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RESEARCH ARTICLE

Clinical Characteristics of Patients Initiated on Long-Term Noninvasive Ventilation Support: A Single-Center Experience

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ABSTRACT

Objective: Long-term noninvasive ventilation (NIV) support is increasingly being used by pediatricians for children with complex medical diseases. However, data on NIV support among children in Turkiye are limited.

Methods: This study included children who received long-term NIV support between July 2022 and July 2024 at a single center. Demographic and clinical characteristics and short-term clinical outcomes were retrospectively evaluated.

Results: A total of 30 patients were included. The median age at NIV initiation was 39.5 months (range: 9–108 months), and the most common underlying etiology was cardiovascular diseases (n = 9, 30%). Twenty-six patients were discharged with long-term NIV support, with a median discharge time of 5.5 days (range: 3–13 days) after NIV initiation. Of the 26 patients discharged with NIV support, four died during follow-up. Three patients, all of whom were from the cardiovascular group, no longer required respiratory support.

Conclusions: NIV can be used effectively for a wide variety of diseases in children. Understanding the current status of NIV support in our clinical setting may help us design a protocol to improve future outcomes.

Keywords: Noninvasive ventilation, pediatrics, cardiovascular diseases

INTRODUCTION

Noninvasive ventilation (NIV) delivers respiratory support via an interface that is applied noninvasively instead of an intubation tube or tracheostomy cannula(1). Noninvasive ventilation support is increasingly recognized by clinicians and used more frequently in pediatric practice because the number of children with special needs and/or chronic respiratory failure is increasing with advanced medical support (1). Noninvasive ventilation (NIV) can limit or delay the need for intubation for acute respiratory failure. Studies have also suggested that NIV aids in weaning from invasive ventilation, reduces intensive care unit (ICU) stay, decreases tracheostomy rates, decreases healthcare costs, and improves the quality of life for patients and caregivers(2-4).

Optimal ventilation requires a good balance between central respiratory drive, respiratory muscle work, and respiratory load. Any condition that disrupts one of these mechanisms, including upper and lower airway obstructions, chronic lung diseases, respiratory muscle diseases, and disorders affecting the control of central respiratory drive, are potential indications for NIV(1, 2, 4). The main methods for NIV support are continuous positive airway pressure (CPAP) and biphasic airway pressure (BPAP). While CPAP simply ensures continuous positive pressure and is used for patients with isolated upper/lower airway obstruction, BPAP delivers an additional positive pressure during inspiration. CPAP increases functional residual capacity and improves oxygenation and gas exchange; however, it does not support spontaneous inspiration. BPAP increases tidal volume and functional residual capacity (FRC), thereby

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improving gas exchange and ventilation more effectively. Biphasic airway pressure is the primary option for patients with central respiratory drive dysfunction and chronic hypercarbic respiratory failure (1, 2, 4). These patients have an increased respiratory load that causes hypoxia and hypoventilation leading to cor pulmonale, growth failure, and neurocognitive sequelae if not treated timely and efficiently(1).

The use of NIV outside intensive care units has dramatically improved over the last two decades. Noninvasive ventilation increases survival and slow respiratory functional decline without decreasing quality of life in patients with chronic respiratory failure. Although only a few randomized controlled studies have been conducted in this area, clinical practice has led to general acceptance of treating acute and chronic respiratory failure with NIV(5-8). Because NIV is rarely initiated outside intensive care units for chronic diseases in our country, our primary aim was to assess the clinical characteristics and short-term clinical outcomes of patients who were initiated on NIV during hospitalization and discharged home with long-term NIV support. Our secondary aim was to assess the factors affecting the success of NIV and to evaluate the short-term clinical outcomes of patients.

MATERIALS AND METHODS

The study included 30 patients who were started on long-term NIV support between July 2022 and July 2024. Long-term NIV was defined as needing NIV support for at least 6 hours per day for at least 3 weeks outside of an acute care setting(9). Patients who were already using NIV before hospital admission were not included in the study. We excluded critically ill patients with acute respiratory failure were not included. In addition, patients were excluded from the study if the families refused the initiation of noninvasive ventilation, did not cooperate, or if the patient was not compliant with the noninvasive ventilation.

Because pediatric polysomnography is not available in our center, the decision to initiate noninvasive ventilation is heavily based on blood gas analysis and clinical findings. Without polysomnography, chronic alveolar hypoventilation, which is often indicated by elevated $PaCO_2$ levels and clinical findings, plays a critical role in guiding treatment. The clinical signs of alveolar hypoventilation include recurrent respiratory infections, cor pulmonale, insomnia, frequent arousals, headaches, shortness of breath, fatigue, decreased intellectual performance, and growth failure(9-11).

During the first initiation of NIV, the patient is monitored and a control blood gas is administered 1 hour after initiation of NIV. If nighttime NIV is not sufficient to provide normocapnia, daytime NIV may be provided. The inspiratory positive airway pressure (IPAP) was increased according to the venous blood gas CO_2 levels. The expiratory positive airway pressure (EPAP) was set at a minimum of 4 cmH_2O and increased if needed according to the oxygen saturation of the patients. The inspiratory time and respiratory rate per minute were age-appropriate(12). All patients were closely followed up with pulse oximetry during the initiation of NIV. The awake morning control blood gas was obtained after the initiation of NIV.

Demographic and clinical characteristics of the patients, day of starting NIV at hospitalization, ventilator settings, mask type, day of discharge after NIV initiation, and short-term clinical outcomes were recorded. Ethical approval was obtained from the Ethics Committee of Basaksehir Cam and Sakura City Hospital (approval number E-96317027-514.10-224467097. Informed consent was obtained from the parents.

Statistical Analysis

The statistical analysis was performed using SPSS for Windows version 20.0. Normality was assessed using normality plots and the Kolmogorov-Smirnov test. Continuous variables that were normally distributed were presented as means and standard deviations, whereas data with asymmetrical distribution are presented as medians and 25-75 th percentiles. Categorical variables are presented as proportions. The statistical significance level was set at a p-value of <0.05.

RESULTS

The study included 30 patients with chronic respiratory distress who received long-term noninvasive ventilation support between July 2022 and July 2024. In 28 of the patients, NIV support was initiated as an inpatient, whereas 2 patients were initiated NIV at the outpatient clinic because the NIV equipment could not be obtained during hospitalization. The median age of patients at the time of NIV initiation was 39.5 (9-108) months; the youngest patient was 2 months old. Eleven patients (36.7%) were aged 1 year. Table 1 presents the baseline demographic and clinical characteristics of the patients.

The most common underlying etiology for NIV support was cardiovascular disease. The median age of the patients at the time of NIV initiation was 9 months (4-10 months) for cardiovascular diseases and 96 months (31-117 months) for neurological diseases. Table 2 presents the main underlying etiology of the NIV requirement.

Table 3 presents the descriptive features of NIV support. Approximately half of the patients (n=16) required NIV with oxygen support. The most common reason for initiating

Table 1. Clinical and demographic characteristics of the patients (n=30)

Age (months)	
Median (25-75 th percentile)	53 (17-120)
Age at NIV initiation (months)	
Median (25-75 th percentile)	39.5 (9-108)
Sex, n(%)	
Female	11 (36.7)
Male	19 (63.3)
Baseline respiratory support, n(%)	
None	27 (90)
Oxygen support	3 (10)
Baseline venous CO_2 levels (mmHg)	
Median, (25-75 th p)	53 (43-60)

NIV: Noninvasive ventilation support, CO_2: carbondioxide

Table 2. The underlying etiology of the NIV requirement (n=30)

The main underlying etiology of NIV requirements	n (%)	Age at initiation of NIV, months (median, 25-75 th p)
Cardiovascular diseases	9 (30)	9 (4-10)
Postoperative diaphragmatic paralysis	3	
Pulmonary hypertension	2	
Tracheobronchial compression	2	
Postoperative prolonged ventilatory support	2	
Neurological	8 (26.7)	96 (31-117)
Epilepsy	7	
Spina bifida	1	
Chronic lung disease	8 (26.7)	79.50 (17-110.50)
Bronchiolitis obliterans	5	
Cyhlothorax	1	
Bronchopulmonary dysplasia	1	
Primary ciliary dyskinesia	1	
Neuromuscular	2 (6.7)	64.50 (19-110)
Spinal muscular atrophy-1	1	
Myopathy	1	
Chest deformity	2 (6.7)	71 (34-108)
Rhizomelyic chondrodysplasia	1	
I-cell disease	1	
Anatomic upper airway obstruction (microretrognathia)	1 (3.3)	6

NIV: Noninvasive ventilation support

Table 3. Descriptive features of NIV support (n=30)

Respiratory support, n(%)	
NIV only	14 (46.7)
NIV and oxygen supplementation	16 (53.3)
Major reason for NIV initiation, n(%)	
Persistent respiratory distress	17 (56.7)
CO_2 retention	9 (30)
Atelectasis	3 (10)
Witnessed apnea	1 (3.3)
Day of hospitalization at the first initiation of NIV	
Median (25-75 th p)	28 (13.50-48)
Mode of NIV, n(%)	
BPAP ST	28 (93.3)
BPAP S	1 (3.3)
CPAP	1 (3.3)
The type of interface mask, n(%)	
Nasal	22 (73.3)
Oronasal	8 (26.7)
EPAP, cmH_2O	
Median (25-75 th percentile)	5 (4-6.5)
IPAP, cmH_2O	
Median (25-75 th percentile)	9 (8-12)
Back-up rate/minute	25 (20-25)

BPAP: Biphasic airway pressure, CPAP: continuous positive airway pressure, S: Spontaneous, ST: Spontaneous/timed, NIV: noninvasive ventilation, EPAP: expiratory positive airway pressure, IPAP: inspiratory positive airway pressure

NIV support was persistent respiratory distress during hospitalization (56.7%, n=17). The median number of days of NIV initiation was 28th day of hospitalization (13.50-48 days). The most commonly selected mode for NIV support was the BPAP ST mode, and the most commonly selected interface was the nasal mask (73.3%).

Table 4. Short-term clinical outcomes of the patients (n=30)

NIV requirement time at discharge (hours)	
Mean±SD	11.6 ±3.2
Current NIV requirement time (hours)	
Median (25-75 th percentile)	5.50 (0-8)
Venous CO_2 levels after NIV initiation (mmHg)	
Median (25-75 th percentile)	45 (40-50)
Median follow-up period after NIV initiation	
Median (25-75 th percentile)	204 (105-274)
Current status of the patients (n=26)	
Reduced need for NIV support	9 (30)
Increased need for NIV support	1 (3.3)
No need for respiratory support	3 (10)
Same as discharge	2 (6.7)
Can not tolerate NIV***	5 (16.7)
Lost to follow-up	2 (6.7)
Exitus	4 (13.3)

NIV: Noninvasive ventilation support, CO_2: carbondioxide
* Reduction in the required pressure or duration of BPAP
**Increased pressure requirement and prolonged BPAP support duration
***Can not tolerate NIV due to adherence problems

The median number of days of discharge after NIV initiation was 5.5 days (3-13 days). Twenty-six patients could be discharged with long-term NIV treatment. Four patients required invasive ventilation during follow-up and could not be discharged with NIV. One patient with rhizomelic chondrodysplasia was transferred to the ICU during follow-up, and two patients with congenital heart disease required invasive ventilation during hospitalization. Another patient with bronchiolitis obliterans initially tolerated NIV, but remained clinically unstable and ultimately required invasive ventilation, and died after ICU transfer. We did not observe any major side effects in any of the

26 patients. Of the 26 patients who were discharged with NIV support, four died during follow-up. Three of the 26 patients no longer needed any respiratory support, and all of these patients were in the cardiovascular (post-cardiac surgery) group. In nine of the 26 patients, the need for NIV support (pressures and/or time for NIV) had decreased. Twelve patients were still on NIV during the follow-up period. The final median EPAP value was 4.5 (4-5.75) cmH_2O while the median IPAP value was 9 (8-11) cmH_2O. There was no significant difference between the final and initial NIMV parameters($p>0.05$ for both). Table 4 presents the short-term clinical outcomes of the patients.

DISCUSSION

This study analyzed the demographic and clinical characteristics and short-term clinical outcomes of patients who were initiated on long-term NIV support at a single center. Although the use of NIV support in pediatric patients is increasing worldwide, it can still be initiated in only few centers in our country, especially outside the intensive care units. Increasing our knowledge in this area will result in a better understanding of NIV, as there is no standard protocol regarding long-term NIV initiation and follow-up programs for pediatric patients in our country.

NIV provides long-term ventilation support for children with a broad range of complex medical conditions, and NIV is a more acceptable alternative to invasive mechanical ventilation with tracheostomy for most of the families(13). The most common underlying etiology for the requirement of NIV was cardiovascular diseases, with a prevalence of 30 %, whereas chronic lung diseases (26.7%) and neurological diseases (26.7%) followed in our study. A systematic review including 289 studies reported that NIV was used for 73 medical conditions, with obstructive sleep apnea (OSA) (33%) and neuromuscular diseases (22%) being the most common causes(13). There are some possible explanations for the difference in the underlying diseases in our study based on the literature. First, our center has one of the largest cardiovascular and cardiac disease centers in Turkey, to which many patients are referred. In addition, we do not have a pediatric sleep center; therefore, we cannot perform polysomnography to diagnose OSA.

The median age at the time of NIV initiation was 39.5 (9-108) months, and 36.7% of the patients were aged 12 months. The age at the time of NIV initiation varies widely between previous studies. Castro-Cadesal et al.. reported the mean age at initiation of NIV as 8±3 years(13). Ikeda et al.. reported that patient age at NIV administration had a bimodal distribution, with a peak under 6 years old and a peak between 9 and 19 years in their study. They reported that neuromuscular disorders, such as severe respiratory distress associated with SMA type 1 or congenital abnormalities, may cause a peak incidence at age 6 years, whereas neuromuscular diseases like DMD, which complicate chronic respiratory failure during adolescence, cause a second peak between 9 and 19 years of age (14). Chatwin et al. reported a median age at initiation of NIV of 10 (3-15) years, and 56 % of the patients had neuromuscular disease in their retrospective cohort study including 496 children. In their study, thirteen percent (n=59) were younger than 1 year old(12). In our study, the median age at NIV initiation was younger than in previous studies. The most common etiology and youngest age group were cardiovascular diseases in our study, with a median age at NIV initiation of 9 months, which may explain the younger median age at NIV initiation in our study. Neurological diseases, predominantly epilepsy, constituted the oldest age group for NIV initiation in our study. Respiratory failure mostly occurs due to damage to the pulmonary parenchyma from aspiration or repetitive infections in this group, which may result in a greater need for ventilation support as the patients age. In addition, previous studies have reported that the median age of patients requiring invasive ventilation is younger than that of patients receiving NIV, as NIV is technically more difficult to adapt for small children(15). As our study is new, we may also suggest that NIV success may be increased by improving technical strategies, including interfaces, which have made a larger proportion of small children suitable for NIV over the years .

Nasal masks were the most commonly preferred interface type in our study (73.3%. Similar to our study, most previous studies have reported that nasal-type interfaces are often selected over oronasal and full-face interfaces(5, 13, 14). Nasal interfaces provide more comfortable respiratory support, a wider range of vision, a lower risk of vomiting aspiration, and greater ability to speak than oronasal and full-face interfaces. We did not use full-face interfaces in our study, as they are more difficult to perform in patients who were not sedated, as most of our patients' NIV support was initiated outside the intensive care unit. More than half of the patients (53.3%) required supplemental oxygen therapy in addition to NIV therapy. Amin et al. reported that 21.7 % of the patients required supplemental oxygen in addition to NIV support in their study, including 313 patients who required NIV during a 20-year period in Canada. They also reported that the most common indication for NIV support was neuromuscular disease(16). Ikeda et al. reported that 60 % of the patients with overall NIV required supplemental oxygen, whereas this rate was 37.7 % for neuromuscular patients on NIV, and there was a significant difference in oxygen requirement between neuromuscular and non-neuromuscular diseases(14). In our study, there were only 2 patients with neuromuscular diseases, and cardiac, neurological, and chronic lung diseases were the most common causes of NIV support with severe respiratory failure. NIV support may be initiated before hypoxia presents due to other clinical findings regarding alveolar hypoventilation in neuromuscular diseases. The most common mode of NIV was BPAP in our study. Similar to previous studies, CPAP is mostly preferred for upper airway obstruction, obesity, and obstructive sleep apnea, whereas BPAP therapy is preferred for patients with neuromuscular and neurological diseases, complex multiple medical conditions, and chronic lung diseases in our study(13). BPAP with a backup rate (ST mode) is the most commonly recommended method for neuromuscular, neurological, and chronic lung diseases (4).

In our study, 26 of 30 patients were discharged home with NIV, and the median discharge day after NIV initiation was 5.5 days.

The median day of hospitalization at the time of starting NIV was 28 days. After initiation of NIV, patients could be discharged with a median time of 5.5 days, which is a relatively short period for children with complex diseases. These results demonstrate the efficacy of NIV for the discharge of children with chronic, complex medical conditions. Four patients could not adapt to NIV, and three of these four patients were aged less than 12 months. It is much more difficult to find an appropriate interface for children and infants. Although there is no standard clinical validation study for limitation, a minimum weight of 5 kg is recommended for NIV treatment from some authors(4). Regarding the current status of the patients who could be discharged on long-term NIV, four of them died (13.3%), 10% did not need further ventilation support, and 16.7% had treatment failure during follow-up due to adherence problems in our study. A retrospective study including a 20-year period in Canada reported a mortality rate of 11% among patients on long-term NIV, whereas 9% of the patients no longer needed ventilation and 3% of the patients had treatment failure (16). In our study, treatment failure was relatively common during the short-term follow-up. As the median age of our patients was younger than that of previous studies, treatment failure during follow-up was not surprising. Another finding of our study was that all three patients who did not need longer respiratory support during follow-up were patients who required NIV after cardiovascular surgery. One patient had postoperative diaphragma paralysis, and two of them had tracheobronchial compression due to cardiovascular abnormalities. Similar to previous case reports, NIV is a successful option to avoid intubation after complications of cardiac surgery including diaphragma paralysis(17, 18). Even though the number of patients in our study was small, these results suggest that NIV may be very beneficial after cardiovascular surgery to bypass the acute period. A retrospective study including 200 patients with NIV reported that the NIV success rate was 85%, with a median duration of NIV of 3 days and mortality rate of 3.9 %(19). Our mortality rate is slightly higher than that of previous studies; however, as patients are younger and cardiac diseases are predominant in our study, mortality may be higher due to complications of the underlying diseases.

This study has some limitations. First, as our study is a single-center study, the sample size is relatively small. Second, polysomnography could not be performed for the titration of NIV support. Lastly, we could not demonstrate the long-term effects of NIV, including hospitalizations and side effects, because the study included a 2-year period.

CONCLUSION

Our study demonstrated the effects of NIV in children with complex medical conditions. Long-term NIV support is increasingly being used worldwide. Patients with cardiovascular diseases, especially during the post-surgery period, may benefit greatly from NIV support by avoiding intubation and intubation-related morbidities. As our patients' median age is younger than that in previous studies, we suggest that NIV support will soon become an increasingly acceptable choice for small children with the improvement of technologies. Although NIV is not appropriate for all children, it is an invaluable tool for the home care of children with chronic respiratory distress. There is a need for further studies to develop a national long-term NIV initiation program and standards of care for children on NIV.

Ethics Committee Approval: This study was approved by the ethics committee of the Ethics Committee of Basaksehir Cam and Sakura City Hospital (approval number E-96317027-514.10-224467097.

Informed Consent: Written consent was obtained from the participants.

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