CHEST Recent Advances in Chest Medicine

Recent Advances in Respiratory Care for Neuromuscular Disease*

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The impact of ventilatory support on the natural history of neuromuscular disease (NMD) has become clearer over the last 2 decades as techniques have been more widely applied. Noninvasive ventilation (NIV) allows some patients with nonprogressive pathology to live to nearly normal life expectancy, extends survival by many years in patients with other conditions (*eg*, Duchenne muscular dystrophy), and in those patients with rapidly deteriorating disease (*eg*, amyotrophic lateral sclerosis) survival may be increased, but symptoms can be palliated even if mortality is not reduced. A growing number of children with NMD are surviving to adulthood with the aid of ventilatory support. The combination of NIV with cough-assist techniques decreases pulmonary morbidity and hospital admissions. Trials have confirmed that NIV works in part by enhancing chemosensitivity, and in patients with many different neuromuscular conditions the most effective time to introduce NIV is when symptomatic sleep-disordered breathing develops.

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Key words: home ventilation; muscular dystrophy; respiratory failure

Abbreviations: ALS = amyotrophic lateral sclerosis; DMD = Duchenne muscular dystrophy; NIV = noninvasive ventilation; NMD = neuromuscular disease; REM = rapid eye movement; SMA = spinal muscular atrophy

Learning Objectives: 1. Noninvasive ventilation (NIV) allows patients with nonprogressive neuromuscular disease to live a near-normal life expectancy, extends survival by many years in other conditions, and can palliate symptoms in patients with rapidly progressive diseases. 2. NIV works in part by enhancing chemosensitivity, and in many neuromuscular conditions the most effective time to introduce NIV is when symptomatic sleep-disordered breathing develops.

Developments in molecular biology have identified the genetic defects in many neuromuscular conditions and hold a very real hope of gene therapy for the treatment of some conditions (*eg*, Duchenne muscular dystrophy [DMD]). Behind the excitement surrounding these important breakthroughs as we await their clinical realization, there has been a quiet revolution in ventilatory support that has had a significant impact on the natural history of a range of inherited and acquired neuromuscular disorders, where respiratory insufficiency is the most common cause of premature mortality. This application of ventilatory assistance, in many cases noninvasively, has extended survival considerably in patients with some conditions, has allowed children affected with other disorders to reach adulthood, and has improved the quality of life in most patients. The following article describes the use of assisted venti-

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This article is a based on the Margaret Pfrommer Honor lecture delivered at the American College of Chest Physicians meeting in Montreal, November 2005, in honor of this pioneer of assistive technology, researcher, champion of independent living, and patient advocate, who herself was a long-term poliomyelitis survivor and user of assisted ventilation. The work is also dedicated to the memory of Dr. Tony Oppenheimer who did so much to advance the care of ventilator-dependent patients, particularly those with amyotrophic lateral sclerosis.

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lation to achieve these objectives and offers an explanation of why it works.

Impact of Ventilatory Support on Survival

Long-term ventilation has an established track record in the management of patients with ventilatory failure due to neuromuscular disease (NMD), having gained currency at the time of the poliomyelitis epidemics in the middle of the last century.

For instructions on attaining CME credit, see page A-92

Many of the old polio patients received treatment with either negative pressure or tracheostomy ventilation, and it was not until the early 1980s that noninvasive ventilation (NIV) with a mask was pioneered by Rideau et al[1] in France and subsequently by Bach et al[2] in the United States. Successive large cohort studies[3–5] have shown that NIV can extend survival in patients with nonprogressive conditions (*eg*, old poliomyelitis) such that these individuals are likely to have a nearly normal life expectancy. In patients with progressive conditions like DMD, the average age of death has increased from 19 to at least 25 years,[6] with 1-year and 5-year survival rate estimates of 85% and 73%,[7] respectively, increasing the numbers of young men with DMD who are now living into their 30s and 40s. Furthermore, the survival profile (Fig 1) suggests a plateau effect over the first 5 or 6 years of ventilation therapy, raising the question once again of whether there is an independent effect of assisted ventilation on the progression of the muscle disease, in addition to a reversal of the respiratory consequences.

Why Does NIV Work?

At first sight, it is surprising that a treatment applied at night can have the sustained effect of correcting arterial blood gas tensions during the day. Over the years, it has been hypothesized that this improvement is mediated by a number of possible mechanisms. Hill[8] has suggested that NIV may work by (1) improving ventilatory mechanics, (2) resting fatigued respiratory muscles thereby improving strength and endurance, or (3) enhancing ventilatory sensitivity to CO_2. In addition, improvement in sleep stage distribution may increase chemosensitivity and enhance sleep quality. It is highly likely that mechanisms playing a key role in patients with restrictive disorders differ from those in COPD patients.

Annane et al[9] measured the effects of NIV on CO_2 responsiveness, noninvasive indexes of respiratory muscle strength, and sleep quality in a mixed group of patients with chest wall restriction or NMD after 6 months and 1 to 3 years of therapy. The mean vital capacity for the group at the start of NIV was 38%

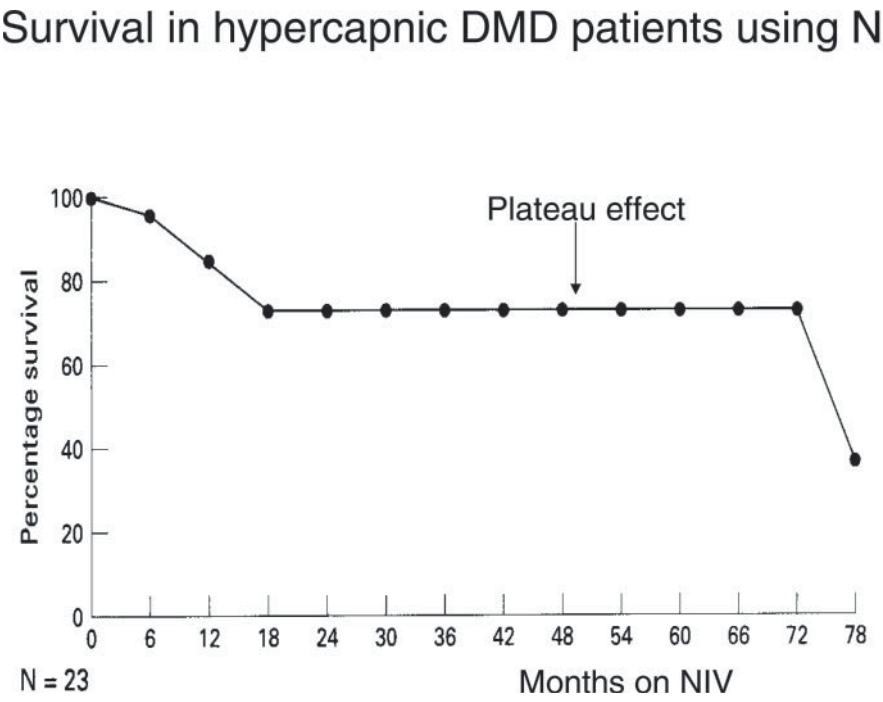

Figure 1. Impact of NIV therapy on survival time in hypercapnic DMD patients. From Simonds et al.[7]