KeurCompany versterkt mensen

OAE en blootstelling aan chemische stoffen...een eerste verkenning

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onderdeel van ARBONED

Inhoud

1 Even voorstellen…

PERSONALIA

- Senior Bedrijfsarts Werkzaam bij Keur Company
- Advisering biologische monitoring gevaarlijke stoffen/ PMO op projectbasis
- Docent Bedrijfsartsopleiding PAOG Heyendael te Nijmegen
- Expertisecentrum Organo psycho syndroom
- Lasrookdeskundige
- Bestuurslid Contactgroep Gezondheid en Chemie
- Expert www.Arboantwoord.nl

2 Inleiding

Interactie ototoxische stoffen en lawaai relatief "nieuw vakgebied"?

- G.P.Pryor e.a.: (1983):hearing loss in rats exposed to toluene
- Barregard en Axelson (1984): interaction noise and solvents ship yard
- Bergstrom Nystrom (1986): hearing loss in paper mill highest with solvent exposed
- Morata (1997): toleen induced hearing loss among rotogravure workers

- "heavy smoking interacts synergistically with noise" (Patty)
- "Chemicals, in different ways,can interact with noise to cause hearing loss" (Patty)

America (ACGIH) Advise Monitoring US Army (1998)

- Initiation enrollment when there is excessive exposures to ototoxins
- Monitoring (same as noise exposure)

Nederland (2009)?

- In Nederland wordt nog geen onderzoek gedaan naar gehoorschade door combinatie van ototoxische stoffen en geluid

OAE de ideale test?

- Schade door Ototoxische stoffen direct meetbaar met OAE!

NB: In de praktijk nauwelijks monitoring van gehoor bij blootstelling aan ototoxische stoffen en geluid

3 Wat is Ototoxiciteit en hoe uit het zich?

Ototoxiciteit

- Schade aan de gehoorcellen door chemische stoffen

NB: sluipend !

Klachten

- Gehoorverlies: meestal beginnend bij hoge tonen
- Hyperacusis (= overgevoeligheid voor geluid)
- Tinnitus (= oorsuizen/piep/ruis in het oor)
- Vergering bestaande tinnitus
- Vertigo (= draaierigheid)

4 Ototoxiciteit: hoe vaak komt het voor?

We weten het niet…?

Schatting 15,000 to 160,000 ototoxische stoffen…(medicatie, chemicaliën en/of zware metalen)

Ototoxische medicatie

- 75% is gering ototoxisch: 1 of 2 per 1,000
- 22% matig ototoxisch: 10-20 per 1000
- 3% ernstig ototoxisch: 100-200 per 1000

5 Historie ototoxische stoffen

Table 1. Some drugs known or implicated to cause ototoxicity

Therapeutic class	Ototoxicity recognized	Examples
Heavy metals	11th century	mercury
Antimalarial drugs	1843	quinine, chloroquine
Non-steroidal anti-inflammatory drugs	1877	salicylate (aspirin), fenprofen, ibuprofen, indomethacin, naproxen, phenylbutazone, sulindac
Anthelmintics	late 19th century	oil of chenopodium (worm seed oil)
Arsenicals	early 20th century	atoxyl, salvarsan
Aminoglycosides	1945	streptomycin, amikacin, gentamicin, kanamycin, neomycin, netilmicin, paromomycin, tobramycin
Other antimicrobial agents	1960s	chloramphenicol, colistin, erythromycin, minocycline, polymyxin B, vancomycin
Loop diuretics	1960s	ethacrynic acid, bumetanide, furosemide
Industrial solvents and chemicals	1970s	toluene, organotins, carbon monoxide, potassium bromate
Topical disinfectants	1970s	chlorhexidine
Antineoplastic drugs	1970s	bleomycin, carboplatin, cisplatin, dichloromethotrexate, nitrogen mustard, vinblastine, vincristine
Chelating agents	after 1980	deferoxamine

6 Mechanismen ototoxiciteit

Mechanismen (voorbeelden)

- Potentiëring door geluid!!!
- Herhaald ontsteking leidt tot cel schade

- Remming K pomp (lis diuretica)
- Remming calcium channels
- Membraan permeabiliteitsveranderingen
- Verminderde endocochleaire potentiaal door O2 tekort

- Oxidatieve metabolisme OHC<
- Prostaglandinde inhibitie (NSAID, quinine)
- Remming enzymen: cyclooxygenase, fosfolipase A2
- Remming van eiwitsynthese

- Verminderde cochleair bloedtoevoer: ischemie
- Oedeem van de stria vascularis (lis diuretica)
- OHC turgor daling
- Vorming van vrije radicalen (Cisplatina, vinblastine,vincristine)
- …

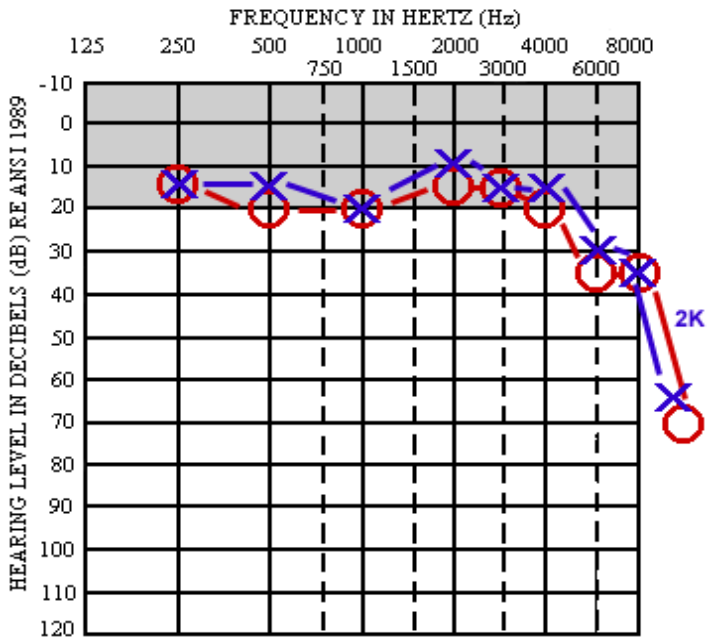
NB: er is nog weinig bekend over de exacte mechanismen…
NB: interactie door lawaai en andere ototoxische stoffen

7 Beroepen met blootstelling aan ototoxische stoffen

Branches

- Brandweer
- Chemische industrie
- Electrotechniek
- Galvaniseerbedrijven
- Gieterijen
- Houtbewerking
- Kunststofindustrie
- Lijmproducenten
- Metaalbewerking
- Schilders/coating
- …

8 Gentamicin : audiogram



- Typical audiogram of person exposed to gentamicin. Hearing is commonly normal through 4000 hz, and then **falls off at higher frequencies.** Often persons with significant vestibular damage from gentamicin do not notice any change in their hearing

8 Gentamycine : trilhaarschade

9 Literatuur en internet

Literatuur

- Neil G Bauman Ototoxic Drugs exposed (ISBN 0-9710943-1-4), 2e edition 2003
- Patty's Toxicology, 5e editie 2001

Internet

- Google: "chemical induced hearing loss"

10 Vragen?

Vragen mag altijd…!

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Bijlage 1: Ototoxische Drugs

Aminoglycosides
- Amikacine
- Gentamicine
- Kanamycine
- Neomycine
- Paromomycine
- Streptomycine
- Tobramycine
- …

Lis diuretica
- Acetazolamide (Diamox)
- Bumetamide (Bumex)
- Ethacryne zuur (Edecine)
- Furosamide (Lasix)
- …

Anti malaria middelen
- Quinine
- Chloroquinine
- …

Bijlage 1: Ototoxische Drugs (Vervolg)

Chemotherapeutica
- Bleomycine
- Carboplatin
- Cisplatin
- Dichloormetotrexaat
- Nitrogen mustard
- Vinblastine
- Vincristine
- …

Pijnstillers/Ontstekingsremmers
- Aspirine
- Fenprofen
- Ibuprofen
- Indomethacine
- Naproxen
- Phenylbutazon
- Sulindac
- …

Bijlage 2: Ototoxische Oplosmiddelen

Alcoholen
- Ethanol
- Methanol

Aromatische koolwaterstoffen
- Benzeen
- Ethylbenzeen
- N-Propylbenzeen
- Styreen
- Tolueen
- Xyleen

Alifatische koolwaterstoffen
- n-Hexaan
- Heptaan

Fuels (jet fuel,benzine

Gechloreerde koolwaterstoffen
- Monochloormethaan
- Tetrachloorkoolstof
- Trichloorethyleen
- Perchloorethyleen

Nitrobenzeen

White spirit

Bijlage 3: Ototoxische metalen

Metalen

- Arseen (pesticiden)
- Cadmium (galvaniseren)
- Chroom VI (lassen, galvaniseren)
- Cobalt (lassen)
- Kwik
- Lood
- Mangaan
- Trimethyltin (antifouling, PUR foam,rubberindustrie,fungicide)
- …

Bijlage 4: Ototoxische stoffen: Pesticiden en overig

Pesticides

- Arseen
- Hexachloorcyclohexaan (Lindaan)
- Organofosfaten (triorthocresylfosfaat)
- Paraquat
- Pentachloorfenol
- …

Overig

- Bromaten
- Koolstofdisulfide=zwavelkoolstof (vezelindustrie)
- Zwaveldioxide?
- Zwaveltrioxide?
- …

Bijlage 5.1 Arsenicum

- Most commonly found in the manufacturing of parasite and micro organism inhibitors
- Arsenic over exposure results in disorders in the Organ of Corti beginning at the apex
- **Hearing losses are greater in the lower frequencies at 125, 250, and 500 Hz**
- Balance problems are also noted

Bijlage 5.2 Carbondisulfide

- Used in solvents and insecticide, the auditory site of lesion is most often retro cochlear
- In noise levels of 86 to 89 dBA, the incidence of hearing loss was 47 % within two years. With three years of exposure the incidence rose to 71%
- Common dysfunctions include abnormal acoustic reflex and central vestibular disorders
- A typical audiogram for carbon disulfide exposure **shows losses in the high frequencies, however, a large number of subjects show additional loss in the lower frequencies regardless of age**

Bijlage 5.3 Koolmonoxide

- In low-dose, oxygen deprivation can result in mild threshold shifts **in all frequencies** usually temporary
- In high-dose, carbon monoxide there are histological changes in the Organ of Corti resulting in oxidative metabolism of the inner ear
- Carbon monoxide is synergistic with noise resulting in large threshold shifts at all frequencies

Bijlage 5.3 Kwik

- Mercury is found in solder, the manufacturing of thermometers and detonators.
- Injury occurs in the early and middle stages in the cochlea with sensory cell destruction. In later stages the injury is retro cochlear as well.
- Hyperadditive with noise, the loss is commonly bilateral with auditory processing difficulties.
- **Hearing loss is in the entire range with greater losses in the high frequencies.** However, loss does not always occur even with severe neurological symptoms. Hearing loss reportedly occurs 80% of the time

Bijlage 5.4 Lood

- This metal causes a demyelination of CN. VIII leaving the cochlea unharmed
- **All frequencies show loss with a greater loss in the high frequencies**
- Vertigo is often a symptom
- It has also been noted that the longer exposure to lead the greater the severity of the hearing loss

Bijlage 5.5: Manganese

- Found in battery manufacturing, electroplating, and the processing of ferrous metals
- The auditory site of lesion is unknown
- However, manganese results in a loss in **both the low and high frequencies with the mid range showing better hearing**

Bijlage 5.6: Organotin

- Organotins are used as heat stabilizers for polyvinyl chloride in piping, siding and window casings
- Also used as catalysts for polyurethane foam, marine paint, wood preservative, fungicides and in the poultry industry.
- TMT hearing losses are possibly reversible and can cause cochlear lesions
- TET results in decreased myelin content in CNS and white matter edema with a rapid onset

Bijlage 5.6: Styrene

- Styrene is used in the production of plastics, synthetic rubber, resins and insulating materials
- Exposure results in sensory cell damage with abnormal acoustic reflex and abnormal ABR
- Lower concentrations of styrene show **losses above 8K Hz** and do not indicate loss other than noise

Bijlage 5.7: Toluene

- 2.6 million metric tons are produced annually via air pollution and auto emissions
- Toluene is the most studied organic solvent. It is used in the manufacturing of chemicals, paints, lacquers, adhesives, rubber, rotogravure printing, leather tanning, spray painting, glue, etc.
- It produces cochlear damage
- The synergistic effects can result in an increased risk 27.5 times
- Balance problems and abnormal acoustic reflexes are significant symptoms
- The audiogram configuration can be flat, bilateral or unilateral; however **the most common configuration is a dip at 3K to 6K Hz** (as noise) even in the absence of noise

Bijlage 5.8: Trichloorethylene

- This solvent is used as a degreaser, dry cleaning agent, spot remover and rug cleaner
- It is used in the production of paints, waxes, pesticides, adhesives and lubricants
- Destruction of sensory cells of the inner ear is suspected
- It results in a bilateral symmetrical high frequency dip **beginning at 2K or 3K Hz and is** associated with balance problems

Bijlage 5.9: Xylene

- Known as the most prevalent, exposing more people, and the most toxic of all the organic solvents, xylene is found in paints, varnishes, and thinners
- It produces damage in the sensory cells of the inner ear