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Muscular Dystrophy

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Research Article

Duchenne Muscular Dystrophy Prolongation of Life by Noninvasive Ventilation and Mechanically Assisted Coughing

ABSTRACT

Gomez-Merino E, Bach JR: Duchenne muscular dystrophy: Prolongation of life by noninvasive ventilation and mechanically assisted coughing. *Am J Phys Med Rehabil* 2002;81:411–415.

Objective: To quantitate prolongation of survival for patients with Duchenne muscular dystrophy with the use of noninvasive intermittent positive-pressure ventilation (IPPV) with and without access to a protocol involving mechanically assisted coughing.

Design: In this retrospective review of all patients with Duchenne muscular dystrophy visiting a neuromuscular disease clinic, patients were trained to use mouth piece and nasal IPPV and mechanically assisted coughing to maintain oxyhemoglobin saturation >94% (protocol). Survival was considered prolonged when noninvasive IPPV was required full time.

Results: Ninety-one of 125 patients used noninvasive IPPV part time for 1.9 ± 1.3 yr, and 51 went on to require it full time for 6.3 ± 4.6 yr. Of the 31 noninvasive IPPV users who died without access to the protocol, 20 died from respiratory causes and seven died from cardiac causes. None of the 34 full-time noninvasive IPPV users with access to the protocol underwent tracheotomy or died from respiratory complications during a period of 5.4 ± 4.0 yr, whereas three died from heart failure. Five patients with no breathing tolerance were extubated or decannulated to continuous noninvasive IPPV.

Conclusions: Noninvasive respiratory aids can prolong survival and permit extubation or decannulation of patients with Duchenne muscular dystrophy with no breathing tolerance.

Key Words: Cough, Noninvasive Mechanical Ventilation, Respiratory Paralysis, Respiratory Therapy, Duchenne Muscular Dystrophy, Exsufflation, Intermittent Positive-Pressure Ventilation

Intermittent positive-pressure ventilation (IPPV) can be delivered via a simple mouth piece for daytime ventilatory support, a mouth piece with lip-seal retention, or a nasal interface for nocturnal support. The In-Exsufflator (J. H. Emerson, Cambridge, MA) is a device that provides maximal lung insufflation via an oronasal mask or invasive airway tube when present, immediately followed by a forced exsufflation to simulate a cough. It is used in conjunction with exsufflation-timed abdominal thrusts to further augment cough flows as part of mechanically assisted coughing (MAC).

It has been estimated that 55%^{1,2} to 90%³⁻⁵ of patients with Duchenne muscular dystrophy die from pulmonary complications associated with respiratory muscle weakness between 16.2 and 19 yr of age and, uncommonly, after age 25.^{4,6} Patients who undergo a tracheostomy have been described to survive an additional 1-7 yr using ventilatory support.⁷⁻⁹ Most patients who do not die from respiratory complications die from cardiomyopathy. Because there is no relationship between the extent of cardiomyopathy and age,¹⁰ some patients without respiratory dysfunction die from congestive heart failure in their teen years, whereas others can survive many years with ventilatory support.

In a recent study, it was found that 90% of episodes of pneumonia and respiratory failure occurred during otherwise benign upper respiratory tract infections (URIs) and were largely caused by an inability to cough effectively.¹¹ In 1993, we introduced a protocol to avoid episodes of pneumonia and respiratory failure. It consisted of using oximetry as feedback to maintain normal oxyhemoglobin saturation (SpO_2) by appropriately using noninvasive IPPV and MAC. In many cases, our patients became continuously dependent on ventilatory support for years, without

ever requiring hospitalization.¹² Although the use of nocturnal-only inspiratory aid can relieve symptoms and ameliorate hypercapnia early on, it does not necessarily prolong survival. The purpose of this report is to evaluate the effect on survival of the use of full-time noninvasive IPPV with and without access to this protocol.

METHODS

A retrospective analysis was undertaken of 125 patients with Duchenne muscular dystrophy referred to a university hospital neuromuscular disease clinic since 1983. The diagnosis was established by absence of dystrophin on muscle biopsy or by DNA analysis. In addition, no patients who could walk beyond their 12th birthday were included. No patients had received glucocorticoid therapy. We considered life to be prolonged from the point at which patients required ongoing full-time ventilator use (without tracheostomy tubes) over 16 hr/day and had limited ventilator-free breathing tolerance, with respiratory distress and blood gas derangements forcing return to ventilatory support.

The cause for death in Duchenne muscular dystrophy was considered to be cardiac related when it occurred suddenly, without evidence or history of recent URI or airway secretion management difficulties, and with a left ventricular ejection fraction documented to be below 20%. Patients were noted to die from respiratory causes when they died during intercurrent URIs, underwent tracheotomy for respiratory failure and subsequently died without meeting the criteria for cardiac death, or had decreases in SpO_2 associated with airway mucus accumulation. Symptomatic, hypercapnic patients, not receiving ventilatory assistance or who discontinued it and became un-

responsive were noted to have died from ventilatory failure.

Before 1993, patients were provided with noninvasive IPPV for ventilatory support and manually assisted coughing but neither MAC nor oximeters for home use. Since 1993, patients have been provided with oximeters, manual resuscitators for deep insufflation therapy to facilitate manually assisted coughing, In-Exsufflators, and access to portable volume ventilators when a high risk for URI-associated acute respiratory failure was identified on the basis of maximum assisted peak cough flows being below 270 liters/min.¹² Because the patients' vital capacities were also below 1000 ml at this point, they were prescribed daily air stacking of manual resuscitator-delivered volumes to maximum insufflation capacities.¹³ They were instructed to monitor their SpO_2 continuously during URIs in a protocol involving the use of noninvasive IPPV and MAC as needed to maintain normal SpO_2 . This ensured effective alveolar ventilation. It also ensured effective airway secretion elimination because any desaturations caused by airway mucus accumulation were promptly reversed, and SpO_2 baseline returned to over 94% after MAC.

Statistical analysis was performed by using the SPSS 8.0 for Windows (SPSS, Chicago, IL). A nonparametric method (Mann-Whitney *U* test) was used in the basic descriptive statistical analysis because the variables measured did not approximate a normal distribution. The Kaplan-Meier survival analysis allowed for variable follow-up times. A *P* value <0.05 was used to establish statistical significance.

RESULTS

A total of 125 patients with Duchenne muscular dystrophy visited a neuromuscular disease clinic. Thirty-four patients (mean, 14.9 ± 6.0 yr) had not yet experienced car-

TABLE 1*Duchenne muscular dystrophy ventilator user mortality*

No Protocol Access	n	Noninvasive IPPV Use, yr		Tracheostomy IPPV, yr	Age at Death, yr
		<16 hr/day	>16 hr/day		
Reason ^a					
CHF	2	0.9 ± 0.1	2		20.5 ± 3.5
CHF	5	2.2 ± 1.8	6.2 ± 1.8		27.5 ± 5.7
ARF	1	0.5			14
ARF	10	2.8 ± 2.7	6.1 ± 5.2		28.4 ± 8.2
AVF ^b	3	1.7 ± 3.1	20.7 ± 1.0		41.3 ± 8.0
Other ^c	1	2.5	13		34
Unknown	3	2.5 ± 2.3	7.7 ± 6.4		29.0 ± 8.2
Posttracheotomy	6	1.9 ± 1.4	6.4 ± 6.8	0.9 ± 1.8	29.1 ± 7.1
With Protocol					
Access					
CHF	3 ^d				16.0 ± 1.0
ARF	0 ^e				

IPPV, intermittent positive pressure ventilation; CHF, congestive heart failure; ARF, acute respiratory failure; AVF, acute ventilatory failure.

^aReasons include CHF, ARF, AVF.

^bThe patients died while sleeping without putting on lipseal at age 29 after 15 years of ventilatory support, following trauma and loss of ventilator interface after 25 years of noninvasive ventilation support, and when using a rocking bed ventilator instead of noninvasive IPPV. His vital capacity was 30 ml, and the rocking bed was ineffective for him.

^cOther deaths were caused by suicide at 34 years of age after 13 years of noninvasive ventilation.

^dWithout ventilator use.

^eWith up to continuous noninvasive IPPV.

diac or respiratory distress and did not use ventilatory assistance or expiratory aids. The remaining 91 patients constituted our study population. These patients had become wheelchair dependent at 9.7 ± 2.2 yr of age. They began to use nocturnal noninvasive IPPV at 19.1 ± 3.3 yr of age, with a mean vital capacity of 411 ± 252 ml, used part-time noninvasive IPPV for 1.9 ± 1.3 yr, and were followed for a mean of 8.5 ± 5.3 yr (range, 1–18 yr). Their mean age was 26.5 ± 7.0 yr at last evaluation, tracheotomy, or death. The probable reasons for death are listed in Table 1. For 11 of the 14 who died from respiratory failure without tracheostomy tubes, the failure was triggered by a URI. None of the seven deaths for which autopsies were performed were caused by pulmonary emboli or non-cardiopulmonary causes.

We lost contact with 14 ventilator users. We considered them in this study from their first to last visits,

but we did not include them in the survival analysis. Three patients were already dependent on tracheostomy IPPV, with no breathing tolerance at their initial visits.

Twelve patients with a mean vital capacity of 265 ± 104 ml and little or no breathing tolerance were able to use glossopharyngeal breathing to volumes of 1273 ± 499 ml. This permitted them a mean of 5.3 ± 4.8 hr of ventilator-free breathing tolerance.

Forty of the 91 patients either died from heart failure before requiring full-time noninvasive IPPV, required the use of noninvasive aids only during intercurrent URIs, or used only part-time noninvasive IPPV at the time of the study. Survival of the other 51 full-time users was prolonged for 6.3 ± 4.6 yr (range, 6 mo to 18 yr), with at least 17 patients still alive at last contact.

Eight of the 10 patients who died from congestive heart failure had had

previous cardiac admissions and complaints of chest, abdomen, or back discomfort and abdominal distention before dying. They had long-standing clinical, radiographic, and laboratory evidence of congestive heart failure, and they had left ventricular ejection fractions <20%. Seven of the patients complained of dyspnea unrelieved by ventilator use.

Five patients with no breathing tolerance were referred to us intubated or using tracheostomy IPPV. We extubated or decannulated them to full-time noninvasive IPPV. Within days after extubation or decannulation, all five patients developed breathing tolerance and were weaned to nocturnal-only noninvasive IPPV for 1–3 yr before requiring it full time. They have now been using full-time noninvasive IPPV for 2, 6, 7, 8, and 9 yr, respectively. Fourteen of the 57 patients without access to oximetry and MAC eventually underwent tracheotomy and survived for an ad-

ditional 4.1 ± 4.5 yr to 28.8 ± 5.1 yr of age.

None of 34 patients with access to the oximetry protocol have been lost to follow-up, undergone tracheotomy, or died from respiratory complications over 1.6 ± 1.6 yr of using noninvasive IPPV part time and, subsequently, 5.4 ± 4.0 yr of using noninvasive IPPV full time. They have avoided episodes of respiratory failure and hospitalizations by using the protocol.¹² The three who died all had left ventricular ejection fractions below 15%. Figure 1 illustrates the causes of death. The 14 patients lost to follow-up and 17 patients still alive were 25.7 ± 4.5 yr of age.

A *P* level of 0.6 was obtained by Mann-Whitney test comparing age of death of patients who died for cardiac reasons with or without protocol access. It was not possible to apply this test to patients who died from respiratory causes because no one using the protocol has died from respiratory causes. A Kaplan-Meier plot shows the survival distributions for protocol users in Figure 2. We applied the log-rank statistical test for equality of survival distributions for protocol users, and a statistic of 18.63 (*P* = 0.0000) was obtained.

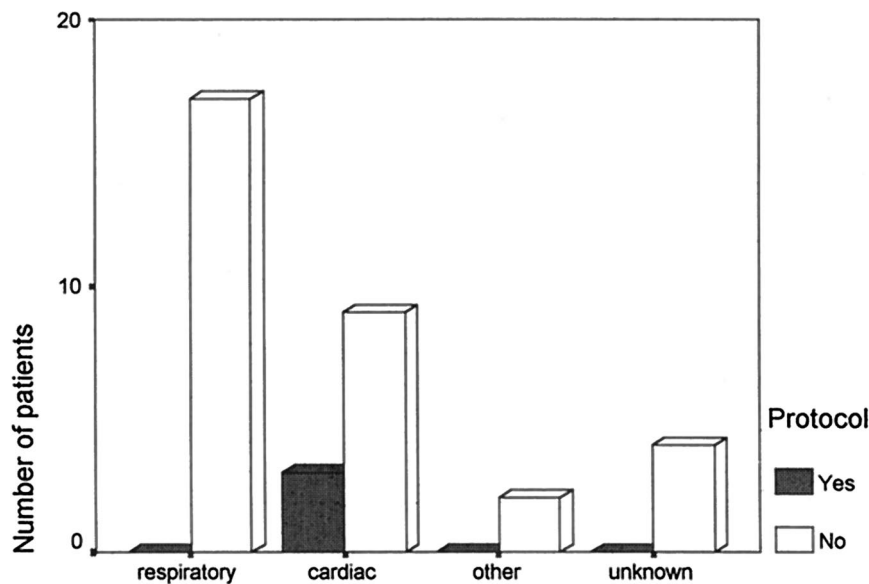


Figure 1: Causes of death in relation to access to protocol.

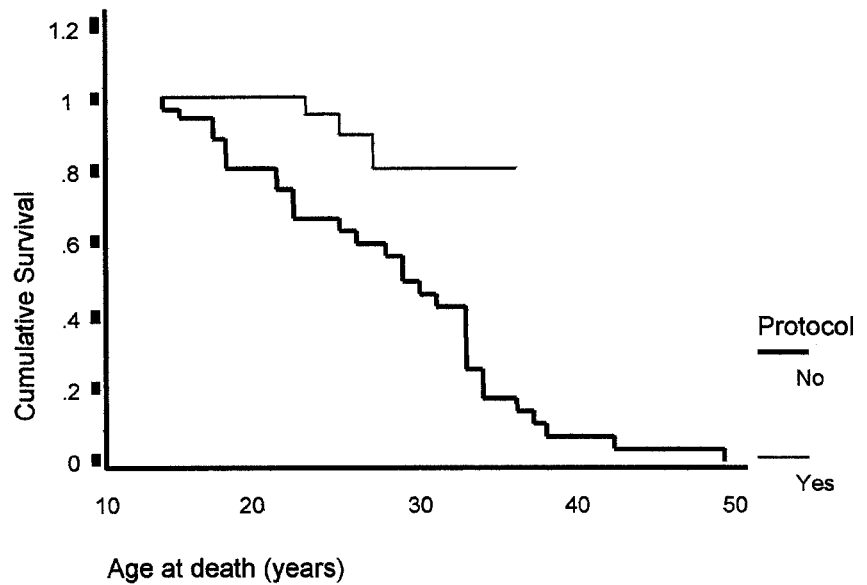


Figure 2: Survival plot for protocol and nonprotocol patients.

DISCUSSION

This study demonstrates that Duchenne muscular dystrophy survival can be prolonged by using noninvasive IPPV and MAC as an alternative to tracheostomy for IPPV and airway suctioning. Since the availability of home oximetry and MAC with the use of SaO_2 monitoring during URIs, we have had no respiratory mortality and only three cardiac deaths.

Even though life can also be prolonged by tracheotomy, noninvasive methods are associated with less pulmonary morbidity and fewer hospitalizations,¹¹ and they are preferred over tracheostomy by patients and their care providers for safety, convenience, verbal communication, sleep, swallowing, appearance, comfort, and general acceptability.¹⁴ By avoiding hospitalizations, expense is also reduced.^{11,15} Thus, noninvasive approaches should be tried before tracheostomy is considered.

A survey of neuromuscular disease clinics noted that the majority of clinics are offering nocturnal nasal ventilation to their patients.¹⁶ However, very few clinics are offering noninvasive IPPV for daytime support or MAC.¹⁶ Failure to do so inevitably results in patients developing pneumonia and acute respiratory failure during intercurrent URIs.¹¹ Although life could be prolonged by full-time noninvasive IPPV before the availability of MAC guided by oximetry, respiratory morbidity and mortality still occurred. Because of the use of home oximetry and MAC, it seems that respiratory mortality will be reduced, making cardiomyopathy a much more prevalent cause of death. It

may, therefore, become particularly important to consider new medical approaches to improve the hemodynamic function of these patients.¹⁷

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