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## Research Article

# Respiratory Management of Myotonic Dystrophy

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## Abstract

Patients with myotonic dystrophy can avoid episodes of respiratory failure by using up to continuous noninvasive ventilatory support (CNVS). Of 154 patients consecutively presenting to a neuromuscular disease clinic, 143 had types 1 or 2 and 11 had congenital myotonic dystrophy. Of the 76 who came multiple times, 41 were prescribed and used at least sleep NVS to relieve symptoms of fatigue and hypersomnolence. They had sleep and end-tidal (Pet) CO<sub>2</sub> with highs over 50 mm Hg and many 4% or greater O<sub>2</sub> desats per hour of sleep and all had mean sleep O<sub>2</sub> sat levels less than 95% before beginning sleep NVS. Thirteen eventually had to extend NVS use into and eventually throughout daytime hours for CNVS. While using NVS during the day their arterial blood gases were within normal limits. When the 41 were using NVS only during sleep, 24 of the 41 also had normalization of diurnal SpO<sub>2</sub> to ≥ 95% and decreased hypercapnia. The 41 patients have been using sleep NVS for 6.70±3.64 (range = 0.75 to 19) years per patient or for 274.7 patient-years. Seventy-two have died or been lost to follow-up. The 13 up to CNVS users have been doing so for 75.7 patient-years or a mean of 5.8±3.2 (range = 0.2 to 10) years per patient. The VC from first visit to most recent visit of all 71 decreased a mean 49.3±168.8 ml or about 1.5% per year. it decreased a mean 52±171 per year for the 41 NVS users over 274.7± 3.64 patient-years.

## Abbreviations

ABG: Arterial Blood Gases; CNS: Central Nervous System; CNVS: Continuous Noninvasive Ventilatory Support; CPF: Cough Peak Flows; DMD: Duchenne Muscular Dystrophy; EPAP: Expiratory Positive Airway Pressure; IPAP: Inspiratory Positive Airway Pressure; VC: Vital Capacity; LVR: Lung Volume Recruitment; MIC: Maximum Insufflation Capacity; NVS: Noninvasive Ventilatory Support; PetCO<sub>2</sub>: End-Tidal Carbon Dioxide; SpO<sub>2</sub>: Pulse Oxyhemoglobin Saturation; VFBA: Ventilator Free Breathing Ability

## Introduction

Myotonic dystrophy has many unique aspects. Virtually all patients complain of hypersomnolence and fatigue. While both can be at least in part relieved by Noninvasive Ventilatory Support (NVS), some hypersomnolence usually remains and may be due to Central Nervous System (CNS) pathology. The chemosensitivity of the respiratory centers (the P<sub>0.1</sub>) is well preserved in patients with myotonic dystrophy, as it is for

patients with other muscular dystrophies. However, even in the absence of weak respiratory muscles, output to breathing is modulated by impaired respiratory mechanics caused by myotonia. The myotonia causes chronic symptomatic alveolar hypoventilation despite Vital Capacities (VCs) and Maximum Insufflation Capacities (MICs) that may be well preserved for many years [1]. Even in the absence of significant central or obstructive sleep apneas [2,3], or chronic diurnal hypercapnia, these patients can exhibit sleep hypercapnia and hypersomnia. Apneas and hypopneas, when present, can be exacerbated by chronic alveolar hypoventilation due to weak and myotonic inspiratory muscles. Even if the respiratory muscles are relatively strong, the myotonia makes it difficult for them to relax and reverse direction, decreasing lung ventilation and leading to hypercapnia.

Despite severe hypercapnia during sleep, because these patients are usually able to walk, because of their frequent general apathy and cognitive impairment, and because of the myotonic nature of the muscle impairment by which they may not feel great benefit by using Noninvasive Ventilatory



Support (NVS), they very often fail to use NVS sufficiently either during daytime hours or overnight to maintain normal Arterial Blood Gases (ABGs). One study reported poor compliance with ventilator use by 62% of 38 patients by comparison with patients with other NMDs [4]. Thus, with many patients not benefiting optimally from NVS, they can be hospitalized repeatedly before succumbing from cor pulmonale and cardiorespiratory failure. Nevertheless, we suspect that those who do cooperate to use at least nocturnal NVS may have improved ABGs, symptoms, and survival [5]. It may be that the weaker patients, those wheelchair dependent with very low VCs, have better prognoses than ambulatory patients who do not appreciate the benefits of NVS and use it sparingly. Ambulatory hypercapnic myotonic dystrophy patients neither want to carry nor pull a ventilator with them while they walk nor do they feel so much benefit as those in wheelchairs who literally can not breathe without up to continuous NVS [6,7].

The objective of this retrospective longitudinal study is to determine changes in VC in populations of patients with myotonic dystrophy that use NVS and active lung volume recruitment vs. those who do not.

## Methods

This is a retrospective longitudinal study of consecutively presenting patients to a neuromuscular disease clinic. Besides demographic information, vital capacity measured in sitting and supine positions, lowest observed value of SpO<sub>2</sub>, highest observed PetCO<sub>2</sub>, maximum insufflation capacity, and Cough Peak Flows (CPF) were recorded for every visit. Patients using low span bi-level PAP were switched to NVS settings on bi-level machines, e.g. inspiratory PAP (IPAP) 20 cmH<sub>2</sub>O, EPAP 4 cmH<sub>2</sub>O, or to portable ventilators volume preset from 700 to 1500 ml. Hours per day of use of NVS was noted, as was if the patient underwent tracheotomy.

## Results

Of 154 patients consecutively presenting to a neuromuscular disease clinic with DNA confirmed myotonic dystrophy, 143 had types 1 or 2 and 11 congenital myotonic dystrophy. Of the 143, 67 came only once. Of the 11 congenital patients, 9 came only once and the other two were not placed on or did not use NVS. Of the 76 who came multiple times, 41 were prescribed and used at least sleep NVS on the basis of symptoms of hypersomnolence, fatigue, and morning headaches. They also had sleep end-tidal (Pet) CO<sub>2</sub> averaging 47 or more mmHg with highs over 50 cmH<sub>2</sub>O and many 4% or greater O<sub>2</sub> desats per hour of sleep. All had mean O<sub>2</sub> sat levels less than 95%. Thirteen of the 41, when feeling dyspneic upon discontinuing NVS in the morning, extended NVS use into and eventually throughout daytime hours. Several lost all ventilator free breathing ability (VFBA). While using NVS during the day their ABGs were within normal limits. When the 41 were using NVS only during sleep, 24 of the 41 also had normalization of diurnal oxyhemoglobin saturation (SpO<sub>2</sub>) to  $\geq$  95% and decreased hypercapnia. The others had normal diurnal SpO<sub>2</sub> levels before beginning sleep NVS but their diurnal PetCO<sub>2</sub> decreased from 46 $\pm$ 1.8 to 42 $\pm$ 1.9 mmHg. Wash out of the end-tidal samples due to the nasal NVS made

nocturnal PetCO<sub>2</sub> quantitations unreliable. Nevertheless, all 41 patients reported symptomatic improvements. The 41 patients have been using and continue to use NVS for 274.7 $\pm$ 3.64 patient-years, at least 6.70 $\pm$ 3.64 (range= 0.75 to 19) years per patient and seventy-two have died or been lost to follow-up. The 13 up to CNVS users have been doing so for 75.68 patient-years or a mean of 5.82 $\pm$ 3.27 (range= 0.2 to 10) years per patient. The VC from first visit to the most recent visit of all 71 managed by NVS decreased a mean 49.3 $\pm$ 168.8 ml or about 1.5% per year whereas normal decrease is 1% for males, 1.2% for females or about 32 ml per year after age 20. It decreased a mean 52 $\pm$ 171 for the 41 NVS users over 274.7 $\pm$ 3.64 patient-years.

For 17 patients beginning NVS at the first visit to the second visit a mean 7 $\pm$ 6.9 (range= 1 to 29) months later the VC increased by 165.2 $\pm$ 99.5 (range = 20 to 330) ml. However, it also increased by 176 $\pm$ 107.14 (range= 70 to 340) ml for 5 of the 30 who did not use sleep NVS but who performed two to three times daily active lung volume recruitment (LVR) from the first visit to the second visit 18.2 $\pm$ 13.16 months later. At least 7 NVS users reported relief of echocardiographic evidence of right ventricular strain. Five of the non-NVS users underwent tracheotomies in their local hospitals during episodes of cardiopulmonary failure (Table 1).

## Discussion

The fact that nine myotonic dystrophy patients underwent tracheotomies locally is in contrast to only 2 of our 279 NVS users with Duchenne Muscular Dystrophy (DMD), none of whom having failed extubation attempts but who underwent emergency tracheotomies during failed intubation attempts. This suggests that the myotonic dystrophy patients did not use NVS adequately to avoid ARF and resort to tracheotomies even though their VCs were much greater than those of the DMD patients, over 100 of whom had VCs less than 250 ml.

Although there are no long term studies on the use of mechanical ventilation by myotonic dystrophy patients, we have managed a handful using Continuous Tracheostomy Mechanical Ventilation (CTMV), and 8 others using CNVS with no VFBA for a prolongation of survival of at least 8 years. In a recent study of 13 hypercapnic patients with some combination of hypersomnolence, dyspnea, morning headaches, and sleep disturbance using nocturnal nasal or oronasal "NIV" which included Continuous Positive Airway Pressure (CPAP) and less than NVS support settings of bi-level PAP, diurnal PaCO<sub>2</sub> decreased from 64 to 53 mmHg, PaO<sub>2</sub> increased from 53 to 65 mmHg, mean nocturnal O<sub>2</sub> sat increased from 80.5 to 90.3%, and transcutaneous PCO<sub>2</sub> decreased from 59.3 to 41.4 mmHg. Three ventilator users died but the other 10 used bi-level PAP for at least 27 months [5].

In another study 32 adult patients diagnosed with sleep-disordered breathing began bi-level PAP with inspiratory PAPs of 8.5 to 18.7 cm H<sub>2</sub>O, expiratory PAP not noted. At 2 year follow-up diurnal PaCO<sub>2</sub> was stable at 41.5 mmHg; PaO<sub>2</sub> decreased from 79.2 to 76.6 mm Hg, mean nocturnal O<sub>2</sub> sat increased from 91.7 to 93.8%, and mean transcutaneous PCO<sub>2</sub> decreased from 46.4 to 40.1 mmHg [8].

**Table 1:** Extent of use of noninvasive ventilatory support.

Myotonic Dystrophy Patients	Males	Females	Mean age $\pm$ s.d.	Mean Vital Capacity (ml) sitting first visit $\pm$ s.d.	Years from first visit to last visit (mean $\pm$ s.d.)	Mean Vital Capacity (ml) sitting most recent $\pm$ s.d.	Cough Peak flows L/min (mean $\pm$ s.d.)
Didn't Use NVS	23	7	32.6 $\pm$ 14.1	3311.3 $\pm$ 1146.1	5.5 $\pm$ 5.2	3213.6 $\pm$ 1044.2	5.6 $\pm$ 1.2
Sleep-only NVS	15	13	40.4 $\pm$ 11.8	2618 $\pm$ 718.3	5.1 $\pm$ 3.8	1780 $\pm$ 703.3	5.1 $\pm$ 1.4
Sleep plus daytime NVS	8	5	45.1 $\pm$ 15.3	1610.7 $\pm$ 679.7	3.8 $\pm$ 3.3	1397.7 $\pm$ 627.2	4 $\pm$ 1.4

Another study considered 12 patients using bi-level PAP. Investigating the effects of a 1-month withdrawal followed by a 1-month reinstatement of bi-level PAP, settings not reported, initial diurnal PaCO<sub>2</sub> 43.1 mm Hg increased to 46.3 mm Hg after the one month withdrawal then decreased back to 43.9 mm Hg after one month of reinstatement; PaO<sub>2</sub> 83.6 mm Hg at baseline decreased to 76.9 mm Hg after one month withdrawal then increased to 80.9 mm Hg after one month of reinstatement. Mean nocturnal O<sub>2</sub> sat 95.0% at baseline decreased to 92.2% after one month withdrawal then increased to 95.1% after one month of reinstatement [9]. None of these studies described patients who, with time, became dependent on continuous ventilatory support. All our 13 patients using CNVS had normal CO<sub>2</sub> and O<sub>2</sub> sat levels while using it and the levels deteriorated and respiratory distress developed upon discontinuation of CNVS, including immediately for 8 patients.

A study of mortality in myotonic dystrophy over a 47 year period indicated a median survival of 60 years for males and 59 years for females with survival to age 65 only 18% by contrast to the normal 78%. The causes of death were about 30% from pneumonia and 30% from cardiac arrhythmias. Half of the patients were wheelchair-bound [10]. Inadequate ventilatory and cough assistance most probably played a big role in the deaths due to pneumonia, cor pulmonale, heart failure and fatal arrhythmias. These patients have periods when their CPF are very poor and they need access to MIE to avoid pneumonia.

Using NVS settings to normalize CO<sub>2</sub> and O<sub>2</sub> sat levels as well as AHI, rather than only low pressure support bi-level PAP, better improves blood gases and can prolong life by CNVS when needed. Some patients are being told that by polysomnography they have no evidence of sleep disordered breathing and do not require treatment despite severe hypercapnia that was not monitored but that we observed on presentation to us. Apnea-hypopnea indices are often normal or normalized by noninvasive ventilation at less than NVS settings despite severe sleep hypercapnia that can result in cor pulmonale.

On conclusion, it is clear that occasional patients with myotonic dystrophy can become CNVS dependent, as an

alternative to undergoing tracheotomy, and this can occur without hospitalization or an episode of acute respiratory failure.

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