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Original Article

Pressure Support Versus Assisted Controlled Noninvasive Ventilation in Neuromuscular Disease

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Abstract

Introduction: Noninvasive ventilation (NIV) is being increasingly used in patients with chronic neuromuscular disorders, but the optimal ventilation mode remains unknown. We compared physiological short-term effects of assist/controlled ventilation (ACV) and two pressure-limited modes (pressure-support ventilation [PSV] and assist pressure-controlled ventilation [ACPV]) in patients with neuromuscular disease who needed NIV.

Methods: Tidal volume was 10 to 12 mL/kg. The ACPV mode used the same respiratory cycle timing as the volume-limited mode. The level of inspiratory support was set to achieve the same tidal volume during the other ventilatory modes.

Results: Thirteen patients with neuromuscular disease who met international criteria for NIV were included. The three ventilatory modes increased alveolar ventilation and decreased respiratory effort indices. However, no difference in breathing or respiratory effort was found among the three modes, with the exception that inspiratory peak flow and percentage of triggered cycles were higher during PSV than volume-limited ventilation. Interestingly, no relationship was observed between subjective patient preference and inspiratory effort indices or percentage of triggered cycles.

Conclusion: In chronic, stable patients with neuromuscular disease, both noninvasive ACV, ACPV, and PSV had similar effects on alveolar ventilation and respiratory muscle unloading, despite some differences in the pattern of breathing and percentage of triggered cycles.

Key Words: Noninvasive ventilation; home ventilation; pressure support ventilation; esophageal pressure time product; neuromuscular disease.

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Introduction

Noninvasive ventilation (NIV) has become a cornerstone in the management of patients with chronic respiratory failure resulting from neuromuscular disease *(1–4)*. Indeed, NIV lowers daytime carbon dioxide partial pressure in arterial blood [$PaCO_2$], raises daytime oxygen partial pressure in arterial blood [PaO_2], and eliminates morning headache and sleepiness.

Volume-limited ventilation remains a standard ventilatory mode for home NIV in patients with neuromuscular diseases *(5)*. Main advantages of assisted/controlled ventilation (ACV) are that it ensures a constant flow and guarantees a minimum level of minute ventilation.

Pressure-support ventilation (PSV) is pressure-limited ventilation activated by the patient's inspiratory effort. Once activated, the ventilator sends into the circuit a flow of

Table 1
Patient Characteristics

N	Diagnosis	Age (year)	Sex	BMI (kg/m^2)	VC (L, %pred)	MIP (cmH_2O)	MEP (cmH_2O)	PaO_2 (mmHg)	$PaCO_2$ (mmHg)
1	Poliomyelitis	33	M	18	1.250 (29%)	57	50	77	47
2	Poliomyelitis	65	M	22	1.180 (31%)	26	50	86	46
3	Sarcoglycanopathy	28	M	27	0.640 (14%)	20	40	96	49
4	Duchenne muscular dystrophy	20	M	24	0.520 (12%)	30	40	71	68
5	Congenital myasthenia	65	M	16	2.740 (69%)	49	80	73	49
6	Poliomyelitis	53	M	35	1.160 (34%)	50	70	64	50
7	Acid Maltase Deficiency	70	F	24	1.027 (46%)	24	47	64	50
8	Myasthenia	76	F	26	1.120 (56%)	26	69	65	59
9	Calpainopathy	65	M	23	0.890 (18%)	20	40	74	49
10	ParsonageTurner Syndrome with diaphragmatic palsy	64	M	30	2.480 (64%)	66	100	68	42
11	Acid Maltase Deficiency	43	M	28	1.920 (43%)	22	51	78	47
12	Sarcoglycanopathy	35	M	19	0.760 (16%)	17	58	83	53
13	Duchenne muscular dystrophy	23	M	47	0.610 (13%)	10	10	67	51

Blood gas results were obtained during spontaneous breathing.
Abbreviations: BMI, body mass index; VC, vital capacity; MIP, maximal inspiratory pressure; MEP, maximal expiratory pressure.

gas that is sufficient to meet the patient inspiratory demand so that the pressure rapidly reaches the set level. A pressure plateau is then achieved and maintained until the inspiratory flow decreases below a predetermined value and, consequently, exhalation occurs. Thus, during PSV, tidal volume (V_T) and inspiratory time are influenced by the patient's respiratory effort. This results in greater patient comfort *(6)*. Currently, PSV is widely used for NIV *(7–10)*. However, the appropriateness of PSV for patients with neuromuscular disease remains a matter of debate.

Another pressure limited ventilatory mode is assist pressure-controlled ventilation (APCV) *(11)*. Despite the fact that APCV is a pressure-limited ventilatory mode, it could be considered as an intermediate mode, with a flow pattern similar to PSV but a respiratory cycling pattern similar to ACV.

The aim of this study was to evaluate and compare the effects of ACV, APCV, and PSV on alveolar ventilation and respiratory muscle activity in stable patients with neuromuscular disease meeting criteria for NIV *(12)*.

Methods

Patients

The study was approved by the appropriate ethics committee. Written informed consent was obtained from all patients. Patients were consecutively enrolled in the study if they were older than age 18 years, had chronic respiratory failure resulting from neuromuscular disease, met international criteria for NIV *(12)*, and had not experienced episodes of acute respiratory failure within the last 2 months. Exclusion criteria were cardiac failure, hemodynamic instability, obstructive respiratory syndrome, allergy to lidocaïne, impaired swallowing, or enrollment in other research protocols. Causes of neuromuscular disease in the patients included in the study are listed in Table 1.

Training Session and Ventilator Settings

During the week preceding the study, patients were familiarized with the NIV modes selected for the study. NIV was carefully explained to the patients and progressively applied several hours each day until the patients felt comfortable with its use. NIV was delivered through a well-fitting nasal mask (Sullivan®, Resmed, Ltd., North Ryde, Australia). No humidification device was added during the study.

For ACV (Eole 3®, SAIME, Savigny le Temple, France), flow rate was constant and the inspiratory/expiratory ratio was half. The recommended V_T in chronic NIV is about 10 and 15 mL/kg *(13)*. In our department, which almost exclusively treats patients with neuromuscular disease, V_T is usually set between 10 and 12 mL/kg. Respiratory rate was set two to three breaths below the awake spontaneous breathing, according to consensus conference *(14)*.

For PSV (Achieva®, Puritan Bennett, Pleasanton, CA), pressure support was initially set at 8 cmH_2O. The initial inspiratory pressure delivery slope was set close to the steepest value. Inspiratory pressure was increased every 5 minutes by 2 cmH_2O until V_T reached 10 to 12 mL/kg. Expiratory flow trigger was set to a value corresponding to a fall in inspiratory flow equal to 75% of the peak flow. The backup rate was set at 10 breaths/minute.

For APCV (Achieva), backup rate and inspiratory/expiratory ratio were the same as those for ACV. Inspiratory pressure was set as for PSV.

Measurement

Flow was measured using a Fleisch no. 2 pneumotachograph (Lausanne, Switzerland) situated between the mask and the ventilatory circuit. Mask pressure (Maw) was measured using a differential pressure transducer (Validyne MP 45 ± 100 cmH2O, Northridge, CA). The flow signal was electronically integrated to calculate V_T and minute ventilation. Leaks were reduced as much as possible according to a difference of less than 10% between inspiratory and expiratory V_T. Esophageal pressure and gastric pressure were recorded using a catheter-mounted transducer (Gaeltec, Dunvegan, Isle of Skye, UK). Appropriate placement was verified by an occlusion test *(15)*. All signals were sampled at 128 Hz and passed to a computer

Table 2
Arterial Blood Gas and Respiratory Parameters During SB, ACV, APVC, and PSV

	SB	*ACV*	*APCV*	*PSV*	*ANOVA, p*
V_T, L	0.31 ± 0.12	0.71 ± 0.20[a]	0.74 ± 0.29[a]	0.77 ± 0.23[a]	<0.0001
RR, breaths/minute	21 ± 6	17 ± 2	16 ± 3	13 ± 3[a]	<0.0001
V_E, L/minute	6.0 ± 1.8	12.2 ± 3.3[a]	11.8 ± 5.0[a]	9.7 ± 1.8	<0.0001
T_I, s	1.42 ± 0.45	1.37 ± 0.24	1.41 ± 0.28	1.64 ± 0.32	0.08
V_T/T_I, L/second	0.23 ± 0.06	0.54 ± 0.20[a]	0.54 ± 0.26[a]	0.48 ± 0.13[a]	<0.0001
Vi max, L/second	0.30 ± 0.10	0.59 ± 0.19	0.76 ± 0.24	0.83 ± 0.19[b]	<0.0001
$PaCO_2$, mmHg	51± 8	43 ± 8	45 ± 13	43 ± 7	<0.005
PaO_2, mmHg	74 ± 10	80 ± 11	84 ± 11	84 ± 12	<0.005
pH	7.39± 0.05	7.43 ± 0.05	7.43 ± 0.06	7.44 ± 0.05	<0.005

Abbreviations: SB, spontaneous breathing; ACV, assisted controlled ventilation; APCV, assisted pressure-controlled ventilation; PSV, pressure-support ventilation; V_T, inspiratory tidal volume; RR, respiratory rate; V_E, minute ventilation; T_I, inspiratory time; V_T/T_I, mean inspiratory flow; Vi max, maximal inspiratory flow.

[a]Statistically significant versus SB ($p < 0.0083$, Bonferroni test).

[b]Statistically significant difference between PSV and ACV, ($p < 0.016$, Bonferroni test).

using an analogic-numeric system (MP100, Biopac System, Goleta, CA).

Study Protocol

All studies were performed in the afternoon, with the patient in a semirecumbent position. The three ventilatory modes were investigated in a random order: ACV, APCV, and PSV. Each ventilatory mode was applied for 25 minutes and separated by a 25-minute spontaneous breathing period (SB). Data were recorded during the last 5 minutes of each 25-minute period, once a stable pattern was observed. Blood was sampled from the radial artery at the end of each period. Patients were asked which NIV mode provided the greatest level of comfort.

Data Analysis

Respiratory pattern parameters were measured using flow signal recording. Based on a breath analysis (flow profile, drop in Maw), we determined percentages of triggered cycles relative to total cycles during ACV, APCV, and PSV for 30–40 consecutive cycles. Esophageal pressure-time products (PTPes), diaphragmatic pressure-time products (PTPdi) and respiratory mechanics were computed, as described in previous studies *(16–18)*.

Statistical Analysis

Data are given as means ± standard deviation (SD). Differences among the ventilatory modes were assessed by repeated-measure ANOVA. (SB, ACV, APCV, PSV). When ANOVA appeared appropriate (F-test with p value less than 0.05), pairwise comparisons were performed using the Bonferroni test.

Results

Patients

Over a 1-year period, 13 patients were recruited for the study. Their anthropometric and baseline respiratory data are shown in Table 1.

Ventilator Adjustments

The inspiratory pressure levels with PSV and ACV were 12.4 ± 2.0 and 12.0 ± 2.0 cmH_2O, respectively. Oxygen therapy was not delivered during NIV.

Breathing Pattern and Gas Exchange

Breathing pattern and arterial blood gas data are shown in Table 2. ACV, APCV, and PSV increased alveolar ventilation, V_T, and minute ventilation and decreased respiratory rate when compared to SB, as reported in Table 2. Inspiratory time was not modified by NIV, as compared to SB. Mean inspiratory flow (V_T/T_I) was higher with ACV, APCV, and PSV than with SB. Maximal inspiratory flow was significantly higher with PSV than with ACV (0.83 ± 0.19 versus 0.59 ± 0.19 L/second, respectively; p less than 0.016). Other breathing patterns and arterial blood gas data were not different among the three ventilatory modes evaluated (Table 2).

Respiratory Effort Parameters

Data on respiratory mechanics are shown in Table 3. Neither dynamic intrinsic end-expiratory positive pressure nor dynamic lung compliance were modified by NIV. ACV, APCV, and PSV all resulted in a significant decrease in PTPes and PTPdi compared with SB. However, PTPes and PTPdi showed no differences among the three ventilatory modes (Table 3).

Cycle Triggering

Triggering results are reported in Tables 3 and 4. Absence of triggering was noted among 3, 9, and 10 patients during PSV, APCV, and ACV, respectively. Despite the absence of triggering, patients produced noticeable inspiratory efforts in phase with ventilator insufflations. In the 10 patients who triggered during PSV, inspiratory efforts were similar during cycles with and without triggering (PTPdi was 14.5 ± 5.0 and 13.0 ± 4.3 cmH_2O. L/second, respectively, p = NS). No correlation was found between the percentage of triggered cycles during PSV and vital capacity ($r = 0.35$, NS) or maximal inspiratory pressure ($r = 0.51$, NS).

Subjective Preferences of the Patients

When asked which NIV mode provided the best level of comfort, 4 of 13 patients preferred ACV, 4 preferred APCV, and 5 preferred PSV. Table 4 shows the preferred ventilatory mode, the ventilatory mode associated with the lowest level of inspiratory effort as determined by PTPes, and the percentage of

Table 3
Mechanical and Respiratory Effort Parameters During SB, ACV, APVC, and PSV

	SB	*ACV*	*APCV*	*PSV*	*ANOVA, p*
$PEEPI_{dyn}$, cm H_2O	0.21± 0.19	0.23 ± 0.19	0.28 ± 0.16	0.23 ± 0.19	NS
CL_{dyn}, L/cm H_2O	0.088 ± 0.074	0.088 ± 0.041	0.088 ± 0.037	0.079 ± 0.047	NS
Swing Pes, cm H_2O	6.39 ± 2.10	1.54 ± 1.02[a]	1.67 ± 1.00[a]	2.10 ± 1.05[a]	<0.0001
Swing Pdi, cm H_2O	7.52 ± 4.12	1.31 ± 1.01[a]	1.36 ± 1.09[a]	2.11 ± 1.11[a]	<0.0001
PTPes, cm H_2O.s/minute	126 ± 35	54 ± 45[a]	62 ± 65[a]	70 ± 42[a]	<0.0001
PTPdi, cm H_2O.s/minute	161 ± 74	59 ± 61[a]	64 ± 52[a]	66 ± 40[a]	<0.0001
Cycle Triggering, %	—	4.5 ± 12.3	14.5 ± 29.4	33.6 ± 26.9[b]	0.007

Abbreviations: SB, spontaneous breathing; ACV, assisted controlled ventilation; APCV, assisted pressure-controlled ventilation; PSV, pressure-support ventilation; $PEEPI_{dyn}$, dynamic intrinsic end-expiratory positive pressure; CL_{dyn}, dynamic lung compliance; Pes, esophageal pressure; Pdi, diaphragmatic pressure; cycle triggering, percentage of cycles triggered by the patient.

[a]Statistically significant versus SB ($p < 0.0083$, Bonferroni test).

[b]Statistically significant difference between PSV and VAC ($p < 0.016$, Bonferroni test).

Table 4
Mode Preferred by Each Patient, Respiratory Unloading and Triggering %

			Triggering %		
Patient no.	*Patient choice*	*<PTPes*	*ACV*	*APCV*	*PSV*
1	PSV	APCV	10	90	50
2	PSV	ACV	0	0	20
3	ACV	ACV	0	0	0
4	PSV	ACV	0	0	10
5	ACV	APCV	0	50	20
6	APCV	PSV	0	0	20
7	APCV	ACV	0	0	0
8	PSV	ACV	20	20	50
9	APCV	ACV	0	0	70
10	ACV	ACV	40	20	60
11	ACV	PSV	0	0	0
12	PSV	APCV	0	0	20
13	APCV	APCV	0	0	50

Abbreviations: SB, spontaneous breathing; ACV, assisted controlled ventilation; APCV, assisted pressure-controlled ventilation; PSV, pressure-support ventilation; < PTPes, ventilatory mode providing the lowest esophageal pressure-time product; Triggering %, percentage of triggered cycles/total cycles.

triggered cycles during the three modes. No relationship was found among these parameters.

Discussion

The main finding of this study was that PSV, APCV, and ACV produced a similar improvement in pattern of breathing and alveolar ventilation and induced a comparable reduction in inspiratory effort in patients with chronic neuromuscular disease requiring NIV. To our knowledge, this study is the first to compare respiratory effort parameters in patients with neuromuscular disease during PSV, ACV, and APCV.

In patients with respiratory failure secondary to neuromuscular disease, home NIV is usually used at night *(2,3)* because of the risk of hypoventilation related to rapid eye movement sleep *(19)*. During sleep, leakage may occur around the mask or through the mouth, resulting in a reduction in the effectiveness of NIV *(20)*. Interestingly, Schonhofer and colleagues *(21)* showed that daytime and nocturnal NIV were similar in reversing hypoventilation. However, our findings cannot be directly extrapolated to nocturnal NIV. The invasive measurements used in our study would be difficult to perform during sleep and might interfere with sleep architecture.

We acknowledge that it would be preferable to use the same ventilator to compare different ventilatory modes. However, during this study, no PSV home ventilator was available that was able to deliver a constant inspiratory flow during ACV mode. For each condition, we used the same expiratory valve (Model T.T 11 372-00; Puritan Bennett), which was considered one of the best expiratory valves *(22)*.

ACV and APCV produced similar improvements in minute ventilation and respiratory muscle unloading compared to SB. In theory, when ACV and APCV are adjusted to obtain a similar V_T, the main difference between the two modes lies in the flow pattern. Indeed, the flow pattern is constant during ACV and decelerates during APCV. Previous studies have suggested that the flow pattern may be of importance in reducing respiratory muscle work during ACV *(23)*. However, Cinnella and colleagues *(24)* showed that the delivery of breaths with a

constant or decelerating flow pattern influenced the inspiratory effort when V_T was small (8 mL/kg) but not when V_T was high (12 mL/kg). Our ventilatory settings and results were similar to those of Cinnella's high V_T group. Furthermore, because our population had an increase in elastic rather than resistive loading *(25)*, the abnormal loading occurred more during the end of inspiration rather than the start of inspiration. In contrast, chronic obstructive pulmonary disease (COPD) is associated with an increase in resistive loading. Thus, a decelerating flow that is maximal at the start of inspiration is unlikely to be beneficial in patients with chronic neuromuscular disease.

In our study, an interesting finding regarding ACV was the low rate of cycle triggering. Similar results have been reported in patients with cystic fibrosis *(10)*. We verified that low triggering rate was not caused by a triggering failure *(26)*. In patients with neuromuscular disease, high output and rapid shallow breaths characterize the spontaneous pattern of breathing *(27)*. When ventilated, these patients tend to reduce their respiratory rate substantially. We found that 10 and 9 patients had no triggering during ACV and APCV, respectively. Interestingly, despite absence of triggering, all patients maintained an effort that was synchronized with the ventilator. Thus, absence of triggering may not indicate absence of effort in this population.

When compared to ACV, PSV produced a similar decrease in inspiratory effort despite a significantly higher rate of cycle triggering. This may be attributable to the good sensitivity of the inspiratory trigger used. This is supported by similar PTPdi values between triggered and nontriggered cycles.

In our study, five patients preferred PS, four preferred ACV, and four preferred APCV. Patient preference seemed to be independent from the respiratory unloading; indeed, patients did not consistently choose the ventilatory mode associated with the greater respiratory unloading. The small sample and design of our study did not permit us to address this issue more extensively. It is noteworthy that similar results have been reported by our group in patients with cystic fibrosis *(10)*, and by others in patients with acute hypercapnic respiratory failure complicating COPD *(28)*.

Because our patients had stable chronic respiratory failure, hypercapnia probably occurred to avoid respiratory muscle failure. In keeping with this assumption, the diaphragm tension-time index (60 PTPdi/per minute × Pimax) *(29)* during SB in each patient remained lower than 0.15, a value considered the critical threshold indicating diaphragmatic fatigue *(29)*. Thus, the objective of mechanical ventilation is to improve alveolar ventilation without increasing respiratory effort, but it is unclear whether an additional objective would be to decrease the respiratory effort. In the study by Jubran and colleagues *(30)*, in patients with COPD, a PTPes less than 125 cmH_2O seconds/minute was considered a desirable level of inspiratory effort during PSV. Interestingly in our study, during SB, five (39%) patients had a PTPes value greater than 125 cmH_2O seconds/minute The latter remained above 125 cmH_2O seconds/minute for two patients during PSV and for one patient during ACV. However, criteria developed for patients with COPD may not be appropriate for patients with neuromuscular disease. Nevertheless, maintaining a reasonable level of inspiratory activity may be desirable. Indeed, it was suggested that inspiratory training may improve respiratory muscle function in patients with neuromuscular disease who were followed for up to two years *(31)*. Finally, because $PaCO_2$ improved and inspiratory effort decreased in all our patients using the three NIV modes, we can consider that these three modes were beneficial.

In conclusion, ACV, APCV, and PSV had similar effects on alveolar ventilation and respiratory muscle unloading despite differences in inspiratory flow pattern and triggered cycle percentage. Patient preference was not based on respiratory effort reduction. These data suggest that PSV and APCV are as appropriate as ACV for patients with chronic neuromuscular disease requiring NIV. Long-term effects of these modes in such patients should to be studied.

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