Weaning from prolonged invasive ventilation in motor neurone disease: analysis of outcomes and survival

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ABSTRACT

Introduction: Non-invasive ventilation (NIV) improves prognosis in patients with Motor Neurone Disease (MND) in the absence of major bulbar involvement. However, some experience a rapid and unexpected decline in respiratory function and may undergo emergency tracheal intubation. Weaning from invasive ventilation can be difficult and reported independence from invasive ventilation is uncommon with poor prognosis. The outcomes of patients with MND referred to a specialist weaning service following emergency tracheal intubation were examined and compared with MND patients electively initiating NIV.

Methods: A case note review was performed on all patients with MND invasively ventilated and referred to a specialist weaning service between 1992 and 2007. Outcomes were compared with those electively commenced on NIV during the same period.

Results: Thirty patients were referred for weaning from invasive ventilation which was started in 17 before MND was diagnosed. Fourteen patients (47%) were weaned from invasive ventilation but still required NIV, 13 failed to wean and three died. Seventeen were discharged home from hospital. Median survival from tracheal intubation was 13.7 months (95% CI 0-30.8) for those previously diagnosed and 7.2 months (95% CI 5.1-9.4) for those not previously known to have MND. Comparison with patients initiated electively on NIV demonstrated similar survival estimates to that from emergency intubation (median 9.4 (95% CI 6.9 – 12.0) vs. 7.8 (95% CI 2.6 – 12.9) months respectively).

Conclusion: The prognosis in MND following acute respiratory failure and intubation is not always complete ventilator dependence if patients are offered a comprehensive weaning programme.

INTRODUCTION

Motor neurone disease (MND) is a progressive neurodegenerative disorder that usually leads to death within 2-4 years. Ventilatory failure is the most common cause of death, caused in varying degrees by respiratory muscle weakness, unsafe swallowing and poor cough.[1] Non-invasive positive pressure ventilation (NIV) can alleviate symptoms, improve quality of life[2] and prolong survival in MND patients,[2,3] particularly in those without severe bulbar dysfunction. However, the initial symptoms of respiratory failure may be subtle and difficult to detect.[1] Some patients experience a rapid and unexpected decline in respiratory function, frequently in the context of respiratory tract infection, and may be invasively ventilated, even before a diagnosis of MND is established.[4,5]

Case series have reported that weaning from invasive ventilation can be difficult, independence from invasive ventilation is rarely achieved and prognosis poor.[4,5] Therefore an emphasis has been placed on the palliation of symptoms.[5] In contrast, the active management of these patients including attempted weaning from invasive ventilation and treatment of associated complications, such as intercurrent infection with physiotherapy, antibiotics and bronchial toilet using bronchoscopy has not been reported.

In this article, the outcomes of 30 patients with MND, referred to a specialist weaning service, who were intubated and ventilated for acute respiratory failure are presented. The aim was to examine whether differences in outcomes justify elective NIV being considered best practice[2] while intubated patients are considered for a more palliative approach due to their reported prognosis.[5]

METHODS

A retrospective case note review was performed on all patients with a diagnosis of MND referred to a specialist weaning centre (Respiratory Support and Sleep Centre (RSSC), Papworth Hospital) between 1st January 1992 and 31st December 2007. The diagnosis of MND was confirmed by a consultant neurologist and appropriate investigations including electrophysiology. The outcomes of patients invasively ventilated and referred for weaning were compared with those of patients referred for consideration of elective NIV during the same time period. In addition patients with a

known diagnosis of MND prior to intubation were compared with those without a diagnosis at intubation.

In those invasively ventilated the demographics, duration of symptoms, duration of tracheostomy, length of stay at referring Intensive Care Unit (ICU) and RSSC, ventilation mode on arrival and discharge from the RSSC and discharge destination were recorded. Patients were categorised as having severe bulbar involvement if their swallow was deemed unsafe. Outcome measures were successful weaning from invasive ventilation, survival to RSSC and subsequent hospital discharge, and long-term survival. Successful weaning was defined as the withdrawal of invasive ventilation, but included continuing support with NIV. Patients with a tracheostomy for airway suction only were regarded as weaned.

The National Health Service Strategic Tracing Service tracked patients and survival was compared from the date of assisted ventilation between patients referred for weaning and those electively initiated on NIV. Patients were followed up to the 31st December 2007 or death, whichever occurred first.

Statistical analysis

Data were analysed using SPSS 16.0 for Windows (Chicago, IL). Normal distribution was established using the Kolmogorov-Smirnov test. Parametric data were compared using independent *t*-tests and non-parametric data compared using the Mann-Whitney U test. Kaplan-Meier survival analysis was performed to estimate survival; the log rank test was used to compare groups. A *p* value of < 0.05 was considered statistically significant.

RESULTS

Thirty (five female) MND patients were admitted for ventilatory weaning between January 1992 and December 2007. All were ventilated via tracheostomy. Twelve had identifiable acute precipitants to ventilatory failure, 9 with pulmonary sepsis. Thirteen patients (43%) had a diagnosis of MND prior to ICU admission (diagnosed patients (DP)) and seventeen (57%) did not (undiagnosed patients (UP)). Fourteen (47%) were weaned from invasive ventilation onto NIV (13 required only nocturnal support).

Three died during their admission on the RSSC. Thirteen failed to wean with 9 requiring continuous ventilatory support and 4 nocturnal support only via tracheostomy.

Seventeen patients were discharged home and they were significantly younger than the 13 who died in hospital (mean 60 (SD 14) vs 70 (6) years, $p = 0.02$). The overall one-year survival rate from tracheal intubation was 43.3%. Of the 27 patients discharged from the RSSC, survival was not significantly different if ventilated via tracheostomy or NIV (mean 14.3 (95% CI 5.5-23.1) vs. 14.0 (95% CI 5.9-22.1) months respectively). Ten of the 14 weaned to NIV (71%) and 7 of 13 (54%) not weaned were ultimately discharged home. The median survival from tracheal intubation was 7.8 (95% CI 2.6 – 12.9) months across the whole cohort. The DP group survived longer (median 13.7 (95% CI 0 – 30.8) months) than the UP group (median 7.2 (95% CI 5.1 – 9.4) months) a non significant difference (log rank test $p = 0.68$). Data comparing the UP with DP groups are presented in Table 1. Fifteen patients had severe bulbar involvement. Five (33%) of these were weaned to NIV in contrast to nine (60%) of those without marked bulbar disease. Eight (62%) of the patients who died in hospital had severe bulbar disease although overall there was no significant difference in survival between those with or without severe bulbar involvement.

During the period examined 332 patients with MND (209 male) were referred electively for ventilatory assessment and 126 patients (88 male) initiated domiciliary NIV. Their mean age was 63.8 (9.9) years. Figure 1 illustrates the survival times of the patients, referred for weaning and elective NIV, from the initiation of assisted ventilation. The median survival in the group referred for weaning was 7.8 (95% CI 2.6 – 12.9) months, this was not significantly different from that for patients electively initiated on NIV which was 9.4 (95% CI 6.9 – 12.0) months.

Table 1

	All (n = 30)	DP Group (n = 13)	UP Group (n = 17)	p-value
Age at onset of symptoms, years	64.2 (12.0)	56.7 (14.1)	70.0 (5.5)	0.006
Age at intubation of trachea, years	67.1 (8.0)	62.0 (7.8)	71.0 (5.8)	0.001
Median time (IQR) between first symptoms and respiratory failure, months	12.9 (18.0)	21.2 (38.8)	9.1 (10.4)	0.02
Length of stay in ICU, days	40.3 (37.8)	28.1 (40.4)	49.6 (34.0)	0.1
Length of stay on the RSSC, days	33.6 (23.9)	27.9 (15.7)	37.9 (28.3)	0.2
Weaned from invasive ventilation	14	6	8	0.02
Time to wean, days	51.4 (38.1)	25.8 (10.3)	70.5 (40.6)	0.03

DISCUSSION

Our findings show that, in contrast to previously published case series,[4-6] 14 from 30 patients with MND were successfully weaned from tracheostomy ventilation, although all had continuing requirements for NIV. Survival to hospital discharge overall was 57% with one year survival of 43.3%. Survival from the initiation of ventilatory support was similar for patients treated with emergency intubation and those started on elective NIV.

Successful weaning removes the complications and cost of prolonged invasive mechanical ventilation. There was no difference in mortality between those weaned and those who continued with tracheostomy ventilation but a higher percentage of those weaned to NIV were discharged home. The majority of the weaned patients only required NIV overnight. We have no data on quality of life in patients weaned to NIV but previous reports suggest it is improved with NIV compared to tracheostomy ventilation[7] and better if cared for at home.[8]

We compared the survival of patients referred for weaning to that of patients who were electively initiated on NIV and found that survival from the date that assisted ventilation was initiated was similar. Survival after the initiation of NIV in our study (median 9.4 months) was equivalent to that of previous studies of MND patients who

were tolerant of NIV (median 8 – 15 months).[2,9-11] Survival is significantly worse in patients who are unable to tolerate NIV.[12] Berlowitz and colleagues report a survival advantage of tracheostomy ventilation compared to NIV and no ventilatory support.[3] However, survival was calculated from symptom onset and tracheostomy ventilation was initiated electively, making comparisons with our study difficult.

The high weaning success rate in the present series could be attributable to selection bias in the referral of patients to a specialist weaning centre. No patients were declined by the RSSC. It is possible that younger patients with less advanced disease were more likely to be referred. All patients had survived prolonged ventilation at the referring ICU, and most were medically stable. However invasive ventilation for over 14 days is associated with increased mortality,[13] and the condition of the patients was poor enough to prohibit weaning by conventional techniques. Seventeen patients were diagnosed with MND following intubation. Compared to the 13 patients with an established diagnosis they were older at symptom onset, had a shorter time from first symptom to respiratory failure, took longer to wean from invasive ventilation and had poorer survival. It may be that older patients with rapidly progressive disease and a known diagnosis were not offered invasive ventilation or not referred for weaning.

During weaning the aim should be to optimize treatment of all associated conditions and infections, provide manual and mechanically assisted cough therapy if required, address nutrition, communication, and psychological aspects of care in addition to reviewing medications and ventilatory requirements.[14] With this approach 57% of patients referred were discharged home compared to 17% in a previous series.[5] Although weaning is possible and outcomes reasonable, the close monitoring of respiratory status in patients known to have MND could avoid invasive ventilation. The acute use of NIV may also be important as this has been shown to reduce intubation rates, length of ICU stay and mortality.[15] Our results show that a more positive approach can be justified in the management of patients with MND following tracheal intubation and ventilation. Many patients can be successfully weaned onto NIV and discharged home with survival overall comparable to that for patients electively initiating NIV.

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