 6–8 mL/kg of ideal body weight; and (2) NAVA through a helmet, setting the neurally-adjusted ventilatory assist level at 15 cm H₂O/ μ V, with an upper airway pressure limit to obtain the same overall airway pressure applied during pressure support through a face mask. We assessed subject comfort, breathing frequency, respiratory drive, arterial blood gases, pressure-time product (PTP) of the first 300 ms and 500ms after initiation of subject effort, inspiratory trigger delay, and rate of asynchrony determined as the asynchrony index. **RESULTS:** Median and interquartile range NAVA through a helmet improved comfort (7.0 [6.0–8.0]) compared with pressure support through a face mask (5.0 [4.7–5.2], $P = .005$). The breathing pattern was not different between the methods. Respiratory drive was slightly, although not significantly, reduced ($P = .19$) during NAVA through a helmet in comparison with pressure support through a face mask. Gas exchange was also not different between the trials. The PTP of the first 300 ms ($P = .92$) and PTP of the first 500 ms ($P = .08$) were not statistically different between trials, whereas triggering performance, patient-ventilator interaction, and synchrony were all improved by NAVA through a helmet compared with pressure support through a face mask. **CONCLUSIONS:** In the subjects with COPD with exacerbation, NAVA through a helmet improved comfort, triggering performance, and patient-ventilator synchrony compared with pressure support through a face mask. *Key words:* noninvasive ventilation; mechanical ventilation; pressure-support ventilation; neurally adjusted ventilatory assist; patient-ventilator interaction; ventilator performance; patient-ventilator asynchrony. [Respir Care 2019;64(5):582–589. © 2019 Daedalus Enterprises]

Introduction

In patients with COPD exacerbation and respiratory acidosis, noninvasive ventilation (NIV) is strongly recommended as a first-line treatment.¹ Most commonly, NIV is applied through a face mask by using a pneumatically triggered and flow-cycled pressure support modality.² However, a face mask can be an uncomfortable interface, and pressure support does not guarantee good patient-ventilator interaction and potentially leads to NIV failure.^{3,4}

The helmet is a well-tolerated interface, which allows prolonged application without NIV discontinuation⁵ and

improved outcomes in patients with ARDS.⁶ However, the helmet is characterized by poorer patient-ventilator interaction and pressurization performance compared with a face mask.⁷ Such drawbacks have been partially improved in a new-generation helmet that introduces some technical advances.^{8,9} In particular, the new-generation helmet is characterized by an annular openable ring placed underneath an inflatable cushion that secures the helmet without the need for armpit braces. Such technical advances have improved patient-ventilator interactions by ameliorating the triggering phase and pressurization performance.^{8,9} In subjects with COPD exacerbation, the new-generation hel-

met has also been found to be an effective interface to improve alveolar ventilation, while also achieving comfort similar to a face mask.¹⁰

Recently, a specific method of applying neurally-adjusted ventilatory assist has been proposed to generate neurally-controlled pressure support in patients who receive either invasive ventilation¹¹ or NIV through a helmet¹² or a face mask.¹³ Compared with pressure support, neurally-controlled pressure support results in better pressurization and triggering performance, and improves patient comfort without affecting gas exchange during NIV.^{12,13} Moreover, NAVA improves patient-ventilator interaction and triggering performance in patients with COPD exacerbation who are intubated when compared with pressure support.¹¹

We hypothesized that the application of neurally-controlled pressure support through a new generation helmet could improve patient comfort compared with cycled-off pressure support through a face mask. This physiologic study aimed to compare NAVA through a helmet with cycled-off pressure support through a face mask with respect to comfort (primary end point), breathing pattern, respiratory drive, gas exchange, pressurization and triggering performance, and patient-ventilator synchrony (additional end points) in subjects with a COPD exacerbation who were receiving NIV.

Methods

The present physiologic, crossover, randomized study was conducted from August to December 2013 in the ICU, Department of Critical Care Medicine, ZhongDa Hospital, Southeast University, School of Medicine, Nanjing, China. The study was approved by the research ethics board of Zhongda Hospital, Southeast University, Nanjing, China (2013ZDSYLL097.0). Written informed consent was obtained from the subjects for publication of their individual details and accompanying images in this article. At the time that the study was conducted, trial registration was not mandatory for this type of investigation.

Subjects

We considered eligible any adult patient with a previous diagnosis of COPD (ie, the presence of dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors, with a post-bronchodilator FEV₁/FVC of

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QUICK LOOK

Current knowledge

Patients with COPD exacerbation and with respiratory acidosis require NIV as first-line treatment. To reduce NIV failure, clinicians attempt to ensure optimal comfort by the choice of a proper interface and ventilator settings. The helmet has been shown to improve patient tolerance to the interface compared with a mask. NAVA has been shown to further improve comfort and patient-ventilator interaction, and to reduce respiratory drive.

What this paper contributes to our knowledge

NAVA through a helmet was more comfortable compared with conventional pneumatically-triggered pressure support through a mask in a group of subjects with COPD exacerbation. Furthermore, as opposed to pressure support through a face mask, NAVA through a helmet improved patient-ventilator interaction and synchrony, without affecting the respiratory drive and pattern.

<0.70 at the spirometry¹⁴), admitted to the ICU for exacerbation and acute respiratory failure, which we defined as pH < 7.35, with P_{aCO₂} > 45 mm Hg while breathing room air or with oxygen supplementation via a air-entrainment mask and required NIV.^{10,14}

The inclusion criteria were the following: (1) the subject was fully cooperative; (2) no infusion of midazolam and propofol in the previous 24 and 4 h, respectively; (3) PEEP ≥ 8 cm H₂O, with a total applied pressure (ie, PEEP plus inspiratory support) of ≤25 cm H₂O; (4) arterial pH > 7.34 during NIV; and (5) breathing frequency ≤ 30 breaths/min. The exclusion criteria were as

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Dr Navalesi discloses relationships with Intersurgical S.p.A., Maquet Critical Care, Hillrom, Philips, Resmed, and Novartis. The remaining authors have disclosed no conflicts of interest.

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follows: (1) the need for analgesic or sedative drugs, (2) recent cervical spine injury, (3) obstructive sleep apnea syndrome, (4) claustrophobia, (5) contraindications to placement of a nasal-gastric feeding tube, (6) face or neck deformities, (7) pregnancy, (8) inclusion in other research protocols, (9) and lack of consent.^{7,13}

Study Protocol

After each subject's enrollment in the study, NAVA catheter (Maquet Critical Care, Solna, Sweden) was placed in the esophagus and correct positioning was ascertained as previously described.¹⁵ The study was performed by using a standard Servo-i ventilator (Maquet Critical Care) equipped with NAVA module and NIV software for air leaks. All the subjects subsequently underwent two 30-min trials (pressure support through a face mask and NAVA support through a helmet) in random order according to a computer-generated random sequence by using sealed, opaque, numbered envelopes. The envelopes were kept in the head nurse's office. The envelope was opened by the nurse in charge of the subject, and the prescribed sequence of modes was communicated to the investigators.

Settings in both modes of ventilation were titrated to obtain the same ventilatory support provided to the subjects before study entry. In particular, the pressure support through a face mask trial was conducted through a face mask individually selected for each subject based on his or her anthropometric characteristics to minimize air leaks and optimize subject tolerance¹³; the face mask was selected from among 2 different models: FreeMotion RT041 Non Vented Full Face Mask (Fisher and Paykel, Auckland, New Zealand) and PerforMax Face Mask (Philips Respironics, Murrysville, Pennsylvania). The ventilator was set as previously clinically indicated by the attending physician. In particular, inspiratory pressure support was ≥ 8 cm H₂O to obtain a tidal volume of 6–8 mL/kg of ideal body weight, with the fastest rate of pressurization and cycling that was between 25 and 50% of peak inspiratory flow.¹⁰

The NAVA through a helmet trial was conducted with a new-generation helmet (Castar Next, Intersurgical, Mirandola, Italy) in NAVA, with the NAVA level set at its maximum (ie, 15 cm H₂O/ μ V), the same PEEP applied during the pressure support through a face mask trial and an upper airway pressure (P_{aw}) limit to obtain the same overall P_{aw} applied during the pressure support through a face mask trial.^{11,16,17} The trigger sensitivity was set at 0.5 μ V, whereas the default cycling was 70% of the peak electrical activity of the diaphragm (EA_{di}), as fixed by the company.¹⁶ F_{IO_2} was set to maintain peripheral (S_{pO_2}) between 90% and 94%,¹⁴ and remained unmodified throughout the study period.

Predefined criteria for protocol interruption were the following: (1) the need for emergency intubation to protect the airway; (2) S_{pO_2} of $<86\%$; (3) acute respiratory acidosis, as defined by $P_{aCO_2} > 50$ mm Hg and $pH < 7.30$; (4) an inability to expectorate secretions; (5) hemodynamic instability (ie, a need for continuous infusion of dopamine or dobutamine of >5 μ g/kg/min, norepinephrine of >0.1 μ g/kg/min, or vasopressin to maintain mean arterial blood pressure of >60 mm Hg); (6) life-threatening arrhythmias or electrocardiographic signs of ischemia; or (7) Glasgow coma scale decline of ≥ 2 points.

Data Acquisition and Analysis

Air flow, P_{aw} , and Ea_{di} were acquired from the ventilator through an RS232 interface at a sampling rate of 100 Hz and were recorded on a computer with dedicated software (ServoTracker V. 4.0, Maquet Critical Care). The last minute of each trial was manually analyzed off-line by using customized software based on Microsoft Excel Microsoft, Redmond, WA, as previously described.¹⁸ Comfort was assessed through an 11-point numeric rating scale, as previously reported.^{9,13,17} Before protocol initiation, all the subjects received a detailed explanation of the numeric rating scale. The subjects evaluated their comfort level at the end of each trial with a number between 0 (worst possible comfort) and 10 (best possible comfort) by using an ICU-adapted large printed scale that included numbers and descriptors. The scores obtained were recorded without additional indications or comments.^{9,13,17} At the end of each trial, arterial blood was also sampled for gas analysis.

Mechanical inspiratory time (T_I) and ventilator rate were determined from the flow tracing. Subject's own (neural) breathing frequency and neural T_I were computed from the Ea_{di} tracing. Subjects' own (neural) breathing frequency and T_I were computed from the Ea_{di} tracing. Mechanical T_I/T_{tot} and neural T_I/T_{tot} inspiratory duty cycle were calculated as the ratio between mechanical T_I/T_{tot} and the ratio between neural T_I/T_{tot} , respectively.^{12,13,19} Leaks were computed as the difference between the volume insufflated to the interface and the exhaled volume back to the ventilator multiplied by the (ventilator rate; leaks were expressed as the rate of the inhaled volume over 1 min.^{13,19} Moreover, we measured the peak P_{aw} , the peak inspiratory flow, and the time to reach peak inspiratory flow from the onset of the subject effort.¹³ The peak Ea_{di} was also calculated as the swing from baseline to its peak to assess the respiratory drive.^{12,13}

The pressurization performance was assessed with the P_{aw} -time product (PTP) of the first 200 ms computed from the onset of ventilator assistance (PTP₂₀₀), excluding the triggering phase, and with the PTP of the first 300 and 500 ms from the onset of subject effort, indexed to the ideal

Table 1. Subject Characteristics

Subject No.	Sex	Age (y)	Weight (kg)	BMI (kg/m ²)	APACHE II Score	PEEP (cm H ₂ O)	PS (cm H ₂ O)	F _{IO₂}	FEV ₁ (%)
1	M	75	65	23.0	21	10	10	0.30	48
2	M	73	60	23.4	28	12	12	0.40	47
3	M	78	70	24.8	23	10	12	0.30	37
4	M	68	56	20.6	25	10	12	0.45	40
5	M	74	60	23.1	25	10	12	0.30	42
6	M	83	72	24.9	22	11	13	0.25	35
7	F	86	60	27.3	22	8	14	0.30	38
8	M	77	70	22.9	19	9	12	0.23	46
9	M	70	70	24.2	10	9	12	0.23	36
10	M	68	80	26.1	15	9	10	0.40	33

BMI = body mass index

APACHE II = Acute Physiology and Chronic Health Evaluation II

PS = inspiratory pressure support above PEEP

PTP (index PTP₃₀₀ and index PTP₅₀₀, respectively).^{8,12,13,20} The ideal PTP was computed by considering a perfectly squared rectangle on the P_{aw}-time tracing, with the height of the actual P_{aw} above PEEP and the width of the time window considered (ie, 0.3 and 0.5 s from the onset of the inspiratory effort, assessed from the EA_{di} tracing, for index PTP₃₀₀ and index PTP₅₀₀, respectively).^{8,12,13,20} The inspiratory trigger delay and the expiratory trigger delay, the PTP during the triggering phase, and the drop in P_{aw} were computed to evaluate the triggering performance.^{8,12,13,20}

To assess patient-ventilator synchrony, we calculated the time of synchrony between diaphragm activity and ventilator assistance indexed to the subject's own neural T_I.^{8,12,13,20} Asynchronies (ineffective efforts, auto triggering and double triggering) were also assessed and expressed as the asynchrony index, that is, the total number of asynchronous events divided by the number of triggered and not triggered breaths.⁴ The asynchrony index of ≥10% was considered to indicate a clinically relevant rate of asynchronies.⁴

Statistical Analysis

Based on preliminary data, to ascertain an average increase in comfort of 2.0 with an expected SD of 2.0 with α risk of 0.05 and β risk of 0.20, a sample of 10 subjects was deemed necessary.¹² Data were reported as median and 25–75% interquartile, unless otherwise specified. All continuous variables were compared by the Wilcoxon signed-rank test. We compared categorical data by using the Fisher exact test, whereas the Spearman rank correlation test was used to determine the correlation between each individual comfort score and the corresponding PTP₂₀₀, index PTP₃₀₀, index PTP₅₀₀, PTP during the trig-

gering phase, inspiratory trigger delay, peak inspiratory flow, and the time to reach peak inspiratory flow. We considered significant 2-sided $P < .05$. All the statistical analyses were performed by using the SigmaPlot v. 12.0 (Systat Software, San Jose, California).

Results

We enrolled 10 consecutive subjects with COPD exacerbation. All the subjects completed the study protocol without any complication and were included in the data analysis. The subjects' demographic and anthropometric characteristics are shown in Table 1.

Comfort

The individual values of the comfort score for all the subjects and their median and interquartile range are depicted in Figure 1. The median and interquartile range NAVA through a helmet slightly, although significantly, improved comfort (7.0 [6.0–8.0]) compared with pressure support through a face mask (5.0 [4.7–5.2]) ($P = .005$). Comfort improvement was not correlated to PTP₂₀₀ ($\rho = -0.286, P = .01$), index PTP₃₀₀ ($\rho = 0.286, P = .22$), index PTP₅₀₀ ($\rho = 0.061, P = .39$), PTP during the triggering phase ($\rho = 0.373, P = .12$), inspiratory trigger delay ($\rho = -0.423, P = .14$), peak inspiratory flow ($\rho = 0.292, P = .21$), and time to reach peak inspiratory flow ($\rho = 0.007, P = .67$).

Breathing Pattern, Respiratory Drive, and Gas Exchange

As reported in Table 2, the breathing pattern was not different between the modes. Air leaks were higher during

Table 2. Breathing Pattern, Respiratory Drive, Gas Exchange, Pressurization and Triggering Performance, and Patient-Ventilator Synchrony

Parameter	Pressure Support Through a Face Mask	NAVA Through a Helmet	P
Breathing pattern and respiratory drive, median (IQR)			
Mechanical respiratory rate, breaths/min	25.2 (18.0–29.5)	25.8 (21.3–32.5)	.99
Patient's own neural breathing frequency, breaths/min	29.3 (23.6–31.6)	25.9 (20.5–31.8)	.49
Mechanical T _I , s	0.72 (0.59–1.04)	0.69 (0.52–0.92)	.99
Neural T _I , s	0.48 (0.64–0.81)	0.70 (0.51–0.80)	.62
Mechanical T _I /T _{tot}	0.26 (0.25–0.31)	0.28 (0.22–0.37)	.32
Neural T _I /T _{tot}	0.31 (0.20–0.35)	0.29 (0.22–0.33)	.99
Peak P _{aw} , cm H ₂ O	23.0 (20.7–26.3)	23.3 (21.2–27.1)	.19
Leaks, %	20.4 (19.2–26.3)	6.2 (4.6–8.0)	.002
Peak inspiratory flow, L/s	1.20 (1.03–1.30)	2.17 (1.86–2.34)	.002
Peak inspiratory flow time, s	0.30 (0.23–0.39)	0.26 (0.24–0.28)	.16
Maximum peak EA _{di} , μV	8.1 (4.7–12.2)	5.1 (3.3–10.2)	.19
Gas exchange, median (IQR)			
pH	7.43 (7.41–7.45)	7.43 (7.42–7.45)	.27
P _{aO₂} , mm Hg	86 (79–88)	81 (78–91)	.62
P _{aCO₂} , mm Hg	46 (41–50)	46 (44–49)	.80
Pressurization and triggering performance, median (IQR)			
PTP ₂₀₀ , cm H ₂ O/s	130 (113–153)	83 (66–109)	.006
Index PTP ₃₀₀ , %	21.6 (8.4–30.4)	22.4 (15.3–26.1)	.92
Index PTP ₅₀₀ , %	41.3 (30.4–50.8)	49.0 (45.5–54.1)	.08
Inspiratory trigger delay, s	0.15 (0.11–0.25)	0.09 (0.08–0.12)	.037
Expiratory trigger delay, s	0.14 (0.05–0.36)	0.07 (0.03–0.12)	.16
Triggering phase PTP, cm H ₂ O/s	5.8 (2.3–9.3)	1.4 (1.1–2.1)	.006
Drop in airway pressure during triggering phase, cm H ₂ O	0.80 (0.60–1.05)	0.52 (0.37–0.85)	.049
Patient-ventilator synchrony			
Synchronous time to neural T _I ratio, median (IQR)	0.79 (0.68–0.88)	0.83 (0.80–0.88)	.37
Asynchrony index > 10%, n/N	6/10	0/10	.01

IQR = interquartile range
T_I = inspiratory time
T_I/T_{tot} = inspiratory duty cycle
P_{aw} = airway pressure
Peak inspiratory flow time = time to reach peak inspiratory flow from the onset of the subject's effort
EA_{di} = electrical activity of the diaphragm
PTP = pressure-time product
PTP₂₀₀ = PTP of the first 200 ms computed from the onset of ventilator assistance
Index PTP₃₀₀ = PTP of the first 300 ms from the onset of patient effort indexed to the ideal PTP
Index PTP₅₀₀ = PTP of the first 500 ms from the onset of patient effort indexed to the ideal PTP

1-y mortality compared with the mask.^{6,21} In particular, the a new-generation helmet used in the present study was characterized by improved pressurization and triggering performance,^{8,9} which also allowed its use in more-challenging patients such as those with a COPD exacerbation.¹⁰ Use in these patients is frequently problematic due to a less-efficient reduction in inspiratory effort and poorer patient-ventilator interaction compared with a mask.⁷

In the present study, the time to reach peak inspiratory flow did not differ between NAVA through a helmet and pressure support through a face mask, whereas the peak inspiratory flow did. This discrepancy with a previous study,¹³ was probably due to the interfaces. PTP₂₀₀, which is computed in the first 200 ms from the onset of ventilator insufflation and did not involve the triggering phase, is an index of

pressurization performance of the interface; this is mainly influenced by the flow delivered from the ventilator (peak inspiratory flow) and the mechanical properties of the interface itself. During pressure support through a face mask, the interface (ie, the mask) has a very low (negligible) compliance, without any displacement during the pressurization. Therefore, the volume (which is the flow over time) delivered to the interface generates all pressurization. On the contrary, NAVA through a helmet is delivered through a helmet that is characterized by a higher compliance compared with an oronasal mask and a cranio-caudal displacement during insufflation.

These also are issues with the a new-generation helmet used in the study, although less so when compared with a standard helmet.^{8,9,12,13} Therefore, even though during NAVA through a helmet, the flow (ie, peak inspiratory

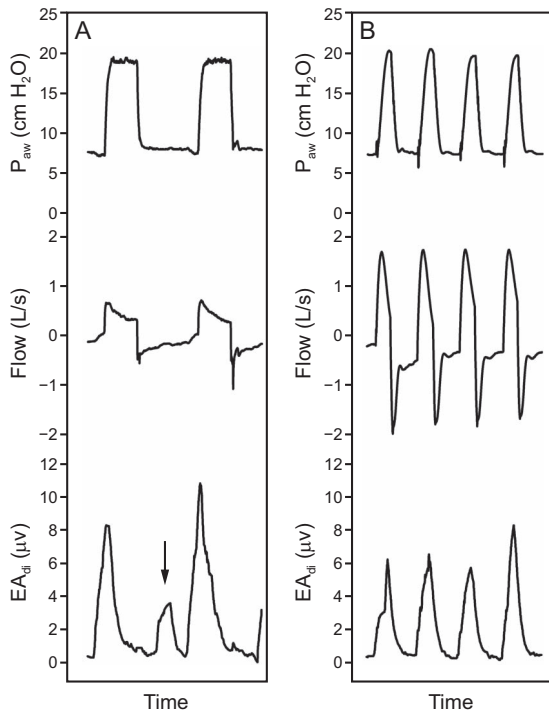


Fig. 2. Airway pressure (P_{aw}), flow, and respiratory drive (electrical activity of the diaphragm [EA_{di}]) tracings are depicted of one representative subject during pneumatically triggered pressure support through a mask (A), and neurally controlled pressure support through a helmet (B). The arrow indicates an ineffective inspiratory effort.

flow) is higher (and almost twice) compared with pressure support through a face mask, the flow does not generate expected pressure due to the mechanical properties of the interface (helmet). In line with this finding, it was already known that neurally triggered modes of ventilation outperform pneumatically triggered ones in subjects with COPD and with exacerbation.¹¹ Furthermore, NAVA has also been largely demonstrated to improve patient-ventilator synchrony during both invasive ventilation^{15,18,22,23} and NIV.^{12,13,19,23-26}

Our study had 2 limitations. First, we tested 2 factors altogether, that is, the interface and the triggering system, without the possibility to ascertain whether improved comfort was attributable to the new-generation helmet or the mode of ventilation, or the combination of both factors. Previous literature reports that comfort during NIV is determined by the interface,^{3,5} patient-ventilator interaction and synchrony,²³ and pressurization and triggering performance.^{12,13} However, this study seemed to indicate that comfort was improved by the interface, rather than the triggering improvement. Second, consistent with previous studies,^{12,13,27,28} we applied the 11-point numeric rating scale to assess comfort, although this scale was formally only validated for pain²⁹ and dyspnea.^{30,31}

Conclusions

In the subjects with a COPD exacerbation and acute respiratory failure, NAVA through a helmet improved comfort, triggering performance, and patient-ventilator synchrony compared with pressure support through a face mask. It remains to be determined whether these physiologic benefits may translate into a reduced NIV failure rate and improved clinical outcomes.

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