New Setting of Neurally Adjusted Ventilatory Assist during Noninvasive Ventilation through a Helmet

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ABSTRACT

Background: Compared to pneumatically controlled pressure support (PS_p), neurally adjusted ventilatory assist (NAVA) was proved to improve patient–ventilator interactions, while not affecting comfort, diaphragm electrical activity (EAdi), and arterial blood gases (ABGs). This study compares neurally controlled pressure support (PS_N) with PS_p and NAVA, delivered through two different helmets, in hypoxemic patients receiving noninvasive ventilation for prevention of extubation failure.

Methods: Fifteen patients underwent three (PS_p, NAVA, and PS_N) 30-min trials in random order with both helmets. Positive end-expiratory pressure was always set at 10 cm H_2O. In PS_p, the inspiratory support was set at 10 cm H_2O above positive end-expiratory pressure. NAVA was adjusted to match peak EAdi ($EAdi_{peak}$) during PS_p. In PS_N, the NAVA level was set at maximum matching the pressure delivered during PS_p by limiting the upper pressure. The authors assessed patient comfort, $EAdi_{peak}$, rates of pressurization (*i.e.,* airway pressure-time product [PTP] of the first 300 and 500 ms after the initiation of patient effort, indexed to the ideal pressure–time products), and measured ABGs.

Results: PS_N significantly increased comfort to (median [25 to 75% interquartile range]) 8 [7 to 8] and 9 [8 to 9] with standard and new helmets, respectively, as opposed to both PS_p (5 [5 to 6] and 7 [6 to 7]) and NAVA (6 [5 to 7] and 7 [6 to 8]; $P < 0.01$ for all comparisons). Regardless of the interface, PS_N also decreased $EAdi_{peak}$ ($P < 0.01$), while increasing PTP of the first 300 ms from the onset of patient effort, indexed to the ideal PTP ($P < 0.01$) and PTP of the first 500 ms from the onset of patient effort, indexed to the ideal PTP ($P < 0.001$). ABGs were not different among trials.

Conclusions: When delivering noninvasive ventilation by helmet, compared to PS_p and NAVA, PS_N improves comfort and patient–ventilator interactions, while not ABGs. **(Anesthesiology 2016; 125:1181-9)**

BOTH ventilator performance and interface tolerance are important determinants of noninvasive ventilation (NIV) success.[1–4] Neurally adjusted ventilator assist (NAVA) is a ventilatory mode where the ventilator is driven by the diaphragm electrical activity (EAdi), rather than by the conventional pneumatic signals, *i.e.*, flow, volume, and airway pressure (P_{aw}). Noninvasive NAVA improves patient–ventilator interaction and reduces asynchronies, compared to pneumatically triggered and cycled-off pressure support (PS_p), the most common mode for NIV delivery.[5–9] The helmet is a relatively novel interface for NIV that, compared to facemasks, improves patient tolerance to NIV and allows NIV administration for longer periods with fewer interruptions and NIV-related side effects[4,10–12] and may reduce intubation rates and 90-day mortality.[13] The helmet, however, is characterized by a less efficient rate of pressurization, poor triggering function, and a higher rate of asynchronies.[14,15]

What We Already Know about This Topic

- Noninvasive ventilation by a facemask or a helmet is used after extubation to reduce the need for reintubation in patients at risk for extubation failure. Due to the large internal volume and the upward displacement (in its standard version), the helmet makes ventilator triggering less efficient and patient–ventilator asynchrony common.

What This Article Tells Us That Is New

- Pressure support (PS) ventilation with a helmet was studied after extubation in 15 patients. Neurally adjusted PS increased comfort and improved patient–ventilator interactions, compared with standard (pneumatic) PS or neurally adjusted ventilatory assist.

In hypoxemic patients receiving NIV through a helmet for treatment of postextubation respiratory failure, compared to PS_p, NAVA improves patient–ventilator interaction

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and synchrony, without determining significant variations in EAdi, respiratory rate, and arterial blood gases (ABGs).[6] When applying NIV with a standard helmet (SH), secured to the patient by armpit braces, the delivery of pressure to the patient's airway is altered by the upward displacement of the interface during insufflation.[16] A modified new helmet (NH) has been shown to improve, as opposed to a SH, triggering and pressurization performance in PS_P on bench,[16] in healthy volunteers,[17] and in critically ill patients.[18]

In the current study, we propose a specific NIV setting to generate a neurally controlled pressure support (PS_N), consisting of increasing the user-controlled gain factor (NAVA level) at maximum (15 cm $H_2O/\mu V$), with the upper pressure limit adjusted to achieve a maximum P_{aw} of 20 cm H_2O, including positive end-expiratory pressure (PEEP).[19] Accordingly, as soon as EAdi rises up, exceeding the trigger threshold (0.5 μV), P_{aw} rapidly increases resulting in a steep pressurization of up to 20 cm H_2O.

We hypothesize that PS_N would improve comfort and reduce EAdi in intensive care unit (ICU) patients undergoing NIV, by improving the rate of pressurization, compared to both PS_P and NAVA, and triggering delays, as opposed to PS_P only. Therefore, we compare the effects of PS_N, PS_P, and NAVA, delivered by both SH and NH, on comfort, respiratory drive, breathing pattern, ABGs, and patient–ventilator interaction and synchrony in patients receiving NIV for prevention of postextubation respiratory failure.

Materials and Methods

The study was conducted in the ICU of the University Hospital "Maggiore della Carità" (Novara, Italy) between July 2012 and January 2013, in accordance with the principles outlined in the Declaration of Helsinki. The institutional ethics committee approved the study (protocol number 484/CE, number of approval 64/12), and patient consent was obtained according to the Italian regulations. At the time the study was conducted, trial registration was not mandatory for this type of investigation. None of the patients in this study had been enrolled in other investigations. Part of the data was previously displayed in abstract form for poster presentations.

Subjects and Study Protocol

We considered eligible any patient aged 18 yr or older on invasive mechanical ventilation with all the following characteristics: (1) previous invasive mechanical ventilation greater than or equal to 48 h; (2) consciousness, as indicated by Glasgow Coma Scale of 11 (*i.e.*, spontaneous eyes opening, obeys command, and no verbal response because of the endotracheal tube in place); (3) no infusion of midazolam and propofol in the previous 24 and 4 h, respectively; (4) readiness for extubation with indication, before extubation, to receive prophylactic NIV to prevent postextubation respiratory failure. Exclusion criteria were as follows: (1) agitation requiring sedation; (2) recent cervical spine injury; (3) obstructive sleep apnea syndrome; (4) pregnancy; (5) contraindications to placement of a nasal-gastric feeding tube; (6) inclusion in other research protocol; and (7) lack of consent.

Patients were considered at risk for extubation failure when meeting at least one of the following: (1) more than one consecutive failure of weaning trial[20]; (2) arterial carbon dioxide tension ($Paco_2$) more than 45 mmHg after extubation; (3) chronic respiratory disorders[20]; and (4) chronic heart failure.[20]

After enrollment, a nasal-gastric feeding tube designed for EAdi detection (NAVA Catheter; Maquet Critical Care, Sweden) was placed, as previously described.[21] All trials were conducted with a Servo-I ventilator (Maquet Critical Care) equipped with a software for air-leak compensation.

We used two separate computer-generated random sequences through sealed, opaque numbered envelops held by physicians and nurses not involved in the study. The first sequence was used for the order of application of the two helmets, while the second for the sequence of administration of the ventilatory modes. Therefore, each patient underwent three consecutive 30-min trials for both helmets with the same random sequence of modes. PEEP was always set at 10 cm H_2O and left unmodified throughout the whole study period. The inspired oxygen fraction, set to obtain oxygen saturation measured by pulse oximetry more than 94% and less than 97% before starting the protocol, remained unmodified throughout the study period. The specific settings of the three modes were as follows: (1) PS_P, inspiratory support of 10 cm H_2O above PEEP, fastest rate of pressurization, expiratory trigger threshold at 50% of the peak inspiratory flow; (2) NAVA, NAVA level set to achieve a comparable peak EAdi ($EAdi_{peak}$) as during PS_P, with a safety P_{aw} upper limit of 30 cm H_2O[6]; and (3) PS_N, NAVA level set at 15 cm $H_2O/\mu V$[19] with an upper P_{aw} limit of 25 cm H_2O, to obtain the same 20 cm H_2O of the overall P_{aw} applied in PS_P.[22] In fact, the maximum pressure applied by the Servo-I ventilator is 5 cm H_2O below the preset upper P_{aw} limit.[22] Fixed by the manufacturer, the default cycling-off during both NAVA and PS_N is 70% of $EAdi_{peak}$.[22]

Predefined criteria for protocol interruption were as follows: (1) need for emergency reintubation; (2) oxygen saturation measured by pulse oximetry less than 90%; (3) acute respiratory acidosis, as defined by $Paco_2$ more than 50 mmHg and pH less than 7.30; (3) inability to expectorate secretions; (4) hemodynamic instability (*i.e.*, need for continuous infusion of dopamine or dobutamine greater than 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$, norepinephrine greater than 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$, or vasopressin to maintain mean arterial blood pressure greater than 60 mmHg); (5) life-threatening arrhythmias or electrocardiographic signs of ischemia; or (6) loss of two or more points on the Glasgow Coma Scale.

Data Acquisition and Analysis

Airflow, P_{aw}, and EAdi were acquired from the ventilator through an RS232 interface at a sampling rate of 100 Hz and recorded on a personal computer by means of dedicated software (NAVA Tracker V. 3.0; Maquet Critical Care). The last minute of each trial was manually analyzed off-line using customized software based on Microsoft Excel (Microsoft Corporation, USA), as previously described.[21]

Mechanical inspiratory time and rate of ventilator cycling (mechanical respiratory rate [RR_{mec}]) were determined from the flow tracing, while the patient's neural TI (TI_{neu}) and RR (RR_{neu}) were obtained from the EAdi tracing.[6] Mechanical and neural inspiratory duty cycles were computed.[6] We measured EAdi from baseline to peak ($EAdi_{peak}$) to assess the neural drive.[23] The peak inspiratory and the mean P_{aw} values were also measured.

The pressurization performance was evaluated with the P_{aw}-time product (PTP) of the first 200 ms computed from the onset of ventilator assistance (PTP_{200}) and of the first 300 and 500 ms from the onset of patient effort, indexed to the ideal PTP and expressed in percentage ($PTP_{300\text{-index}}$ and $PTP_{500\text{-index}}$, respectively).[16,18,24] The ideal PTP was computed considering a perfectly squared rectangle on the P_{aw}-time tracing, having the height of the actual P_{aw} above PEEP and the width of the time window considered (*i.e.*, 0.3 and 0.5 s from the onset of the inspiratory effort, assessed from the EAdi tracing, for $PTP_{300\text{-index}}$ and $PTP_{500\text{-index}}$, respectively).[16,18,24] The drop in P_{aw} ($\Delta P_{trigger}$) and the PTP during the triggering phase (PTP_t) were determined to evaluate triggering performance.[16,18,24]

We calculated the inspiratory ($Delay_{TR\text{-}insp}$) and expiratory trigger delays[6] and the time of synchrony between diaphragm activity and ventilator assistance, indexed to patient's own (neural) TI.[18,24] The asynchrony index (AI%) was computed as the sum of ineffective efforts, autotrigger, and double trigger, divided by the overall number of triggered and nontriggered breaths.[25] We considered an AI% greater than or equal to 10% to indicate a clinically relevant rate of asynchronies.[25]

At the end of each trial, arterial blood was sampled for ABGs and comfort was assessed using the 11-point numeric rating scale (NRS), as previously reported.[18,26,27] Briefly, patients were asked to indicate a number between 0 (worst possible comfort) and 10 (no discomfort at all) on an ICU-adapted, large printed scale including numbers and descriptors.[27] Before protocol initiation, all patients received a detailed explanation about the 11-point NRS. The scores obtained were recorded without further indications or comments.[18]

Statistical Analysis

To calculate the sample size necessary to ascertain a 50% NRS increase with PS_N, we have utilized the values from a database of patients previously evaluated with a SH in PS_P, with a mean NRS of 5.0 and a SD of 2.7. To detect an increase in comfort of 2.5, with α risk of 0.05 and β risk of 0.20, a sample of 12 patients were deemed necessary. Because this calculation is based on a Student's paired *t* test and we performed comparisons among three conditions, we have applied Bonferroni correction, reducing the α risk from 0.05 to 0.017, which increases the sample up to 15 patients.

Data are reported as median (25 to 75% interquartile range) unless otherwise specified. All continuous variables were compared between modes with both helmets. The effects of the three modes were assessed separately for each helmet by the Friedman test and then by the Wilcoxon rank text, with Bonferroni correction for multiple comparisons ($P < 0.017$). We compared categorical data by the McNemar test, while the Spearman rank test was used to determine the correlation between each individual comfort scores and the corresponding $PTP_{300\text{-index}}$, $PTP_{500\text{-index}}$, PTP_t, and $Delay_{TR\text{-}insp}$; for these comparisons, we considered two-sided $P < 0.05$ significant. Statistical analysis was performed using the Sigmaplot v. 12.0 (Systat Software Inc., USA).

Results

We enrolled 15 consecutive patients, after obtaining written informed consent. Patients' characteristics at ICU admission are provided in table 1. The main reason for ICU admission was hypoxemic acute respiratory failure (ARF). All patients completed the study protocol without complications. Two patients were reintubated before 48 h after extubation: one because of severe dyspnea and the second due to respiratory acidosis

Table 1. Patient Characteristics at Intensive Care Unit Admission

Patient	Gender	Age	Weight	BMI	Admission Pathology	SAPS II
1	F	78	90	27.8	Pneumonia	34
2	M	62	88	28.1	Septic shock	37
3	M	57	72	23.5	Polytrauma	32
4	M	67	80	23.2	Pneumonia	39
5	F	75	82	28.4	Septic shock	46
6	M	69	70	25.1	Pancreatitis	68
7	M	31	67	21.1	Chest trauma	18
8	F	45	55	21.0	Postsurgical ARF	25
9	F	37	59	21.2	Chest trauma	18
10	M	56	62	22.2	Septic shock	30
11	M	74	73	23.8	Septic shock	40
12	F	76	78	25.5	Pneumonia	34
13	F	73	75	24.5	Pneumonia	33
14	F	63	64	22.4	Postsurgical ARF	32
15	M	59	70	22.9	Septic shock	33

ARF = acute respiratory failure; BMI = body mass index; F = female; M = male; SAPS II = Simplified Acute Physiology Score II.

Comfort

Figure 1 shows individual scores and median values of comfort for all trials. With SH (left panel), PS_N (8 [7 to 8]) improved the comfort score, when compared to both PS_P (5 [5 to 6]; $P < 0.001$) and NAVA (6 [5 to 7]; $P = 0.001$). Similarly, with NH, PS_N (9 [8 to 9]) outperformed both PS_P (7 [6 to 7]; $P < 0.001$) and NAVA (7 [6 to 8]; $P = 0.003$). The comfort scores were directly correlated to $PTP_{300\text{-index}}$ ($\rho = 0.52$; $P < 0.001$) and $PTP_{500\text{-index}}$ ($\rho = 0.50$; $P < 0.001$) and inversely correlated to $Delay_{TR\text{-insp}}$ ($\rho = -0.56$; $P < 0.001$) and PTP_t ($\rho = -0.53$; $P < 0.001$).

Breathing Pattern, Respiratory Drive, and ABGs

As depicted in table 2, RR_{neu}, TI_{neu}, and neural inspiratory duty cycle were unaffected by the ventilatory mode with both helmets. Also shown in table 2, PS_N significantly decreased RR_{mec}, as compared to PS_P while not to NAVA, when delivering NIV by NH. Conversely, RR_{mec} was no different at all between modes when delivering NIV by SH. Irrespective of the interface, mechanical inspiratory time and mechanical inspiratory duty cycle were greater with NAVA and PS_N than with PS_P. Figure 2 displays P_{aw}, flow, and EAdi tracings of a representative patient during PS_P, NAVA, and PS_N delivered by SH. Compared to both PS_P and NAVA, PS_N reduced $EAdi_{peak}$. Group median values confirm that $EAdi_{peak}$ is reduced by PS_N, as opposed to both PS_P and NAVA (table 2). ABGs were not different between trials (table 2).

Triggering Performance and Rates of Pressurization

Figure 3 displays P_{aw} profiles of single breaths during PS_P (solid line), NAVA (dotted line), and PS_N (dashed line), with both interfaces from one patient. The arrow indicates the initiation of diaphragm effort, as assessed by EAdi. Irrespective of the interface, both PS_N and NAVA show a shorter $Delay_{TR\text{-insp}}$, as opposed to PS_P, while the pressurization rate looks steeper in PS_N than in PS_P and NAVA. In keeping with these observations, group median data, as displayed in table 2, show that compared to PS_P, both PS_N and NAVA improved triggering performance irrespective of the interface, while all the indices of pressurization were significantly improved by PS_N, as opposed to both PS_P and NAVA, with no significant difference between PS_P and NAVA. Also shown in table 2, compared to PS_P, NAVA improved $PTP_{300\text{-index}}$ and $PTP_{500\text{-index}}$ with SH, while not with NH.

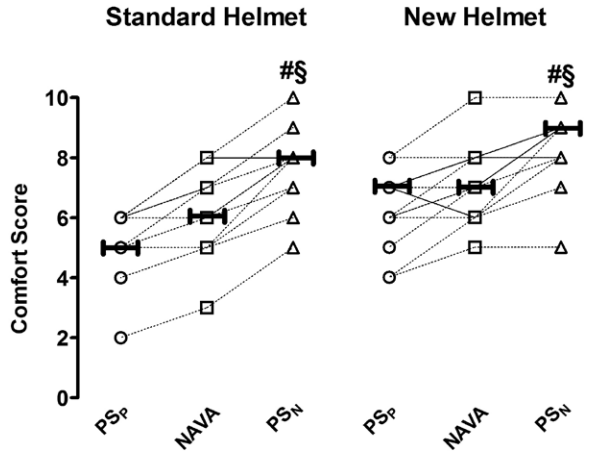

Fig. 1. *Hollow circles* (pneumatically controlled pressure support [PS_P]), *squares* (neurally adjusted ventilatory assist [NAVA]), and *triangles* (neurally controlled pressure support [PS_N]) indicate the individual comfort scores given by the 15 patients on the numeric rating scale with standard helmet (*left*) and new helmet (*right*). *Solid etched lines* depict median values. #$P < 0.017$ PS_N *versus* PS_P; §$P < 0.017$ PS_N *versus* NAVA.

Patient–Ventilator Synchrony

As shown in table 2, irrespective of the interface, PS_P and NAVA significantly improved the ratio between time during which respiratory effort and ventilator assistance were synchronous and the TI_{neu}, as opposed to PS_P. No patient had an AI% greater than or equal to 10% with PS_N and NAVA, while in PS_P, the patients with AI% greater than or equal to 10% were 8 with SH ($P = 0.02$, compared to both PS_N and NAVA) and 5 with NH ($P = 0.04$, compared to PS_N and NAVA).

Discussion

We found in patients receiving NIV by helmet that, irrespective of the interface, compared to both PS_P and NAVA, PS_N improves patient comfort, reduces EAdi, and results in better pressurization and triggering performance, while it does not affect ABGs and respiratory rate. Both PS_N and NAVA improve patient–ventilator synchrony, as opposed to PS_P, with no significant difference between the two modes.

Although several studies proved that, compared to PS_P, NAVA ameliorates patient–ventilator interactions and synchrony during NIV,[5–8] none demonstrated a reduction of EAdi, which is the best estimate of the respiratory drive[28] and reflects diaphragm effort.[29] In fact, in one study, EAdi is slightly, although significantly, higher in NAVA than in PS_P,[8] while in the others, EAdi is no different between the two modes.[5–7] In keeping with these findings, we find similar $EAdi_{peak}$ in NAVA and PS_P, while PS_N significantly reduces $EAdi_{peak}$.

With PS_N, a towering NAVA level and a safety P_{aw} limit are set on the ventilator. Accordingly, as soon as EAdi rises up exceeding the trigger threshold (0.5 μV), the ventilator immediately applies a boost of pressure to the helmet determining a steep pressurization up to 20 cm H_2O. Briefly, the upper pressure limit is achieved when the rise in EAdi reaches 1.5 μV; in fact, 1.5 μV (EAdi) × 15 H_2O/μV (NAVA level) > 20 cm H_2O. Consequently, as depicted in figure 3, the shape of the airway pressure in PS_N is nearly squared, as in an ideal PS_P, but EAdi determines on and off cycling instead of flow.

Patient comfort is a major determinant of NIV success[30] and depends on both interface tolerance and ventilator performance.[31] NIV by helmet reduces the inspiratory effort, compared to spontaneous breathing, although to a lesser extent than by facemask.[14,15] Vargas *et al.*[15] showed that a specific ventilator setting for helmet NIV, consisting of a 50% increase in both the expiratory and inspiratory pressures, lessens diaphragm

Table 2. Respiratory Drive and Timing, Arterial Blood Gases, Pressurization Rate, and Triggering Performance

	Standard Helmet				New Helmet			
	PS_P	NAVA	PS_N	*P* Value	PS_P	NAVA	PS_N	*P* Value
Respiratory drive and timing								
$EAdi_{peak}$, μV	14.8 [9.9 to 22.6]	14.6 [12.5 to 22.1]	12.2 [5.69 to 16.6]*,†	0.038	16.9 [12.7 to 19.8]	15.3 [10.7 to 18.8]	10.2 [7.1 to 16.2]‡,§	0.005
RR_{mec}, breaths/min	20 [15 to 25]	20 [16 to 29]	21 [15 to 26]	0.420	26 [21 to 28]	23 [15 to 28]	22 [16 to 26]‖	0.017
RR_{neu}, breaths/min	20 [15 to 24]	20 [16 to 29]	21 [15 to 26]	0.766	23 [20 to 27]	23 [15 to 28]	22 [16 to 26]	0.420
TI_{mec}, s	0.69 [0.67 to 0.79]	0.91 [0.84 to 1.09]#	0.92 [0.79 to 1.00]**	0.015	0.60 [0.51 to 0.68]	0.85 [0.75 to 1.18]††	0.87 [0.75 to 1.08]‡	< 0.001
TI_{neu}, s	0.87 [0.73 to 1.10]	0.83 [0.72 to 1.00]	0.89 [0.70 to 1.00]	0.936	0.77 [0.72 to 0.96]	0.80 [0.73 to 1.10]	0.85 [0.75 to 1.00]	0.549
$TI/TTOT_{mec}$	0.24 [0.19 to 0.27]	0.33 [0.29 to 0.41]#	0.32 [0.26 to 0.37]‡	0.002	0.25 [0.23 to 0.30]	0.35 [0.28 to 0.39]††	0.32 [0.24 to 0.36]*	0.007
$TI/TTOT_{neu}$	0.29 [0.23 to 0.35]	0.29 [0.27 to 0.38]	0.28 [0.24 to 0.35]	0.189	0.33 [0.27 to 0.38]	0.32 [0.26 to 0.36]	0.32 [0.24 to 0.36]	0.549
$Time_{synch}/TI_{neu}$	0.62 [0.49 to 0.76]	0.86 [0.82 to 0.90]††	0.87 [0.81 to 0.93]‡	< 0.001	0.69 [0.60 to 0.81]	0.83 [0.77 to 0.89]††	0.89 [0.84 to 0.93]‡	0.001
Arterial blood gases								
pH	7.44 [7.38 to 7.46]	7.43 [7.40 to 7.48]	7.43 [7.39 to 7.47]	0.344	7.43 [7.38 to 7.47]	7.44 [7.39 to 7.49]	7.44 [7.39 to 7.49]	0.184
$PaCO_2$, mmHg	42.4 [36.5 to 55.1]	42.3 [35.6 to 53.7]	41.1 [40.0 to 53.8]	0.135	41.0 [36.9 to 53.0]	38.5 [36.1 to 51.4]	40.6 [33.9 to 51.7]	0.633
PaO_2/FIO_2, mmHg	250 [206 to 270]	233 [192 to 290]	230 [217 to 260]	0.449	235 [181 to 266]	225 [199 to 262]	240 [190 to 340]	0.374
Pressurization rate								
P_{awpeak}, cm H_2O	20.7 [19.7 to 20.9]	21.0 [19.4 to 22.5]	20.5 [19.8 to 20.8]	0.174	20.6 [19.7 to 20.9]	21.4 [19.9 to 22.3]	20.5 [20.0 to 20.9]	0.558
P_{awmean}, cm H_2O	11.1 [10.8 to 11.3]	11.5 [11.3 to 12.5]‡‡	12.2 [11.3 to 12.5]§§	< 0.001	11.4 [11.0 to 11.5]	11.8 [11.3 to 12.4]	12.0 [11.6 to 12.7]‖‖	0.003
PTP_{200}, cm H_2O/s	10.5 [8.8 to 20.4]	14.1 [9.0 to 20.3]	30.5 [21.0 to 35.7]‡,##	< 0.001	28.6 [23.6 to 35.5]	20.0 [16.2 to 28.4]	32.4 [26.5 to 37.3]***,†††	0.038
$PTP_{300\text{-}index}$, %	1.0 [0.2 to 3.2]	6.1 [1.3 to 13.2]	11.9 [4.7 to 14.7]†,‡	< 0.001	2.8 [1.0 to 7.3]	5.3 [3.0 to 14.3]	12.3 [8.1 to 19.4]§,§§	0.002
$PTP_{500\text{-}index}$, %	6.6 [1.9 to 17.0]	19.3 [10.5 to 34.8]§§§	35.3 [21.9 to 41.7]‡,§	< 0.001	16.8 [8.7 to 26.1]	23.4 [17.2 to 36.7]	39.6 [29.8 to 47.3]‡,§	0.002
Triggering performance								
$Delay_{TR\text{-}insp}$, s	0.31 [0.26 to 0.44]	0.13 [0.10 to 0.17]††	0.11 [0.09 to 0.13]‡	< 0.001	0.23 [0.19 to 0.30]	0.16 [0.12 to 0.20]‡‡	0.11 [0.08 to 0.12]‡	0.001
$Delay_{TR\text{-}exp}$, s	0.18 [0.13 to 0.24]	0.11 [0.10 to 0.16]###	0.09 [0.05 to 0.12]§§	0.022	0.13 [0.08 to 0.30]	0.15 [0.13 to 0.18]	0.11 [0.06 to 0.17]	0.189
PTP_t, cm H_2O/s	28.6 [15.2 to 42.5]	5.1 [1.7 to 14.7]††	3.7 [1.1 to 5.8]‡	< 0.001	18.5 [11.2 to 22.5]	6.0 [2.7 to 11.6]‖‖‖	3.0 [1.6 to 4.4]‡	< 0.001
$\Delta P_{trigger}$, cm H_2O	−1.8 [−2.0 to −1.1]	−0.1 [−1.8 to −0.6]###	−0.8 [−1.2 to −0.5]‡	0.012	−1.4 [−1.8 to −1.2]	−0.8 [−1.2 to −0.5]§§§	−0.9 [−1.3 to −0.5]****	< 0.001

P values refer to Friedman test, while symbols (*, †, ‡, and others) refer to statistically significant *P* values from the Wilcoxon rank test.

*$P = 0.01$ PS_N *versus* PS_P. †$P = 0.007$ PS_N *versus* NAVA. ‡$P < 0.001$ PS_N *versus* PS_P. §$P < 0.001$ PS_N *versus* NAVA. ‖$P = 0.008$ PS_N *versus* NAVA. #$P = 0.001$ NAVA *versus* PS_P. **$P = 0.016$ PS_N *versus* PS_P. ††$P <$ 0.001 NAVA *versus* PS_P. ‡‡$P = 0.003$ NAVA *versus* PS_P. §§$P = 0.005$ PS_N *versus* PS_P. ‖‖$P = 0.009$ PS_N *versus* PS_P. ##$P = 0.002$ PS_N *versus* NAVA. ***$P = 0.013$ PS_N *versus* PS_P. †††$P = 0.004$ PS_N *versus* NAVA. §§§P = 0.013 NAVA *versus* PS_P. ‖‖‖$P = 0.004$ NAVA *versus* PS_P. ###$P = 0.015$ NAVA *versus* PS_P. ****$P = 0.002$ PS_N *versus* PS_P.

$Delay_{TR\text{-}exp}$ = expiratory trigger delay; $Delay_{TR\text{-}insp}$ = inspiratory trigger delay; $EAdi_{peak}$ = maximum peak of the diaphragm electrical activity; FIO_2 = inspired oxygen fraction; NAVA = neurally adjusted ventilatory assist; $\Delta P_{trigger}$ = drop in airway pressure during triggering phase; P_{aw} = airway pressure; P_{awmean}= mean P_{aw}; P_{awpeak} = peak of P_{aw}; $PaCO_2$ = arterial carbon dioxide tension; PaO_2 = arterial oxygen tension; PaO_2/FIO_2 = ratio between PaO_2 and FIO_2; PS_N = neurally controlled pressure support; PS_P = pneumatically controlled pressure support; PTP = pressure-time product; PTP_t = PTP during the triggering phase; PTP_{200} = PTP of the first 200 ms computed from the onset of ventilator assistance; $PTP_{300\text{-}index}$ = PTP of the first 300 ms from the onset of patient effort, indexed to the ideal PTP; $PTP_{500\text{-}index}$ = PTP of the first 500 ms from the onset of patient effort, indexed to the ideal PTP; RR_{mec} = mechanical respiratory rate; RR_{neu} = patient own neural respiratory rate; TI_{mec} = mechanical inspiratory time; TI_{neu} = neural inspiratory time; $TI/TTOT_{mec}$ = mechanical inspiratory duty cycle; $TI/TTOT_{neu}$ = neural inspiratory duty cycle; $Time_{synch}/TI_{neu}$ = ratio between time during which respiratory effort and ventilator assistance were synchronous and the TI_{neu}.

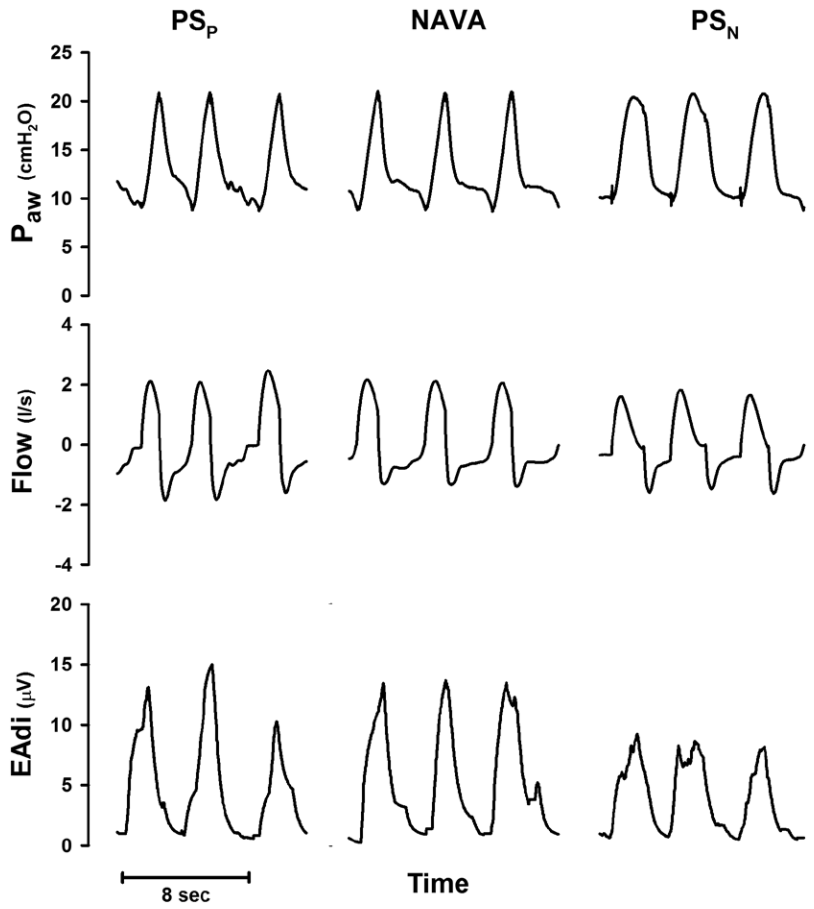

Fig. 2. Examples of tracings from a representative patient breathing during pneumatically controlled pressure support (PS_P), neurally adjusted ventilatory assist (NAVA), and neurally controlled pressure support (PS_N), delivered through a standard helmet. Airway pressure (P_{aw}), flow, and electrical activity of the diaphragm (EAdi) are displayed from *top* to *bottom*. PS_N reduces EAdi as opposed to both PS_P and NAVA.

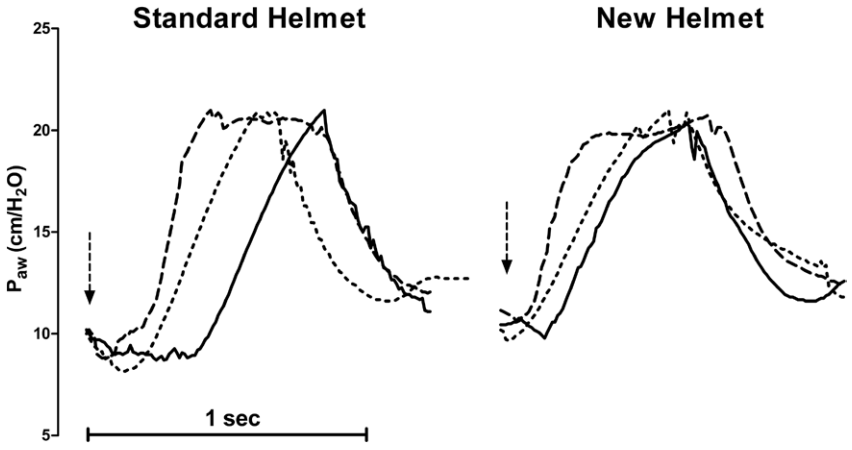

Fig. 3. Airway pressure (P_{aw}) profiles of single breaths during pneumatically controlled pressure support (*solid line*), neurally adjusted ventilatory assist (*dotted line*), and neurally controlled pressure support (*dashed line*) with both standard helmet (*left*) and new helmet (*right*), from another patient. In both panels, the *arrow* indicates the commencement of diaphragm effort, as assessed by diaphragm electrical activity.

effort down to the values observed during mask NIV; these specific settings, however, did not improve patient comfort. We recently demonstrated NH to be superior to SH in terms of patient comfort and triggering and pressurization performance; the median value of $EAdi_{peak}$, however, was lower with NH than with SH, without achieving statistical significance.[18] Notably, in the current study, EAdi is significantly reduced by PS_N with both helmets, compared to both PS_P and NAVA.

Moerer *et al.*[32] showed in healthy individuals that, compared to conventional pneumatic triggering during PS_P, EAdi triggering significantly improves comfort. In our study, both PS_N and NAVA settings improved trigger delays and PTP_t, compared to PS_P, with no significant difference between NAVA and PS_N. While Moerer *et al.*[32] in healthy volunteers set PEEP at 5 cm H_2O, we applied PEEP at 10 cm H_2O because the main reason for ICU admission was hypoxemic ARF; indeed, as shown in table 2, the median arterial oxygen tension/inspired oxygen fraction ratio never exceeded 250 mmHg throughout the study protocol. In patients undergoing NIV for prevention of postextubation respiratory failure, Vargas *et al.*[15] found that increasing PEEP from 5 to 8 cm H_2O reduced the work of breathing and improved patient–ventilator interaction overall, without affecting patient's comfort.

In hypoxemic patients undergoing invasive PS_P, Chiumello *et al.*[33] found that both the lowest and highest pressurization rates were associated with the worst level of comfort. In patients with chronic obstructive pulmonary disease (COPD) who are receiving PS_P through a facemask while recovering from an episode of acute hypercapnic respiratory failure, Prinianakis *et al.*[34] also observed that the highest speed of pressurization worsened patient comfort. Different from the study performed in intubated patients,[33] Prinianakis *et al.*[34] found the inspiratory muscle effort to be inversely related to the rate of pressurization.[34] Importantly, in the study by Prinianakis *et al.*,[34] the highest speed of pressurization caused air leaks that are well-known determinants of patient's intolerance to NIV. Worth mentioning, both the endotracheal tube and facemask are characterized by very low compliance, which makes ventilator-delivered pressure entirely transmitted to the airway. Quite the opposite, the helmet is inefficient in pressurizing the airway partly because of the soft compliant wall and the increased internal compressible volume[14] and primarily consequent to the downward displacement of the soft collar during ventilator insufflation in its standard version.[16–18]

Our study has some limitations deserving discussion. The number of patients enrolled is relatively small, as in the majority of the physiologic investigations.[3,5–8,14,15,18,21,33] We powered our study to detect a 50% improvement in comfort, as assessed by the NRS, with PS_N, as opposed to PS_P, for at least one of the two interfaces. PS_N significantly improves comfort with both interfaces, by 60% and 29% with SH and NH, respectively. Of note, PS_N improves comfort with respect to both PS_P and NAVA, with small and nonsignificant differences between the latter two modes.

We studied a mixed patient population with mainly hypoxemic ARF, including individuals with diverse underlying diseases, having in common only the indication for prophylactic NIV to prevent extubation failure and reintubation.[20] We chose this patient population because, for proper comfort assessment, we consider including awake, nonsedated, and cooperative patients important, which may be problematic in more acutely and severely ill patients.[35] In keeping with previous studies, we assess patient comfort by NRS[18,26,27]; this scale, however, is just formally validated for the assessment of pain[36–38] and dyspnea.[39]

We use the 10% threshold to indicate a clinically relevant rate of asynchronies, which may not be correct for NIV. Very recently, Doorduin *et al.*[9] found, in a selected population of COPD patients, that ineffective efforts increase drastically after timing errors between EAdi and airway pressure, reaching 20%. As we do not study COPD patients and do not take into account timing errors in the computation of the AI%, while considering only "major" asynchronies (ineffective efforts, autotriggering, and double triggering), we deem the 10% threshold appropriate, in keeping with several previous studies dealing with asynchronies in NIV.[5–8,18,25]

Finally, because of their specific characteristics, the helmets are the interfaces with the highest potential for improvement with PS_N, compared to both PS_P and NAVA. In fact, the improvements observed are generally less prominent with the more performing NH than with the SH.[16–18] It is uncertain whether the physiologic benefits we observe may occur when applying NIV by mask.

Conclusions

In patients receiving NIV by helmet for preventing extubation failure and reintubation, compared to both PS_P and NAVA, PS_N ameliorates patient comfort, while reducing the neural drive and effort and enhancing the pressurization rates. In addition, as opposed to PS_P, while not to NAVA, PS_N improves triggering performance and patient–ventilator synchrony. Whether these benefits may take place with other interfaces or when applying NIV to other categories of patients remains unclear and needs further evaluation.

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Competing Interests

Dr. Navalesi contributed to the development of the helmet Next (Castar Next; Intersurgical S.p.A., Mirandola, Italy), whose license for patent belongs to Intersurgical S.p.A., and received royalties for that invention. Dr. Navalesi received honoraria/speaking fees from Maquet Critical Care (Solna, Sweden), Covidien AG (Segrate, Italy), Draeger Medical GmbH (Corsico, Italy), Breas (Saint-Priest, France), Hillrom (Bussigny, Switzerland), and Linde AG (Munich, Germany). The other authors declare no competing interests.

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Address correspondence to Dr. Navalesi: Department of Translational Medicine, Eastern Piedmont University "A. Avogadro," Via Solaroli 17, 28100, Novara, Italy. paolo.navalesi@med.uniupo.it. Information on purchasing reprints may be found at www.anesthesiology.org or on the masthead page at the beginning of this issue. ANESTHESIOLOGY's articles are made freely accessible to all readers, for personal use only, 6 months from the cover date of the issue.

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The Ultimate Anesthetic? The Endlessly *Sleeping Endymion* of Cornacchini

Chiseled from marble in 1716, *Sleeping Endymion* (*right*) reflects the Rococo-Period prowess of Italian sculptor Agostino Cornacchini (1686 to 1754). According to classical Greek mythology, the handsome Endymion was a shepherd prince who was the first mortal to observe the moon. Personified as a Titan goddess named Selene, the Moon (*left*) reciprocated, unable to keep her eyes off the charming young man. She turned to her cousin, the king of the gods, to immortalize her dear Endymion. Zeus obliged by giving her lover the ultimate anesthetic, leaving Endymion forever young but forever sleepy. (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology.)

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