Vestibulotoxicity

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Background

Imbalance caused by drug-induced damage to the vestibular system ("vestibulotoxicity") is a significant cause of morbidity and mortality

Vestibulotoxicity can lead to limited mobility and social isolation, falls, injury, and death (Rogers 2011)

Unlike hearing loss, imbalance cannot be treated with an implant.

Ototoxic medications may more commonly affect balance function than auditory function (Handelsman 2017)

Degree of hearing loss does not correlate with degree of vestibular damage (Handelsman 2017)

Vestibular anatomy and physiology

- The inner ear's *semicircular canals* respond to head rotations and *otolith organs* respond to head tilt
- Cilia projecting from thousands of "hair cells" in each inner ear respond by bending in opposite directions. The difference between the ears corresponds to the amount of rotation or tilt
- The brain uses this information to move the eyes to compensate for head movement (the "vestibulo-ocular reflex") and to help maintain postural stability
- If the hair cells or the neurons leading from the hair cells to the brain are damaged, the inner ear is less sensitive to rotations or tilts. This reduces visual acuity during head movements and causes imbalance. Asymmetric damage leads to a sensation of rotation (vertigo)

Vestibulotoxic medications

- Many aminoglycoside antibiotics, especially gentamicin, tobramycin, and streptomycin, are ototoxic (DiSogra 2019)
- Aminoglycosides are commonly used in subacute bacterial endocarditis, sepsis, cystic fibrosis, non-tuberculous mycobacterial infections, and multi-drug-resistant bacterial infections
- Some antineoplastic agents, such as cisplatin or carboplatin, may also be vestibulotoxic (Prayuenyong 2018)(Baguley 2020)
- Very limited evidence links vestibular loss to the use of loop diuretics, macrolide antibiotics, and arsenic-based antineoplastic agents

Diagnosis of vestibulotoxicity (Handelsman 2018)

- Patient symptoms are NOT reliable indicators.
  - Patients may attribute their disequilibrium to their disease itself, other medications, or deconditioning whereas very sick patients are often bedridden and unable to perceive any imbalance
  - Patients may have severe symmetric bilateral loss despite a reassuring lack of vertigo
  - The brain may compensate somewhat, masking the true extent of vestibular loss
- Serum drug levels are NOT correlated with vestibulotoxic effects

Diagnosis of vestibulotoxicity (Handelsman 2018)

- Bedside tests:
  - Head impulse (or “head thrust”)—do patient’s eyes keep up when moving head rapidly?
  - Dynamic visual acuity—can patient can read eye chart while moving head?
  - Romberg—can patient stand on an unstable surface?
- Laboratory tests:
  - Video head impulse
  - Caloric
  - Rotational chair
  - Vestibular-evoked myogenic potential

Prevention of vestibulotoxicity

- Use of other medications, when possible
- Regular monitoring of function (Rogers 2011; Handelsman 2018). This is often done with bedside dynamic visual acuity testing, where the patient reads an eye chart while moving the head side to side. A loss of more than three lines of acuity may indicate vestibular damage
- Substitution of second-line therapy when needed
- Use of chemoprotective drugs such as antioxidants (experimental)
- Careful pre-dosage counseling as to possible side effects and encouraging attention to development of imbalance during treatment (Leis 2015)

Treatment of vestibulotoxicity

- Vestibular damage rarely recovers spontaneously
- Physical therapy is the mainstay of treatment (Meldrum 2019)
  - Recalibrates brain to reduced vestibular input, increasing sensitivity and restoring normal reflexive eye movements
  - Enhances use of other balance-related sensory inputs, such as vision and proprioception
- Vestibular prosthesis (currently in human trials) (van de Berg 2020)
- Genetic or chemical therapies to reconstitute vestibular hair cells (experimental) (Forge 2020)

Citation

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Hullar, T; Konrad-Martin, D; Nofstker, K; Hulswit, J. (2020). “Vestibulotoxicity”. VA RR&D National Center for Rehabilitative Auditory Research (NCRAR)

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