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Original Article

CT-abnormalities, bacteriology and symptoms of sinonasal disease in children with Cystic Fibrosis

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Abstract

Background: Sinonasal pathology in adults with Cystic Fibrosis (CF) is common but the extent of CT-abnormalities and symptoms of sinonasal disease in children with CF and the age of onset are less frequently studied.
Methods: In this observational, cross-sectional study 58 children with CF from two CF centres were included. All subjects completed a questionnaire regarding sinonasal symptoms, underwent a CT scan of the paranasal sinuses, and in each subject a culture of the upper airways was performed. Subjects were divided in 6 age cohorts (0–2, 3–5, 6–8, 9–11, 12–14 and 15–17 years) and were divided into severe and mild CF based on their CFTR mutation. Opacification of the sinonasal system of the subjects was compared with opacification on MRI-scans of an age-matched control group without CF.
Results: Most frequently reported symptoms were nasal obstruction and posterior/anterior nasal discharge. Opacification was abundant in every age cohort of the study group and was significantly more compared to the control group. In patients with severe CF the opacification was higher than subjects with mild CF. Upper airway cultures showed predominantly *Staphylococcus aureus*, *Haemophilus influenzae* and *Pseudomonas aeruginosa.*
Conclusion: CT-abnormalities indicating sinonasal disease and symptoms are present from shortly after birth which may argue for a thorough examination of the upper airways in children with CF.

Keywords: Cystic Fibrosis; Children; Rhinosinusitis; CT scan; Microbiology; Genotype

1. Introduction

The prevalence of sinonasal pathology in patients with Cystic Fibrosis (CF) is high. Due to the defect Cystic Fibrosis Transmembrane conductance Regulator (CFTR) protein, stasis of viscous mucous and impaired mucociliary transport are believed to contribute to the development of chronic rhinosinusitis (CRS). However, not all predisposing factors are identified yet [1]. Acknowledgement of sinonasal disease in CF patients is important because symptoms of rhinosinusitis can decrease a patient's quality of life. Furthermore the paranasal sinuses can constitute a niche for pathogens from which cross infection to the lungs can occur and lung infections can be facilitated [2].

Recently more aggressive treatment strategies of sinonasal disease have been applied to improve pulmonary outcomes. Early detection and treatment of pathogens in the upper airways can prevent or postpone cross infection of the lungs [3,4]. For early detection however, it is necessary to gain data on the clinical characteristics of sinonasal disease from children with CF.

In adult patients with CF the prevalence of rhinosinusitis is approximately 63% and the prevalence of nasal polyps around

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25% [5]. The exact prevalence in children with CF, however, is unknown. In the literature the prevalence of nasal polyps ranges from 32 to 45% [6]. For ethical concerns studies performed in children with CF often did not include children in the 0 to 4 age group. Moreover investigations to ascertain the diagnosis of rhinosinusitis, such as a CT scan and nasendoscopy are often omitted in children. For these reasons a proper statement on the prevalence among children in different ages was difficult to obtain.

Clinical manifestations of sinonasal disease in CF which can be found on additional examination include nasal polyps, abnormalities on computed tomography (CT) of the sinuses and cultures from the upper airway positive for CF pathogenic microorganisms. In adults with CF *Pseudomonas aeruginosa* is most frequently cultured from the upper airways, followed by *Staphylococcus aureus.*

CT scans of the paranasal sinuses often show opacified sinuses, which indicates inflammation of the epithelium lining the sinuses [7]. Furthermore, hypoplasia and aplasia of the frontal and sphenoid sinus have been described [7,8]. Another radiographic finding in patients with CF is osteitis/neoosteogenesis predominantly of the maxillary sinus walls [7]. This has been hypothesized to be associated with increased severity of inflammation [9]. These developmental and inflammatory changes in adult patients indicate a chronic course of rhinosinusitis. However, to date the age of onset of the sinonasal pathology is unknown.

Sinonasal manifestations of CF seem to be associated with genotype, with more severe sinonasal disease in patients with class I–III mutations in the CFTR gene [5,10]. However, research in this possible correlation is scarce.

In the present study several aspects of sinonasal disease in children with CF were investigated. This is one of the scarce studies that includes CF children from the age of 0 years [11,12]. The aim of this study was to gain more knowledge on CT-abnormalities, microbiology and symptoms of sinonasal disease in children with CF.

2. Study design

2.1. Patients

This multicentre, observational study was performed in two CF-centres in the Netherlands (Academic Medical Centre (AMC) in Amsterdam and Haga Teaching Hospital in The Hague). From September 2013 to September 2014 children with a diagnosis of Cystic Fibrosis, based on a positive sweat test and/or a confirmed CF genotype, from 0 to 17 years of age were enrolled in this study. Subjects were divided into 6 cohorts of age; 0–2, 3–5, 6–8, 9–11, 12–14 and 15–17 years. The intended number of patients was ten in each cohort. The subjects were divided into two groups according to the mutations in their Cystic Fibrosis transmembrane regulator (CFTR) gene. Patients who were homozygous or compound heterozygous for class I–III mutations were considered as having severe CF. Subjects who carried at least one class IV–VI mutation were assessed as having mild CF. If one or both of the mutations were unknown, pancreatic function and age at diagnosis were used to allocate subjects to one of the two groups. Since a strong correlation between pancreatic function and severity of CF is reported [13] and age at diagnosis is known to correlate well with genotype [14] in this study patients with pancreatic insufficiency or an age at diagnosis <10 years were considered as having severe CF. History of sinonasal surgery and current drug use were recorded for each subject. The study was performed in accordance with the Declaration of Helsinki and was approved by a local medical ethics committee. Written informed consent was obtained from both parents/caretakers and assent was obtained from a participant of 12–17 years old.

2.2. Computed tomography

Computed tomography (CT) of the paranasal sinuses was performed in all subjects. In the Haga Teaching Hospital the SOMATOM Definition Flash CT scan was used and in the AMC the Philips Brilliance CT scan. In both hospitals a low-dose protocol was used, with an effective dose of 1 millisievert. Axial computed tomography was performed with a slice thickness of 0.5 mm and images were reconstructed at 1.0 mm to coronal and sagittal images. In both centres the scan ranged from the upper border of the frontal sinuses tot the lower part of the teeth in the maxilla. No intravenous contrast nor anaesthesia was used. In patients that objected to the CT scan after two attempts, the procedure was stopped because too much movement during the CT scan would interfere with the quality of the scan.

Opacification of the paranasal sinuses was analysed using a modified Lund–Mackay (L–M) score. The Lund–Mackay scoring system grades every sinus as 0: normal, 1: partial opacification, or 2: total opacification. With this system the opacification of the maxillary, anterior ethmoid, posterior ethmoid, sphenoid and the frontal sinus of both sides is graded. Moreover the ostiomeatal complex is scored as 0: patent and 2: occluded [15]. In case all sinuses are present, the L–M score can range from 0 to 24. However, in this study modification of the L–M system was necessary since the prevalence of non-developed sinuses in children is high. The total L-M score was divided by the amount of elements present, resulting in a score for opacification per element of the sinonasal system. Two observers (F.K. and M.C.B) who were blinded for genotype and previous outcomes of the study, analysed all CT scans.

Lund–Mackay scores on CT scans of patients with CF were compared with L–M scores on MRI-scans of children without CF. This group consisted of children in which a MRI of the head was performed for other reasons than rhinosinusitis. The MRI scans were collected from a database of the Radiologic Department of the Haga Teaching Hospital and personal data were removed before they were used in the analysis. MRI scans were included when the reason for MRI-scan was not otorhinolaryngologic pathology and the lower border of the maxillary sinus was depicted. The study group and the control group were matched for age.

In addition, the CT scans of CF patients were evaluated for the presence of anatomical variations, such as bulging of the lateral nasal wall, the anatomy of the uncinate process and the