Original Article
Yonsei Med J 2022 Jun;63(6):578-584
https://doi.org/10.3349/ymj.2022.63.6.578
Yonsei Medical Journal
YMJ
pISSN: 0513-5796 · eISSN: 1976-2437

Clinical Implications of Routine Monitoring of Pulmonary Function and Ventilation in Patients with Duchenne Muscular Dystrophy

Han Eol Cho[1*], Jang Woo Lee[2*], Won Ah Choi[1], and Seong-Woong Kang[1]

[1]Department of Rehabilitation Medicine, Gangnam Severance Hospital, Rehabilitation Institute of Neuromuscular Disease, Yonsei University College of Medicine, Seoul;
[2]Department of Physical Medicine and Rehabilitation, National Health Insurance Service Ilsan Hospital, Goyang, Korea.

Purpose: To investigate the effect of regular monitoring of pulmonary function and ventilatory status on the initiation of non-invasive ventilation (NIV) between patients who were routinely monitored before receiving NIV and those who were not.

Materials and Methods: This retrospective cohort study included subjects with Duchenne muscular dystrophy (DMD) who first received NIV between 2010 and 2019. The subjects were assigned to either the regular-follow-up (REG) group or the non-REG group, according to their follow-up status, before initiating NIV. We compared the number of emergent cases, the results of nocturnal ventilatory monitoring, and the pulmonary function of each group at initial ventilatory support.

Results: In total, 73 subjects were enrolled in the REG group and 47 subjects in the non-REG group. There were significantly more emergency cases due to respiratory insufficiency in the non-REG group (12/47, 25.5%) than in the REG group (3/73, 4.1%). At the time of initial ventilatory support, hypoventilatory symptoms were more common and relatively severe in the non-REG group (37/47, 78.7%) than in the REG group (18/73, 24.7%). The average age at initial ventilatory support of the non-REG group was 2.15 years older than that of the subjects in the REG group. Moreover, subjects who were not regularly monitored exhibited greater deterioration in pulmonary function compared to those who were regularly followed up.

Conclusion: Regular evaluation of pulmonary function and ventilatory status before the onset of ventilatory insufficiency is crucial to reduce the risk of patients with DMD requiring emergency care due to ventilatory insufficiency.

Key Words: Muscular dystrophy, Duchenne; respiratory insufficiency; hypercapnia; mechanical ventilations; noninvasive ventilation; respiratory function tests

INTRODUCTION

In the past, respiratory insufficiency has been considered to be responsible for most of the deaths in patients with Duchenne muscular dystrophy (DMD), one of the most common X-linked genetic disorders worldwide.[1] However, life expectancy and the quality of life in patients with DMD have shown significant improvements through active pulmonary rehabilitation using means such as non-invasive ventilation (NIV).[2,3] Several studies have suggested the optimal time to initiate NIV in patients with DMD,[4-7] as hypoventilation should be diagnosed at an early stage to prevent deleterious effects of acute respiratory failure. However, in clinical practice, it is difficult to determine the optimal time to initiate NIV, due to two main reasons. One is that patients often miss symptoms associated with respiratory insufficiency. Patients with DMD are often unaware of symptoms related to respiratory failure since dyspnea rarely affects them as their mobility is severely restricted; moreover, other hypoventilatory symptoms may be subtle and non-specific in early stages of ventilatory insufficiency.[8] The other reason

Received: October 28, 2021 **Revised:** March 16, 2022
Accepted: March 17, 2022
Corresponding author: Seong-Woong Kang, MD, PhD, Department of Rehabilitation Medicine, Gangnam Severance Hospital, Rehabilitation Institute of Neuromuscular Disease, Yonsei University College of Medicine, 211 Eonju-ro, Gangnam-gu, Seoul 06273, Korea.
Tel: 82-2-2019-3492, Fax: 82-2-2019-3499, E-mail: kswoong@yuhs.ac

*Han Eol Cho and Jang Woo Lee contributed equally to this work.
•The authors have no potential conflicts of interest to disclose.

is that symptoms of ventilatory insufficiency initially presents during sleep, and hypercapnia due to ventilatory insufficiency extends throughout sleep and finally into waking hours.[9] To overcome these difficulties and provide mechanical ventilatory support at an accurate time, regular evaluation at hospitals that have special clinics for pulmonary rehabilitation and neuromuscular disease are recommended. However, the effectiveness and importance of regular examinations of pulmonary function and ventilatory status in patients with DMD have not been systematically investigated.

Therefore, this study aimed to investigate the clinical implication of regular pulmonary function and ventilatory status evaluation by comparing subjects with DMD who were routinely monitored prior to the initiation of NIV to those who were not regularly followed up.

MATERIALS AND METHODS

Monitoring of pulmonary function and ventilatory status

Patients with DMD are recommended to visit the outpatient department (OPD) every 3 to 12 months, based on their age and pulmonary function, at our center. Routine pulmonary evaluation at our center includes assessment of forced vital capacity (FVC), peak cough flow (PCF), maximal inspiratory pressure (MIP), maximal expiratory pressure (MEP), and end-tidal CO_2 ($EtCO_2$). Recommendation for admission to perform continuous monitoring of ventilatory status overnight was considered if the subject reported possible symptoms of ventilatory insufficiency including nightmares, morning headaches, daytime sleepiness, fatigue, dyspnea, and orthopnea[10] over the course of detailed interviews; the FVC of the subject is much less when the subject is in the supine position compared to being in the sitting position; the subject requires two or more pillows to fall asleep; the FVC is below −40% of the predicted normal value in any position; the $EtCO_2$ indicates daytime hypoventilation ($EtCO_2$ when awake is greater than 44 mm Hg); and the daytime oxygen (O_2) saturation decreases below 95% without suspected lung disease.[11]

Criteria for NIV application

According to previous consensus indications for mechanical ventilation, we determined NIV application based on the arterial partial pressure of carbon dioxide ($PaCO_2$) over 45 mm Hg with the presence of symptoms of ventilatory insufficiency[6] or results from nocturnal continuous monitoring of the subject's ventilatory status [peak transcutaneous partial pressure of carbon dioxide ($TcCO_2$) > 48.7 mm Hg][7] with or without symptoms of ventilatory insufficiency.

Study population

This retrospective cohort study included subjects with DMD who first received mechanical ventilation due to ventilatory insufficiency at tertiary hospital between January 2010 and December 2019. We excluded subjects who obtained NIV immediately after surgery to correct scoliosis since the subjects may need NIV during acute stage of post-operative recovery.[12-14] We also excluded subjects who could not be evaluated accurately due to intellectual disability.

The subjects included in the study were categorized into two groups according to their follow-up status before NIV initiation. The regular-follow-up (REG) group had been followed-up regularly at least twice a year and their pulmonary function evaluated at the OPD over 1 year before applying NIV. The non-REG group comprised of subjects who had never visited the hospital for ventilatory insufficiency until the initiation of NIV or those who missed OPD follow-up for more than 1 year before applying NIV.

We defined severe cases as subjects who had been applied mechanical ventilation in the emergency room (ER) due to emergent conditions, such as severe desaturation or loss of consciousness due to CO_2 narcosis.

Clinical variables and nocturnal hypercapnia measurement

We collected the following clinical data at initial ventilatory support: age at initial ventilatory support, height, weight, body mass index (BMI, kg/m^2), existence of scoliosis (cases with a Cobb's angle over 20 degrees or having already received scoliosis correction operation), hypoventilatory symptoms, pulmonary function parameters, and nocturnal ventilatory status. Height was measured in joint segments with the patient positioned supine on an examination table with the hip and knee joints straightened as much as possible. Using a straight edge, the following segments were measured: top of the head to the right greater trochanter, right greater trochanter to the right femoral condyle, and right femoral condyle to the distal point of the calcaneus. The median of the three measurements was recorded. BMI was calculated as body weight divided by the square of height. We categorized hypoventilatory symptoms as "presence of breathing difficulty," "difficulties with sputum expectoration or recurrent chest infections," "morning headaches," "fatigue/daytime somnolence," "poor sleep quality," "anxiety," "chest discomfort," and "general weakness or poor oral intake."

The pulmonary function parameters, including FVC, PCF, MIP, and MEP, were evaluated. FVC was measured in the sitting positions using a hand-held spirometer (Micro Medical Ltd., Rochester, Kent, UK). PCF was measured using a peak-flow meter (Philips Respironics, Guildford, UK). MIP and MEP were measured in the sitting positions using a mouth pressure meter (Micro Medical Ltd.). Percentages of the normal predicted values were calculated for FVC, MIP, and MEP.[15-17] Arterial blood gas analysis (ABGA) was performed prior to ventilatory support upon initial admission while the patient was still awake. Those who performed intubation on initial ventilatory support

were excluded from the result analysis of ABGA, as it could not be done in some emergency situations.

Nocturnal $TcCO_2$ and O_2 saturation were measured continuously and noninvasively using a transcutaneous method (SenTec System, SenTec AG, Therwill, Switzerland) during the first night of hospitalization without ventilatory support.

Statistical analysis

The chi-square test was used to compare the number of severe cases in each group at initial ventilatory support and existence of scoliosis. Independent t-test was used to compare the results of nocturnal ventilatory monitoring between the groups. However, severe cases were excluded since they required emergency management and it was usually impossible to accurately evaluate spirometric data or perform nocturnal ventilatory monitoring, before applying ventilatory support. All statistical analyses were performed using SPSS (version 25, IBM Corp., Armonk, NY, USA).

Ethical approval

This study was approved by the Institutional Review Board of Gangnam Severance Hospital, Seoul, Republic of Korea (IRB number 3-2019-0371-001). The study protocol was in accordance with the Declaration of Helsinki.

RESULTS

Among the 136 subjects with DMD who received ventilatory support during the study period, 16 subjects were excluded from our analysis as NIV was applied immediately after scoliosis correction surgery (n=13) and intellectual disability (n=3). Finally, 120 subjects were included in the study (Fig. 1).

There were 73 subjects in the REG group and 47 subjects in the non-REG group. The non-REG group consisted of 39 patients who never visited a hospital that have special clinics for pulmonary rehabilitation and neuromuscular disease and eight patients who had not visited one of these hospitals for more than 3 years since the most recent visit. Patient characteristics are presented in Table 1. The average age at starting mechanical ventilatory support was 20.77±4.75, and 93.3% (112/120) of the patients were applied with NIV from initial ventilatory support. When the two groups were compared, the average age at initial ventilatory support in the non-REG group was 2.15 years older than that of the REG group. The non-REG group showed significant deterioration of FVC, PCF, and MIP compared to the REG group. In ABGA, $PaCO_2$ (REG group 40.55±6.02 vs. non-REG group 48.34±15.05, p=0.003) and bicarbonate (REG group 25.30±3.36 vs. non-REG group 28.92±6.02, p=0.001) were significantly high in the non-REG group than in the REG group, while O_2 saturation, arterial partial pressure of oxygen, and pH showed no significant differences.

A comparison of the nocturnal ventilatory status of subjects

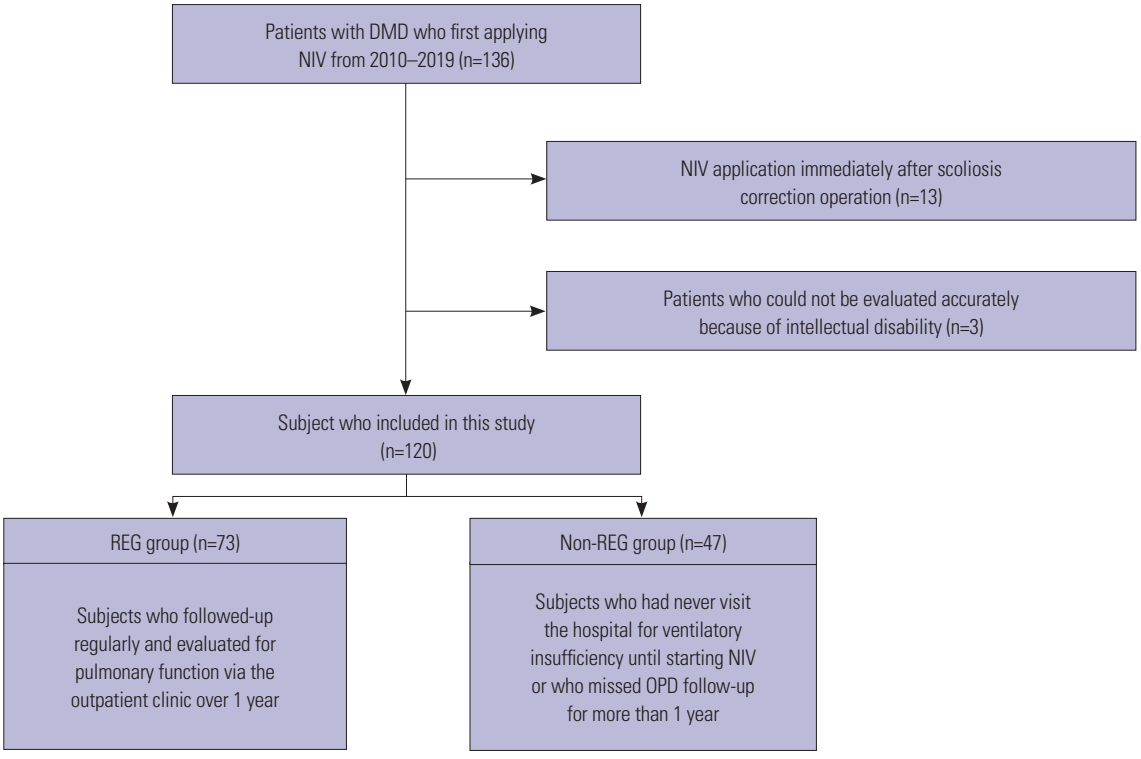

Fig. 1. Flow diagram of subject grouping. DMD, Duchenne muscular dystrophy; NIV, non-invasive ventilation; REG, regular-follow-up; OPD, outpatient department.

https://doi.org/10.3349/ymj.2022.63.6.578

Table 1. Basic Characteristics of Study Population at the Time of Ventilatory Support

Parameters	Total (n=120)	REG group (n=73)	Non-REG group (n=47)	*p* value
Age at mechanical ventilation (years)	20.77±4.75	19.90±4.02	22.05±5.46	0.024
Height (cm)	159.54±9.06	159.78±9.61	159.19±8.22	0.730
Weight (kg)	45.81±15.63	45.46±15.80	46.37±15.51	0.757
BMI (kg/m^2)	17.82±5.36	17.62±5.34	18.13±5.45	0.613
Scoliosis†	80 (66.7)	51 (69.9)	29 (61.7)	0.428
Apply NIV from initial ventilatory support	112 (93.3)	72 (98.6)	40 (85.1)	0.004
Pulmonary function				
FVC (%)‡	19.63±10.42	21.69±9.10	16.61±11.53	0.009
PCF (L/min)	153.19±71.24	167.97±63.44	130.0±77.16	0.005
MIP (%)‡	19.97±16.86	22.58±18.02	15.49±13.74	0.034
MEP (%)‡	14.58±9.70	15.29±8.82	13.36±11.06	0.319
ABGA*	(n=112)	(n=72)	(n=40)	
O_2 saturation (%)	97.16±3.47	97.57±2.78	96.46±4.38	0.151
pO_2	106.39±32.40	107.55±31.32	104.42±34.47	0.630
pH	7.39±0.04	7.40±0.03	7.39±0.05	0.142
$PaCO_2$ (mm Hg)	43.43±10.93	40.55±6.02	48.34±15.05	0.003
HCO_3^-	26.64±4.83	25.30±3.36	28.92±6.02	0.001

BMI, body mass index; NIV, non-invasive ventilation; pO_2, arterial partial pressure of oxygen; $PaCO_2$, arterial partial pressure of carbon dioxide; FVC, forced vital capacity; PCF, peak cough flow; MIP, maximal inspiratory pressure; MEP, maximal expiratory pressure; REG, regular-follow-up; ABGA, arterial blood gas analysis.
Data are presented as mean±standard deviation or n (%).
*Excluded emergency intubation; †Cobb's angle over 20 degrees or had already undergone scoliosis correction operation; ‡These values were calculated to the percentage of normal predictive values.

Table 2. Comparison of Overnight Monitoring of Ventilatory Status Before the Application of Non-invasive Ventilation (Without Considering Severe Cases)

Overnight monitoring	REG group (n=70)	Non-REG group (n=35)	*p* value
Mean O_2 saturation (%)	96.87±1.58	94.50±4.48	0.004
Maximum $TcCO_2$ (mm Hg)	52.49±5.13	57.81±10.16	0.006
Mean $TcCO_2$ (mm Hg)	45.50±4.39	50.22±8.80	0.005

$TcCO_2$, transcutaneous partial pressure of carbon dioxide; REG: regular-follow-up.

in the REG groups and non-REG groups without including severe cases revealed that the REG group exhibited average O_2 saturation of 96.87±1.58%, maximum $TcCO_2$ of 52.49±5.13 mm Hg, and average $TcCO_2$ of 45.50±4.39 mm Hg, whereas the non-REG group exhibited average O_2 saturation of 94.50±4.48%, maximal $TcCO_2$ of 57.81±10.16 mm Hg, and average $TcCO_2$ of 50.22±8.80 mm Hg, according to the data obtained immediately before initial ventilatory support. Additionally, the non-REG group showed significantly higher average and maximum $TcCO_2$ values compared to the REG group (Table 2).

Table 3 shows the hypoventilatory symptoms that the patients had when they initiated ventilatory support. In the REG group, 55/73 (75.3%) were asymptomatic, while 10/47 (21.3%) were asymptomatic in the non-REG group (p<0.001). A total of 27 hypoventilatory symptoms were observed in 18/73 patients (24.7%) in the REG group, and 108 hypoventilatory symptoms were observed in 37/47 patients (78.7%) in the non-REG group. In the REG group, headaches were the most common symptom. In the non-REG group, breathing difficulty and fatigue/daytime somnolence were the two most common hypoventilatory symptoms.

Table 3. Hypoventilatory Symptoms of Initial Ventilatory Support

	REG group (n=73)	Non-REG group (n=47)	*p* value
No symptoms	55 (75.3)	10 (21.3)	<0.001
Presence of hypoventilatory symptoms	18 (24.7)	37 (78.7)	
Total number of initial hypoventilatory symptoms*	27	108	
Category			
Presence of breathing difficulty (discomfort in breathing, dyspnea, orthopnea, cyanosis, decreased O_2 saturation, etc.)	4	24	
Difficulties with sputum expectoration or recurrent chest infections	0	15	
Morning headaches	9	15	
Fatigue/daytime somnolence	6	22	
Poor sleep quality (insomnia, nightmares, wakes up several times a night, night sweating, etc.)	5	15	
Anxiety	2	4	
Chest discomfort	1	2	
General weakness or poor oral intake	0	11	

REG, regular-follow-up.
Data are presented as n (%) or n.
*Symptoms were allowed to overlap.

At the time of initial ventilatory support, the non-REG group was more often in emergency condition. In the REG group,

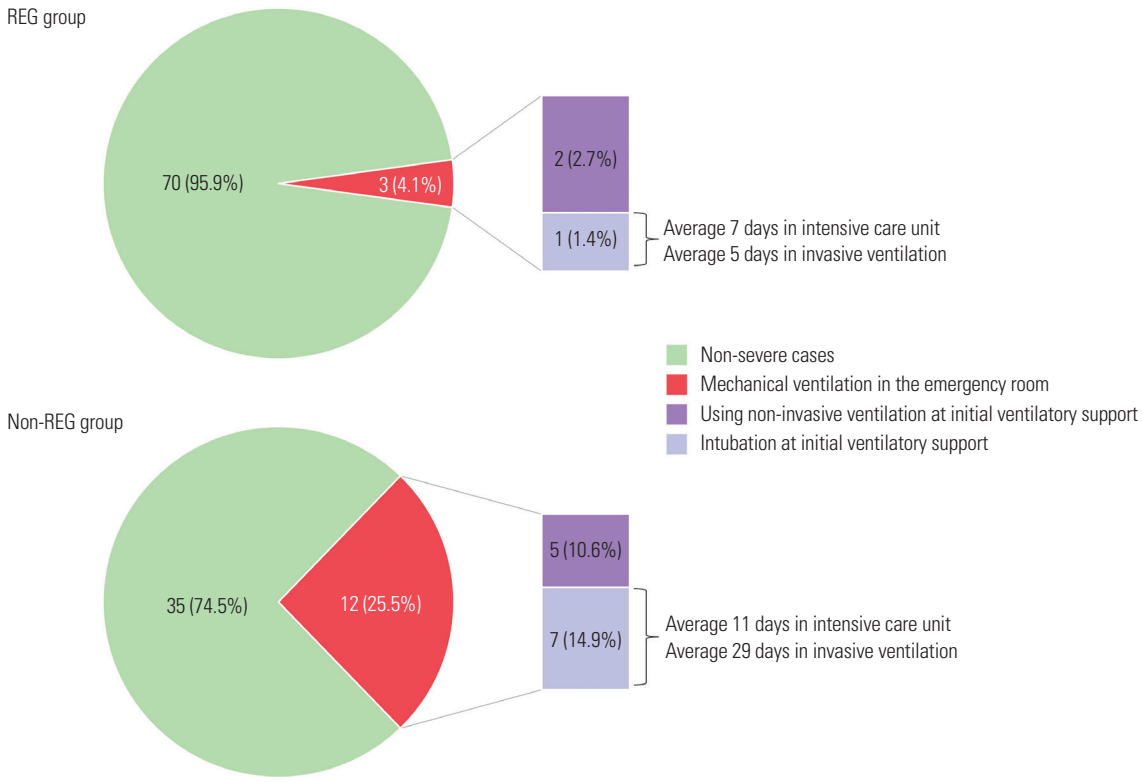

Fig. 2. Initial admission status of subjects at the initiation of mechanical ventilation. REG, regular-follow-up.

3 (4.1%) subjects required emergency initiation of ventilation while 12 (25.5%) subjects received mechanical ventilation in the ER in the non-REG group (p=0.001). Only 1 (1.4%) in the REG group required intubation and intensive care unit (ICU) care, and 7 (14.9%) were intubated at initial ventilatory support and needed ICU care in the non-REG group (p=0.004). The severe patient in REG group stayed in the ICU for 7 days, and maintained invasive ventilation for 5 days. However, severe patients in non-REG group stayed in the ICU for 11 days (7 to 18 days) on average, and used invasive ventilation for 29 days (6 to 91 days) (Fig. 2).

DISCUSSION

Among individuals who had their pulmonary function and ventilatory status checked regularly, those without REG were more prone to emergent situations due to ventilatory insufficiency. This indicates that regular pulmonary monitoring before NIV application is important in patients with DMD who do not require the use of ventilators yet.

Mechanical ventilatory support is inevitable, as ventilatory insufficiency eventually occurs in DMD. However, deciding when to initiate ventilatory support is like an art. Appropriate timing is important since applying the NIV too early wastes medical resources and increases discomfort for patients, whereas late initiation places the patients at risk. There have been several studies regarding the level of hypercapnia that determines whether to initiate ventilatory support. For example, Ward, et al.[7] suggested peak $TcCO_2$ >6.5 kPA (48.8 mm Hg) as nocturnal hypoventilation, as it is easy to define and predictive of worsening nocturnal hypoventilation. Our study emphasized that continuous and regular observation is required to apply those criteria accurately in clinical fields, since patients with DMD tend to gradually deteriorate with aging.

In this study, the REG group received adequate ventilatory support at proper timing through annual follow-up observation, while the non-REG group did not. Most patients in the REG group had no or only one mild symptom; however, a significant number of patients in the non-REG group showed multiple symptoms that were relatively severe. This can also be inferred by checking $PaCO_2$ on ABGA and $TcCO_2$. Patients with DMD develops nocturnal hypercapnia first, which is followed by daytime hypercapnia as the disease progresses.[7] For this reason, measuring nocturnal hypercapnia is a major criterion for determining ventilatory assistance.[7,18] In our results, $PaCO_2$ of ABGA was measured in the awake state in the afternoon, while $TcCO_2$ was measured during sleep. $PaCO_2$ was out of the normal range with an average of 48.34 mm Hg only in the non-REG group, whereas the maximal $TcCO_2$ value was high in both REG and non-REG groups. In other words, the REG group began with ventilatory support at early stage of hypoventilation where hypercapnia only occurred at night, while the non-REG group began ventilatory support after nocturnal and daytime

https://doi.org/10.3349/ymj.2022.63.6.578

hypercapnia.

Our results demonstrate that the application of ventilator support in the non-REG group has been significantly delayed, by at least 2 years on average, compared to that of the REG group.

This delay of the ventilatory support period made the patients in the non-REG group more prone to emergency situations. Compared to the REG group, the non-REG group started mechanical ventilation in the ER six times more, and experienced invasive ventilation 10 times more. Subjects in the non-REG group missed their hypoventilatory symptoms for a long time which resulted in severe events such as respiratory arrest, whereas the REG-group visited the ER due to acute events that had occurred on the same day. In detail, only one patient from the REG group required intubation following cardiopulmonary resuscitation due to an (aspiration pneumonia from) unforeseen choking event. This demonstrates a clear difference from the non-REG group, as severe cases in the non-REG group showed gradual progression due to the lack of appropriate care, which subsequently led to respiratory arrest with mental change or severe desaturation events (Supplementary Table 1, only online). This difference resulted as severe cases in the non-REG group might not have been able to take appropriate action, since they did not know that their symptoms were due to the lack of ventilation. Another interesting point is that severe patients in the non-REG group tended to stay in the ICU and were more likely to require invasive ventilation for a longer period of time. This suggests the possibility that patients who have been previously managed will be able to recover easily from serious situations.

In addition, the period of exposure to hypoventilation with hypercapnia may adversely affect patients with DMD. Uncorrected hypercapnia caused by the weakness of respiratory muscles further exacerbates respiratory muscle weakness. In animal experiments, hypercapnic conditions were shown to change the contractile properties of the diaphragm and the activity of ATPase.[19] In human studies, hypercapnia has been demonstrated to increase the workload of respiratory muscles in healthy adults as well as in patients with chronic obstructive pulmonary disease.[20,21] In other words, it can increase the workload and cause fatigue in inspiratory muscles.

This study had some limitations. First, even after the exclusion of severe cases, subjects in the non-REG group showed significant deterioration in pulmonary function. However, this is because non-REG subjects visited the hospital to receive NIV about 2 years later on average compared to the REG group. Therefore, it is understandable that the pulmonary function was worse in the older group. The other limitation is that the effect of management on weakened cough may have been ignored. Subjects in the REG group received comprehensive pulmonary rehabilitation, including assistive cough method, which might affect the incidence of pneumonia. Various additional disease management techniques, such as steroid use, nutritional support, and physical therapy, may have been better fulfilled in subjects in the REG group, which could have affected the time at which patients need ventilatory support. However, it is clear that patients with DMD cannot avoid ventilatory support on some days, even with all of these treatments. The present study focused on the effects of regular evaluation of pulmonary function and ventilatory status to evaluate the appropriate timing of ventilatory support and patient safety. Therefore, the effect of additional therapy did not undermine the importance of our results. Lastly, and perhaps most importantly, this study did not investigate why the non-REG group failed to receive REG in hospitals that have special clinics for pulmonary rehabilitation and neuromuscular disease. Further research is needed to establish strategies to increase the rate of regular ventilatory follow-up observation.

In conclusion, regular evaluation of pulmonary function and ventilatory status before the onset of ventilatory insufficiency is crucial in patients with DMD to reduce the risk of emergencies due to ventilatory insufficiency. In addition, appropriate ventilatory support can potentially reduce the deterioration of pulmonary function due to hypercapnia.

ACKNOWLEDGEMENTS

This work was supported by the Rehabilitation Institute of Neuromuscular Disease, Yonsei University College of Medicine.

AUTHOR CONTRIBUTIONS

Conceptualization: Seong-Woong Kang. Data curation: Han Eol Cho and Jang Woo Lee. Formal analysis: Han Eol Cho and Jang Woo Lee. Funding acquisition: Seong-Woong Kang. Investigation: Han Eol Cho and Jang Woo Lee. Methodology: all authors. Project administration: all authors. Resources: Won Ah Choi and Seong-Woong Kang. Software: Han Eol Cho and Jang Woo Lee. Supervision: Won Ah Choi and Seong-Woong Kang. Validation: Han Eol Cho and Jang Woo Lee. Visualization: Han Eol Cho. Writing—original draft: Han Eol Cho and Jang Woo Lee. Writing—review & editing: all authors. Approval of final manuscript: all authors.

ORCID iDs

Han Eol Cho https://orcid.org/0000-0001-5625-3013
Jang Woo Lee https://orcid.org/0000-0002-2634-0375
Won Ah Choi https://orcid.org/0000-0003-0403-8869
Seong-Woong Kang https://orcid.org/0000-0002-7279-3893

REFERENCES

1. Dooley J, Gordon KE, Dodds L, MacSween J. Duchenne muscular dystrophy: a 30-year population-based incidence study. Clin Pediatr (Phila) 2010;49:177-9.
2. Ishikawa Y, Miura T, Ishikawa Y, Aoyagi T, Ogata H, Hamada S, et al. Duchenne muscular dystrophy: survival by cardio-respiratory interventions. Neuromuscul Disord 2011;21:47-51.
3. Eagle M, Baudouin SV, Chandler C, Giddings DR, Bullock R, Bushby K. Survival in Duchenne muscular dystrophy: improvements in

life expectancy since 1967 and the impact of home nocturnal ventilation. Neuromuscul Disord 2002;12:926-9.
4. Bourke SC. Respiratory involvement in neuromuscular disease. Clin Med (Lond) 2014;14:72-5.
5. Bushby K, Finkel R, Birnkrant DJ, Case LE, Clemens PR, Cripe L, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: implementation of multidisciplinary care. Lancet Neurol 2010;9:177-89.
6. Consensus Development Conference Committee. Clinical indications for noninvasive positive pressure ventilation in chronic respiratory failure due to restrictive lung disease, COPD, and nocturnal hypoventilation--a consensus conference report. Chest 1999; 116:521-34.
7. Ward S, Chatwin M, Heather S, Simonds AK. Randomised controlled trial of non-invasive ventilation (NIV) for nocturnal hypoventilation in neuromuscular and chest wall disease patients with daytime normocapnia. Thorax 2005;60:1019-24.
8. Böing S, Randerath WJ. Chronic hypoventilation syndromes and sleep-related hypoventilation. J Thorac Dis 2015;7:1273-85.
9. Smith PE, Edwards RH, Calverley PM. Ventilation and breathing pattern during sleep in Duchenne muscular dystrophy. Chest 1989; 96:1346-51.
10. Han JJ, Kilmer DD. Myopathy. In: Frontera WR, DeLisa JA, Gans BM, Walsh NE, Robinson LR, editors. DeLisa's physical medicine and rehabilitation: principles and practice. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2010. p.757-80.
11. Bach JR. Guide to the evaluation and management of neuromuscular disease. Philadelphia: Hanley & Belfus; 1999.
12. Barsdorf AI, Sproule DM, Kaufmann P. Scoliosis surgery in children with neuromuscular disease: findings from the US National Inpatient Sample, 1997 to 2003. Arch Neurol 2010;67:231-5.
13. Khirani S, Bersanini C, Aubertin G, Bachy M, Vialle R, Fauroux B. Non-invasive positive pressure ventilation to facilitate the postoperative respiratory outcome of spine surgery in neuromuscular children. Eur Spine J 2014;23 Suppl 4:S406-11.
14. Racca F, Mongini T, Wolfler A, Vianello A, Cutrera R, Del Sorbo L, et al. Recommendations for anesthesia and perioperative management of patients with neuromuscular disorders. Minerva Anestesiol 2013;79:419-33.
15. Morris JF. Spirometry in the evaluation of pulmonary function. West J Med 1976;125:110-8.
16. da Costa JL. Pulmonary function studies in healthy Chinese adults in Singapore. Am Rev Respir Dis 1971;104:128-31.
17. Wilson SH, Cooke NT, Edwards RH, Spiro SG. Predicted normal values for maximal respiratory pressures in caucasian adults and children. Thorax 1984;39:535-8.
18. Kang SW. Pulmonary rehabilitation in patients with neuromuscular disease. Yonsei Med J 2006;47:307-14.
19. Shiota S, Okada T, Naitoh H, Ochi R, Fukuchi Y. Hypoxia and hypercapnia affect contractile and histological properties of rat diaphragm and hind limb muscles. Pathophysiology 2004;11:23-30.
20. Bégin P, Grassino A. Inspiratory muscle dysfunction and chronic hypercapnia in chronic obstructive pulmonary disease. Am Rev Respir Dis 1991;143(5 Pt 1):905-12.
21. Takasaki Y, Orr D, Popkin J, Xie AL, Bradley TD. Effect of hypercapnia and hypoxia on respiratory muscle activation in humans. J Appl Physiol (1985) 1989;67:1776-84.

https://doi.org/10.3349/ymj.2022.63.6.578