Ototoxicity monitoring of adults with cystic fibrosis

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INTRODUCTION

Cystic fibrosis (CF) causes thickened mucus in the respiratory tracts leading to blockage, infection and respiratory failure. According to the Cystic Fibrosis Foundation (CFF), approximately 30,000 people in the US have CF, and the annual incidence is about 0.0009%[1]. The median life expectancy in 2005 was 37 years.

These respiratory infections are treated using aminoglycoside antibiotics like tobramycin that can be ototoxic; in 2004 over 15,300 CF patients were prescribed tobramycin[2], which has reported cochleotoxicity and vestibulotoxicity incidences of 14% and 3%, respectively[3]. Optimizing the care of CF patients requires treating the classical effects of CF while maintaining cochleovestibular function. Ototoxicity monitoring can ensure medication regimens are balanced with audiologic care when possible, but currently there is no monitoring standard.

Nationwide there are 115 CFF-accredited care centers including 95 adult programs and over 50 affiliate sites. Despite considerable data showing aminoglycoside ototoxicity, it is not clear if the CFF care facilities have identified patients with ototoxicity-related hearing loss and dizziness, or more importantly if they are monitoring.

The objective of this research was to develop a practical ototoxicity monitoring protocol for use with adult CF patients based on literary recommendations, analysis of patient data from the UCSD Adult CF Center, and survey of CFF adult care facilities.

METHODS

This research was approved by the Institutional Review Board (IRB) at SDSU as well as the IRB at UCSD.

❖ CF PATIENT DATA ANALYSIS

- Inpatient & outpatient, bilateral audiologic results from 10/26/04-7/25/07 retrospectively reviewed (1-9 tests per patient) at the UCSD Adult CF Center
- 114 patients (58 male), age 17-62 years (mean 32) as of 7/25/07
- Patient questionnaire about tinnitus, dizziness & noise exposure
- Pure-tone air conduction (PT) thresholds from 500-8,000 Hz
- Distortion product otoacoustic emissions (DPOAEs) from 842-7,996 Hz (f_2/f_1=1.20, L_1=65 dB, L_2=55 dB) recorded using an Otodynamics ILO OAE system
- Outpatients & most inpatients tested in a quiet room using a TA-7B portable audiometer with TDH-50P supra-aural earphones
- Some inpatients tested in a sound booth using a GSI-61 clinical audiometer with TDH-50P or E-A-RTONE 3A insert earphones
- Equipment disinfected between each patient; sound booth usage limited to one CF patient in 24 hrs
- All audiologic interpretations, which were based on the worst ear, provided by same audiologist using established PT threshold norms[4], UCSD DPOAE amplitude norms[5] & patient histories

❖ CFF ADULT CARE FACILITY SURVEY

- 101 care facility administrators contacted via email with Statement of Informed Consent
- 10-question anonymous online survey
- Survey data collected from 10/22/07-12/20/07

RESULTS

❖ CF PATIENT DATA ANALYSIS

- As illustrated in Figure 1, 52.6% (60 patients) had cochleotoxicity identifiable based on PT thresholds &/or DPOAEs; 31.7% of these had normal PT thresholds w/ abnormal DPOAEs (Early Ototoxicity)
- Sensitivities & specificities are shown in Table I; all cases of ototoxicity identified had abnormal DPOAEs (100% sensitivity)

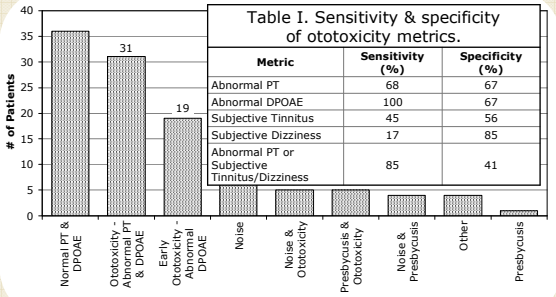

Table I. Sensitivity & specificity of ototoxicity metrics.

Metric	Sensitivity (%)	Specificity (%)
Abnormal PT	68	67
Abnormal DPOAE	100	67
Subjective Tinnitus	45	56
Subjective Dizziness	17	85
Abnormal PT or Subjective Tinnitus/Dizziness	85	41

Figure 1. Distribution of 114 audiologic interpretations.

- 44.5% & 16.4% reported tinnitus or dizziness, respectively, at the time of at least one test
- 31.6% of Early Ototoxicity patients reported tinnitus &/or dizziness at the time of at least one test

❖ CFF ADULT CARE FACILITY SURVEY

- 26 survey respondents (19.3% of facilities)
- 96.2% & 61.5% think they have patients with possible ototoxicity-related hearing loss & dizziness, respectively
- 42.3% & 30.8% monitor for cochleotoxicity & vestibulotoxicity, respectively; 81.8% of those do not follow a protocol
- Figure 2a shows that 72.7% of those who monitor outpatients do so using PT at ≤ 8,000 Hz; Figure 2b illustrates that an audiologist administers the monitoring at 54.5% of facilities

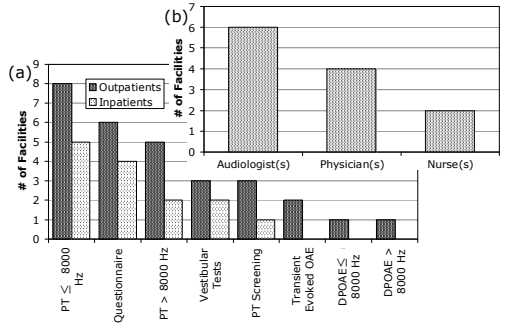

Figure 2. Monitoring (a) methods & (b) staff at facilities.

DISCUSSION

These patient data suggest incidences of cochleotoxicity (52.6%) and vestibulotoxicity (16.4%) for adults with CF are higher than reported by Govaerts et al. (1990). They also imply that among adult patients with CF and ototoxicity there is 68% probability of abnormal PT thresholds at ≤ 8,000 Hz as well as a 100% chance of abnormal DPOAEs. In addition, there is 85% probability that patients with CF and ototoxicity will have abnormal PT thresholds at ≤ 8,000 Hz or subjective tinnitus or dizziness.

These survey data indicate the following: CFF adult care facilities have identified possible cases of ototoxicity; most care facilities do not monitor; when performed monitoring usually involves only patient questionnaire and/or PT at ≤ 8,000 Hz and not per a specified protocol; and monitoring often is not conducted by an audiologist.

Based on these data, a minimum ototoxicity monitoring protocol is proposed in Figure 3. PT audiometry at ≤ 8,000 Hz in combination with patient questionnaire is a feasible and cost-effective means of audiologically monitoring the adult CF population; however, there is a large body of literature that recommends the use of DPOAEs or PT thresholds at > 8,000 Hz for earlier detection of ototoxicity.

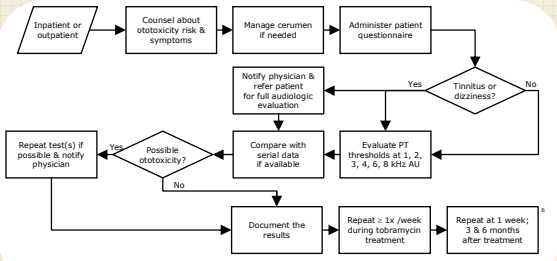

Figure 3. Proposed minimum ototoxicity monitoring protocol.

Abnormal DPOAE results were not confirmed using other tests. Ototoxic effects of other medications may be involved. Survey responses may not be an unbiased representation of the CFF adult care facilities.

CONCLUSIONS

- ❖ The incidence of ototoxicity found in this population is much greater than reported in the literature, emphasizing a need for increased awareness among the CFF adult care facilities.
- ❖ Minimally ototoxicity monitoring of adult CF patients should include PT thresholds at standard frequencies and a patient questionnaire; implementation of this protocol appears feasible and cost effective.
- ❖ DPOAEs also should be used for monitoring if possible.

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