CONTINUING EDUCATION

EDUCATIONAL OBJECTIVES

After participating in this activity, clinicians should be better able to

- Define three risk factors for ototoxicity in cancer treatment in the pediatric population
- Identify the appropriate audiologic testing for infants and children
- Identify the mechanisms of ototoxicity of three types of ototoxic drugs
- List the preventive measures for ototoxicity

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Understanding ototoxicity risks for pediatric oncology patients

Karen MacDonald, RN, BSN, CPON

STATEMENT OF NEED/PROGRAM OVERVIEW

Hearing loss is one possible adverse effect of childhood cancer treatment. Partial or complete hearing loss can result in communication difficulties and impaired speech and language development. Most cancer treatments for children include agents that put patients at risk for ototoxicity. Knowledge of the risk factors for ototoxicity and understanding the appropriate interventions can help promote continued social and emotional development in these young patients.

CE INFORMATION

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CONTINUING EDUCATION

EDUCATIONAL OBJECTIVES

After participating in this activity, clinicians should be better able to

- Define the risk factors for ototoxicity in cancer treatment in the pediatric population
- Define the three main types of hearing loss
- Identify the appropriate nursing considerations in the care of a child with hearing loss

Understanding ototoxicity risks for pediatric oncology patients

Audiometric testing, awareness of the symptoms, and knowledge of which drugs are ototoxic are preventive measures for nurses to share with patients'

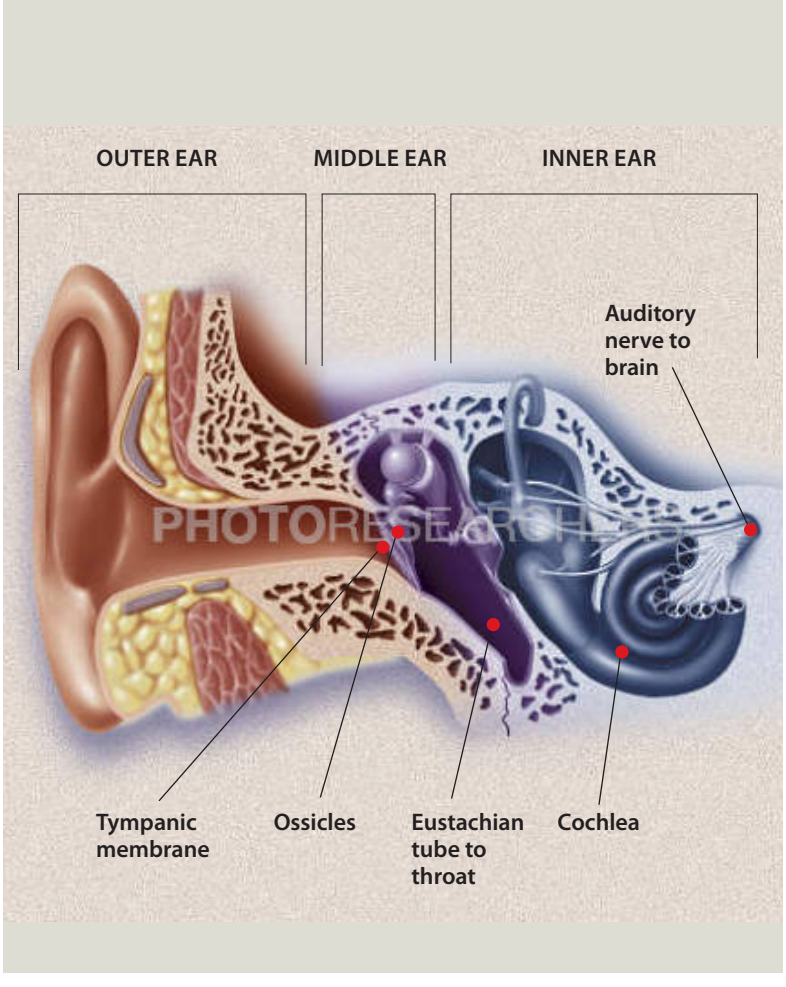

FIGURE 1. Anatomy of the auditory canal

KAREN MACDONALD, RN, BSN, CPON

Long-term survival is a likely outcome for children diagnosed with cancer today. As a result of improved cancer treatment and supportive care measures, more than 250,000 patients who had childhood cancer are survivors. The combined 5-year survival rate increased from less than 50% in the 1970s to the current rate of 80%.[1] The Children's Oncology Group (COG) estimates that 1 in 570 young adults aged 20 to 34 years is a childhood cancer survivor.[1] With these statistics is an increased awareness of the need to reduce the long-term effects of treatment and improve quality of life for these patients.

Hearing loss is one possible adverse effect of childhood cancer treatment. Partial or complete hearing loss can result in communication difficulties and impaired speech and language development. The time most conducive to learning language is before puberty. Children form a hypothesis about linguistic rules and apply them in their own way based on the language heard.[2] An inability to learn language skills in this way because of hearing loss may lead to delays in emotional and social development for the child. Most cancer treatments for children include agents that put patients at risk for ototoxicity. Knowledge of the risk factors and an understanding of the appropriate interventions

can assist the nurse with planning appropriate care for his or her patients.

HEARING AND HEARING LOSS

Sound waves entering the external auditory canal hit the tympanic membrane (eardrum) and cause the ossicles (auditory bones) of the middle ear to vibrate (**Figure 1**). The vibration of the ossicles moves the fluid within the cochlea. Inside the cochlea is the organ of Corti—this holds hair cells. The movement of the fluid in the cochlea stimulates these hair cells, which are nerve receptors for hearing. Specific hair cells react to specific sound frequencies; therefore, the pitch determines which hair cells are stimulated. Signals from the stimulated cochlear hair cells are then transformed into nerve impulses and transmitted to the brain via the acoustic nerve. These hair cells cannot regenerate; any damage that occurs to them is permanent.[3]

The three main types of hearing loss are described according to the site of damage. *Conductive* hearing loss is a result of damage to the outer or middle ear that prevents sound waves from progressing into the inner ear. Conductive loss is usually temporary, often a result of fluid in the middle ear or otitis media. *Sensorineural* hearing loss is the result of damage to the inner ear or the auditory nerve. This loss can make accurate perception of speech difficult. A mixed hearing loss is the third type. In this case, both conductive and sensorineural components disrupt the transmission of sound.[3]

RISK FACTORS IN PEDIATRIC ONCOLOGY PATIENTS

Several factors place a pediatric oncology patient at risk for ototoxicity: presence of CNS tumor, radiation treatment, diminished renal function, IV infusion of ototoxic agents, and age 3 years or younger at the time of ototoxic agent administration.[4,5] Agents considered to be ototoxic include platinum-based chemotherapy agents, loop diuretics, and aminoglycoside antibiotics (**Table 1**). Aminoglycosides and loop diurectics have a synergistic relationship. The risk of damage to the organ of Corti is greater if an aminoglycoside is administered prior to a loop diuretic.[3,4,6]

Radiation therapy directed at the head is a risk factor for ototoxicity; therefore, hearing loss is a symptom of a brain tumor as well as an adverse effect of its treatment. Radiation therapy-related hearing loss ranges from self-limiting to irreversible, especially if the patient's tumor is a midline, pontine, or brainstem lesion. The loss can be sudden or manifest 3 to 10 years after completion of therapy. Radiation therapy-related hearing loss is conductive through fibrosis or thickening of the tympanic membrane and the ossicles. Otitis media and tinnitus are self-limiting conditions caused by radiation therapy. Atrophy of the organ of Corti and the auditory nerve can cause sensorineural hearing loss. In rare cases, irreversible profound hearing loss manifests up to 8.5 years after radiation therapy to the brain.

The child's age at treatment is a significant factor. The auditory system in children 3 years and younger is still developing and therefore more susceptible to damage. The pharmacokinetics of platinum chemotherapy are different in younger children as well, which may result in slower clearance and increased exposure to the drug.[7] Lastly, many chemotherapeutic agents are nephrotoxic, and diminished renal function is associated with an increased risk of ototoxicity.

Tinnitus and vertigo indicate vestibular injury and impending hearing loss; however, many children are asymptomatic. A parent or caregiver may notice that a young child does not turn toward sound or a teacher may notice inattentiveness at school. High-frequency hearing loss is indicative of future loss in the speech ranges if ototoxic therapy continues, in some cases with as little as one additional course.[6]

TABLE 1. Ototoxic effects of chemotherapeutic agents

Class	Drug(s)	Adverse effect	Results
Platinum-based chemotherapy	• Carboplatin (Paraplatin, generics) • Cisplatin (Platinol, generics)	Destruction of outer sensory hair cells followed by inner sensory hair cells in the cochlea	• Irreversible sensorineural hearing loss initially in the high frequencies then progresses • Ototoxicity in 23%-54% of patients receiving cisplatin
Loop diuretics	Furosemide (Lasix, generics)	Electrolyte and/or enzyme changes in inner ear	• Loss can develop quickly; however, usually reverses after treatment cessation • Problems with nerve transmission caused by fluid changes within the inner ear • Transient severe deafness, tinnitus, and high frequency hearing loss
Aminoglycoside antibiotics	• Gentamicin (Garamycin, generics) • Tobramycin (Nebcin, generics)	Destruction of outer sensory hair cells of cochlea, occurs most commonly during prolonged serum trough levels of drug	• Usually irreversible high-frequency hearing loss

TABLE 2. Age-appropriate audiometric tests

Age	Auditory test	Measurement obtained	Interpretation	Nursing considerations
Birth to 9 mo	BAER	Electrophysiologic measurement of function of auditory nerve pathway	Hearing evaluated by reviewing the size of the peaks and time to form them	• 15-min test • Child must be asleep/sedated • Electrodes placed on child's head record electrical response to sound stimuli
9 mo to 2.5 y	VRA[a]	• Child will turn head when sound is introduced at specific frequencies • Head turns are reinforced with a lighted toy	• Assesses hearing of better ear, if earphones are worn • Evaluates hearing of frequencies ranging from 500-4,000 Hz	• 30-min test • Child sits on parent's lap between two speakers or wears earphones • Test performed in sound-proof room
2.5-5 y	Play audiometry[a]	Auditory thresholds in response to speech or specific tones	Assesses child's auditory perception	• 30-min test • Child performs a repetitive task each time sound is heard • Earphones used (if child refuses to wear earphones, test is administered in a sound field)
≥5 y	Conventional audiometry[a]	Auditory threshold in response to brief clicks	Assesses child's auditory perception	• 30-min test • Child raises hand when sound is heard • Earphones are used
All ages	OAE	Cochlear hair cell response to auditory stimuli	Determines whether hearing loss is present	• 10-min test • Cannot determine degree of hearing loss • Results can appear normal in children who received carboplatin because drug affects inner cochlea hair cells only • Signals are generated by the cochlear hair cells

[a] Extended high-frequency audiometry may be performed. Test is extended to include 8,000-20,000 Hz. Used to check for early changes in hearing.

Key: BAER, brainstem auditory evoked response; Hz, Hertz; OAE, otoacoustic emissions test; VRA, visual reinforcement audiometry.

MONITORING OTOTOXICITY

Several audiometric tests are available for monitoring treatment effects on hearing, and the type utilized is based on the child's age, state of health, and ability to cooperate. **Table 2** lists audiometric tests with their appropriate ages for administration.[3] Baseline measures are obtained before initiating treatment. Typically, newly diagnosed cancer produces great anxiety and stress for the family; therefore, explaining why the hearing test is being performed and what to expect not only reduces anxiety but may instill the child's cooperation.

The Children's Oncology Group guidelines for monitoring audiometric measures throughout treatment recommend that high-risk patients be tested before each course of platinum-based chemotherapy. Patients who are considered high-risk are 3 years or younger, have received radiation to the brain or ear, received a diagnosis of CNS neoplasm, are currently receiving ototoxic or investigative agents, or have received a cumulative dose of more than 360 mg/m^2 of cisplatin (Platinol, generics) or a cumulative dose of more than 1,000 mg/m^2 of carboplatin (Paraplatin, generics). All other children are considered to have a lower risk and should undergo hearing tests before every other course of platinum-based chemotherapy.

All patients should undergo auditory tests at least 3 weeks after completing a course of platinum-based chemotherapy because hearing deficits may be delayed. In addition, patients should be tested 6 to 8 weeks after their final chemotherapy course. Annual audiometric testing is recommended for children who are off treatment and had received platinum-based chemotherapy and/or radiation to the ear, midline of brain, or brainstem. However, children older than 8 years who are able to self-report symptoms can undergo screening every other year. COG also recommends that children who have been treated with aminoglycoside antibiotics and loop diuretics should undergo periodic audiometric testing, depending on the frequency and duration of treatment with these agents.[6]

Results of visual reinforcement audiometry (VRA), play audiometry, and conventional audiometry are plotted on an audiogram (**Figure 2**). Pitch frequency, which is measured in

Hertz (Hz), is plotted on the horizontal axis from lowest to highest (left to right, respectively); sound intensity, which is measured in decibel (dB), is plotted on the vertical axis from softest to loudest (top to bottom, respectively). The audiogram provides a representation of the softest sounds a patient can hear at a particular frequency, known as the *threshold*. An X represents air conduction threshold from the left ear, and an O represents air conduction threshold from the right ear. Lower plot points indicate reduced hearing. **Figure 3** is an audiographic representation of degree of hearing loss. Typical conversation produces sound at approximately 60 dB, and a whisper produces sound at approximately 30 dB.[8]

NURSING INTERVENTIONS FOR HEARING-IMPAIRED PATIENTS

Nursing care for a child with hearing deficits centers on providing support and guidance and should be directed toward making the child feel at ease. Maintaining eye contact, smiling, and using nonthreatening body language are actions that can establish trust and enhance rapport with the patient. Educating the patient's family about support services and assistive devices that are available can help them adjust to their child's hearing loss.[4]

There are a variety of technologic devices available for the child who has a hearing loss. An auditory trainer, or FM trainer, is a listening device that allows a child to receive audio output directly from the teacher or parent into their hearing aid. This device reduces any background noise. Many school districts have these available in the classrooms.[4,6] Other assistive devices include telephone amplifiers, text telephones, closed captioning, and adaptive appliances. The family of a child who wears hearing aids should be instructed to have the devices refitted every 6 months and that most batteries need to be replaced every 1 to 2 weeks. Nurses should also assess the family for any educational needs in regards to cleaning and care of hearing aids.[4]

Patients and families should also be educated about community and educational resources that may be available to them. In the United States, hearing impairment is considered a disability. In-home speech and occupational therapy, as well as specialized daycare placement, are available for children from birth to 3 years who have a hearing loss. An individualized family service plan (IFSP) is required for this age group. An IFSP outlines the interventions that can maximize the child's abilities. Children older than 3 years are eligible for placement in the public education system. Individualized education plans (IEPs) are developed to outline specific interventions and goals for the child.[6] The Centers for Disease Control and Prevention (CDC) Web site lists links to Web sites that provide family support services (www.cdc.gov/ncbddd/hearingloss/links.html).

PREVENTIVE MEASURES

Recent studies indicate that ototoxic therapy-related hearing loss ranges from minimal to more than 80%. **Table 3** lists various preventive measures.[9]

The American Speech-Language-Hearing Association (ASHA) states that noise and ototoxic therapy have a synergistic relationship. Patients should be instructed to avoid excessively noisy situations (ie, loud music or television) during treatment and for 6 months after completion of treatment. Apple offers a program that limits the maximum volume on its iPods. The

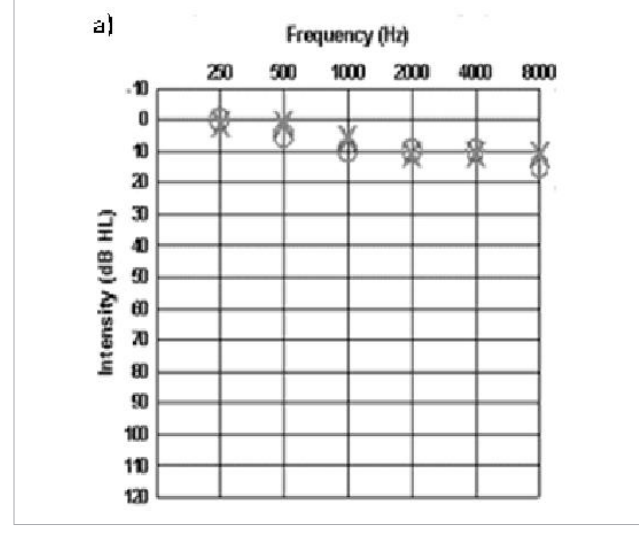

FIGURE 2. Audiogram depicting normal hearing to a slight loss

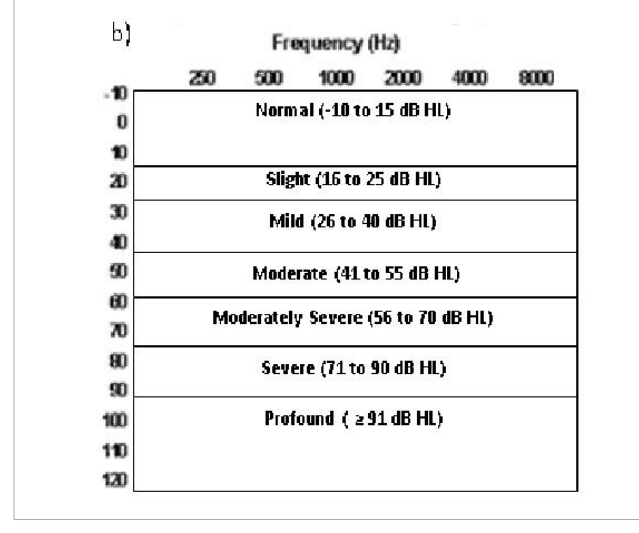

FIGURE 3. Degree of hearing deficits mapped on an audiogram

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TABLE 3. Ototoxicity preventive measures

Therapy	Preventive measure
Platinum-based chemotherapy	Monitor cumulative dosage (cisplatin, ≤360 mg/m^2; carboplatin, <1,000 mg/m^2)
Loop diuretics	• Avoid rapid infusion • Recommendation administration: <4 mg/min
Aminoglycoside antibiotics	Keep trough levels <2.5 µg/mL for gentamicin and tobramycin and <7.5 µg/mL for amikacin
Radiation	• Cochlear shielding for use of high-energy linear accelerators to avoid hot spots in the ear • 3D (IMRT) is conformal, XRT can delivery radiation to intended site while avoiding surrounding tissues • Administer platinum-based therapy before radiation and avoid platinum-based therapy after radiation

Key: IMRT, intensity modulated radiation therapy; XRT, external radiation therapy.

program can be downloaded for free from www.apple.com/ipod/download, and it works with any headphone or accessory that is plugged into the iPod headphone jack.[9]

Researchers are investigating amifostine (Ethyol, generics) and sodium thiosulfate (Nithiodote) as otoprotectant agents for pediatric oncology patients. The medications are used in conjunction with cisplatin and carboplatin. Initial COG trial results on the otoprotective features of amifostine are disappointing; however, sodium thiosulfate is promising and is currently in clinical trials. Oxaliplatin (Eloxatin), a cell cycle nonspecific platinum-based chemotherapy agent, has been found somewhat effective in treating pediatric patients with refractory solid tumors without achieving significant ototoxicity.[10] The major side effects of oxaliplatin are numbness or tingling sensation in the mouth, throat, arms, and legs (may be worse with cold temperatures); stomach cramps; diarrhea; and constipation. Patients should avoid drinking or eating cold food or liquids during administration.[11]

CONCLUSION

Children undergoing cancer treatment are at great risk for adverse effects both during and after therapy. Ototoxicity is one potential adverse effect. The pediatric oncology nurse should have knowledge of the risk factors and understand the appropriate interventions in order to promote continued social and emotional development in this population. ■

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