Automatic air-leak compensation in neuromuscular patients: A feasibility study

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Dual modes;
Neuromuscular disease

Summary
Air leaks often result in alveolar hypoventilation in mechanically ventilated patients with neuromuscular disease. The primary objective of this study was to assess the feasibility, efficacy and tolerance of a ventilator equipped with an automated air-leak compensation system in a clinical situation. Fourteen neuromuscular patients with nocturnal air leaks during home ventilation were included in a prospective randomised crossover study. A modified VS Ultra ventilator was studied during two consecutive nights and patients were randomly ventilated with and without a leak-compensation system, respectively. Tolerance, minute ventilation, blood gas values, sleep parameters, and nocturnal oxygen saturation were assessed. Leak compensation significantly increased the mean inspiratory and expiratory tidal volumes (731 ± 312 vs. 1094 ± 432 ml [p = 0.002] and 329 ± 130 vs. 496 ± 388 ml [p = 0.006], respectively) and inspiratory and expiratory flows (51.7 ± 8.2 vs. 61.8 ± 12.4 l/min [p = 0.016] and 63.3 ± 26.2 vs. 83.3 ± 37.8 l/min [p = 0.013], respectively). The system acted by increasing both inspiratory time (from 1355 ± 230 to 1527 ± 159 ms, p = 0.038) and inspiratory pressure (from 14.0 ± 2.8 to 18.3 ± 3.4 cm H2O, p = 0.002). Leak compensation improved arterial PCO2 (6.18 ± 0.9 vs. 5.21 ± 1.0 kPa, p = 0.004), slow-wave-sleep latency (119 ± 69 vs. 87 ± 35 min, p = 0.04), and tolerance. Air-leak compensation is feasible and may produce

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Introduction

Long-term home ventilation is an established treatment for neuromuscular patients with respiratory failure, as it improves clinical symptoms, daytime function, arterial blood gas values, sleep quality,^1^ quality of life,^2^ and survival.^3^ No specific recommendations regarding the choice between volume-cycled and pressure-cycled ventilators are made in guidelines about positive-pressure ventilation for patients with chronic respiratory failure.^4^ Despite increased interest in the less expensive pressure-cycled ventilators, volume-targeted ventilators remain widely used for non-invasive ventilation (NIV) in patients with neuromuscular disease.5 Advantages of volume-cycled ventilation may include greater patient comfort and correction of nocturnal and diurnal hypoventilation.^6^ In addition, volume-cycled ventilators deliver a constant volume independently from respiratory impedance, and they have better alarm capabilities^7^ compared to pressure-cycled ventilators. The main drawback of volume-cycled ventilation is that the set volume is not delivered in the event of air leaks or increased airway resistance.^8,9^ Pressure-cycled ventilators are characterised by greater sensitivity of flow triggering, better patient-ventilator synchronisation, and an ability to compensate for air leaks.10 However, the use of pressure-targeted modes in patients with neuromuscular diseases remains controversial, because the delivered tidal volume (Vt) varies according to chest-wall compliance and airway resistance. Leak-compensating capabilities may be overwhelmed if the ventilator is unable to maintain inspiratory and expiratory cycling, stay at the targeted pressure, and lengthen the insufflation time.7,11 Air leaks may result in persistent hypercapnia^8^ and may occur despite adequate adherence to the prescribed mechanical-ventilation regimen. Air leaks are of special concern during REM sleep,12 when muscle hypotonia increases the risk of alveolar hypoventilation in the event of inadequate ventilator assistance. Minimizing air leaks may be among the best ways to improve the efficiency of assisted ventilation.13 However, several measures used to avoid leaks are associated with poor tolerance in dependent patients 8,14,15 and require frequent arterial blood gas measurements and/or repeated sleep recordings to achieve optimal ventilation. We designed a volume-assured pressure-targeted mode to counterbalance leaks. Volume-assured pressure-targeted modes combine the advantages of pressure-targeted and volume-targeted modes.16–18 We modified the algorithm of the commercial software to render the inspiratory time and delivered pressure dependent on the patient’s respiratory volume, thereby minimizing hypoventilation in the event of leakage. Here, we report preliminary results obtained in a clinical situation with this air-leak compensating system in 14 home-ventilated neuromuscular patients who had nocturnal air leaks.

Methods

Patients

We studied patients who had neuromuscular disease requiring home ventilation and who had nocturnal air leaks identified on the basis of dry mouth or symptoms of nocturnal hypoventilation (e.g., daytime sleepiness or morning headaches) and/or persistent hypercapnia >6.0 kPa despite adequate adherence to the ventilation regimen. Non-inclusion criteria were unwillingness to provide consent to participation in the study, age younger than 18 years, respiratory distress, and need for oxygen therapy.

Ventilator settings

We used the VS Ultra ventilator (SAIME, Savigny le Temple, France), which is a home ventilator capable of volume- and pressure-targeted modes. The VS Ultra ventilator is usually proposed in a single circuit configuration. An optional double limb configuration is also available incorporating an expiratory spirometry. The ventilator was used both in pressure-controlled mode and in a double-circuit configuration.19 The back-up rate, inspiratory time (Ti), and inspiratory pressure (Ipap) settings were those normally used by the patient at home. Pressure was set at the usual level of Ipap if the patient used a pressure-targeted mode at home. In patients who normally used volume-targeted ventilation, Ipap was set during the day to achieve the same Vt as with the home ventilator. Adjustments were made to obtain a daytime arterial PCO2 equivalent to the PCO2 observed with the home ventilator. No Epap was prescribed. The trigger was set at 3 (1 being the most and 6 the least sensitive trigger value).

When the leak-compensation mode is active, the ventilator monitors the patient’s expiratory tidal volume (Vte) cycle by cycle, and an algorithm automatically adjusts the ventilator parameters to maintain a minimum level of ventilation. The ventilator continuously calculates the mean of the previous and current Vte value. A security volume (Vts) is set based on the home ventilator parameters: Vts is the set Vt if the usual mode is volume-cycled and the Vt measured by the ventilator if the usual mode is pressure-cycled. When leaks occur, the ventilator tries to maintain Vte at Vts or higher. If Vte falls below Vts, the ventilator automatically increases Ti cycle by cycle, in steps of +11%, to lengthen the insufflation while keeping the pressure constant, to a maximum of +33% of the initial Ti (Ti_max). The ventilator stops the increase procedure at the Ti that achieves the Vts. When Vts is not achieved at Ti_max, the ventilator then automatically increases Ipap cycle by cycle, in steps of +1 cm H2O, to a maximum of +5 cm H2O (Ipap_max). The ventilator stops the increase
procedure at the Ipap value that achieves the Vts. If Vts is still not achieved, the ventilator functions at Ti$_{\text{max}}$ and Ipap$_{\text{max}}$. If Vts is achieved, the ventilator returns gradually to the previous settings, as long as Vte remains above Vts. The leak-compensation procedure starts at the first drop in Vte. For this study, we developed a counter that recorded the number of times the air-leak compensation procedure was started.

**Study design**

We used a prospective randomised crossover design. The study was approved by our institutional review board, and written informed consent was obtained from all patients prior to study inclusion. After the randomisation procedure, the patients were studied during two nights. They used their own interface during both nights. Patients were unaware of the ventilation modes used during the two nights.

**Measurements**

Full polysomnography was performed using the BRAIN-NET system (Medatec, Brussels, Belgium). Electrophysiological recordings included three electro-encephalogram channels, two electro-oculogram channels, a chin electromyogram, an electrocardiogram (V2 lead), and electromyograms of the right and left tibialis muscles. Inspiratory and expiratory flows were measured using a pneumotachograph (Fleisch #2, Lausanne, Switzerland) situated between the interface and the ventilatory circuit (after the Y piece). Interface pressure was measured using a differential pressure transducer (Validyne MP 45 ± 100 cm H$_2$O, Northridge, CA). Abdominal and thoracic movements were recorded using respiratory inductive plethysmography (Respitrace; Ambulatory Monitoring, Ardsley, NY). Gas exchanges were assessed by continuous recording of oxygen saturation (SpO$_2$) (Ohmeda Biox, BOC Healthcare, Boulder, CO) and of transcutaneous carbon dioxide tension (PtCO$_2$) (Radiometer TCM3, Copenhagen, Denmark).

**Data analysis**

Minute ventilation, Vte and Vti, mean inspiratory and expiratory flow ($F_{\text{inspi}}$ and $F_{\text{expi}}$), Ti, Ttot, Ipap, and respiratory rate (RR) were measured continuously during both nights. Morning arterial blood gas values were measured at the end of each night just before disconnection of the ventilator.

Tolerance was assessed at the end of each night using a 10-cm visual analogue scale (VAS) on which 0 indicated very poor tolerance and 10 very good tolerance. At the end of the study, the patients were asked whether they would like to use the leak-compensation mode.

Sleep data for all patients were read by the same operator (GM), who was blinded to the ventilation mode. Sleep was staged in 30-s periods using Rechtschaffen and Kales criteria. If arousals were evaluated using American Sleep Disorders Association (ASDA) criteria. Time of sleep onset, total sleep period (TSP, time in minutes from sleep onset to final wakening), total sleep time (TST, time in minutes spent sleeping during the TSP), sleep efficiency index (TST/TSP × 100), number of arousals, percentage of TST spent in each sleep stage (stage 1, stage 2, stages 3–4 or slow-wave-sleep, and rapid-eye-movement sleep [REM]), duration of delta sleep (stages 3 and 4) in minutes, and REM latency were recorded.

Apnoeas and hypopnoeas were scored using inductive plethysmography as previously described. Minimal and mean SaO$_2$ were measured, as well as the time in minutes and percentage of time spent with SaO$_2$ < 90%. The difference in peak PtCO$_2$ between wakefulness and sleep (Delta PtCO$_2$) was calculated.

**Statistical analysis**

All data are expressed as mean (SD) values. Respiratory and sleep parameters with or without leak compensation were compared using the non-parametric Wilcoxon rank test. Values of $p$ smaller than 0.05 were considered significant.

**Results**

**Patients characteristics**

Fourteen patients were randomised. Nocturnal PtCO$_2$ was recorded in only 10 patients. Mean Vc was 1178 ± 493 ml in the seated position and 1049 ± 484 ml in the supine position. Mean Pr$_{\text{max}}$ was 40 ± 20 cm H$_2$O and mean Pe$_{\text{max}}$ was 40 ± 19 cm H$_2$O. Of the 14 patients, 13 used a ventilator at home during the night only and one required 24-hour ventilation. All 14 patients complained of nocturnal leaks and five patients had persistent hypercapnia during mechanical ventilation. Patient characteristics are reported in Table 1. With the home ventilator, mean $V_t$ was 665 ± 142 ml, mean RR was 15.5 ± 2.6 breaths/min, and mean Ti was 1.25 ± 0.14 s.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Respiratory parameters and morning blood gas values with and without the leak-compensation system.</th>
</tr>
</thead>
<tbody>
<tr>
<td>$N = 14$</td>
<td><strong>No compensation</strong></td>
</tr>
<tr>
<td>$V_{ti}$, ml</td>
<td>731 ± 312</td>
</tr>
<tr>
<td>$V_{te}$, ml</td>
<td>329 ± 130</td>
</tr>
<tr>
<td>$F_{\text{inspi}}$, L/min</td>
<td>51.7 ± 8.2</td>
</tr>
<tr>
<td>$F_{\text{expi}}$, L/min</td>
<td>63.3 ± 26.2</td>
</tr>
<tr>
<td>Ti, ms</td>
<td>1355 ± 230</td>
</tr>
<tr>
<td>Ti/tot</td>
<td>0.40 ± 0.05</td>
</tr>
<tr>
<td>RR</td>
<td>17.9 ± 3.4</td>
</tr>
<tr>
<td>Ipap cm H$_2$O</td>
<td>14.0 ± 2.8</td>
</tr>
<tr>
<td>pH</td>
<td>7.39 ± 0.04</td>
</tr>
<tr>
<td>PaCO$_2$, kPa</td>
<td>6.18 ± 0.9</td>
</tr>
<tr>
<td>PaO$_2$, kPa</td>
<td>11.2 ± 2.0</td>
</tr>
<tr>
<td>CO$_2$ total, mmol/l</td>
<td>29.2 ± 3.5</td>
</tr>
<tr>
<td>SaO$_2$%</td>
<td>95.7 ± 2.1</td>
</tr>
</tbody>
</table>

Abbreviations: $V_{ti}$, inspiratory tidal volume; $V_{te}$, expiratory tidal volume; $F_{\text{inspi}}$, inspiratory flow; $F_{\text{expi}}$, expiratory flow; Ti, inspiratory time; Tot, total duty cycle; RR, respiratory rate; Ipap, inspiratory pressure.
Mechanical ventilation parameters with and without air-leak compensation

Respiratory and ventilator parameters
Mean set Ipap was 15.5 ± 3.1 cm H2O and mean set Vts was 633 ± 118 ml (Tables 1 and 2). Without leak compensation, 50% of the target Vts was achieved, compared to 74% with leak compensation (Table 2). Mean percentage of compensated cycles ([number of compensated cycles/number of effective cycles] × 100) was 97.5% (8687/8907 cycles). With leak compensation, Vti, Ti, Ttot, and Ipap increased significantly (Table 2, Fig. 1). Significant increases in Finspi and Fexp were noted (Table 2). Mean ventilation time was similar in the two study nights (9.1 ± 0.7 vs. 8.9 ± 1.2 h, p = 0.60).

Arterial blood gas values
Immediately before ventilator disconnection, arterial P\(CO_2\) was significantly lower and pH significantly higher with air-leak compensation (Table 2). No significant effects on alkaline reserve or PO\(2\) were noted.

Sleep parameters
The VAS scores indicated that tolerance of ventilation was better with the air-leak compensation system (Table 2). We found no effects on TST or sleep efficiency. Significant decreases were noted in slow-wave sleep latency and non-significant decreases in stage 1 and REM-sleep latencies. No differences in sleep-stage durations were found, and neither was there any effect on sleep arousal indices or the incidence of hypopnoea/apnoea. With air-leak compensation, the percentage of time spent with SaO\(_2\) <90% tended to be lower, and there was a non-significant increase in delta P\(t\)CO\(_2\). At the end of the study, nine (66%) patients stated that they would like to use the air-leak compensation system at home.

Discussion
In this short-term study conducted in home-ventilated neuromuscular patients who complained of nocturnal air leaks, an automated air-leak compensation system improved minute ventilation, blood gas values, and sleep parameters.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Sleep parameters with and without leak compensation.</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 14</td>
<td>No compensation</td>
</tr>
<tr>
<td>VAS score</td>
<td>6.4 ± 2.0</td>
</tr>
<tr>
<td>TST, min</td>
<td>332 ± 87</td>
</tr>
<tr>
<td>Sleep efficiency, %</td>
<td>76.3 ± 13.2</td>
</tr>
<tr>
<td>Stage 1 sleep latency, min</td>
<td>66 ± 48</td>
</tr>
<tr>
<td>Stages 3, 4 sleep latency, min</td>
<td>119 ± 69</td>
</tr>
<tr>
<td>REM sleep latency, min</td>
<td>188 ± 114</td>
</tr>
<tr>
<td>Arousal/(\mu) arousals index, n/h</td>
<td>20.1 ± 13.2</td>
</tr>
<tr>
<td>Apnoea/hypopnoea index, n/h</td>
<td>7.5 ± 13.0</td>
</tr>
<tr>
<td>Mean SaO(_2) %</td>
<td>93.8 ± 2.6</td>
</tr>
<tr>
<td>Minimal SaO(_2) %</td>
<td>86.4 ± 6.6</td>
</tr>
<tr>
<td>% Time SaO(_2) &lt;90%</td>
<td>7.4 ± 17.4</td>
</tr>
<tr>
<td>Delta P(t)CO(_2) (mm Hg)</td>
<td>3.52 ± 6.85</td>
</tr>
</tbody>
</table>

Abbreviations: VAS, visual analogue scale; TST, total sleep time; REM, rapid-eye-movement sleep; \(\mu\) arousals, micro-arousal; SaO\(_2\), oxygen saturation; P\(t\)CO\(_2\), transcutaneous P\(CO_2\).
Air leaks raise major problems during mechanical ventilation in patients with chronic or acute respiratory failure. In home-ventilated patients, leaks can occur during invasive or non-invasive ventilation. Air leaks are particularly common around nasal masks but occur also with other interfaces such as oronasal masks and uncuffed tracheostomy tubes. Air leaks during the day were reported to decrease the effective Vt by up to 34%; leak severity correlated to PCO₂, and the most common cause of leakage was an inadequate seal between the interface and the patient. During sleep, Vt reduction due to air leaks may have severe adverse effects in neuromuscular patients. Although these methods can other leak-related complications, such as upper airway obstruction, swallowing disorders, and difficulty clearing the airway. A tightly applied mask may cause pressure sores. In tracheostomised patients, using a cuffed tube may reduce leaks but also limits phonation and carries a risk of tracheal lesions in the long term. In addition, in the event of ventilator failure, the dependent patient is unable to remove an oronasal mask in order to call for help. Furthermore, methods designed to improve the patient-interface seal are not effective in all patients. Another strategy, which is used empirically, consists in increasing Vt during volume-targeted ventilation, or pressure during pressure-targeted ventilation, in order to increase Vti. This strategy is usually well tolerated and efficient with volume-targeted ventilation but increases upper airway pressure during leak-free periods with pressure-targeted ventilation. Although these methods can reduce the risk of hyperventilation, they fail to eliminate other leak-related complications, such as upper airway dryness, nasal obstruction, and ineffective triggering. On the other hand, we could have used a commercial volume-assured-pressure support, in this study, to achieve a sufficient minute ventilation in case of leaks. These devices increase the Vti especially when working with a simple circuit configuration without monitoring of the expiratory volume. It may expose to inefficient compensation especially when inspiratory leaks are present.

It has been suggested that leaks may induce arousal. However, despite an increase in absolute leak size, we found that increasing air leaks via the compensation system failed to induce arousal. Our air-leak compensation system was well tolerated, although our patients were severely disabled and dependent. Few studies have sought to determine the optimal mode of ventilation in neuromuscular patients. Pressure- and volume-targeted modes seem to have similar effects on alveolar hypoventilation. Home ventilators vary markedly regarding their ability to compensate for air leaks. Pressure-targeted ventilators have better compensation capabilities than do volume-targeted ventilators, and Vt delivered during leakage is best maintained by pressure-targeted modes. Effectiveness in compensating for air leaks depends on the ability of the ventilator to reach and to maintain a sufficient inspiratory flow rate, and large leaks often overwhelm compensation capabilities. Pressure support compensates for air leaks by increasing Ti, often without appropriate adjustment of inspiration duration, which may lead to excessive insufflation time and to inversion of the inspiration/expiration ratio. We used pressure-targeted ventilation in our study to obtain optimal control of both Ipap and Ti and to determine which of these adjustments was most effective for leak compensation. The studies were done with zero end-expiratory pressure, because the system may overestimate leaks when positive end-expiratory pressure is present; in addition, neuromuscular patients usually have very low levels of intrinsic positive end-expiratory pressure. Our leak-compensation mode shares similarities with pressure-augmentation modes. It more closely resembles volume-targeted ventilation than volume-assured or average-volume-assured pressure-support modes, which combine the benefits of pressure- and volume-targeted ventilation. These modes were first used for brief periods in patients who had acute respiratory failure or were undergoing weaning. Recently, they were used for the long-term treatment of obesity-related hypoventilation syndrome. In these studies, the goal was to adjust for acute changes in ventilatory demand or to improve work of breathing in patients with acute unstable respiratory failure. In our study, in contrast, the goal was to counterbalance the effects of air leaks in patients with chronic stable respiratory failure. Our air-leak compensation system also shares similarities with expert-based knowledge modes, which have been used to automatically assist in weaning by allowing a minimal acceptable level of pressure or, more recently, to maintain alveolar ventilation in patients with acute respiratory failure. The original feature of our leak compensation mode is that a Ti increase is combined with an Ipap increase to maintain sufficient minute ventilation based on monitoring of the patient’s Vte. The ventilator takes the amount of leakage into account, cycle by cycle, and increases Vti to obtain a Vte value as close as possible to the set Vts. When the leak compensation program is activated, Vti is increased, first by increasing Ti (by up to 33% if needed) then by increasing Ipap. Significant Ti and Ipap increases occurred in our study, indicating that both adjustments were effective in compensating for leaks and maintaining Vts. Surprisingly, the Ti increase was smaller than expected (13% on average). Thus, the ventilator stopped the Ti increase procedure before the maximal set limit of +33%, thereby limiting the risk, in clinical situation, of inspiration/expiration inversion and autocycling, by maintaining the Ti/Ttot ratio below 0.5. One important limitation of our system is that expiratory leaks may lead to errors by decreasing the Vte detected by the ventilator. The result may be inappropriately large increases in Ti, inspiratory flow, and Ipap, possibly producing lung overinflation. Excessive pressure level increases due to the leak-compensation system may also increase the size of the leaks and worsen dynamic hyperinflation, as reported in patients with obstructive lung disease. The impact of such hyperinflation is probably
more limited in neuromuscular patients. Furthermore, we limited the Ipap increase to a maximum of $+5$ cm H$_2$O, which probably helped to limit leak increases and drops in mask occlusion pressure, as well as to avoid cycling-off failure$^{39}$ and barotrauma. However, the limitations placed on the Ti and Ipap increases for safety reasons also limited the leak-compensation capabilities of the system. Therefore, in the event of large leaks, compensation was only partial, which restricted the ability of the system to more improved sleep and respiratory parameters.

Conclusion

We studied a dual-control mode that targeted a Vte value, in order to compensate for nocturnal air leaks in patients with neuromuscular disease. This mode improved minute ventilation, blood gas values, and several sleep parameters. It was well tolerated despite the presence of severe neuromuscular disease in our patients. It was effective with both invasive and non-invasive ventilation in our short-term study. Our leak-compensation system is probably less effective in compensating for inspiratory leaks than insipiratory leaks and may be ineffective when the entire Vte leaks around the interface. Nevertheless, our results support the feasibility of air-leak compensation and suggest beneficial effects in neuromuscular patients. Our leak-compensation system deserves to be assessed in long-term studies of efficacy and tolerance comparatively to other modes of ventilation capable of leak compensation, such as pressure-support ventilation.

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Conflict of interest statement

David Orlikowski, Ghassane Mroue, Helene Prigent, Catherine Moulin, Mikaelle Bohic, Maria Ruquet, Jean Claude Raphael MD, Djillali Annane, Frederic Lofaso have no financial and personal conflict of interest to disclose.

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