Non-Invasive Ventilation Support for People with Amyotrophic Lateral Sclerosis: Multidisciplinary Team Management

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Abstract

Purpose of review:

To summarise recent developments in the use of Non-invasive ventilation (NIV) for people with amyotrophic lateral sclerosis (pwALS), with a specific focus on how multidisciplinary teams (MDT) can support best practice.

Recent findings:

We included 13 papers, 12 with observational designs and one qualitative interview design. The review is structured using four content domains: prognosis, effectiveness of NIV, NIV tolerance, and MDT structure and delivery. Findings suggest a modest survival benefit of NIV for pwALS. Further evidence is needed to consider the appropriate time of initiation in the context of respiratory status and the influence of NIV on cognitive function over the course of the disease. A key emerging determinant of tolerability of NIV is secretion load. Palliative care professionals

within the MDT can play a key role in supporting pwALS to consider the potential benefits of NIV in the context of their preferences, prognosis, symptom burden, and ALS variant.

Summary:

ALS MDTs allow timely information sharing about NIV between experts that is likely to improve outcomes. MDT practice must continually adapt to reflect pwALS's preferences for care and ensure those caring for them at home have access to support using digital innovations.

Keywords:

Amyotrophic Lateral Sclerosis, Non-invasive ventilation, Multidisciplinary team.

Introduction

ALS is an incurable illness characterised by progressive neurological degeneration. Non-invasive ventilation (NIV) forms an important part of the management of ALS, where mode of death is commonly due to respiratory failure. NIV is one of the only interventions that can improve survival for pwALS, whilst preserving quality of life [1, 2]. For this reason, NIV is often used until the end of life.

In the absence of promising pharmacological agents, attention has understandably been given to the factors which optimise NIV use in this population, such as improved diagnostics to identify respiratory failure at an earlier opportunity therefore maximising survival benefits [3]. Co-ordinated multidisciplinary care is likely to impact upon survival and quality of life in pwALS. [3-5] The benefits of an MDT approach (e.g. specialist palliative care support) in achieving optimal treatment with NIV appears to be of critical importance. [6-8]

The purpose of this review is to summarise recent developments and understanding of the use of NIV in pwALS, with a specific focus on how an MDT can support best practice in this area. [9] As

Covid-19 has disrupted care activity, it is a timely opportunity for teams to reflect upon the aspects of MDT care which are most helpful in the management of pwALS.

Method and Results

The review team, led by clinicians from the Norfolk and Norwich University Hospital Centre for Neurosciences with support from an academic researcher and librarian, followed rapid review guidance. [10] We conducted database searches in MEDLINE and Embase (via OVID), Web of Science, and Google Scholar. The search strategy used medical subject headings combined with keyword searches (with term and spelling variants). Results were restricted to peer-reviewed articles published in the English language from July 2019 onwards describing primary research using experimental or observational cohort designs. We included thirteen articles; summary characteristics are provided in (Appendix 1).

Prognosis

As the majority of patients with ALS will die of respiratory failure, use of NIV is intrinsically linked to a person's prognosis. Whilst objective measurements of respiratory function (e.g. Forced Vital Capacity, FVC) provide an indication of prognosis, further understanding is needed about how less easily quantifiable interventions, e.g. optimal care structure of the ALS MDT, may affect the prognosis of those using NIV.

Klavzar et al describe MDT outcomes for pwALS cared for by a Slovenian centre which developed in maturity over a ten-year period. [11] This study provides longitudinal data about the impact of MDT care on survival. The risk of death for pwALS receiving NIV was three times lower at the end of the reporting period in comparison to when the centre was first established (Hazard ratio = 2.7 vs. 7.9; NIV use * Late group interaction hazard ratio = 0.34, 95% Confidence Interval 0.12–0.96, p= 0.041).

Two main factors are hypothesised for improved hazard ratios. Firstly, a greater number of pwALS used NIV in the latter years of the study, in comparison to when the centre was first established. Secondly, over time, there was improved knowledge and skills in the use of NIV by the MDT clinical teams, which was felt to translate to improved survival. A notable absence from the Slovenian MDT was a palliative care specialist. [11]

The presence of airway secretions may influence survival for pwALS using NIV. Hesters et al aimed to assess the prognostic factors for survival for gastrostomy placement in pwALS. Patients who were NIV dependent were found to have a significantly higher 30-day mortality risk. [12] Notably, the presence of recurrent airway secretions was independently associated with a worse prognosis, to the extent that the authors conclude this symptom should be a key decision-making criterion when considering gastrostomy placement in NIV users. [12]

The Hesters et al study raises important issues for the ALS MDT. [12] Suitability for gastrostomy is often determined by respiratory function, as measured via spirometry. Symptom burden from airway secretions do not routinely form part of assessment for suitability for gastrostomy. In the UK, support for the management of excess secretions may be provided by a specialist palliative care professional, who may not routinely participate in decision making about gastrostomy insertion. We do not know from this study whether the mortality risk associated with accumulation of upper airway secretions would be ameliorated by better symptom management with local and/or systemic medications. Whilst anti-muscarinic drugs are routinely used first line for the management of secretions, there is a limited evidence base to determine what drug should be used and at what dose. [13] The UK National Institute for Health and Care Excellence (NICE) has recommended future research in this area. [9]

The notion of determining suitability for gastrostomy on a pulmonary function threshold alone is coming into question. Whilst the NICE guidance is clear that FVC should be >50% of predicted to perform the procedure safely, [9] Kim et al reported outcomes suggesting that gastrostomy

insertion can be performed safely in patients with a FVC <30%, irrespective of ventilatory support. [14] These findings may be interpreted with caution given contradictory findings about mortality risk in NIV dependent individuals observed in contemporaneous studies, but does suggest that the relationship between NIV use, pulmonary function and survival post gastrostomy may not be as linear as initially thought.

Effectiveness of NIV

The survival benefit of using NIV for most is measured in months not years. [1] Understanding and delineating the factors affecting NIV are important to ensure that patients who receive NIV treatment have the best chance of benefitting from this intervention, which otherwise may complicate or worsen quality of life.

Whilst previous studies examining the benefits of NIV may have been cofounded by variation in usage, symptomatology and patient selection, future controlled trials are unlikely given the well-established nature of NIV in the management of ALS. [15] The MDT must therefore adopt a more nuanced approach in establishing the effectiveness of NIV for their population.

Ackrivo et al performed a stratified survival analysis of retrospective data to understand the factors likely to confer the greatest survival advantage for pwALS. [15] There was an association between longer use of NIV and lower rates of death overall. Those who used NIV for greater than four hours/day had a 33% reduction in rate of death. The survival advantage was predominantly observed for those with limb-onset ALS.

For those with bulbar ALS and neurocognitive deficits, the effectiveness of NIV is less clear cut. Achieving effective NIV use for patients with bulbar symptoms may be more time consuming for the healthcare professionals involved in care. [15]

Sancho et al have aided understanding of how those with bulbar onset MND may not find NIV effective. [16] They studied 30 pwALS on NIV prospectively. There was a strong association

between upper airway obstruction with decreased central drive (ODCD) events and an upper motor neuron pattern of bulbar weakness. The ODCD events reduce NIV effectiveness and produce an unstable breathing pattern. There are no known treatments for ODCD events; thought to be caused by forceful glottic closure in response to central apnoea.

Ineffective NIV is due most commonly to air leak or ODCD events. [16] As ODCD events are not improved by altering ventilatory settings, distinguishing between these two causes is important for the ALS MDT to ensure support is provided by the most appropriate clinician. For those with upper motor neuron bulbar weakness, this may include an earlier focus on palliative care where NIV is not providing satisfactory results.

For patients with neurocognitive deficits, the benefits of NIV may have been understated. There is an association between respiratory dysfunction and reduced cognitive function, with a linear relationship between cognitive and respiratory decline. [17] Treating respiratory dysfunction with NIV may influence the course of cognitive decline. Achieving effective NIV use in this population, who may have impaired mental capacity to consent to treatment, can provide challenges for the ALS MDT. [18] The presence of neurocognitive impairments may form part of the exclusion criteria for some ALS NIV trials and therefore further information is needed about the effectiveness of NIV in this specific population. [17]

NIV Tolerance and Adherence

Patients only receive the prognostic benefits of NIV if they are able to tolerate ventilation for the required number of hours per day. Inability to tolerate NIV for the length of time needed to compensate for respiratory failure is likely to result in a shorter prognosis and death. Understanding what factors affect an individual's ability to tolerate NIV is important to promote adherence and address treatable causes.

Paradoxically, whilst presence of symptoms may affect the tolerability of NIV, patients are more likely to accept NIV if they are experiencing respiratory symptoms. For those with orthopnea, the odds of NIV use may increase four - eight fold. [19]

An accelerated rate of decline in lung function has been associated with future NIV adherence. [20]. Indeed, whilst rate of decline in FVC is independent of NIV use, observational studies may incorrectly attribute slowing FVC decline to NIV initiation, by overlooking the impact of improved adherence to therapy. [20]

Aside from respiratory function, for those with bulbar involvement, inability to swallow saliva can effect tolerability of NIV. A study by Cazzolli (2020) aimed to assess the validity of an Oral Secretions Scale in determining tolerance of NIV and survival of those who use it. [21] Patients with evidence of saliva pooling at initiation of NIV were less likely to tolerate NIV. Patients with minimal problems with saliva at initiation of NIV were more likely to be able to tolerate NIV for 24 hours/day and a survival benefit was observed.

The link between sialorrhea and NIV tolerability is supported in a study by Russo et al, where no significant correlation was found between “general” bulbar symptoms and NIV compliance, but rather with hypersalivation alone. [22] These findings are relevant to palliative care professionals involved in the MDT management of pwALS who often oversee the management of excessive oral secretions.

The Russo et al study is also notable for its in-depth analysis of how the neurocognitive effects of ALS (present in 50% of their study population) negatively influence NIV adherence, specifically due to impairments in insight and goal-orientated behaviors (e.g. motivation). In such cases, appropriate training and support of carers was identified as a key factor in promoting adaptation to life with NIV. [22]

In this study, NIV was started in an inpatient setting, which was felt to contribute to 95% adherence to NIV. In areas such as the UK where this approach may not be feasible, it is important to consider other ways in which services can be inclusive and understanding of the challenges faced by those with neurocognitive deficits, and those close to them, when initiating NIV.

In general, an improving trend has been observed in the proportion of patients who tolerate NIV for the required period. Whilst technological advances in NIV machines and mask fitting may play a part in this, greater MDT understanding of how to support pwALS to use NIV effectively is likely to play an important role. [23]

MDT Structure and Delivery

An MDT approach may vary from healthcare professions working across healthcare settings in a co-ordinated way, to a full "MDT clinic" with multiple professionals providing a whole day assessment of a person's care needs.

The latter model was recently described by a Swiss team in a four-year, longitudinal study. [24] A MDT approach to the management of respiratory failure meant that, in 89% of cases, NIV was started electively, rather than from an emergency presentation. In comparison to UK practice, in 85% of cases NIV was initiated during an elective inpatient admission, rather than in an outpatient setting. Median survival figures in this study were higher than in other published data (50 months [interquartile range 24 - 95] from onset of symptoms).

A key difference between this MDT structure and NICE Guidance was the inclusion of an Ear, Nose and Throat (ENT) specialist. [9] The task of the ENT specialist within this MDT was to assess glottic function (to mediate risk of aspiration) and for treatment of sialorrhea via Botulinum injections and radiotherapy to salivary glands. [24]

As upper airway dysfunction is associated with ineffective or impaired NIV use, integration or inclusion of ENT specialists within the ALS MDT may be considered as a potential future service development for UK MDTs, where these roles are not already performed by other professionals.

A key benefit of the Covid pandemic has been the acceleration in the use of digital technology within healthcare settings. Telehealth technology offers distinct benefits to this patient group, given the challenges for some in attending face to face hospital appointments. The use of telehealth, has been evaluated for pwALS using NIV; both for videoconferencing and remote monitoring of NIV usage. [25]

Thematic analysis of services users' experiences positively links NIV and telehealth. Aside from the reduced burden in hospital clinical visits, telehealth was seen to enhance the care experience and wellbeing through regular assessment, prompt access to intervention and continuity of care. Users described an increased sense of autonomy and awareness of their condition, despite some technical challenges. Use of telehealth may help provide coordinated care for those who are unable to attend clinic, in line with current guidance. [9]

As ALS progresses, it is important to recognise that it may be the carer, rather than the pwALS themself, who is the core user of teleheath and therefore future work must be inclusive of their pivotal role in care delivery.

Discussion

Palliative care aims to improve quality of life for individuals living with life limiting illnesses by providing holistic care in line with a person's wishes and values. ALS is a progressive terminal condition, for which therapeutic options are limited. Professionals with palliative care expertise are an important part of the ALS MDT to ensure that the benefits of treatments such as NIV are balanced against the burdens of intervention. Recognition of the limited benefits of NIV in certain

patient groups must be acknowledged and recognised by MDTs to reduce the risk of therapeutic obstinacy towards the end of life.

The mechanism through which MDT working improves outcomes for pwALS using NIV is yet to be fully understood. [6-8] It is likely, however, to be due in part to the information exchange between healthcare professionals and the development of specialist expertise in this, fairly rare, condition. Furthermore, MDT optimisation of troublesome symptoms (e.g. sialorrhea) may have a role in improving NIV adherence and patient outcomes.

Clinically, MDT working provides common ground in which the technical knowledge about the optimal conditions for NIV use can be combined with a sensitive exploration about an individual's preferences for care and goals of treatment. This may involve discussion about symptom management and cessation of NIV for those approaching the end of life.

Consideration must also be given to the carer burden inherent in this condition and how medical interventions influence the carer's ability and confidence to provide care, with an understanding of the socioeconomic determinants at play.

Conclusion

Given the modest survival benefit that NIV confers, it is necessary to establish further information about the quality, not just quantity of life gained, and the costs to the system in delivering this type of care. [23] The use of tracheostomy ventilation in ALS has wide geographic variations and complexities related to funding and care provision. Despite this, recent years has seen emerging interest in tracheostomy use as a core element of ALS management and clinicians should remain open minded about developing the skills needed to support its use within their MDT.

Keypoints:

- The ALS MDT approach has a role not just in providing specialist expertise, but also in providing a forum for “information exchange" about NIV and combined decision-making which is likely to improve outcomes
- Secretion load is emerging as a key determinate of tolerability of NIV, prognosis and outcomes following gastrostomy
- Palliative care professionals within the MDT can play a key role in helping pwALS understand the potential benefits of NIV in the context of their prognosis, ALS variant, symptom burden and their own preferences.
- The ALS MDT may wish to evaluate established criteria for NIV initiation, management and cessation in light of emerging evidence about outcomes in certain populations, particularly those with neuro-cognitive impairment.
- In the post pandemic period, the ALS MDT must evolve to reflect patient preferences around place of care, carer involvement, and digital innovations

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Conflicts of interest
We declare no conflicts of interest.

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