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Original Article

Audiometric assessment of pediatric patients with cystic fibrosis

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Abstract

Background: The purpose of this study was to evaluate hearing impairment in pediatric patients with cystic fibrosis (CF).
Methods: This is a retrospective analysis of the AudGen database generated by Children's Hospital of Philadelphia. Audiograms were analyzed for type of hearing loss (HL), pure-tone-average (PTA), laterality, and change in hearing over time. Medical charts were reviewed to identify factors that influence development and progression of hearing loss.
Results: 217 patients with CF were included in this study. 69 (31.8%) had hearing loss on initial audiogram. Chronic otitis media (OR: 2.4, 95% CI: 1.3–4.5, $p < 0.01$), Eustachian tube dysfunction (OR: 2.4, 95% CI: 1.4–5.4, $p < 0.01$), and otorrhea (OR: 6.3, 95% CI: 1.6–24.7, $p < 0.01$) were positive predictors of HL. Children with a diagnosis of diabetes had more decline in hearing over time than those without diabetes (12.4 ± 17.2 dB worsening vs. −5.7 ± 9.8 dB improvement in PTA, $p = 0.014$).
Conclusion: This is the largest comprehensive analysis of all types of hearing loss in pediatric patients with CF. Our data suggest that children with more severe sinus disease may be at lower risk for inflammatory middle ear disease and subsequent hearing loss. Patients who develop complications of CF such as diabetes should be monitored frequently, and the use of ototoxic drugs should be limited if possible.

Keywords: Cystic fibrosis; Hearing loss; Audiogram; Conductive hearing loss; Sensorineural hearing loss; Otitis media

1. Introduction

Cystic Fibrosis (CF) affects >70,000 people worldwide and is caused by a mutation in the epithelial CFTR protein, which is an anion transporter (CF foundation patient registry). These mutations cause a disturbance of ion and water homeostasis on epithelial surfaces resulting in viscous mucus collection and bacterial colonization. This ultimately leads to chronic inflammation and recurrent infections in the respiratory tract and nasal sinuses [1,2].

Although the middle ear and Eustachian tube are lined with respiratory mucosal epithelium, CF does not appear to cause frequent middle ear disease. Studies comparing patients with CF to age-matched controls have found no greater incidence of middle ear disease [3,4]. In fact, one study found a lower prevalence of otitis media in patients with CF than controls [4]. Anatomical studies reveal comparable pneumatization and mucosal histology of middle ear between temporal bones of patients with and without CF [5,6]. One theory that explains these findings is that the CFTR protein might play a more limited role in anion transport in middle ear mucosa compared to nasal epithelium [7].

The prevalence of overall hearing loss in patients with CF ranges from 8% to 39% [8–11]. Several prior studies have

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examined sensorineural hearing loss (SNHL) related to ototoxic antibiotic use for treatment of pseudomonas infections in children with CF [12,13]. Estimates of SNHL in patients with CF range from 0 to 44% [12,13], and might correlate directly with the number of courses of antibiotics taken [12]. The present study utilizes a large pediatric audiologic database to provide what we believe is the largest comprehensive analysis of all types of hearing loss in pediatric patients with CF.

2. Materials & methods

2.1. Subjects

Institutional Review Board exemption from the Medical University of South Carolina was obtained for this study. AudGen is a publically available online database funded by the National Institutes on Deafness and Other Communication Disorders of the NIH. The database is HIPAA compliant and draws information from electronic health records, audiological instruments, radiology reports, and clinical genetics results. Information on medical therapies (e.g. antibiotics or other drugs prescribed) is not available in the database. At the time we accessed the AudGenDB Database [14], it contained information on approximately 105,000 pediatric patients, populated from the electronic medical records of Children's Hospital of Philadelphia (CHOP) and Vanderbilt University; since that time, records from Boston Children's Hospital have been added, but were not included in our study.

The patients for this study were drawn from a database query of children who had received a diagnosis of cystic fibrosis according to ICD-9 coding. Genetic confirmation of this diagnosis was not available. Patient data were organized by age (up to age 21), gender, ethnicity, availability of audiometric data, and presence of hearing loss on audiograms.

2.2. Audiologic evaluation

Pure-tone air and bone conduction audiometry and sound-field testing were used to evaluate hearing outcomes. When available, ear-specific air-conduction thresholds were collected at octave frequencies of 0.25 to 8.0 kHz and at interoctave frequencies of 3.0 to 6.0 kHz. Both masked and unmasked bone-conduction thresholds were analyzed when available at octave frequencies of 0.25 to 4.0 kHz and at the interoctave frequency of 3.0 kHz. Audiograms were categorized based on presence of hearing loss, type of hearing loss, severity, and ear affected (right, left, bilateral). Sound-field testing measures the better ear, thus patients with hearing loss on sound-field testing were recorded as having bilateral hearing loss.

The most complete audiogram that demonstrated the earliest evidence of hearing loss was used to characterize the type of hearing loss, severity, and laterality. Patients with hearing loss on at least one audiogram were classified as having hearing loss. Hearing loss was defined as at least one threshold >15 dB (pure-tone audiometry) or 20 dB (sound-field) at any frequency, or >25 dB at any frequency for infants <1 year of age [15–19]. In general, we classified hearing loss as:

1. Conductive: normal bone conduction threshold, air conduction threshold of >15 dB HL and air-bone gap of 10 dB or more at any recorded frequency,
2. Sensorineural: bone conduction threshold of >15 dB HL with an air-bone gap of <10 dB at any recorded frequency,
3. Mixed: bone conduction threshold of >15 dB HL with an air-bone gap of >10 dB at the same recorded frequency, or conductive and sensorineural components were both present but at different frequencies, and
4. Undefined: there were insufficient data to determine the loss type (e.g. audiograms without bone-conduction testing or for non-ear-specific sound field audiograms) [16].

Pure-tone average (PTA) was calculated for air-conduction thresholds bilaterally using the frequencies 0.5, 1.0, 2.0, and 4.0 kHz in accordance with the American Academy of Otolaryngology- Head and Neck Surgery guidelines for pure-tone averages. PTA was used to classify severity of hearing loss via the following guidelines: normal (PTA ≤15 dB), slight (16–25 dB), mild (26–40 dB), moderate (41–55 dB), moderately severe (56–70 dB), severe (71–90 dB), and profound (90+ dB) as delineated by the PTA [16]. It is possible for an ear to have hearing loss (defined as >15 dB at any frequency) but have a PTA that is still in the normal range. We refer to these ears as "HL with PTA ≤ 15 dB". Tympanometry data including middle ear pressure (MEP), static compliance (SC), and external canal volume (ECV) were used to calculate tympanogram type (A, B, C) based on guidelines from the American Speech and Hearing Association.

2.3. Chart review

For each patient with cystic fibrosis, common medical and otologic ICD-9 diagnoses were noted. These included: otologic, ocular, neurological, cardiac, pulmonary, and gastrointestinal disorders. Specific otologic conditions of interest included: otitis media, Eustachian tube dysfunction, otorrhea, cerumen impaction, cholesteatoma, and placement of ear tubes. Number of episodes of otitis media and cerumen impaction were calculated based on number of times the ICD-9 code was noted in a patient encounter.

2.4. Statistical analysis

All statistical analyses and graphs were performed in R version 3.2.4 (Free Software Foundation's GNU General Public License) [20]. Categorical variables were summarized by frequency and percentage. Continuous variables were summarized by mean ± standard deviation, range, and median where appropriate. All continuous variables were assessed for normality using the Shapiro-Wilk test. To analyze change in hearing loss over time, change in PTA was calculated from the patient's first audiogram to their last. Cases were also stratified by PTA outcome (improved, no change, worse) with "no

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