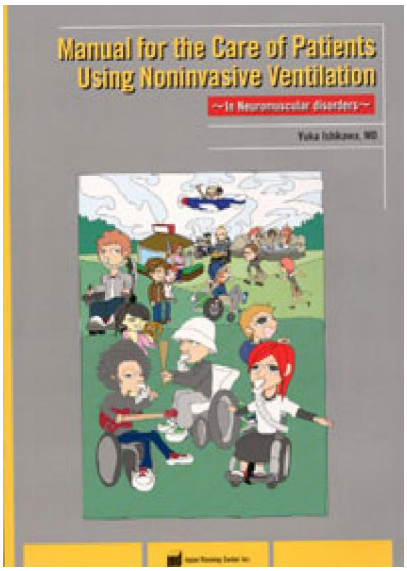
イタリアでは、今度石川悠加先生が 2004 年に日本語で出版した**「非侵襲的換気療法ケアマニュアル～神経筋疾患のための～」**をイタリアの呼吸器科の医師がイタリア語に訳し 9 月末には出版となります。

10 月初めに、イタリアのジェノバのイタリア呼吸器学会で、贈呈式と記念講演会があります。

イタリア理学療法士学会会長が、普及の旗手になっているそうです。

■ 非侵襲的人工呼吸ケアマニュアル　～神経筋疾患のための～



編著　石川 悠加　小児科医長

この本は、医師、看護士、理学療法士、作業療法士、臨床工学士、臨床工学士、臨床検査技師、指導員、保育士等、当院スタッフが呼吸機能評価や呼吸リハビリテーション、気管内挿管の抜管などから日常的な全身ケア、旅行や外泊、在宅人工呼吸療法、そして今後の展望などを、医療関係者だけでなく、患者さんやご家族をはじめ多くの方々にも読んで頂けるように、「できる限り専門用語を用いずに」「実例を具体的にご紹介してイメージし易いように」を意識して知恵を絞った 1 冊です。

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ついに非侵襲的人工呼吸ケアマニュアルの英語版が登場！　世界に広がれ　みんなの思い！

デュシェンヌ型筋ジストロフィーの NPPV による延命について、イタリアのボローニャの医師が、米国リハビリテーション医学雑誌に先月論文を出しました。

「デュシェンヌ型筋ジストロフィーの NPPV による延命効果を、米国バック先生、日本の石川先生、カナダの McKim、ベルギーのトゥサーンが医学論文で公表しています。気管切開人工呼吸を回避して、NPPV で十分な延命ができるという明らかな効果を示しています。

これら４か所の施設が、それぞれ、自身のデータを示していても、ヨーロッパ全体が、パラダイムシフトしているまでには至っていません。

そこで、イタリアは、個々に示すデータを基に、デュシェンヌ型筋ジストロフィーにおいて、気管切開人工呼吸を回避して、NPPV で十分な延命ができるというパラダイシトをしたと宣言します。」というような内容です。

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ORIGINAL RESEARCH ARTICLE

Duchenne Muscular Dystrophy

Life Prolongation by Noninvasive Ventilatory Support

ABSTRACT

Villanova M, Brancalion B, Mehta AD: Duchenne muscular dystrophy: life prolongation by noninvasive ventilatory support. Am J Phys Med Rehabil 2014;93:595–599.

Objective: American, Japanese, and Canadian centers have demonstrated that noninvasive intermittent positive pressure ventilatory support (NVS) can be used continuously and in the long-term by people with Duchenne muscular dystrophy as a definitive alternative to tracheostomy mechanical ventilation. The aim of this study was to report this for the first time in Europe.

Design: In this study, more than 300 patients with Duchenne muscular dystrophy were followed. End-tidal carbon dioxide, oxyhemoglobin saturation, and vital capacity were measured at each visit. Of the 300 patients, 79 used NVS for 8 hrs or more per day and 20 of these became continuously dependent on NVS.

Results: A total of 20 patients have continuously depended on NVS for survival, for a total of 336 patient-years, up to 16 yrs in one case. Nocturnal NVS was begun for symptomatic hypoventilation when the vital capacity had decreased to a mean of 831 ± 173 ml, and continuous dependence on NVS was necessary when the vital capacity had decreased below 297 ± 113 ml.

Conclusions: Noninvasive respiratory management can prolong survival without resorting to tracheotomy and without hospitalization.

Key Words: Duchenne Muscular Dystrophy, Noninvasive Ventilation, Italy, Paradigm

Without ventilatory support and mechanical insufflation-exsufflation (MIE), most patients with Duchenne muscular dystrophy (DMD) die between 16 and 19 yrs of age.[1,2] Ninety percent of the time, they die during upper respiratory tract infections that develop into pneumonias and acute respiratory failure (ARF).[3] Most often, conventionally managed DMD patients develop ARF; are hospitalized and intubated; and when ventilator weaning fails, undergo tracheotomy for a lifetime of home nursing care or institutionalization.[1] However, Alexander et al.[4] first described prolongation of life for DMD by continuous noninvasive mechanical ventilatory support including noninvasive intermittent positive pressure ventilatory support (NVS) in 1979. Bach and Martinez reported 101 continuous NVS (CNVS) users with DMD in 2011.[5] They noted that many of the patients became CNVS dependent for 20–27 yrs without being hospitalized or developing ARF.[5] In 2009, Ishikawa et al.[2] reported, in Japan, that 88 DMD patients survived 10 yrs longer using CNVS to a mean age of 39.6 yrs than the 24 previously managed patients who used tracheostomy mechanical ventilation to age 28.9 yrs. Despite the work of these American and Japanese centers and a subsequent study of 12 such patients by McKim et al.[6] in Canada in 2013, no one in Europe has reported that tracheotomy can be eliminated for DMD by using CNVS and MIE to avoid pneumonias and episodes of ARF[5,7] and to permit the successful extubation of ventilator unweanable patients. The purpose of this article was to demonstrate prolongation of survival for DMD by using CNVS and MIE, without any hospitalizations for respiratory failure, in Italy.

METHODS

More than 300 consecutively referred patients with DMD have been studied since 1995. All the patients had their diagnosis confirmed by both muscle biopsy and genetic analysis,[8] except one for whom the diagnosis was made by DNA analysis and muscle biopsy of a maternal cousin with clinically apparent DMD. All were wheelchair dependent before the age of 13 yrs. No patients received glucocorticoid therapy. Patients older than 11 yrs were screened for symptoms of hypercapnia, including morning headaches, daytime somnolence, depression, nocturia, weight loss, and fatigue. Sixty patients were already using sleep NVS at presentation, so their previous pulmonary function studies were reviewed to determine vital capacity (VC) at onset of sleep NVS. At every visit, they underwent end-tidal carbon dioxide ($ETCO_2$) and pulse oxyhemoglobin saturation monitoring (SpO_2) and spirometry for VC. All patients whose VCs had passed lifetime maximum (plateau) values (and were therefore decreasing) were prescribed air stacking three times a day for lung volume recruitment to improve compliance, increase cough peak flows, prevent atelectasis, and improve speech volume.[9]

Patients having hypoventilation symptoms and restricted lung function who were not already using sleep NVS were prescribed it. Patients with questionable symptoms underwent sleep ($ETCO_2$) and SpO_2 monitoring to support persuading those with abnormal results to try nocturnal NVS. Sleep $ETCO_2$ averaging greater than 40 mm Hg and especially when exceeding 50 mm Hg with or without multiple SpO_2 dips per hour were demonstrated to the patients as implying that they would be likely to feel better by using nocturnal NVS. However, when patients felt that the burden of using NVS exceeded the benefits that they derived from it, they were advised to return in 6 mos for reevaluation and perhaps another NVS trial. Polysomnography was not used because it is programmed to assess for central and obstructive apneas and hypopneas rather than for hypoventilation.

Portable ventilators, most often the Trilogy series (Philips-Respironics, Murrysville, PA) and the Elysée 150 (Saime, Savigny le Temple, France), were used on assist/control mode volume cycling at

FIGURE 1 *Patient with Duchenne muscular dystrophy using mouthpiece NVS.*

800–1500 ml delivered volumes and at physiologic backup rates to maximize inspiratory muscle rest during sleep and allow patients to vary their tidal volumes. Patients were switched to pressure cycling if severe aerophagia occurred.

When patients experienced dyspnea when discontinuing nasal NVS in the morning and continued nasal ventilation into daytime hours, they were switched to mouthpiece NVS if they had enough strength to grab a 15-mm angled mouthpiece with their lips (Fig. 1). If not, then nasal prongs were used instead. During intercurrent upper respiratory tract infections, CNVS and MIE were used with oximetry feedback to maintain or return ambient air Spo_2 to 95% or greater. They were instructed to seek medical attention if they could not maintain an Spo_2 of 95% or greater during waking hours. They were also told that if intubated, they might be extubated back to CNVS and MIE without undergoing tracheotomy.[5,7,10,11] Life was considered to be extended by CNVS when its discontinuance resulted in immediate dyspnea and oxyhemoglobin desaturation.[10]

RESULTS

Of the more than 300 referred patients, 60 were already using sleep NVS upon presentation. Symptoms were used as the criterion to introduce NVS for the other 19 patients, all of whom had $etCO_2$ of 42 or greater and normal Spo_2 at the time of its introduction and 7 of whom went on to require CNVS. Of the 79 total NVS users, 20 became CNVS dependent, with only seconds to minutes of ventilator-free breathing ability and without being hospitalized for ARF. Table 1 provides demographics and pulmonary function for the 19 still extant, all of whom have $etCO_2$ less than 40 and normal Spo_2 at last evaluation. In addition to the 19, one DMD CNVS-dependent patient for 7 yrs died suddenly at age 35 yrs with severe cardiomyopathy; another 23-hr/day NVS user died suddenly at age 36 yrs, as well as a nocturnal-only NVS user at age 23 yrs and one who was unaided at age 20 yrs. In all 4 cases, death was presumed to be of cardiac etiology. One additional ventilator user, patient 9 in Table 1, had been hospitalized once for cardiac failure. Of the 79 ventilator users, only 1 underwent tracheotomy (Table 1, 13), when he developed an upper respiratory tract infection that developed into pneumonia, in a distant region of Italy and could not be transferred to a center to extubate him to CNVS and MIE.[11] Other than the patient who underwent tracheotomy at a distant center, none of the patients ever developed ARF or were hospitalized for ARF either before or after starting NVS. The oldest DMD CNVS user is 51 yrs old (Table 1, 14). He initially used an iron lung for nocturnal assistance at age 25 yrs but was switched to nocturnal nasal NVS and at age 41 yrs became CNVS dependent.

TABLE 1 Characteristics of patients with DMD dependent on continuous noninvasive mechanical ventilation

Age, years	NVS Begun, years	VC at NVS Onset, ml	Onset of CNVS, years	VC at Onset of CNVS, ml	LVEF, %
31	16–17	730	24	320	43
34	19	830	25	270	60
35	15	980	30	350	45–50
39	15	1100	33	220	20
33	17	950	30	440	35
32	15	980	25	400	65
35	16	710	30	220	32
24	12	780	22	370	40–44
34	20	650	30	280	32
38	20	940	25	340	45–50
35	16–17	980	33	100	63
25	18	930	24	320	52
37[a]	18	870	30	140	40–45
51	25–26	300–350	43	120	65
26	18	920	24	580	45
39	14	850	22–23	280	52
33	17	860	25–26	310	48–50
38	14	680	25	280	45
40	25	720	34	300	50

[a]Patient who underwent tracheotomy at a distant center when transfer for extubation to noninvasive management could not be arranged.

LVEF indicates left ventricular ejection fraction.

DISCUSSION

This study's outcomes are consistent with those of Ishikawa et al.,[2] who reported survival to age 28.9 yrs for DMD continuous tracheostomy mechanical ventilation (CTMV) users but to age 39.6 yrs by noninvasive management. The 19 patients in this study are currently 34.7 ± 4.1 yrs old. This figure is 34.2 ± 4.2 yrs if the ages of the three deceased NVS users are added. Remarkably, none of the patients have had any hospitalizations for respiratory failure. Thus, when optimally managed, these patients can become CNVS for life without hospitalization or tracheostomies. This was also the case with the 88 patients reported by Ishikawa et al.,[2] but their patients all resided in a facility and were under their care from admission. On the other hand, in Bach and Martinez,[5] only 30% of DMD CNVS users became CNVS dependent without hospitalization because many of their patients came from long distances and were not initially under their care.

Despite articles from five centers on three continents over the last 34 yrs and a recent consensus statement that concluded that there should be a paradigm shift from invasive to noninvasive respiratory management,[12] extremely few DMD patients are offered CNVS in any country and no literature of patient-family support organizations in the United States or Europe recognizes the capacity for noninvasive management to eliminate need to resort to tracheotomy for survival. Accomplishing this requires both ongoing outpatient preventative interventions—the initiation of NVS and monitoring it to eventual CNVS dependence—and the extubation of ARF patients unable to pass spontaneous breathing trials or ventilator weaning parameters. This requires specifically trained therapists and physicians in both pediatric and adult specialties or at least one physician who can manage all. Because hospital and physician compensation is greater for invasive interventions than for noninvasive, preventative measures, this has only been reported by three centers that have individual physicians who provide both long-term and critical care.[2,5,6] Thus, it is generally incumbent on the patients themselves to demand the noninvasive path. For this, rehabilitation healthcare professionals can be crucial because DMD patients almost invariably receive physical, occupational, and respiratory therapy services long before developing the ARF that conventionally results in tracheotomy, and physiatrists, as opposed to neurologists and pulmonologists, typically treat both pediatric and adult populations.

In 2005, Toussaint et al. reported 42 Belgian DMD patients who used mouthpiece NVS to a mean Kaplan-Meier analysis predicted survival of 31 yrs, only slightly better than by invasive management (29.1 ± 8.5 yrs; range, 15.9–42.0 yrs)[2] and inferior to that reported in other centers.[2,5,8] In addition, at least 4 of the 11 who died did so from ARF,[13] and all who subsequently developed ARF and were transferred from their boarding institution to acute hospitals were intubated and underwent tracheotomies.[14] They rightfully concluded that the principal reason that the patients developed ARF was that MIE was not available to them. However, they also used high nonphysiologic ventilator backup rates of 19 ± 3 per minute and low ventilator delivered volumes, 688 ± 19 ml, which would also have contributed to their long-term noninvasive management failures and relatively poor survival by limiting the patients' ability to air stack in order to cough more effectively.[15] In addition, the fact that all who had to be intubated underwent tracheotomy demonstrates what should now be considered suboptimal management because most, if not all, could have been extubated to CNVS.[11] Furthermore, in their study, the patients were instructed to begin nocturnal NVS for hypercapnia, but not for symptomatic hypercapnia, so they began it with VCs over 1 liter. Even after 7 yrs of using mouthpiece NVS, their VCs were 354 ± 129 ml; thus, many were not CNVS dependent and yet developed ARF and underwent tracheotomies. In a later report, again because of failure to extubate unweanable patients with DMD, these authors stated, "tracheostomy may be provided when mechanical techniques of cough-assistance are useless to treat chronic cough insufficiency."[9] Kohler et al.[16] likewise published a study in 2005 on disability and quality-of-life in DMD and, as an aside, noted that some patients were CNVS dependent but did not report any daytime mouthpiece NVS nor MIE use and noted no unweanable patients being extubated so recourse to tracheotomy would ultimately become necessary to avoid premature death.

Consistent with previous successful studies, it was found that onset of nocturnal NVS for symptomatic hypoventilation occurred when the VC was a mean of 831 ± 173 ml and CNVS dependence occurred when the VC had decreased to below 297 ± 113 ml. Bach and Martinez[5] reported means of 694 ± 278 ml and 320 ± 240 ml, respectively, for these figures; and McKim et al.,[6] a mean of 900 ± 400 ml and 570 ml, respectively. Bach and Martinez,[5] Ishikawa et al.,[2] and McKim et al.[6] reported a total of 1157.2 patient-years of ventilator use among their patients. The 19 patients in Table 1 have a total of 329 patient-years of ventilator use. In a study of 69 CNVS dependent patients with neuromuscular respiratory muscle failure who had been decannulated after 1 mo or more of tracheostomy mechanical ventilation and switched to CNVS, all preferred noninvasive management for speech, swallowing, appearance, convenience, security, and unanimously overall and none were retracheed.[17]

Without mechanical ventilation, the mean age at death has been described as 18.6 ± 2.9 yrs for 56 people with DMD, with 95% of deaths caused by respiratory failure.[2] Using tracheostomy mechanical ventilation, more than 50% of patients die of cardiac disease, with most of the remainder dying of respiratory complications associated with tracheostomy. Stewart et al.[18] reported that there is no correlation between age and extent of cardiomyopathy in random DMD patients, which is why patients can die of heart failure long before requiring ventilator assistance and others with relatively preserved left ventricular ejection fractions can survive into their 40s. In the Ishikawa et al.[2] study, using CNVS and MIE, of 96 total patients, 24 of the 25 who died did so of cardiac disease, including 8 who died before requiring respiratory assistance. Thus, with noninvasive management, the limiting factor to survival is cardiac, and noninvasive management is warranted for all patients with DMD. Thus, the authors conclude that the paradigm shift to noninvasive management has begun in Italy.

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