Original Article

The Effect of Noninvasive Positive Pressure Ventilation on Pneumonia Hospitalizations in Children With Neurological Disease

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Abstract

The aim of this retrospective single-institution observational study was to identify whether the frequency of hospitalizations for pneumonia would change before and after the initiation of noninvasive positive pressure ventilation in children with neurological conditions. Included patients were 1 to 18 years old with an underlying neurological disease and had been prescribed nocturnal noninvasive positive pressure ventilation. The authors excluded patients with a tracheostomy or those who used noninvasive positive pressure ventilation solely for obstructive sleep apnea. A total of 14 patients were included in the study, among whom there was no significant change in the mean number of pneumonias 2 years before versus after the initiation of noninvasive positive pressure ventilation (mean difference = −0.714, standard deviation = 2.4, $P = .312$). These findings suggest that while noninvasive positive pressure ventilation may not reduce absolute pneumonia frequency, it may have the beneficial value of preventing an increase in the frequency of pneumonias over time, especially in children with progressive respiratory compromise.

Keywords

noninvasive ventilation, neurologic disease, respiratory failure, pneumonia, neuromuscular disease

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Noninvasive positive pressure ventilation refers to the administration of air at 2 different pressure settings (ie, inspiration and expiration) through a device with a tightly fitting nasal or oral mask. The use of noninvasive positive pressure ventilation has been shown to decrease work of breathing, dyspnea, and tachypnea[1] in different patient populations.

For children with neurological diseases who frequently develop respiratory failure secondary to their muscle dysfunction, and often die of respiratory complications, the use of noninvasive positive pressure ventilation is an important treatment option. The mechanism of respiratory morbidity in these patients varies depending on the specific underlying disease and can range from peripheral muscle weakness to blunted respiratory drive or progressive scoliosis.[2,3] Each of these conditions can lead to hypoventilation.

In previous studies of adults and children with amyotrophic lateral sclerosis or Duchenne's muscular dystrophy, noninvasive positive pressure ventilation has been established as a means to treat hypoventilation and improve quality of life.[4-6] However, in addition to hypoventilation, children with neurological diseases often have an increased risk of aspiration and/or impaired cough clearance, due to respiratory muscle weakness, lack of central drive, or impaired swallowing. Recurrent pneumonias may eventually lead to chronic lung disease and respiratory failure; pulmonary infections are often the cause of death in these patients. Noninvasive positive pressure ventilation has been used in patients with progressive neuromuscular diseases as a means to decrease pulmonary infections. This is based on the supposition that improved inflation of the lungs by the use of noninvasive positive pressure

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ventilation may prevent areas of atelectasis that would otherwise be prone to infection and chronic inflammation.[1] Noninvasive positive pressure ventilation may also allow patients to rest more effectively at night, thereby giving them more energy to maintain ventilation and cough during the day while awake.[1]

There are only a limited number of studies that have examined the effect of noninvasive positive pressure ventilation on the frequency or severity of respiratory infections in children with neuromuscular diseases, and these have produced conflicting results. Bach and Wang treated 10 patients with spinal muscular atrophy with assisted coughing techniques and intermittent positive pressure. They found that patients had significantly fewer respiratory complications and improved speech and oral feeding following these interventions.[7] Another retrospective study from Portugal of 22 patients with spinal muscular atrophy also noted a decrease in the frequency and severity of respiratory infections after the initiation of noninvasive positive pressure ventilation.[8] On the other hand, a similar and more recent study by Lemoine of 49 children with spinal muscular atrophy type 1 treated with noninvasive positive pressure ventilation plus mechanical cough assist found that these children in fact had more hospitalizations for respiratory insufficiency but longer survival times.[9]

These previous studies examining respiratory infections as an outcome post initiation of noninvasive positive pressure ventilation have all been conducted in children with spinal muscular atrophy. To date, there have not been any studies to examine the rate of pneumonias following the initiation of noninvasive positive pressure ventilation in children with other neurological diseases such as Duchenne's muscular dystrophy or static encephalopathies with significant motor impairment.

The aim of this study was to determine whether the initiation of noninvasive positive pressure ventilation would be associated with a decrease in the number of episodes of severe pneumonia requiring hospitalization in patients with static or progressive neurological diseases.

Methods

Patients and Setting

The authors conducted a retrospective chart review of patients aged 1 to 18 years, who had been followed at any time between January 1, 2000, and January 1, 2015, at the Children's Hospital, London Health Sciences Centre, London, Ontario, Canada, due to an underlying neurological or neuromuscular disease and had been prescribed nocturnal noninvasive positive pressure ventilation for hypoventilation. Hypoventilation was diagnosed based on formal polysomnography or close observation in the pediatric intensive care unit and monitoring of work of breathing, oxygen saturation, transcutaneous carbon dioxide trends, and capillary blood gas values before, during, and after sleep. Home nocturnal noninvasive positive pressure ventilation was prescribed for those patients who demonstrated improvement in sleep parameters on polysomnography or improved work of breathing and estimation of alveolar oxygen and/or carbon dioxide tensions following the application and titration of noninvasive positive pressure ventilation.

The caregivers of all patients prescribed home nocturnal noninvasive positive pressure ventilation were provided education on the goals of therapy, how to safely and effectively use the machine and apply the interface, and methods for troubleshooting alarms by an experienced registered respiratory therapist using a standardized education checklist. Patients initiated on home nocturnal noninvasive positive pressure ventilation were assessed regularly in a multidisciplinary home ventilation clinic approximately every 3 months to ensure adherence to therapy and continued benefit of the treatment. Adherence was assessed at every visit based on patient/caregiver self-report and by analysis of usage data downloaded from each patient's noninvasive positive pressure ventilation machine. Table 1 includes a composite assessment of adherence to noninvasive positive pressure ventilation therapy for each patient. In keeping with accepted practice definitions, adherence was defined as an estimated minimum of 4 hours of noninvasive positive pressure ventilation use for at least 50% of nights.[10]

For inclusion in this study, patients were all less than 18 years of age at the time of noninvasive positive pressure ventilation prescription but may have been observed beyond 18 years of age to allow for 2 years of follow-up post noninvasive positive pressure ventilation. Neurological diagnoses were defined as per the treating pediatric neurologist and identified through review of the patient's hospital and clinic charts. Eligible patients were identified through the clinical records (ie, noninvasive positive pressure ventilation clinic list) of the pediatric respirologists or neurologists at the Children's Hospital of Western Ontario, Canada. If a child died before the end of the study period, the authors reviewed information up until the date of death.

The authors excluded patients who were receiving invasive ventilation through a tracheostomy or were using noninvasive positive pressure ventilation for the treatment of obstructive sleep apnea alone. Figure 1 summarizes our methodology for this study.

Outcomes

The main outcome was the total number of hospitalizations for pneumonia. This was compared in the 2 years prior to the initiation of noninvasive positive pressure ventilation versus in the 2 years after the initiation of noninvasive positive pressure ventilation. The case definition of pneumonia was the presence of clinical symptoms consistent with pneumonia (such as fever, cough, increased or change in secretions) as well as new infiltrates on chest radiograph, identified during a hospital admission.

Patient Characteristics

Data collection included each patient's neurological diagnosis, adherence to noninvasive positive pressure ventilation, the use of ancillary pulmonary treatments, whether each patient had a static or progressive neurologic disease, details of hospital admissions due to pneumonia, any comorbid diagnoses that would typically predispose to pneumonia (eg, asthma, heart disease, aspiration, immune dysfunction), the method of enteral feeding, height, and weight.

Analysis

Due to the nonparametric nature of the data collected, a Wilcoxon signed rank sum test was done to compare the mean number of episodes of pneumonia before and after the initiation of noninvasive positive pressure ventilation. The authors also performed 2 additional Wilcoxon signed rank sum tests to compare the mean frequency of pneumonias before and after noninvasive positive pressure ventilation separately in (1) children with central neurologic diseases and (2) in children with peripheral neurologic diseases.

Table 1. Patient Characteristics.[a]

Study ID	Sex (M/F)	Central vs Peripheral Disease	Age, years	Age at NiPPV Start, years	Static Disease (Y/N)	Compliant With NiPPV (Y/N)	Asthma (Y/N)	Heart Disease (Y/N)	Other Comorbid Conditions	Aspiration Risk? (Y/N)	G Tube (Y/N)	GJ Tube (Y/N)	Chest Physio (Y/N)	Assisted Cough (Y/N)
1	M	Peripheral	20	17	N	Y	–	Y	Y	Y	N	N	Y	N
2	M	Peripheral	20	14	N	Y	–	N	N	Y	N	N	N	Y
3	M	Peripheral	23	18	N	Y	N	Y	Y	N	N	N	Y	Y
4	M	Peripheral	21	14	N	Y	N	N	N	Y	N	N	Y	Y
5	M	Peripheral	17	8	N	Y	Y	N	N	Y	Y	N	Y	Y
6[b]	M	Peripheral	3.5	2.5	N	N	[c]Y	N	N	Y	Y	N	Y	Y
7	F	Central	11	7	Y	Y	N	N	Y	Y	Y	N	N	N
8[d]	F	Central	12	9	N	Y	N	N	Y	Y	Y	N	Y	Y
9	M	Central	8	3	Y	Y	N	N	Y	N	N	N	N	N
10	F	Central	19	7	N	[e]	[e]	N	Y	Y	N	N	N	N
11	F	Peripheral	12	10	N	Y	N	N	Y	Y	N	N	N	N
12	F	Central	3	0.5	N	Y	N	Y	Y	N	Y	N	N	N
13	F	Central	9	5	N	Y	Y	N	Y	Y	Y	Y	[e]	[e]
14	M	Central	12	9.5	Y	Y	N	N	Y	Y	Y	N	Y	Y

Note: F, female; G tube, gastrostomy tube; GJ tube, gastrojejunostomy tube; M, male; N, no; NiPPV, noninvasive positive pressure ventilation; Physio, physiotherapy; Y, yes.
[a]To avoid revealing identifying information for some of the rare diseases, patients have not been identified by disease.
[b]Diagnosis not certain.
[c]It is unclear whether this patient has asthma, but he is on salbutamol as needed.
[d]Patient who has died.
[e]Missing or unknown data.

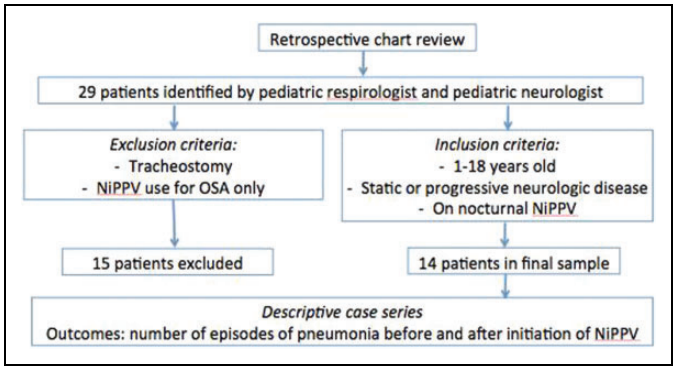

Figure 1. Method of chart review and descriptive case series. NiPPV indicates noninvasive positive pressure ventilation; OSA: obstructive sleep apnea.

Results

A total of 29 patients were identified for possible study inclusion by the pediatric neurologists and respirologists. Fifteen patients were excluded due to the presence of a tracheostomy or use of noninvasive positive pressure ventilation solely for obstructive sleep apnea.

Fourteen patients were included in this study, with 7 patients in each category of peripheral and central nervous system disorders. Table 1 lists the characteristics and treatments received by these patients. The diagnoses of the patients with peripheral nervous system disease included Duchenne's muscular dystrophy, limb girdle muscular dystrophy, Pompe disease, spinal muscular atrophy type 2, and myotonic dystrophy type 1. The diagnoses of those with central nervous system disorders included trisomy 18, Leigh syndrome, Prader-Willi, and cerebral palsy. Table 2 provides a summary of the characteristics of each patient and the raw data for the number of episodes of pneumonia before and after the initiation of noninvasive positive pressure ventilation.

There was no significant change in the mean number of pneumonias 2 years before versus after the initiation of noninvasive positive pressure ventilation (mean difference $= -0.714$, standard deviation $= 2.4$, $P = .312$). When participants were divided into those with central and peripheral neurological disorders, the mean number of pneumonias before and after noninvasive positive pressure ventilation still did not significantly differ. In children with central neurological disorders, this difference was -0.85 (2.9), $P = .5625$; the mean number of pneumonias before and after noninvasive positive pressure ventilation in children with peripheral neurological disorders was -0.57 (1.99), $P > .99$. Among the 7 patients who used airway clearance techniques (chest physiotherapy or assisted cough), 2 had a reduced number of pneumonias over the 2 years post initiation of noninvasive positive pressure ventilation, whereas none of the 6 patients who were not using airway clearance techniques had a reduction in pneumonia frequency.

Discussion

This study was performed to observe the effectiveness of noninvasive positive pressure ventilation in preventing hospitalizations for pneumonia in patients with static or progressive

Table 2. Number of Episodes of Pneumonia by Patient.

Disease Type	Description	Pneumonia Before NiPPV	Pneumonia After NiPPV
Peripheral nervous system	Patient 1 (20 years old): On NiPPV for approximately 3 years; uses breath-stacking	0	0
	Patient 2 (20 years old): On NiPPV for approximately 6 years	0	0
	Patient 3 (23 years old): On NiPPV for 5 years; also uses breath-stacking	0	0
	Patient 4 (21 years): On NiPPV for approximately 7 years; compliant with NiPPV, chest physiotherapy, and assisted cough	1	0
	Patient 5 (17 years old): On NiPPV for 8 years; uses both chest physiotherapy and assisted cough; has been admitted to ICU 3 times (once for respiratory failure after a dental procedure and twice more for pneumonia)	0	5
	Patient 6 (3.5 years old): Inconsistent NiPPV use, and the use of chest physiotherapy and assisted cough has all been inconsistent since diagnosis	0	0
	Patient 11 (12 years old): On NiPPV intermittently since the age of 10; no use of pulmonary toileting methods	0	0
Central nervous system	Patient 7 (11 years old): On NiPPV for 4 years	2	2
	Patient 8 (12 years old): On NiPPV for 3 years; uses chest physiotherapy, assisted cough, and home suctioning; admitted to ICU many times for pneumonia; died of respiratory complications at age 12 years	5	7
	Patient 9 (8 years old): On NiPPV for 5 years; had tonsillectomy and adenoidectomy	0	0
	Patient 10 (19 years old): On NiPPV for 12 years; has restrictive lung disease and is on continuous oxygen supplementation	0	3
	Patient 12 (3 years old): On NiPPV since infancy; receives supplemental oxygen at home at baseline	0	3
	Patient 13 (9 years old): On NiPPV for 4 years; use of pulmonary toilet methods unknown; number of reported pneumonia may be underestimated due to use of home IV antibiotics	12	7
	Patient 14 (12 years old): On NiPPV for 3 years; good compliance with NiPPV and chest physiotherapy	2	5

Abbreviations: ICU, intensive care unit; NiPPV, noninvasive positive pressure ventilation.

neurologic diseases. Our results indicate that there was no difference in the number of episodes of pneumonia 2 years prior to using noninvasive positive pressure ventilation versus 2 years after noninvasive positive pressure ventilation in the patients sampled, even when children were divided into those with central or peripheral nervous system disorders. Although our hypothesis was that noninvasive positive pressure ventilation would reduce the frequency of pneumonias in children, it is possible that the use of noninvasive positive pressure ventilation did prevent an increase in the frequency of pneumonias over time. That is to say, in children with progressive neurologic conditions, especially once there is already evidence of respiratory failure (ie, hypoventilation requiring noninvasive positive pressure ventilation), the frequency of pneumonias would be expected to increase over time. Even children with static neurologic disease, such as cerebral palsy, may have progressive scoliosis over time, which could lead to worsening respiratory status and more frequent pneumonias. But, in the present study, the authors did not see an increase in the frequency of pneumonias. Furthermore, there were no mortalities during the study observation period and only 1 patient in the cohort died before the age of 18 years.

It is also possible that the use of noninvasive positive pressure ventilation caused bias toward a lower threshold for the treatment of pneumonia within a hospital setting. As respiratory caregivers follow these patients more closely, they may be more likely to bring these patients to urgent care centers if there is clinical deterioration. Adjustment of pressure settings, provision of suction, and so on, may be done more easily in a hospital, and this may increase the frequency of hospitalization for pneumonias that could otherwise be treated in an ambulatory setting if noninvasive positive pressure ventilation was not being used.

It should be noted that all patients in this study, with the exception of 2, were ascertained to be adherent to their prescribed noninvasive positive pressure ventilation therapy. A sensitivity analysis performed after excluding both of these nonadherent patients did not result in any change in the overall study findings (data not shown).

The small sample size and the lack of a control group in this study do not allow us to determine whether noninvasive positive pressure ventilation may have in fact reduced the frequency of pneumonias in these patients compared to if they had not used noninvasive positive pressure ventilation; the study may have also been underpowered to show an effect on pneumonia rates over time. There were a number of confounders in our study, the most significant of which was heterogeneity of the underlying neurologic diagnosis of each child. Because of the small number of patients reviewed, subanalyses by neurological diagnosis were not possible. Another potential confounder was the inconsistent use of airway clearance techniques such as chest physiotherapy or assisted cough within the study cohort. Given the small sample size, it is not possible to

determine whether this may have affected the impact of noninvasive positive pressure ventilation on the frequency of pneumonias.

Given these limitations, the authors are cautious about the generalizability of the results from this study, though they are provocative and suggest a possible benefit of the use of noninvasive positive pressure ventilation for preventing an increase in the frequency of pneumonias over time in these children. The authors propose that future studies involving a multicenter prospective cohort design with an intervention and control arm and long-term follow-up should be performed to more rigorously examine this question. Alternatively, a matched analysis using data within a large health database might be another method to determine the efficacy of noninvasive positive pressure ventilation for the prevention of pneumonias in children with neurological diseases and respiratory insufficiency.

Conclusion and Future Directions

The authors did not identify a change in the frequency of pneumonias in children with static and progressive neurologic disease following treatment with noninvasive positive pressure ventilation. While this could imply failure of noninvasive positive pressure ventilation to prevent pneumonias, it could also be interpreted as the success of noninvasive positive pressure ventilation in preventing the progression of infection-related respiratory morbidity over time among these children. In the future, larger studies using a prospective multicenter cohort design or population-based data sets will be valuable in understanding the full benefits of noninvasive positive pressure ventilation and the degree to which this intervention may minimize respiratory morbidity in children with neurological disease.

Author Contributions

AZH, CC and DR together conceptualized and designed this study. AZH performed all data collection and DR performed data analysis. All authors participated in data interpretation. AZH prepared the manuscript and CC and DR edited and revised the manuscript. All authors approve of the final manuscript.

Declaration of Conflicting Interests

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Ethical Approval

Research ethics approval for this study was obtained from The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects at Western University and Lawson Health Research Institute, London, Ontario (File Number 104573).

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