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Review

Ototoxicity and Noise

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Abstract: In most cases, hearing loss is the result of exposure to high levels of noise for extended periods of time or as an effect of aging. Although this is found in most situations, hearing can also be damaged by certain chemical agents in pure state, or as a combination. These chemicals can even include parts of drugs used for the treatment of illnesses for which there are no other remedies. Ototoxic chemicals are also found in the workplace, in most occasions as solvents. The effects from these elements are worst when combined with exposure to a high level of noise. This paper examines the effects of these chemicals in isolation or in combination with noise and gives recommendations on how to deal with this problem.

Keywords: hearing conservation; hearing loss; ototoxicity

1. Introduction

"Ototoxicity is the property of being toxic to the ear (*oto-*), specifically the cochlea or auditory nerve and sometimes the vestibular system, for example, as a side effect of a drug" [1]. In practical terms, ototoxicity deals with chemical agents that may affect hearing in general but also the body equilibrium.

The existence of such agents is nothing new. Avicenna (Abu Ali al-Husayn ibn Abd-Allah ibn Sina Balkhi), the Persian philosopher and medical scholar, is considered to be the first person to describe the harmful effect of a chemical substance on ear function. In his Canon of Medicine, completed almost 1000 years ago, he warned that when mercury vapor was used to combat head lice, the host could be deafened by the treatment.

The effects from high noise levels can be enhanced by the presence of ototoxic agents, therefore increasing the risk of hearing loss. Thus, it is so important to deal with this problem.

The American Congress of Governmental Industrial Hygienists (ACGIH) state in their TLV Documentation for Audible Sound that: "While audiometric data is useful for any worker exposed to any measurable level of a chemical substance, yearly audiograms are highly recommended for workers whose exposures are at 20% or more of the TLV for the substance in question. This 20%, while somewhat arbitrary, will ensure data from sub-TLV exposures." [2].

The Occupational Safety and Health Administration (OSHA) standards require employers to limit exposure to the specific substance to or below the permissible exposure limit (PEL). However, synergistic effects from the combined ototoxicant and noise exposure could result in hearing loss even when exposures are below the PEL [3].

Several European countries as well as Australia recommend that when ototoxic agents are present in the workplace, the daily noise exposure level should be reduced to 80 dBA instead of 85 dBA (the existing standard) [4].

The situation is quite complex, since ototoxic chemicals are used in everyday life as well as in the workplace. In the latter, noise and ototoxic chemicals are present in activities as diverse as painting, printing, boat building, construction, furniture making, manufacturing of metal and fiberglass, leather and petroleum products, aircraft maintenance, assay labs, radiator repair, fueling vehicles and aircraft,

fire-fighting, pesticide spraying, weapons firing, etc. Therefore, it is possible that a detected hearing loss may not be solely due to excessive noise, but also to the presence of ototoxic substances [5].

2. Studies on This Subject

A quick look through the bibliography on the hearing effects of ototoxic chemicals and noise shows that the bulk of studies deal with pharmaceutical drugs and that many studies are carried out either by modeling or using animals.

3. Effects from Noise and Ototoxic Chemicals

There are many differences and similitudes between noise and ototoxic agents regarding their entry into the human body and their effects thereafter.

As is well known, noise is a single physical agent where the external ear canal is the port of entry, basically affecting the cochlea. In general, the progression of noise induced hearing loss ceases when the noise is eliminated. There are, however, some data suggesting a progression of cochlear and possibly neural dysfunction even after the noise exposure was terminated [6].

In contrast, the number of known ototoxic chemical agents (alone or in combination) is in the thousands. There are not one, but three routes of entry: ingestion, inhalation and skin penetration. The effects occur not only in the cochlea and the semicircular canals, but on the central nervous system as well. The effects can go well beyond hearing acuity, resulting in compressed loudness, reduced frequency, and temporal resolution and diminished spatial resolution, as well as dizziness and tinnitus.

The effects of some ototoxic chemicals (alone or in combination with noise) continue even after the cause is removed: The mechanism is most likely a combination of cochlear and neural involvement.

Unlike noise induced hearing loss, the auditory effects of chemical exposure may not be bilateral or even symmetrical. As with the noise induced hearing loss, it most likely occurs first in the high frequency region. The effects are also related to the individuals' exposure history: The longer and the higher the exposure, the greater the effects.

Synergetic and additive effects may occur when chemical ototoxic agents and noise are both present. The synergetic effect from the combination can be larger than if the two were acting separately. The additive effect occurs when the effect of both participants is equal to the sum of the individual effects. The most studied combination is that of noise and solvents.

4. Ototoxic Substances

The list of recognized and suspected ototoxic substances is quite extensive, especially when considering that they may also be a part of a complex compound. Also, the exact knowledge of their "safe" limits is scarce. As mentioned above, studies in toxicity involving humans are very few and far between. There are many animal studies, but questions remain of how their results can be applied to humans [7].

In general, ototoxic substances are grouped into:

1. Pharmaceuticals drugs:
    (a) Aminoglycosides (streptomycin, kanamycin, neomycin, gentamicin, tobramycin, amikacin and netilmicin, commonly used to treat gram-negative bacterial infections).
    (b) Platinum-derivates (cisplatin and carboplatin anti-cancer drugs).
    (c) Loop diuretics (ethacrynic acid, furosemide and bumetanide, widely used as part of the treatment for high blood pressure and swelling due to congestive heart failure).
    (d) Acetyl salicylic acid (aspirin; >2.5 g/day).
    (e) Anti-tuberculosis drugs (e.g., Amikacin).
2. Aromatic solvents.
3. Asphyxiate gases.

4. Metals and compounds.

Substances from the first group (ototoxic pharmaceutical drugs) are probably the most well-known. Despite the risk of hearing disorders, they are used to treat serious health conditions for which they may be the only remedy [8,9].

Among the solvents, the main culprits are usually styrene, toluene, xylene and trichloroethylene. All of these solvents are extensively used in many industries. The combined exposure of solvents and noise increases the risk of occupational hearing loss in a synergistic (more than additive) manner, especially if the noise is impulsive in nature.

Among the gases, those most often cited are the asphyxiants that interfere with cell respiration. In animal models, they are not toxic when acting alone, but can become ototoxic when combined with high levels of noise. The only exception appears to be CO from smoking, which presumably is implicated in hearing loss, even in the absence of noise exposure.

The list of metals includes lead, cadmium, arsenic, manganese, cobalt, tin, platinum and copper. Among them, lead has been often cited as the cause for the deafness of Beethoven. Apparently, it was used to improve the taste of wine, something the great composer was addicted to.

To complete the list, we should also add some pesticides and PCBs; all of these studies are based on animal models only.

5. Recommended Actions

Typically, we should be concerned with what we can do to reduce/eliminate the effects of ototoxic substances. The answer lies in the implementation of a hearing conservation program.

As in any hazard management program, the first step is determining if the substance(s) is (are) present in the workplace. If that is the case, the measurement of the exposure of the workers will indicate the degree of the hazard.

Limiting the exposure is the obvious second step. This should be done by implementing engineering measures or through the compulsory use of personal protective equipment. The latter requires an in-depth search of existing appropriate equipment and then a proper training of its use for the exposed personnel.

The last step is the introduction of a thorough audiometric program to ensure that there are no adverse effects from the substances and noise in the workplace. The program should be more thorough than what is traditionally carried out when only high noise levels are present.

It is important to have management and workers aware of the combined effects of noise and chemicals. Their exposure should be reduced to "safe" levels that are recommended to be lower than the maximum permissible levels, when only noise or only ototoxic chemical are present.

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