Domiciliary-Assisted Ventilation in Patients With Myotonic Dystrophy*

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Study objectives: Respiratory failure is found in many neuromuscular diseases, even when the lungs may be healthy, because of an inadequacy of the ventilatory pump. Long-term domiciliary ventilation is a well-established treatment in conditions such as postpoliomyelitis; however, its use in patients with respiratory failure secondary to myotonic dystrophy has not been well described. The purpose of this study was to review the use of domiciliary-assisted ventilation in these patients and to assess their response to treatment.

Design: Descriptive analysis of retrospective and prospective clinical data.

Setting: Inpatient, noninvasive respiratory-care unit in a tertiary referral center.

Patients: Sixteen patients with myotonic dystrophy, 13 of whom required ventilatory support.

Interventions and measurements: A retrospective study of all patients with myotonic dystrophy referred for assessment for assisted ventilation was performed, including results of arterial blood gas analysis, pulmonary function tests, and overnight oxygen saturation and transcutaneous carbon dioxide levels. A prospective reassessment of all patients established on domiciliary ventilation was performed, including measurements of quality of life.

Results: Results of arterial blood gas analysis showed a fall in mean Pa CO2 from 64.3 to 53.8 mm Hg (p < 0.05) on discharge after starting ventilation and a rise in mean PaO2 from 53.0 to 65.3 mm Hg (p < 0.05). There were three deaths, at 5 months, 32 months, and 57 months, respectively. The survivors received assisted ventilation for a mean period of 27 months (range, 2 to 76 months). At reassessment, improvements in arterial blood gas levels were maintained, with mean PaCO2 of 52.4 mm Hg and PaO2 of 59.0 mm Hg. Mean overnight mean arterial oxygen saturation rose from 80.5 to 90.3% after the start of treatment (p < 0.001) and was maintained at 90.4% at reassessment. Mean transcutaneous PCO2 during sleep fell from 59.3 to 41.4 mm Hg (p < 0.05), and to 43.7 mm Hg at reassessment. There were no significant changes in spirometry or maximum mouth pressures. Compliance with treatment for our test group was lower than compliance in a group of age- and sex-matched postpoliomyelitis patients.

Conclusion: Use of domiciliary-assisted ventilation in patients with myotonic dystrophy is associated with prolonged survival and a sustained improvement in arterial blood gas tensions.

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Key words: mechanical ventilation; myotonic dystrophy; noninvasive positive-pressure ventilation; respiratory failure

Abbreviations: HAD = hospital anxiety and depression scale; SaO2 = arterial oxygen saturation

Myotonic dystrophy is an autosomal dominant multisystem disease characterized by muscle weakness and myotonia (failure of the muscles to relax). Other features include frontal balding, cataracts, testicular atrophy, and mental retardation.

Cardiac complications are common and can be associated with respiratory failure.1 Respiratory failure is found in many neuromuscular diseases because of an inadequacy of the ventilatory pump despite healthy lungs. It can occur because of a reduced central drive, upper-airway obstruction, respiratory muscle weakness, or reduced chest wall compliance. Each of these mechanisms can be demonstrated in subjects with myotonic dystrophy.1–3 Both central and obstructive apneas have been demonstrated during sleep,4,5 and the breathing pattern at rest during

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wakefulness may be irregular.6,7 Domiciliary-assisted ventilation is a well-established treatment for ventilatory failure in other neuromuscular and chest wall disorders;8 however, its use in patients with myotonic dystrophy has not been well described. The purpose of this study was to review the indications for domiciliary-assisted ventilation in patients with myotonic dystrophy, to monitor the physiologic response to treatment, and to assess the quality of life of a group of patients when established on home ventilation.

MATERIALS AND METHODS

Patient Selection

All patients with myotonic dystrophy who were referred to the Respiratory Support and Sleep Center, Papworth Hospital, were identified and their case records were reviewed retrospectively. From 1989 to 1997, 16 patients were referred. Of the original 16 patients, 3 patients did not receive assisted ventilation and 3 patients died. The remaining 10 patients were admitted for reassessment between October 1997 and April 1998.

Initial Assessment

Clinical history was obtained from all patients, including presenting symptoms, details of myotonic dystrophy, smoking habits, and medication. A full physical examination was performed. Hemoglobin concentration was measured. Arterial blood gas analysis (PaO₂ and PaCO₂) when breathing air was performed if possible before starting any assisted ventilation. Pulmonary function tests were performed with measurement of FEV₁ and FVC using a dry spirometer (Vitalograph; Bucks, UK); maximal mouth pressures during inspiration and expiration were recorded using a pressure transducer (PK Morgan; Kent, UK) as a measure of respiratory muscle strength.

Where possible, before starting assisted ventilation, overnight levels of arterial oxygen saturation (SaO₂) and transcutaneous PCO₂ were recorded. SaO₂ was measured using a pulse oximeter (Biox 3700; Ohmeda; Herts, UK), and transcutaneous PCO₂ was measured using a heated polarographic electrode (TCM3; Radiometer; Copenhagen, Denmark). A two-channel recorder was used to produce a hard copy. From the paper tracings, the mean and minimum SaO₂ levels, the desaturation index (the number of dips in SaO₂ > 4%/h), and the mean transcutaneous PCO₂ level and recorded. For the 13 patients requiring assisted ventilation, the indications for and type of ventilatory support were noted. The progress of the patients was recorded, including results of arterial blood gas analyses and overnight SaO₂ and transcutaneous PCO₂ at discharge, as well as PaO₂ and PaCO₂ on subsequent hospital admissions at 3- to 6-month intervals. Where relevant, details of death were obtained.

Reassessment

Ten patients were admitted to the hospital overnight for reassessment. Clinical histories were obtained, including current symptoms and perceived subjective benefit from ventilation. Arterial blood gas analysis was performed with the patients at rest and breathing room air. Venous blood was taken for measurement of hemoglobin concentration, and a sample was also sent for genetic analysis to quantify the number of cytosine-thymine-guanine trinucleotide repeats on the myotonin gene, which are known to be increased in patients with myotonic dystrophy.9 Pulmonary function tests were repeated, including spirometry and maximal mouth pressures. Overnight recording of SaO₂ and transcutaneous PCO₂ was performed using ventilatory support. Quality of life was assessed using three questionnaires: the Short Form-36 health survey,10 the hospital anxiety and depression scale (HAD),11 and the Beck depression inventory.12 Compliance was monitored in all patients using a clock on each ventilator that recorded the number of hours of ventilator function. The additional hours used from the previous assessment (within the preceding 6 months) allowed the daily hours of ventilator use to be calculated. Comparison was made with postpoliomyelitis patients who were provided with long-term assisted ventilation from our center. Postpoliomyelitis patients were selected as a control group because there were enough patients in the database to obtain age- and sex-matched control subjects with complete records of compliance for comparison.

Statistical Analysis

Comparison of test results before starting ventilation, after being established on ventilatory support, and at reassessment was made using the Wilcoxon signed-rank test. Between-group comparisons were made using the Mann-Whitney U test. All p values < 0.05 were regarded as statistically significant.

RESULTS

Patient Characteristics

Of the 16 patients initially referred for assessment, 3 patients were found to have satisfactory physiologic results at initial assessment (PaCO₂ < 49 mm Hg and PaO₂ > 60 mm Hg) and did not require assisted ventilation after a mean follow-up period of 2.5 years (range, 1.5 to 3.0 years). Of the 13 patients who commenced ventilatory support, there were 6 men and 7 women with mean age 47.9 years (range, 36 to 69 years). All were referred with a previously established diagnosis of myotonic dystrophy by a consultant neurologist, with the exception of three patients for whom the diagnosis was suspected at our initial assessment and confirmed by genetic analysis. All patients who were tested (n = 11) had an expansion of cytosine-thymine-guanine trinucleotide repeats (> 40) on the myotonin gene on chromosome 19, confirming a diagnosis of myotonic dystrophy. All patients had typical facial appearances of myotonic dystrophy with muscle wasting, ptosis, and frontal balding, the latter being most marked in male patients. All had peripheral muscle weakness, with the exception of one patient who died after peripheral muscle weakness with worsening respiratory failure. Eight patients used a wheelchair to go outdoors, two of whom were wheelchair bound. The mean interval from diagnosis of myotonic dystrophy to initiation of long-term ventilatory support was 8.4 years (range, 0 to 29 years). One patient had required short-term
invasive ventilation 11 years before starting long-term ventilation because of pneumonia. The most frequent symptoms at presentation included excessive daytime sleepiness (n = 9) and shortness of breath (n = 7), whereas a smaller number of patients complained of sleep disturbance (n = 2) and morning headache (n = 2).

**Commencing Assisted Ventilation**

Any patient with symptoms of chronic respiratory failure and proven hypercapnia (or acute respiratory decompensation) was considered for ventilatory support. The indications for assisted ventilation included chronic hypercapnic respiratory failure with PaCO₂ > 49 mm Hg (n = 11), respiratory arrest requiring immediate intubation (n = 1), and nocturnal hypoventilation with transcutaneous PCO₂ rising to > 56 mm Hg (n = 1). Assisted ventilation was non-invasive in all patients, with the exception of the patient who required immediate intubation. All but one patient had at least one ongoing symptom in keeping with chronic respiratory failure, including excessive daytime sleepiness, shortness of breath, morning headache, or insomnia.

The results of baseline investigations before starting ventilatory support are shown in Table 1. It was not possible to obtain overnight recordings of SaO₂ and transcutaneous PCO₂ for three patients: one patient required immediate intubation at another hospital and was transferred to our center for weaning, and two patients were commenced on non-invasive ventilation on the day of hospital admission because of severe respiratory failure with PaO₂ < 49 mm Hg and PaCO₂ > 68 mm Hg.

Patients were maintained on intermittent positive-pressure ventilation using either volume preset ventilators (Monnal D; Taema; Paris, France [n = 4]; Companion 2801; Puritan Bennett; Carlsbad, CA [n = 1]) or pressure preset machines (Nippy 1; Friday Medical; London, UK [n = 5]; Nippy 2; Friday Medical [n = 1]; BiPAP-ST, Respironics; Murrysville, PA [n = 1]). One patient had predominantly obstructive sleep apnea and was started on treatment with continuous positive airway pressure (Somnus; Friday Medical). Patients used either a nasal mask (Respironics [n = 7]) or a face mask (Laerdal Medical; Kent, UK [n = 6]). The patient requiring immediate intubation went on to undergo a tracheostomy but was weaned to a nasal mask, allowing removal of the tracheostomy tube. Only one patient required additional oxygen during the day while self-ventilating to maintain adequate oxygenation, and it was possible to discontinue this after 2 months. All patients required assisted ventilation during sleep only.

**Long-term Response to Assisted Ventilation**

During follow-up, two patients had changed interfaces with the ventilator. One patient changed from a nasal mask to a face mask after 10 months because of mouth leaks, and one patient changed from a nasal mask to tracheostomy after 3 years because of retained secretions. Three patients died since starting assisted ventilation at home. One patient died from cardiac failure after 5 years of successful pulmonary treatment. Another patient died after 32 months with recurrent sigmoid volvulus and bronchopneumonia. The third patient died of respiratory failure after 5 months of treatment with which she did not comply adequately. The remaining 10 patients received assisted ventilation for a mean period of 27 months (range, 2 to 76 months) at reassessment, and five patients received treatment for > 2 years. At reassessment, eight patients experienced an overall benefit from treatment; in particular, they experienced less daytime sleepiness and improved nocturnal sleep. Of the two patients who experienced no improvement from treatment, one patient was poorly compliant with use of the ventilator, and the other patient was treated for only 2 months. The patient with poor compliance had respiratory arrest and had no symptomatic benefit from ventilator use.

**Physiologic Responses to Assisted Ventilation**

Arterial blood gas analysis before the start of ventilatory support showed hypoxemia (mean PaO₂, 53.0 mm Hg) and carbon dioxide retention (mean PaCO₂, 64.3 mm Hg). As shown in Table 1, there was a significant improvement before discharge, with a rise in mean PaO₂ to 65.3 mm Hg and a fall in mean PaCO₂ to 53.8 mm Hg. At reassessment in the survivors, these improvements were maintained.

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**Table 1—Hemoglobin Level, Arterial Blood Gas Analysis, and Overnight SaO₂ and Transcutaneous PCO₂ Before and After Starting Assisted Ventilation and at Reassessment**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Baseline (n = 13)</th>
<th>Discharge (n = 13)</th>
<th>Reassessment (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin, g/dL</td>
<td>15.4 (0.7)</td>
<td>14.8 (0.6)</td>
<td>14.8 (0.6)</td>
</tr>
<tr>
<td>PaO₂, mm Hg</td>
<td>53.0 (3.3)</td>
<td>65.3 (2.0)</td>
<td>59.0 (1.9)</td>
</tr>
<tr>
<td>PaCO₂, mm Hg</td>
<td>64.3 (3.9)</td>
<td>53.8 (1.4)</td>
<td>52.4 (1.4)</td>
</tr>
<tr>
<td>Mean SaO₂, %</td>
<td>90.5 (1.9)</td>
<td>90.3 (1.2)</td>
<td>90.4 (1.5)</td>
</tr>
<tr>
<td>Minimum SaO₂, %</td>
<td>43.0 (4.4)</td>
<td>68.5 (3.8)</td>
<td>82.3 (1.9)</td>
</tr>
<tr>
<td>Desaturation index</td>
<td>21.2 (5.1)</td>
<td>6.7 (0.9)</td>
<td>4.0 (0.9)</td>
</tr>
<tr>
<td>Transcutaneous PCO₂, mm Hg</td>
<td>59.3 (4.6)</td>
<td>41.4 (3.2)</td>
<td>43.7 (4.6)</td>
</tr>
</tbody>
</table>

*Data are presented as mean (SEM).

†p < 0.05.

‡p < 0.001.
Figure 1 shows the changes in arterial blood gas results with time from start of ventilation.

Pulmonary function tests showed a restrictive pattern initially with a reduction in maximal mouth pressures in keeping with respiratory muscle weakness (Table 2). At reassessment, there had been no significant change in FEV₁, FVC, or maximal mouth pressures, suggesting that treatment may have halted the decline in respiratory function.

**Compliance With Assisted Ventilation**

Records of compliance were available for nine patients at reassessment. They were to use the ventilator when going to sleep at night and for naps during the day. The number of hours used per 24 h on the ventilator was significantly lower for patients with myotonic dystrophy compared with postpoliomyelitis patients (mean, 6.3 h; SEM, 1.2 h) compared with 8.8 h (SEM, 0.4 h), respectively (p < 0.05). Three of the patients with myotonic dystrophy achieved < 5 h of use of the ventilator, whereas all of the postpoliomyelitis patients achieved > 7 h per 24 h of use of the ventilator. Although most patients overestimated hours of usage, reasons for poor compliance included difficulty sleeping with the ventilator, nasal blockage, and lack of improvement in daytime symptoms.

**Quality of Life**

The results of the Short Form-36 survey that showed the greatest differences were in physical function and role limitation caused by physical limitations, which were both 72% lower in subjects when compared with age- and sex-matched control subjects. The smallest differences were in mental health and role limitation caused by emotional problems, which were 8% and 18%, respectively. In the HAD questionnaire, where a score > 10 suggests clinically relevant anxiety or depression, no patient reached that level of anxiety; however, two patients had raised scores for depression. In the Beck Depression Inventory, four patients had a score > 15, suggesting moderate-to-severe depression.

**Discussion**

Chronic hypercapnia is a common finding in patients with myotonic dystrophy and can occur with minimal signs of peripheral muscle weakness. There are few reports of long-term use of noninvasive ventilatory support in this condition. In a previous study, all patients with myotonic dystrophy required tracheostomy for long-term ventilation. Factors that may contribute to difficulties in establishing patients with myotonic dystrophy on noninvasive treatment include an irregular respiratory drive, upper-airway obstruction, facial muscle weakness, and intellectual and emotional problems. However, noninvasive ventilation is preferable because a tracheostomy tube reduces cough efficiency, provokes secretions, may lead to aspiration into the trachea, and may increase the frequency of respiratory infections.

This study has shown that patients with myotonic dystrophy can be established on prolonged ventilatory support at home with immediate and sustained improvements in physiologic parameters. This has been shown in other disorders including scoliosis, thoracoplasty, postpoliomyelitis, and other neuromuscular diseases. Although there was no control group in this study because we believed it would be unethical not to offer ventilatory support to a patient with respiratory failure, there seems to be prolonged survival on assisted ventilation with more than one half of the patients receiving treatment for > 2 years.

**Table 2—Pulmonary Function Test Results**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Baseline</th>
<th>Reassessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁, L</td>
<td>1.27 (0.21)</td>
<td>1.15 (0.23)</td>
</tr>
<tr>
<td>FVC, L</td>
<td>1.66 (0.30)</td>
<td>1.40 (0.22)</td>
</tr>
<tr>
<td>Pmax, cm H₂O</td>
<td>28.1 (5.9)</td>
<td>29.5 (3.2)</td>
</tr>
<tr>
<td>Pe max, cm H₂O</td>
<td>43.0 (5.5)</td>
<td>42.5 (5.5)</td>
</tr>
</tbody>
</table>

*Data are presented as mean (SEM). Pmax = maximal inspiratory mouth pressure; Pemax = maximal expiratory mouth pressure.

**Figure 1.** Arterial blood gas values (mean ± SEM) over 24 months with the number of patients shown at each time point. pre = before initiation of assisted ventilation; post = after initiation of assisted ventilation; m = month.
The most common presenting symptom in this study was excessive daytime sleepiness. This is well recognized in patients with myotonic dystrophy and may also occur in the absence of respiratory failure.\(^4,20,21\) Explanatory factors may include sleep disruption associated with frequent apneas\(^3\) and a central neurogenic abnormality.\(^20\) Although the excessive sleepiness may not be corrected with treatment, the majority of patients in this study felt more alert after starting assisted ventilation. Other symptoms, including shortness of breath, sleep disturbance, and morning headache, also improved.

Important aspects of management in this group of patients included selection of an appropriate ventilator and interface for each patient. When selecting a ventilator, consideration was given to trigger sensitivity and the ability to deliver positive expiratory pressure, in particular if there was evidence of obstructive apneas. We noted that a considerable number of patients had mouth leaks of air when using a nasal mask, and they required a face mask. This was most likely caused by facial muscle weakness. Even with a face mask, there could be considerable air leaks, and it was important to have a range available to ensure that the mask fit well.

The patients often appeared to be poorly motivated, and repeated education with both patient and family or the caregiver regarding treatment was essential. Depressive tendencies as well as low intelligence and personality disturbances have previously been noted in patients with myotonic dystrophy, and it is unclear whether the depression is a direct result of brain dysfunction or a secondary reaction to the physical disability.\(^16,22\) Given the neuropsychological problems in this group of patients, we were concerned about compliance with treatment. The overall number of hours of ventilation used was lower for patients with myotonic dystrophy compared with a group of age- and sex-matched post-polio myelitis patients. Compliance appeared to be a particular problem in one third of the patients who used the ventilator for < 5 h/d. The poorly compliant patients rarely admitted to not using the ventilator and were often adamant that they were complying. It is important to note that compliance with treatment may be a problem with these patients; ventilator hours of use should be monitored regularly, and the benefits of treatment to patient and caregiver need to be reinforced.

An attempt was made to evaluate quality of life while receiving treatment. Unfortunately, patients did not complete questionnaires before starting treatment, so the information obtained is limited. From the Short Form-36 questionnaire, the most marked difference from healthy control subjects was a reduction in physical function, which is to be expected given the muscle weakness associated with myotonic dystrophy. However, there were no significant differences in mental health and role limitation caused by emotional factors. The HAD and Beck Depression Inventory suggested the presence of depression in a small proportion of the patients, although the proportion did not differ significantly from a survey from UK general practice.\(^23\) Cost of treatment was not addressed directly in this study; however, long-term domiciliary ventilation is cheaper than monitoring patients in hospital. The capital cost of the equipment is relatively small at approximately $5,000 per ventilator.

In conclusion, this study has shown that use of domiciliary-assisted ventilation in patients with myotonic dystrophy is associated with prolonged survival and an improvement in arterial blood gas tensions that is maintained. Quality-of-life assessment shows a similar emotional status compared with control subjects, despite a marked reduction in physical function. Domiciliary-assisted ventilation should be considered in patients with myotonic dystrophy in whom respiratory failure develops. This treatment can be successfully implemented despite the physical and psychological disabilities in patients with myotonic dystrophy.

**References**