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Predictors of severe chest infections in pediatric neuromuscular disorders

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Abstract

Chest infections are serious complications in neuromuscular disorders. The predictive values of lung and respiratory muscle function including peak cough flow still remain unclear.

We performed retrospective analysis of 46 children and adolescents (12.7 ± 3.7 years) in whom lung function, respiratory muscle function and peak cough flows had been obtained. Data were related to: (1). number of chest infections and days of antibiotic treatment the year prior to the study and (2). history of severe chest infection requiring hospital admission.

The number of chest infections and the number of days treated with antibiotics correlated with Inspiratory Vital Capacity IVC, peak cough flow PCF and Peak Expiratory Pressure PEP. Twenty-two patients were hospitalized at least once due to severe chest infection. IVC (0.65 vs. 1.44 l; $P < 0.0001$) and PCF (116 vs. 211 l/min; $P < 0.0005$) in these patients were significantly lower than in the non-hospitalized group. IVC < 1.1 l and PCF < 160 l/min were specific and sensitive thresholds to discriminate between patients who had already suffered severe chest infections and those who had not. Therefore, spirometry and peak cough flow are reliable tests to identify patients at high risk for severe chest infections.

Patients with IVC below 1.1 l and/or PCF below 160 l/min should be well monitored and introduced to assisted coughing techniques.

Keywords: Spirometry; Respiratory muscle function; Peak cough flow; Severe chest infection

1. Introduction

Patients with neuromuscular disorders are often threatened by respiratory complications like peumonia and atelectasis which may cause acute respiratory failure [1–3]. Mortality due to pneumonia has been reported in 30% of patients with ALS and adult-onset-myotonic dystrophy [4,5]. In spinal muscular atrophy type I respiratory complications [6,7] lead to death during the first year, if patients were not treated by tracheotomy or recurrent invasive ventilation. Incidence of pneumonia in Duchenne patients was 0.8/year and in other myopathies 1/year [8].

Clearance of airway secretions is determined by mucociliary debris transport and a sufficient cough mechanism [9,10]. This system may become overloaded in case of excessive bronchial secretions. Upper respiratory tract infections due to otherwise non-virulent viruses then lead to pneumonia and atelectasis.

In the literature respiratory complications have been related to different parameters of respiratory function testings. Respiratory failure occurred in patients with severe restrictive ventilatory defect [11] and impaired respiratory muscle strength [12]. ALS patients with peak expiratory cough flows < 3 l/s had to undergo tracheotomy to prolong survival [13]. Chaudri et al. [14] showed a correlation between the absence of cough expiratory spikes and mortality in motor neuron disease.

In pediatric patients with neuromuscular disorders, spirometry was proven to discriminate between patients with nocturnal hypoventilation and those without [15]. A review of the current literature showed no description of the relation between respiratory function parameters and chest infections for patients at school age. Aim of the study was to investigate if simple bed side tests (spirometry, respiratory muscle function, peak cough flow) could identify pediatric patients at high risk for severe chest infections like pneumonia and/or atelectasis.

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2. Methods

2.1. Patients

We performed a retrospective chart review of 46 patients with neuromuscular disorders who were referred to the Ruhrlandklinik in Essen and the University Hospital of Essen for respiratory assessment from years 2000 to 2004. Mean age was 12.7 ±3.6 years and ranged from 6 to 20 years. Twenty-eight male and 18 female patients were enrolled. Underlying diagnosis was Duchenne muscular dystrophy (DMD) in 16 patients, spinal muscular atrophy (SMA) in 14 patients (5 type Ib, 9 type II), congenital muscular dystrophy (CMD) in 10 patients, hereditary sensory and motor neuropathy (HSMN) in 3 patients and acid maltase deficiency (Pompe's disease), nemaline myopathy and congenital myopathy in one patient each. No patient was tracheostomized. Nineteen patients were already using nocturnal non-invasive ventilation, but none was performing assisted coughing techniques at the point of the study.

2.2. History of chest infections

At time of respiratory assessment we asked patients and their caregivers (1) how often they had suffered from chest infections during the year prior to the visit, (2) how many days they had been treated with antibiotics for chest infections during the year prior to the visit and (3) if they had at least once been admitted to a hospital due to severe chest infection after their second year of life.

2.3. Lung function and respiratory muscle function

All measurements were obtained in the seated patient wearing a nose clip. Inspiratory vital capacity (IVC) and forced expiratory lung volumes (FVC, FEV_1) were measured with a hand-held spirometer (*ZAN* 100, ZAN Meßgeräte, Obertulba, Germany). The best of three successive efforts (<5% variability) was chosen. Predicted values were derived from published data [16]. In patients with severe scoliosis height was measured with a brace. Peak inspiratory pressure (PIP) was measured after exhalation to functional residual capacity FRC and peak expiratory pressure (PEP) after inspiration to IVC, both against occluded airways using a handheld manometer (ZAN Meßgeräte, Obertulba or Respironics, Inc., Murrysville, PA, USA). The highest pressure of three subsequent efforts was used. P01 was assessed as mouth occlusion pressure after 0.1 s of inspiration at tidal breathing. Respiratory muscle strain was defined as P01/PIP (%), the relation of inspiratory muscle pressures at quiet breathing and at maximum inspiratory effort. Peak cough flow (PCF) was measured in the seated patient wearing a nose clip and performing a maximum cough into a pocket peak flow meter (Pocketpeak™, Ferraris Medical Limited, Enfield, UK).

2.4. Statistics

Analysis was performed with Statistica 6.0 software package (StatSoft, Inc., Tulsa, OK). Data are presented as mean and standard deviation. Comparison of two groups were performed using the Mann-Whitney-*U*-test. Correlations were calculated by Spearman's rank test. $P<0.05$ was considered significant. Multiple regression analysis was used to identify the major determinant of severe chest infections. Receiver operator curves (ROCs) were constructed for four variables. Cut-off points separating patients with a history of severe chest infections from those without were calculated by bi-dimensional analysis and with equal sensitivity/specifity (ratio 1:1). The variable with the largest area under the curve (AUC) was considered strongest predictor of a history of severe chest infections.

3. Results

Mean lung function and respiratory muscle function values were as follows: IVC 1.08±0.68 l (37.6±21.6% pred.), FEV1 0.90±0.58 l (37.6±23.3% pred.), PCF 167.9±83.8 l/min, P01 0.29±0.17, PIP 3.19±1.71 kPa, P01/PIP 11.4±8.1% and PEP 2.72±1.17 kPa. PCF highly correlated with IVC ($R=0.87$), FEV1 ($R=0.88$), PEP ($R=0.59$) and respiratory muscle strain ($R=-0.65$); $P<0.0001$ for all. Weaker correlations were found between PCF and PIP ($R=0.41$) and PCF and P01 ($R=-0.42$); $P<0.01$ for all. PCF did not correlate with age ($R=0.27$), but with BMI ($R=0.58$, $P<0.001$).

During the year prior to the study, the average rate of chest infections was 0.84±0.94 and the average number of days treated with antibiotics was 5.5±6.0.

Table 1

	History of severe chest infection ($n=22$)	No history of severe chest infection ($n=24$)	P
IVC (l)	0.65±0.42	1.44±0.65	<0.00001
IVC % pred.	28±13	47±24	<0.005
FEV1 (l/s)	0.53±0.36	1.21±0.55	<0.0001
PCF (l/min)	116±62	211±74	<0.0005
PIP (kPa)	2.7±1.1	3.6±2.1	n.s.
PEP (kPa)	2.4±1.1	3.0±1.3	n.s.

Comparison of spirometry and respiratory muscle function in patients with a history of chest infections and patients without.

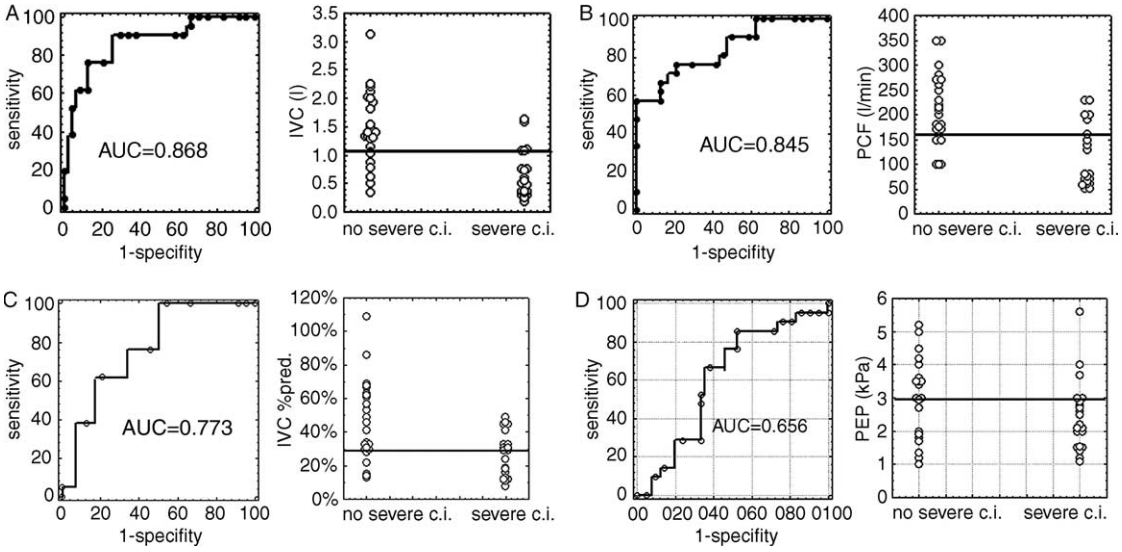

Fig. 1. A–D: On the right raw data of IVC (A), PCF (B), IVC% (C) and PEP (D) for patients with and without a history of severe chest infections. On the left the corresponding receiver operator curves with the area under the curve (AUC). The line indicates the optimal cut-off point for the predictors calculated with bi-dimensional analysis.

IVC ($R_c = -0.63$, $R_a = -0.57$; $P < 0.0001$), IVC %pred. ($R_c = -0.48$, $R_a = -0.41$; $P < 0.01$), FEV1 ($R_c = -0.62$, $R_a = -0.57$; $P < 0.0001$), FEV1%pred. ($R_c = -0.51$, $R_a = -0.44$; $P < 0.0005$) PCF ($R_c = -0.60$, $R_a = -0.57$; $P < 0.0005$), PEP ($R_c = -0.38$, $R_a = -0.35$; $P < 0.05$), P01 ($R_c = 0.42$, $R_a = 0.43$; $P < 0.01$) and P01/PIP ($R_c = 0.47$, $R_a = 0.43$; $P < 0.005$) highly correlated with both chest infections and days of antibiotic treatment, whereas PIP was not related ($R_c = -0.17$, $R_a = -0.10$).

Twenty-two patients had at least once been admitted to a hospital due to pneumonia. Patients who had suffered pneumonia showed significantly lower IVC, IVC %pred., PCF and FEV1 values. Concerning PIP and PEP no differences between these two groups could be detected (see Table 1).

In the group of patients with a history of severe chest infections, three patients were admitted at least once to intensive care unit. Two patients suffered from severe pneumonia and one suffered from acute gastrointestinal bleeding. One patient required intubation. The lung function values and PCFs were at the lowest range (PCF 50, 60, and 80 l/min; IVC 0.29, 0.29, and 0.42 l).

Multiple regression analysis revealed reduced IVC as strongest risk factor for pneumonia out of diagnosis, age, BMI, respiratory muscle function (PIP, PEP) and scoliosis (adjusted $R^2 = 0.38$, $P < 0.005$). Due to the dependence of FEV1 and PCF on IVC, FEV1 and PCF were not considered as independent variables.

Receiver-operator-curves were performed for respiratory function values (Fig. 1) considering the history of severe chest infections as the dependant value. Sensitivity, specifity, positive predictive value and negative predictive value are given in Table 2.

4. Discussion

Our study is the first systematic analysis of respiratory assessment and its relation to incidence and risk of chest infections in children and adolescents with neuromuscular disorders. Not surprisingly, pediatric patients with neuromuscular disorders experience a rising risk of chest infections with progressive deterioration of lung function and peak cough flows. Therefore, patients at high risk can be easily identified by providing simple bed side tests measuring inspiratory vital capacitiy (IVC) and peak cough flow (PCF). Interestingly, respiratory muscle function, scoliosis, age and diagnosis play a less important role.

Analysis of data is limited by the fact that we performed a retrospective chart review and also by the heterogeneity of the study population.

Recurrent chest infections are a major complication of advanced neuromuscular disorders. The average rate in our study population was almost 1/year. Half of the patients had at least once been hospitalized with pneumonia. As chest infections determine morbidity and often mortality in neuromuscular disorders prevention of chest infections should be a major goal of treatment. Therefore, in these

Table 2

Severe chest infections	IVC ≤ 1.1 l (%)	IVC ≤ 30% pred. (%)	PCF ≤ 160 - l/m (%)	PEP ≤ 3 kPa (%)
Sensitivity	90.5	61.9	75.2	85.7
Specifity	70.8	79.2	79.2	47.3
Ppv	73.1	63.2	79.2	62.1
Npv	89.5	65.4	76.2	76.9

IVC, inspiratory vital capacitiy; IVC pred., inspiratory vital capacity of predicted; PCF, peak cough flow; PEP, peak expiratory pressure; Ppv, positive predictive value; Npv, negative predictive value.

patients pulmonary clearance of secretions should be improved when necessary. But to clear airways from mucus a sufficient cough has to be maintained. We could show that diminished PCF in neuromuscular disorders is the result of restrictive lung defect (IVC) and to a lesser degree of expiratory muscle weakness (reduced PEP). Inspiratory muscle strength (PIP) showed only a very weak influence on PCF. Therefore, to produce cough augmentation, the major goal should be an increase of lung volumes above IVC. Additional support of expiratory muscles by manual abdomino-thoracic compression can further enhance PCF. Several studies have shown an increase of PCF by hyperinsufflation to a maximum insufflation capacity (MIC) and a further increase of PCF by additional expiratory aids. Different devices and methods have proven to promote this effect: Glossopharyngeal breathing, volume targeted ventilators, intermittent positive pressure breathing devices (IPPB) and the in- ex-sufflator [17–25].

The present study showed that IVC and PCF are strong predictors of severe chest infections. Therefore, these testings can discriminate between patients at high risk and patients at low risk to develop pulmonary infectious complications. An IVC $<$ 1.1 l or a PCF $<$ 160 l/min both have high sensitivity and specifity values for severe chest infections. This PCF threshold confirms a former established value in adults by Bach et al. [26]. This research group could demonstrate that a PCF $<$ 160 l/min in ALS patients predicted weaning failure of invasive ventilation.

Detection of the above mentioned thresholds are of high clinical importance in children with NMD. They mark the latest date when caregivers should start to initiate patients on assisted coughing methods, even in the absence of respiratory complications in the medical history. At that stage of disease patients should also be well monitored and introduced to a treatment protocol: Assisted coughing techniques should be performed once to twice daily. During chest infections the frequency should be enhanced according to the amount of pulmonary secretions. With these measures and with non-invasive ventilation the oxygen saturation should be maintained above 95%. In a retrospective review, the frequency of chest infections and the frequency of hospital admissions could both be reduced using this protocol [27]. Further investigation is needed to prospectively prove this effect.

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