The Role of Noninvasive Ventilation in Neuromuscular Disorders

A summary of highlights from presentations at the 1st Respiratory Failure and Mechanical Ventilation Conference 2020 by Wolfram Windisch (Cologne, Germany), Anita Simonds (London, United Kingdom) and Peter Wijkstra (Groningen, Netherlands)

Pulmonary comorbidities, including chronic obstructive pulmonary disease (COPD), asthma and congestive heart failure, are frequently found in adults with neuromuscular diseases (NMD), particularly those with rapidly progressive disease such as motor neurone disease or amyotrophic lateral sclerosis (ALS).[1] As a result, healthcare utilisation for pulmonary complications is substantial, and depends on the age of the patient, with a higher frequency in those aged over 70 years. In a population study, more than one-third of adults with neuromuscular disease had undergone pulmonary outpatient clinic visits with a mean 6 visits per patients, pulmonary function testing in about a third, sleep studies in 14% and 16% having intensive care unit (ICU) admissions. There were disparities according to income level, and only a minority received ventilatory support. In patients with ALS, 6% received home mechanical ventilation (HMV).[1] Blood gases and lung function parameters vary substantially between patients with differing neuromuscular disorders when started on HMV: patients with ALS are very likely to have HMV but are typically referred late in the disease, compared with Duchenne muscular dystrophy (DMD) patients who tend to receive HMV earlier in the disease course.[2]

When considering the benefits of artificial ventilation, it is important to remember that the respiratory system consists of two components: the lungs and respiratory pump. Pulmonary failure leads to hypoxaemic respiratory failure, whereas pump insufficiency and ventilatory failure lead to hypercapnic respiratory failure. Oxygen therapy is not indicated in the latter scenario; artificial ventilation is needed. The management of respiratory failure in NMD requires the use of artificial ventilation to assist the respiratory muscles in order to correct the alveolar hypoventilation and ameliorate gas exchange.

The benefits of artificial ventilation were first demonstrated in 1953 during a polio epidemic, when the use of 24 hour manual ventilation caused mortality to plummet from 92 to 25%.[3] Since then, a wide range of NMD have been found to benefit from artificial ventilation, primarily by noninvasive ventilation (NIV). National guidelines have algorithms recommending when patients should be referred and offered NIV. German guidelines recommend considering NIV when patients are symptomatic, there is evidence of respiratory muscle weakness or forced vital capacity (FVC) falls below 70% of the predicted value. The decision should be individually tailored but it is important to start early when patients start to become hypercapnic.[4] Improved survival with NIV has been demonstrated in patients with progressive NMD, and also in some subgroups of patients with COPD, suggesting that the effect is NIV is not limited

to the respiratory pump.[5] In hypercapnic patients with DMD, NIV has a substantial impact on long term survival.[6] Other neuromuscular conditions include where NIV may be used include spinal muscular atrophy (SMA), X-linked myotubular myopathy, congenital muscular dystrophy and mitochondrial disorders.

Deciding when to initiate NIV can present challenges in patients with rapidly progressing NMD. It can be difficult to predict how quickly a disease is going to progress in a newly diagnosed person with ALS. Patients can be broadly categorised as rapidly progressive or less rapidly progressive but the decision can be difficult on an individual basis. Younger age at diagnosis, delay between symptom onset and diagnosis, and FVC are useful prognostic factors for respiratory insufficiency in ALS.[7] A recent study showed that the decline in vital capacity was rapid at first but slowed after about 17 months.[8] The introduction of NIV in childhood is associated with an increase in survival in a range of progressive conditions,[9] and has a favourable long-term impact on nocturnal and diurnal gas exchange.[10]

Identifying biomarkers of disease progression would be useful to inform treatment decisions. A randomised controlled trial in patients with ALS found that NIV improved survival in the subgroup of patients with mild/moderate bulbar weakness on study entrance. In patients with severe bulbar impairment, NIV improved sleep-related symptoms, but did not confer a large survival advantage.[11] Sleep disordered breathing, particularly nocturnal hypoventilation (NH) is a complication of respiratory involvement in NMD that can evolve into symptomatic daytime hypercapnia if not treated with NIV.[12] Respiratory polygraphy is generally used to detect NH; oxycapnography may also be used. Paediatric patients with NMD can develop NH in the absence of clinical symptoms or other signs of nocturnal altered gas exchange. Monitoring of nocturnal

hypoventilation should, therefore, be included among nocturnal respiratory assessments of these patients as an additional tool to determine when to initiate NIV.[13]

Cough is impaired in NMD and therefore cough assisting is an important part of the management of the condition. Inspiratory weakness leads to a reduction of inspiratory volume, bulbar weakness impairs the glottis closure and expiratory weakness reduces cough pressure. Maximum insufflation capacity (MIC) and peak cough flow (PCF) should be measured at each clinic. The latter is most important in terms of deciding when to start treatment. Peak cough flow should be 360–840 L/min. In clinical practice, a PCF between 160 and 200 L/min is considered an effective cough.
Airway clearance techniques include cough augmentation (assisted inspiration/expiration) and sputum mobilisation.[14] Manually assisted coughing and mechanical insufflation/exufflation (MI-E) are effective and safe methods for clearing airway secretion in patients with NMD.[15] Breath stacking or airstacking with a mask and one way valve can achieve significantly increased lung volumes in NMD patients.[16,17]

In weaker patients, MI-E is the most appropriate choice. It has been shown to increase PCF, reduce dyspnoea and reduce the duration of the session, which is important for the patient.[18] It has also been found to be beneficial in NMD patients with upper respiratory tract infections.[19] It is important that inspiratory and expiratory timing/pressures are individualized. Patients with ALS are likely to benefit from lower pressures, triggered insufflation and longer insufflation time. Greater exsufflation pressures than insufflation pressures, together with a shorter insufflation time than exsufflation time, should be used. Subjects who produced daily secretions are more likely to use MI-E every day.[20]

The use of MI-E is not supported by a strong body of clinical trial evidence; a 2013 Cochrane review found that only 5 studies with a total of 105 participants were eligible for inclusion, and concluded that there was insufficient evidence for or against the use of MI-E in people with NMD.[21] But despite the lack of evidence, experts consider that it must be used in weak patients with NMD.

In summary, this summary has demonstrated that management of respiratory failure in patients with NMD requires the use of NIV and that the management of cough impairment in weak patients requires MI-E. As patients with some NMDs are living longer, long term consequences of these interventions will arise; Clinical experience shows older patients now experiencing new, and some potentially fatal, complications of NIV. Further research is needed on how best to address these.

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