

Pseudomonas aeruginosa in children with cerebral palsy: a prospective study

Katrien Romaen¹, Isabelle Van Ussel², Carolin Van Rossem³, Sandra Kenis¹, Berten Ceulemans¹, Kim Van Hoorenbeeck⁴, and Stijn Verhulst⁴

¹Universitair Ziekenhuis Antwerpen

²AZ Voorkempen

³ZNA Koningin Paola Kinderziekenhuis

⁴Universiteit Antwerpen

July 11, 2023

Abstract

As we know life expectancy in CP can improve by both preventive measurements as initiation of early therapy concerning respiratory morbidity. The prevalence of PA in this prospective study of children with CP is low, gram-negative bacteria were most commonly found. Therefore, it is recommended to repeat and expand this study since the prevalence of respiratory tract infections is again increasing in the post-covid era.

Pseudomonas aeruginosa in children with cerebral palsy: a prospective study

Katrien Romaen, MD^{1*}; Isabelle Van Ussel, MD^{2*}; Carolin Van Rossem^{3*}; Sandra Kenis MD¹; Berten Ceulemans MD, PhD¹; Kim Van Hoorenbeeck, MD, PhD⁴; Stijn Verhulst MD, PhD⁴

¹ Department of Paediatric Neurology, Antwerp University Hospital/University of Antwerp, Belgium.

² Department of Paediatrics, AZ Voorkempen, Malle, Belgium.

³ Department of Pediatrics, ZNA Queen Paola Children's Hospital, Antwerp, Belgium.

⁴ Department of Paediatric Pulmonology, Antwerp University Hospital and Lab of Experimental Medicine and Pediatrics, University of Antwerp, Antwerp, Belgium.

* These authors contributed equally

Correspondence : Katrien Romaen, department of Pediatric Neurology, Antwerp University Hospital. Drie Eikenstraat 655 2650 Edegem, Belgium.

E-mail: Katrien.romaen@uza.be

To the Editor.

Children with cerebral palsy (CP) often present with chronic respiratory symptoms. This is an important risk factor for increased morbidity and mortality in children with CP. *Pseudomonas aeruginosa* (PA), is a known pathogen associated with more severe respiratory disease. Due to its ability to change its phenotype, an infection with PA is often chronic and PA is very difficult to eradicate. CP is often accompanied by multisystem medical concerns like epilepsy, secondary musculoskeletal problems and impairment in cognition, communication, behavior, perception, motor control and sensation (1,3,4,5). The degree or severity of motor disability is classified by the Gross Motor Function Classification System (GMFCS), a higher score indicates

increasing severity and lower life expectancy (1,5). Patients with CP have a shorter life expectancy than the general population and the observed morbidity and mortality is especially linked to respiratory disease (1,2,4,5). The impact of respiratory morbidity on the quality of life cannot be underestimated (1,3,5). The reasons for these respiratory complications are probably multifactorial. Risk factors for hospital admission include the severity of gross motor disfunction reflected by GMFCS score, epilepsy, axial hypotonia, limited shoulder movement, severe kyphoscoliosis, swallowing problems, gastroesophageal reflux disease (GERD), gastrostomy feeding and absence or impairment of spontaneous cough (1,4). Other medical conditions also influence hospitalization rate, quality of life and life expectancy, including overt or silent aspiration, impaired mucociliary clearance, kyphoscoliosis, upper or lower airway obstruction and recurrent infections leading to bronchiectasis. One study showed that the presence of abnormal bacterial flora (including *Pseudomonas* and *Klebsiella* species) in children with CP who are critically ill occurred twice as frequent compared to those critically ill without CP (2).

From experience in children with cystic fibrosis, it is known that chronic colonization of the lower airways with PA is a risk factor for repeated lung infections, deterioration in lung function and shortened survival (6). It is also known that early therapy will prevent chronic colonization (6). Preventive actions to eradicate this bacterium and to improve the respiratory condition of children with CP could therefore be of interest. The prevalence and role of PA, however, is relatively unknown in this population. Therefore, we assessed the prevalence of PA and its association with respiratory disease in a prospective study including patients, aged 0-18 years, with a diagnosis of CP who attended either specialised day care centres in Flanders and/or the Antwerp Reference Centre of Cerebral Palsy in the Antwerp University Hospital. Exclusion criteria included a known presence of PA defined as a throat swab with a positive culture for PA and eradication treatment in the last month before inclusion. Inclusion was done during two periods. Informed parental consent was obtained. First inclusion was done between August 2017 to January 2018. To further expand the study, new inclusions were done from January 2020 to September 2020. Demographic data, respiratory characteristics and data of comorbidities from patient records were extracted from the electronic medical records (*Table 1*). Follow-up of respiratory symptoms was done by the Liverpool respiratory symptom questionnaire (LRSQ) after 3 months. Throat swabs were used to evaluate lower airway microorganisms. A throat swab and a completed LRSQ after 3 months were received from 79 children with CP. Most children had a GMFCS of I (24.1%) or V (24.1%). Feeding difficulties, malnutrition, cough efficiency, airway clearance therapy and epilepsy were statistically significant associated with GMFCS stages. Twenty-eight patients (35%) were found to have at least one positive respiratory culture. Only 4 patients (5%) were infected with PA. Gram negative bacteria were isolated in 22% of the positive throat swabs, *S. aureus* was found in 14%. Most pathogens were found in patients with higher GMFCS score (GMFCS III, IV and V) (*Table 2*). Results of the LRSQ showed that 52% of these patients reported having 1 cold in the past 3 months. Only 3 patients were admitted to the hospital, none of these patients were colonized with PA. No statistically significant relation could be found between the number of colds and/or pneumonia, the use of antibiotics or hospitalization, and having a positive culture, colonization with *S. aureus*, *P. aeruginosa* or gram-negative bacteria.

Although respiratory disease is an important risk factor for morbidity and mortality in children with CP, we demonstrated that the prevalence of PA in our population of children with CP without known chronic lung disease is low. Despite several study limitations, colonization with PA or other bacteria in a large sample of children with CP does not seem to be a major cause of respiratory morbidity and mortality. Previous studies, including the study by Gerdung et al. showed that children with CP with a positive culture for gram-negative bacteria, and mainly PA, had more severe respiratory disease, more Paediatric Intensive Care Unit (PICU) hospitalizations, more need for mechanical ventilation, larger pleural effusions and a longer hospitalization (2). Our study showed that there is a correlation between GMFCS score and colonization with gram-negative bacteria. The short-term respiratory consequences of being colonized with these bacteria were limited in our prospective study. We could not demonstrate a statistically significant correlation between number of colds, pneumonia, the use of antibiotics or hospitalization with having a positive culture, colonization with *S. aureus*, *P. aeruginosa* or gram-negative bacteria. Possible explanations

for this could be the COVID-19 pandemic with two lockdowns and therefore less exposure to pathogens due to less social contact and extensive hygienic measures, no visitors in specialized day-care centers and closed schools.

As we know life expectancy in CP can improve by both preventive measurements as initiation of early therapy concerning respiratory morbidity. The prevalence of PA in this prospective study of children with CP is low, gram-negative bacteria were most commonly found. Therefore, it is recommended to repeat and expand this study since the prevalence of respiratory tract infections is again increasing in the post-covid era.

Table 1

Patient characteristics n = 79

Age (years)	Mean	8.44 (SD ¹ ± 4.74)
Gender	M : F	37 : 42
Gross Motor Function Score	Level I	19 (24.1%)
	Level II	18 (22.8%)
	Level III	9 (11.4%)
	Level IV	14 (17.7%)
	Level V	19 (24.1%)
Respiratory characteristics		
OSA ²	Yes : No	4 : 75 (5.1% : 94.9%)
Asthma	Yes : No	2 : 77 (2.5% : 97.5%)
Bronchiectasis	Yes : No	1 : 78 (1.3% : 98.7%)
Antibiotic prophylaxis	Yes : No	3 : 76 (3.8% : 96.2%)
Chronic respiratory medication ³	Yes : No	9 : 70 (11.4% : 88.6%)
Chronic airway clearance therapy (e.g. Physiotherapy)	Yes : No	9 : 70 (11.4% : 88.6%)
Chronic oxygen therapy	Yes : No	1 : 78 (1.3% : 98.7%)
NIV ⁴	Yes : No	5 : 74 (6.3% : 93.7%)
Comorbidities		
GER ⁵	Yes : No	10 : 69 (12.7% : 87.3%)
Feeding difficulties	Yes : No	34 : 45 (43% : 57%)
Malnutrition	Yes : No	12 : 67 (15.2% : 84.8%)
Scoliosis (<i>missing n = 1</i>)	Yes : No	7 : 71 (8.9% : 89.9%)
Epilepsy (<i>missing n = 1</i>)	Yes : No	28 : 50 (35.4% : 63.3%)

TABLE 1 demographic characteristics. ¹Standard Deviation; ²Obstructive sleep apnea;

³Chronic respiratory medication: Salbutamol, Fluticasone propionate, Salmeterol/Fluticasone propionate, Acetylcysteine;

⁴Non-invasive ventilation;⁵Gastroesophageal reflux

Table 2

	Positive culture of any bacteria	Positive culture of any bacteria	Positive culture of any bact
Predictors	No	Yes	P value
GMFCS			.016
I-II	29 (36.7%)	8 (10.1%)	
III-IV-V	22 (27.8%)	20 (25.3%)	

TABLE 2 Descriptive statistics and chi square tests for positive culture, gram-negative bacteria, and S. aureus. A P-value < 0,05 is considered statistically significant.

References

1. Boel L, Pernet K, Toussaint M, Ides K, Leemans G, Haan J, et al. Respiratory morbidity in children with cerebral palsy: an overview. *Dev Med Child Neurol.* 2019;61(6):646-53.
2. Gerdung CA, Tsang A, Yasseen AS, 3rd, Armstrong K, McMillan HJ, Kovesi T. Association Between Chronic Aspiration and Chronic Airway Infection with *Pseudomonas aeruginosa* and Other Gram-Negative Bacteria in Children with Cerebral Palsy. *Lung.* 2016;194(2):307-14.
3. Young NL, McCormick AM, Gilbert T, Ayling-Campos A, Burke T, Fehlings D, et al. Reasons for hospital admissions among youth and young adults with cerebral palsy. *Arch Phys Med Rehabil.* 2011;92(1):46-50.
4. Kuo TJ, Hsu CL, Liao PH, Huang SJ, Hung YM, Yin CH. Nomogram for pneumonia prediction among children and young people with cerebral palsy: A population-based cohort study. *PLoS One.* 2020;15(7):e0235069
5. Gibson N, Blackmore AM, Chang AB, Cooper MS, Jaffe A, Kong WR, et al. Prevention and management of respiratory disease in young people with cerebral palsy: consensus statement. *Dev Med Child Neurol.* 2021;63(2):172-82.
6. Silva Filho LV, Ferreira Fde A, Reis FJ, Britto MC, Levy CE, Clark O, et al. *Pseudomonas aeruginosa* infection in patients with cystic fibrosis: scientific evidence regarding clinical impact, diagnosis, and treatment. *J Bras Pneumol.* 2013;39(4):495-512.

Author names

Katrien Romaen, MD^{1*}; Isabelle Van Ussel, MD^{2*}; Carolin Van Rossem³; Sandra Kenis MD¹; Berten Ceulemans MD, PhD¹; Kim Van Hoorenbeeck, MD, PhD⁴; Stijn Verhulst MD, PhD⁴

Affiliations

¹ Department of Paediatric Neurology, Antwerp University Hospital/University of Antwerp, Belgium.

² Department of Paediatrics, AZ Voorkempen, Malle, Belgium.

³ Department of Pediatrics, ZNA Queen Paola Children's Hospital, Antwerp, Belgium.

⁴ Department of Paediatric Pulmonology, Antwerp University Hospital and Lab of Experimental Medicine and Pediatrics, University of Antwerp, Antwerp, Belgium.

* These authors contributed equally

Conflict of interest statement

No disclosure

Correspondence

Katrien Romaen, department of Pediatric Neurology, Antwerp University Hospital. Drie Eikenstraat 655 2650 Edegem, Belgium.

E-mail: Katrien.romaen@uza.be