Audiological Management of Ototoxicity

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Ototoxic Drugs

1- Approximately 200 drugs have been labeled ototoxic (Govaerts et al., 1990; Lien, Lipsett, & Lien, 1983, Rebuke, 1986).

2- Permanent or temporary damage

3- Varying degree

4- Those of greatest concern for permanent effects are the aminoglycosides and the chemotherapeutic agents

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Incidence of Drug-Induced Ototoxicity

1- Aminoglycosides-induced ototoxicity has been reported to range from 0% (Powell, Thompson, & Luthe, 1983) to 63% (tabl, Reyes, Rintelmann, & Lerner, 1984).

2- Cisplatin-induced ototoxicity from 3% (Forastiere, Takasugi, Baker, Wolf, & Kudla-Hatch, 1987) to 100% (Kopelman, Budrick, Sessions, Kramer, & Wang, 1988).
Aminoglycosides

1- It has been estimated that about **four million patients annually** are potentially at risk for hearing loss associated with aminoglycosides in the USA each year (Kumin, 1989).

2- Kanamycin & Gentamycin appear to be approximately equal in ototoxicity (47%), followed by tobramycin (32%), then netilmicin (24%)
Aminoglycosides

Aminoglycosides are cleared more slowly from inner ear fluids than from serum (Federspil, 1981), leading to a significant latency in the ototoxic effects following cessation of therapy (Gatell et al., 1984; Meyerhoff et al., 1989) thus:

1. Cumulative effect will be greater than what serum level reflects.
2. Serum levels do not reflect drug concentration in the perilymph.
Chemotherapy and Ototoxicity

Cisplatin (Platinol):

- Although very effective in treating a variety of cancers in adults and children, cisplatin is the most potent of known ototoxic drugs (Barr-Hamilton, Matheson, & Keay, 1991).

- It produces irreversible effects in the high frequency region of the cochlea (Fausti et al., 1993; Pollera et al., 1988)

- Other drugs including Ifosfamide, Loop diuretics potentiate cisplatin ototoxicity (McHaney et al., 1992)

- Prior radiation (McHaney, 1992)

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Carboplatin

An analogue of cisplatin, was developed as a less ototoxic alternative to its parent drug (Calvert et al., 1982), but adverse effects on hearing have since been documented (Kennedy, Fitzharris, Colls, & Atkinson, 1990; Wake et al., 1993).
HOW WE HEAR

- Nerve cells in the cochlea are tuned to specific frequencies
- Base of the cochlea is sensitive to high frequency sounds
- Tip of the cochlea is sensitive to low frequency sounds
HOW WE HEAR

- Sound waves cause the eardrum to vibrate
- Bones in middle ear transmit vibrations to cochlea
- Receptors (hair cells) in cochlea convert vibrations to electrical energy
- Brain interprets these electrical impulses as sound
**HOW WE HEAR**

17-year old girl
- **Low noise exposure**
- **Normal cochlea**
- **Receptors intact**

76-year old man
- **Low noise exposure**
- **Fewer receptors but still intact**

59-year old man
- **High noise exposure**
- **Damaged cochlea**
- **Receptors destroyed**
Identification of at-risk patients

1. Advanced age
2. Prior hearing loss or ear injury
3. Prior use, administration and concomitant use of ototoxic drugs
4. Liver failure
5. Renal failure
6. Vascular disorders that predispose to vascular occlusion or fat emboli: Leukemia, aplastic anaemia, autoimmune thrombocytopenic purpura, polycythemia, sickle cell
EOAEs

Evoked otoacoustic emissions (EOAEs) are considered a by-product of outer hair cells transduction and represent frequency region in the cochlea, in response to transient stimuli, that are detected as measurable sounds (release of energy) in the external auditory canal (EAC) (Kemp, 1980; Brownell, 1983)
EOAEs

- Pre-neural in origin and are dependent on outer hair cell integrity and movement.
- Outer hair cell movement is the source of generated mechanical energy propagated outward by the middle ear mechanisms and is measured by a microphone seated within EAC; in other words, a reversal of normal acoustic transduction (Kemp et al., 1978)
EOAEs

Because EOAEs are always present in a non-pathologic ear with normal hearing, their primary advantage is:

- objective evaluation of a frequency specific regions of the cochlea and
- a level of auditory sensitivity

Both parameters analogous to the pure-tone behavioral audiogram (Lonsbury-Martin and Martin, 1990)
Evoked Otoacoustic Emissions (EOAEs):

Evoked Otoacoustic Emissions (EOAEs) are a property of the ears of all normally hearing individuals.

This observation has been supported by the results of the following recent studies on human EOAEs:

Kemp et al (1986)
Harris & Glattke (1988)
Probst, Antonelli, & Pieren (1989)
Prevalence of EOAEs:

Kemp (1987)
Grandori (1983)
Kemp et al. (1986)
Probst et al. (1986)
Bonfils et al. (1988)
Stevens (1988)
EOAEs

• Thus, the presence of middle ear pathology or Organ of Corti dysfunction will reduce or eliminate the EOAEs.

• An objective measure of *peripheral auditory sensitivity* (Owens et al., 1992; Robinette, 1992).

• EOAE test is an excellent tool in the assessment of normal and *pathologic* cochlea.
Baseline testing

- Optimal timing for testing depends largely on the drugs the patient is receiving:

  **Aminoglycosides:** testing should be done prior to or within 72 hours of the first treatment dose (Brummett, 1983; Brummett & Fox, 1982; Fausti et al., 1992).

  **Cisplatin:** Prior to the first dose (Fausti et al., 1993).
Audiological Criteria for Ototoxicity:

Change in hearing sensitivity is always computed relative to baseline measures:

- ≥ 20 dB decrease at any frequency
- ≥ 10 dB decrease at any two adjacent frequencies.
- Loss of response at three consequetive frequencies.
- Reduction in amplitude or absence of EOAEs.


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Elements of Monitoring Ototoxicity:

1. Specific criteria for identification of ototoxicity.
2. Identification of at-risk patients.
3. Pre-treatment counseling regarding potential ototoxicity.
4. Valid baseline measures (pre-or early in treatment).
5. Monitoring testing at sufficient intervals to document progression or fluctuation of hearing loss.
6. Follow-up testing for post-treatment effects.
Monitoring schedule and follow-up:

- Immediate post-treatment to document auditory status at the end of drug treatment.
- Patients on aminoglycosides should be tested weekly.
- Patients on cisplatin should be tested 24 hour prior to each course of treatment.
- Follow-up testing at 3 and 6 months post treatment (Fausti et al., 1992; Beck, Maurer, Welkoborsky, & Mann, 1992; Plinkert & Krober, 1991)
Pre-treatment counseling

- Potential effects on auditory system
- Signs and symptoms of cochlear damage: tinnitus, fullness, dizziness, and hearing loss
- Potential effects on communications
- Avoid exposure to noise during and after chemotherapy

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Post-treatment Aural Rehabilitation:

If hearing loss results in communication deficits, the audiologist should recommend aural rehabilitation (including amplification, assistive listening devices, speech reading, and other modalities).

Intervention should begin as soon as possible after hearing loss has been identified.
Conclusions:

Hearing loss in the critically ill patients can lead to both short- and long-term disability. If the diagnosis is suspected in those at-risk for hearing loss, audiological intervention should be performed to monitor and to apply the rehabilitation measures.

Objective, easy to introduce audiological testing is available for this category of patients.

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