

Noise Induced Hearing Loss: The Impact of Acoustic Trauma on the Ear

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Abstract

Noise-induced hearing loss (NIHL) is a pervasive disability that affects millions of people across the world. It is characterized by a decrease in hearing sensitivity to sounds that fall between 3000–6000 Hz (known as the “notch”). NIHL is caused by either a sudden acoustic trauma or long-term exposure to noise levels above 85 dB. The noise exposure induces overproduction of free radicals within the cells of the cochlea, overpowering of the ear’s antioxidant defense systems. The free radicals then destroy cell membranes and hair cell nuclei, causing necrosis and apoptosis, leading to hair cell death. This upsets the mechanical structure and the metabolic homeostasis within the ear, impeding hearing function. Studies have shown that some people are more susceptible to NIHL, either due to environmental factors or genetic factors. NIHL is preventable; OSHA and the EPA have sought to regulate sound levels on job sites and encourage the use of hearing protective devices at work, and researchers are developing new imaging tests to accurately diagnose NIHL before severe hearing loss sets in. There are also ongoing studies regarding the prophylactic and therapeutic use of pharmacological agents (antioxidants and glucocorticoids) and vitamins in the prevention and treatment of NIHL. This paper is a review of the literature available on NIHL and the ongoing studies related to diagnosis, treatment, and genetic factors in the disorder. The literature was found on a number of research databases, with most of the source material coming from the Academic Search Complete (EBSCO) database.

Introduction

Millions of people across the globe are exposed each day to acoustic overstimulation – noise – in their daily activities, whether at their jobs or during their leisure activities. Noise is one of the most common sources of environmental stress, and it can cause both mechanical and metabolic damage to an individual’s ear. As a result, noise-induced hearing loss (NIHL) is a disability that is widespread among individuals exposed to either prolonged loud noise or excessively loud noise. More than 600 million people around the world endure excessive noise at their jobs and are thus at risk for NIHL. Millions more expose themselves to excessive noise during leisure activities, particularly when listening to or playing music, and they too place themselves at risk to developing NIHL.

The susceptibility to NIHL has been shown to have both environmental and genetic factors. Environmental variables that increase a person’s likelihood of developing NIHL include noise exposure that is combined with extreme temperatures, chemical solvents, and prolonged vibration. Individual environmental factors including smoking, high blood pressure, and high cholesterol levels, have also been shown to increase an individual’s risk of developing NIHL. Currently, the genetic factors that increase a person’s susceptibility to NIHL are largely unknown. Many animal studies are currently ongoing to identify genetic polymorphisms linked with NIHL.

This paper will explore how noise impacts both the mechanical structure of the ear and the metabolic processes within the ear. Additionally, it will examine recent and ongoing studies regarding the genetic factors that increase a person’s susceptibility to developing NIHL, as well as the preventative and therapeutic interventions that are currently in use or being tested in experimental stages.

Methods

The information in this paper was synthesized from literature reviews and studies published in peer-reviewed journals. The articles were selected using databases, primarily the Academic Search Complete (EBSCO) database made available through the Touro College virtual library. Data was extracted according to relevance, with special attention given to NIHL statistical data; mechanical and metabolic disruption in the ear as a result of noise trauma; and the diagnosis, treatment, and genetic factors related to NIHL.

Discussion

The word noise is derived from the Latin word *nausea*, which means “impulsive, unwanted, and unpleasant” (Taneja, 2014). In medical terms, noise has been defined as a “physical agent capable of causing damage to the human body with the short and medium term effects” (Metidieri et al., 2013). Sound is measured in units known as decibels (dB), and normal sounds are generally less than 75 dB and are unlikely to cause any damage to the ear or cause hearing loss. However, sounds that are higher than 85 dB can cause physical damage to the structures of the ear. This includes excessively loud noises that are short and sudden, such as gunshots or explosions. Moreover, an individual who is frequently exposed to noises that are continuously and moderately loud can experience damage to hearing structures that results in NIHL. NIHL can involve functional limitations for a number of hearing processes, including “changes in frequency selectivity, temporal and spatial resolution, recruitment, and tinnitus as well as changes in hearing sensitivity” (Metidieri et al., 2013). NIHL is the second most common hearing loss after age-related hearing loss (Levey et al., 2012).

Excessive noise in public areas has been called noise pollution, and it is considered an environmental problem along with other forms of pollution, such as smog or water pollution. In fact, noise pollution affects the largest number of people worldwide, according to the World Health Organization (WHO) (Metidieri et al., 2013). In research on NIHL, noise is classified in three categories: (i) continuous noise, which is noise that persists for minutes or hours at about the same level of intensity; (ii) impact noise, which is a high level but short duration noise that occurs when two objects collide; and (iii) impulse noise, which is a high level but short duration noise that results from an explosion or gunfire (Bielefeld, 2015). NIHL can be diagnosed as either acoustic trauma or chronic NIHL. Acoustic trauma is defined as a sudden but permanent hearing loss caused by a one-time exposure to a forceful sound, with sound pressure levels of approximately 130–140 dB. The extent of damage after an acoustic trauma will vary from mild to profound. In contrast, chronic NIHL results from gradual exposure to less forceful noise over an extended period of time, and this can result in either mild or profound hearing loss (Rajguru 2012).

Approximately 25% of workers across the globe are exposed to noise levels that can induce NIHL. It is the most common work injury (Metidieri et al., 2013). Noise exposure is often experienced with other causal agents of NIHL, including chemical exposure. For example, when an individual is exposed to carbon monoxide and noise simultaneously, he has a higher risk of developing NIHL, even though exposure to carbon monoxide alone rarely induces hearing loss (Kashani et al., 2011). Smoking cigarettes while being exposed to noise both raises the risk of NIHL and increases the extent of the hearing damage. This may be due in part to the carbon monoxide exposure related to cigarette smoke (Liuyan et al., 2013). Other causal agents include vibrations, medications, and one's individual susceptibility to hearing loss (Metidieri et al., 2013).

The National Institute for Occupational Safety and Health (NIOSH) estimates that in the United States alone, there are 5–30 million workers who are exposed to dangerous noise levels each year (Bielefeld, 2015). NIHL is an insidious condition, as those exposed to loud noise are generally unaware that damage is occurring until it is too late (Levey et al., 2012). It is characterized by a decrease in hearing sensitivity to sounds that fall between 3000–6000 Hz (known as the “notch”). The decrease in hearing sensitivity is often asymmetric. Typically, there is greater hearing loss in the left ear than in the right ear (Phillips et al., 2010).

Individuals from all segments of the population are at risk for NIHL, though there is a higher prevalence among men (Pelosi, 2014). Among Americans aged 20–69, there are 23 million people (12.8% of this demographic) who have NIHL (Bielefeld,

2015). However, the risk of developing NIHL is unrelated to age (Phillips et al., 2010). In fact, the pervasiveness of NIHL rises steadily over childhood and adolescence (Pelosi, 2014). The American Academy of Audiology estimated in 2008 that one in eight children has sustained NIHL. In 2010, a similar estimate was made in which 16% of teenagers were thought to have sustained NIHL. Among younger demographics, NIHL is typically caused by exposure to excessively loud music over an extended period of time, particularly on personal listening devices such as iPods, MP3 players, or CDs. Children's toys that emit loud sounds have also been found to cause NIHL. A study conducted with 329 student musicians between the ages of 18 to 25 years found that 45% of the students had sustained NIHL, with 78% of the hearing loss happening at 6000 Hz (Levey et al., 2012).

Noise exposure at work is often associated with factory workers who spend their working hours in cramped spaces with loud, industrial machinery. However, there are less conventional occupations that have high risk of NIHL as well. As many as 60 percent of military personnel involved in active duty return home with NIHL or tinnitus, and have both (Pelosi, 2014). This is likely due to their excessive gun use (Berg et al., 2014). Firefighters, too, are at high risk for NIHL, as the noise they are exposed to regularly is usually high in intensity and short in duration (Hong et al., 2013).

Individuals who do not work in noisy environments or listen to loud music can also be at risk for NIHL in their daily lives. Neitzel et al. found that New York City subway riders are exposed to noise louder than the limits recommended by WHO and the United States Environmental Protection Agency (EPA). This presents a heightened risk for NIHL to those who use mass transit often, especially those who remain on the subways for a longer period of time (Nietzel et al., 2009).

Mechanical Structure and Metabolic Processes of the Ear

The prevalence of NIHL demonstrates how the ear is a complex and vulnerable organ. The cochlea is the inner ear organ that converts sound for the process of hearing. The cochlea holds the organ of Corti, which is comprised of hair cells that serve as the sensory receptors of sound. There are two types of hair cells: inner hair cells and outer hair cells. The inner hair cells use the auditory nerve to communicate with the brain to create sound perception. The outer hair cells amplify sound, increasing hearing sensitivity by ~40 dB. The organ of Corti also contains a number of supporting cells that form the physical structure of the ear that is necessary for the mechanical movement that occurs when sound waves reach the ear.

The organ of Corti requires metabolic homeostasis to properly convert sound waves and auditory signals. Noise exposure can

Figure 1

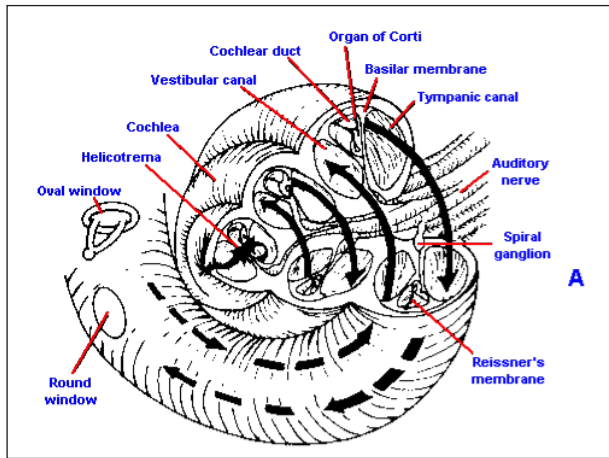


Figure 2

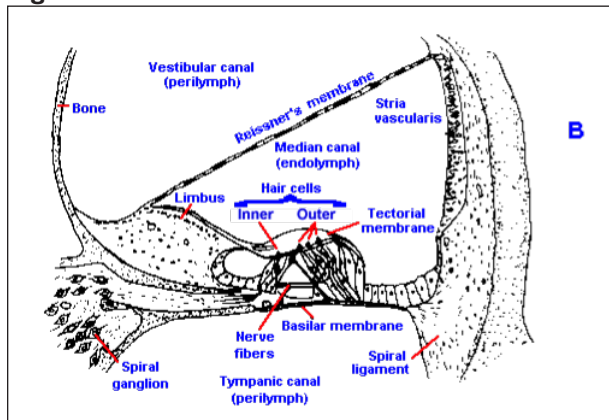


Figure 1: Diagram of the cochlea cut through along the modiolus. Arrows demonstrate the pathway of pressure waves that originate in the oval window. (Curtis et al., 1970)

Figure 2: Cochlear partition and the organ of Corti. (Curtis et al., 1970)

damage the cochlea both metabolically and mechanically, and NIHL can occur from either metabolic or mechanical deterioration, as well as from a combination of both (Bielefeld, 2015). (Figures 1 and 2)

Normal Ear Function

The hearing process is a complex series of steps that occurs when a sound is emitted. Sound waves travel to an individual's ear, where the hair cells act as receptors for the energy from sound waves and then convert the sound waves into nerve signals that reach the brain (Pelosi, 2014). Sound waves first enter the outer ear and then traverse the ear canal to reach the eardrum. When the sound waves strike the eardrum, it begins to vibrate, and the vibrations reach the middle ear. In the middle

ear, bones (also known as "ossicles") called the malleus, incus, and stapes, amplify the sounds. The vibrations are then sent to the inner ear, known as the cochlea, which is a fluid-filled organ with an elastic membrane known as the basilar membrane. Attached to the basilar membrane, there are sensory cells, known as outer and inner hair cells. The vibrations that reach the inner ear generate a traveling wave that runs along the basilar membrane as a result of the electromotility of the outer

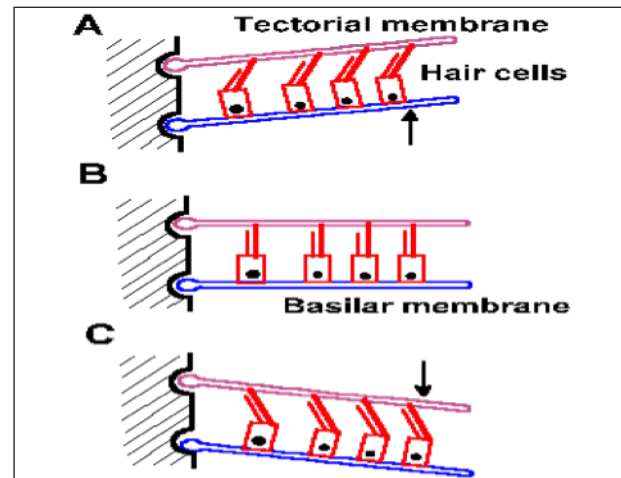


Figure 3:
Movements of the basilar membrane and the deflection of the stereocilia:
A. Upward movement of the basilar membrane (arrow) deflects hairs away from the modiolus.
B. The basilar membrane is at rest is
C. Downward movement (arrow) deflects hairs toward the modiolus. (Klinke, 1978)

hair cells. The movement induces stereocilia, spiky structures on the apical surface of the inner hair cells, to rub up against the tectorial membrane and thus release neurotransmitters that travel across the synapse between the inner hair cell and the auditory nerve. Figure three depicts these movements. This process allows for sound waves to change into electrical signals that are carried to the brain by the auditory nerve, and the brain allows the individual to perceive the sound he is hearing (Levey et al., 2012).

Development of NIHL

Most cell populations in the cochlea are vulnerable to noise damage. Noise can impair or kill: the pillar cells, which provide the structural support for the organ of Corti; the fibrocytes of the lateral wall, which allow potassium recycling necessary for the depolarization of the hair cells; and the outer and inner hair cells, which are vital for reducing hearing thresholds, discriminating between sound frequencies, and delivering auditory information to the brain. The synapses between the inner hair

cells and afferent auditory nerve neurons are also susceptible to noise damage, and damage to these synapses can result in long-term auditory nerve neuropathy (Bielefeld, 2015). An individual with NIHL will experience deterioration of the ciliated cells of the organ of Corti (Metidieri et al., 2013). Figure 4 shows the destruction of a region of the organ of Corti. The noise exposure induces overproduction of free radicals. While free radicals are often present in cells, they can be destructive when they are overproduced, resulting in an overpowering of the ear's antioxidant defense systems. These free radicals are made up of reactive oxygen species (ROS) (Levey et al., 2012). ROS are molecules with an odd number of electrons and thus highly reactive and destructive to the body. The accumulation of ROS causes damage to the mitochondria, which is the driving force of the cell and produces more than 98% of the energy used in our bodies. When ROS impair the mitochondria, they lose their capacity to produce energy. Ultimately, this reduces the amount of energy available for normal inner ear function, causing hearing loss (Seidman, 1999).

When the ear is exposed to excessive noise, the outer hair cells in the cochlea require high levels of energy and consume more oxygen. This generates a number of byproducts that mix with other molecules in the cochlea to generate high levels of ROS. This upsets the metabolic homeostasis of the cochlea. Additionally, the ROS then destroy cell membranes and hair cell nuclei, which causes tissue death (necrosis) and apoptosis (cell self-destruction), ultimately leading to hair cell death. Once it is dead, the hair cell will break into pieces, and this upsets the mechanical structure of the ear. Eventually, the hair cells are replaced with scar tissue. While the scar tissue ensures that the basilar membrane of the ear remains intact, it cannot play a role in the hearing process, and thus the individual with NIHL will experience hearing loss (Levey et al., 2012).

Cochlear microcirculation is vital for hearing transduction. Sensory hair cells of the cochlea are at risk of ischemia during noise exposure, and studies have shown that inadequate blood flow is associated with the development of NIHL. An important component of cochlear microcirculation is the diameter of the spiral modiolar artery, a branch of the anterior inferior cerebellar artery, which meets the lateral cochlear wall to form the striavascularis. The spiral modiolar artery has been shown to constrict during and after noise exposure (Arpornchayanon et al., 2013), and this is an additional cause of NIHL.

Another contributing factor in the development of NIHL is calcium homeostasis in the cochlea. Calcium plays the role of second messenger in a cell's physiological activities, and an upset calcium homeostasis has been linked to trauma-induced neuronal injury (Bao et al., 2013). In the cochlea, calcium participates

in a number of functions, including mechano-electric transduction, hair cells' voluntary contractions, the inner ear's frequency selection, basal membrane vibration, and the release of neurotransmitters (Liu et al., 2012). Calcium homeostasis is sustained through a number of different calcium channels, including voltage-gated calcium channels (VGCCs). VGCCs are comprised of two groups: high-voltage-activated (L-type) and low-voltage-activated calcium channels (T-type) (Bao et al., 2013). L-type VGCCs provide access for calcium to enter hair cells and are essential for the regulation of calcium homeostasis. After noise exposure, the levels of calcium in hair cells have been shown to increase, and an excessive amount of calcium in a cell has been linked to cell injury and cell death. Thus, too much calcium in the cochlea, brought on by excessive noise, has been linked to NIHL (Liu et al., 2012).

Genetic link

Although there is much research about the link between environmental agents and NIHL, less is known about the genetic basis for the impairment. Various animal studies have provided significant evidence of a genetic predisposition for NIHL. Mitochondrial dysfunction and ROS production have been shown to play significant roles in neurodegenerative conditions. As ROS overproduction is a result of noise exposure, mitochondrial genes and endogenous antioxidant defense-related genes have been thought to be the genes associated with NIHL. There are a number of antioxidant enzymes at work in the cochlea. Glutathione-S-transferase (GST) enzymes catalyze the conjugation of glutathione with xenobiotics and are vital for antioxidant protection. GST is comprised of a number of gene classes (GSTA, GSTM, GSTP, GSTT, GSTZ, GSTS, GSTK, GSTO). Humans have genetic variability of GSTM1 and GSTT1. For example, approximately half of the European population has null genotypes for GSTM1, and 25–40% of Europeans do not have GSTT1. A person with a null genotype is unable to conjugate certain metabolites for these enzymes, and this makes him or her more susceptible to damage from oxidation. Therefore, it has been suggested that an individual with a null genotype is more likely than his peers to develop NIHL when exposed to excessive noise (Liu et al., 2012).

There are also genetic mutations that reduce susceptibility to NIHL. A1555G in MTRNR1 is the mitochondrial mutation most frequently linked to hearing loss, typically with aminoglycoside-induced deafness and non-syndromic deafness. MTTSI is another mitochondrial gene with a number of mutations. A1555G or other mitochondrial variants in the MTRNR1 and MTTSI have been suggested as factors that lessens susceptibility to NIHL.

Abreu-Silva et al. conducted a study to evaluate genetic factors

in susceptibility to NIHL. The researchers compared persons with NIHL and persons without NIHL, as well as their family history of hearing loss and whether they had genetic mutations that have been linked with hearing loss (including deletions in GSTM1 and GSTT1, A1555G in the MTRNR1 gene). Their sample was comprised of 255 bus drivers and workers at a printing facility in São Paulo, Brazil. Both groups were regularly exposed to excessive noise. The subjects of the study included 107 people whose audiograms showed NIHL, 44 people with hearing impairment and audiograms that did not show NIHL, and 104 people with normal hearing. Data was collected regarding each subject's age, regularity of noise exposure, family history of hearing loss, alcohol consumption, smoking habits, and geographic origin of their ancestors. Subjects also provided blood samples for DNA screening and genotyping. The researchers found that family history of hearing loss is significantly associated with NIHL, which supports a genetic susceptibility to the impairment. Moreover, the researchers found that the existence of at least one allele in both genes (GSTM1 = 1/? and GSTT1 = 1/?) increases the risk of NIHL, and that individuals of mitochondrial haplogroup L1 were disproportionately affected by NIHL. However, no significant findings were made regarding variants in the MTRNR1 and MTTST1 genes (Abreu-Silva et al., 2011).

Additional research on the genetic susceptibility to NIHL has focused on Human 8-oxoG DNA glycosylase I (hOGG1), a key enzyme in the human base excision repair pathway. NIHL occurs as a result of DNA damage to cochlear hair cells, causing necrosis and apoptosis. At the same time, a number of DNA repair pathways, including base excision repair, help to maintain the integrity of the cell and stave off cell death. This DNA repair has been shown to be essential in maintaining hearing after noise exposure.

The 8-oxoguanine (8-oxoG) DNA lesion, which is caused by the overproduction of ROS, is a common cause of oxidative damage associated with NIHL. HOGG1 in the base excision repair pathway eliminates 8-oxoG. Research has suggested that the Ser326Cys polymorphism (rs1052133) in exon 7 of hOGG1 gene can impact the activity of hOGG1 enzyme and thus may be useful as a genetic marker for vulnerability to different diseases. Shen et al. conducted a study to evaluate whether there is a link between the hOGG1 Ser326Cys polymorphism in the human base excision repair pathway and susceptibility to NIHL. The researchers genotyped 615 workers with NIHL and 615 normal hearing workers in China. The workers had not been regularly exposed to any other causal agents of NIHL, like chemical solvents, heat, or vibrations, and they had no other medical conditions that could have impacted their hearing.

The researchers found that the hOGG1 Cys/Cys genotype was statistically associated with NIHL. There was a higher number

of persons with the hOGG1 Cys/Cys genotype among NIHL workers than among normal hearing workers, suggesting the hOGG1 Cys/Cys genotype may have a lesser capacity for restoring 8-oxoG damage, and thus a higher susceptibility for NIHL. The researchers also found that the hOGG1 Ser326Cys polymorphism had a synergistic effect when combined with noise exposure time, noise exposure level, whether the individual is a smoker, and whether the individual drinks alcohol regularly (Shen et al., 2014).

Diagnosis

Early detection of NIHL would help decrease the social and economic burdens related to the condition (Meinke et al., 2013). Moreover, early detection can help stop the progression of hearing loss and prevent damage to speech frequencies (i.e., 500, 1000, 2000 and 3000 Hz) (Mehrparvar, 2011). NIHL is diagnosed when an individual is found to have a hearing level change, compared to a baseline audiogram, of an average of 10 dB or more at 2000, 3000, and 4000 Hz in either ear (Levey et al., 2012). Generally, NIHL results in hearing loss in the higher frequencies (3000-6000 Hz), so during hearing tests, hearing loss is observed at 4000 Hz with improvement in hearing at 8000 Hz. However, among elderly patients, the improvement at 8000 Hz is often lost, and this presents difficulty in determining whether the hearing loss is from NIHL, age, or another cause. Tympanometry is used to test the condition of the middle ear. Asymmetric hearing losses are evaluated using a brainstem auditory evoked response or a high resolution CT scan of the inner ear and internal auditory canal (Seidman, 1999).

Researchers are currently evaluating a potential new means of diagnosing and monitoring NIHL known as distortion product otoacoustic emission (DPOAE) level mapping. The goal of DPOAE is to detect early signs of cochlear damage and then track changes in cochlear function, but the maps have mostly been used in trials with animals. A study was conducted in which they performed DPOAE level mapping on 17 individuals without a history of noise exposure and then compared the results to maps created with 19 individuals with mild/moderate NIHL. The DPOAE maps presented accurate data in a color pattern, a "visual snapshot" of cochlear function between the frequencies of 0.5 kHz and 6.0 kHz. This graphic form of data presentation enables for more detailed data collection and supports rapid comparison of maps for an individual. With further research, DPOAE maps may become the standard tool for detecting and monitoring NIHL (Meinke et al., 2013).

Prevention

NIHL is not a new phenomenon. Reports from as early as 600 B.C. tell of the Sybarites, who prohibited metal-working or the possession of roosters within their city limits due to the dangers

of excessive noise. Other historical documents show that individuals living near the waterfalls of the Nile River experienced more hearing loss than those at a greater distance from the waterfalls' noise (Seidman, 1999). NIHL is an impairment that is both avoidable and foreseeable (Metidieri et al., 2013). The implications of NIHL can extend beyond hearing loss; it can result in the development of a range of secondary diseases, including hyperacusis (over-sensitivity to certain frequency and volume ranges of sound), tinnitus, or depression related to social isolation (Tziridis et al., 2014).

The federal government has long sought to regulate noise exposure and prevent NIHL. In 1936, the Walsh-Healey Public Contracts Act was instituted to oversee workplace noise exposure, though it was not properly enforced. In 1970, the Occupational Safety and Health Administration (OSHA) was founded to both monitor and regulate workplace noise exposure. Currently, OSHA allows for exposure to 90 dB for 8 hours a day, while the EPA allows for a level of 85 dB. However, on-the-job inspections are typically infrequent, and fines for noise-level violations are often low.

The key to preventing NIHL is avoiding damaging noise exposure (Seidman, 1999), beginning with an assessment of risk of an environment. It is advisable to have workers rotate tasks to ensure that no individual is exposed to continuous hazardous noise over an extended period of time (Singh et al., 2012). Additionally, acoustic attenuation devices or engineering controls can be used to reduce the noise dose to which an individual is exposed (Bielefeld, 2015). If sounds often go above 85 dB, hearing protection is essential to preventing damage. OSHA mandates the distribution of free hearing protective devices (HPDs) in work places such as these. Protective devices may include ear plugs or ear muffs (Pelosi, 2014). Earplugs can reduce between 10 dB and 22 dB of sound diminution, and protective earmuffs can reduce sound by 20-55 dB. When earplugs are used together with earmuffs, the benefit is additive (Seidman, 1999).

However, there are a number of barriers to the use of HPDs. First, many work sites require ongoing communication with colleagues, and this is hindered by the use of ear protectors. Additionally, Reddy et al. (2012) conducted surveys with workers in high-noise environments, and their findings suggest that there is a "fatalist belief among workers that noise is an acceptable and unavoidable part of the job." This perception often leads workers to avoid using HPDs, not recognizing that these devices can prevent permanent hearing loss (Reddy et al., 2012). Hong et al. (2013) explain that the perceptual factors involved in HPD use include perceived self-efficacy, perceived benefits, perceived barriers, perceived susceptibility to hearing loss, and perceived severity of hearing loss. In a study conducted by Nodoushan et al. (2014), HPDs were found to be used more frequently and more

effectively when workers received training about the reasons for HPD use, as well how they can be properly fitted in the ear.

In addition to HPD use, scientists continue to investigate a number of less conventional approaches to reducing the damage from noise exposure. Experimental methods for preventing NIHL include reducing body temperature, stimulating a number of neural structures, treatment of the ear with a number of compounds, increasing oxygenation, interfering with ROM activity, and sound conditioning. In some cases, these alternative approaches have achieved partial protection. In particular, the concept of sound conditioning has received a lot of attention from scientists. Conditioning allows for the toughening of the cochlea through exposure to non-damaging levels of sound before being exposed to noise trauma. Resistance can develop after the exposure to stimuli that varies in duration, frequency, and continuity. This is due to brain and nerve adaptability; during sound conditioning, the cochlea's outer hair cells perform similarly to a muscle (Seidman, 1999).

Treatment

Research has also focused on the use of pharmacological agents in the prevention and treatment of NIHL. While there is no widely-accepted protocol for pharmacological treatment of NIHL, there are a number of ongoing research studies that are testing substances on both animals and humans, including antioxidants that decrease oxidative stress by eliminating ROS; glucocorticoids; and agents that improve cochlear blood flow, stimulate inhibitory transmitter systems, or obstruct apoptosis pathways in hair cells (Tziridis et al., 2014).

There are a number of antioxidants currently being tested for their efficacy in both preventing and treating NIHL. The antioxidant α -tocopherol has been shown to reduce the noise-induced damage in guinea pigs (Kashani et al., 2011). N-Acetyl-L-Cysteine (NAC), an antioxidant which has been shown to inhibit lipid peroxidation and destroy ROS by increasing levels of glutathione within the cell, has been found in a number of animal studies to be effective in treating NIHL if given immediately after noise exposure (Rajguru, 2012).

Antiepileptic drugs and glucocorticoids are also being tested in the treatment of NIHL. Bao et al. conducted a study regarding prophylactic treatment of NIHL. Their study sought to reduce the risk of NIHL by administering anticonvulsant drugs to block T-type calcium channels in the organ of Corti, and thus prevent an injurious disturbance to calcium homeostasis that may occur after exposure to noise. This approach had been found to be effective in protecting neurons after a stroke. The researchers administered to mice two anticonvulsant drugs - ethosuximide and zonisamide - to block T-type

calcium channels, and then exposed them to high levels of noise. The mice were also administered synthetic glucocorticoids, dexamethasone and methylprednisolone (Bao et al., 2013). Glucocorticoids were used because they activate the enzyme Na, K-ATPase, which has been linked to restoring cellular osmolarity and neuronal conduction. Additionally, glucocorticoids have been found to be effective in both cells and dendrites (Rajguru, 2012).

In Bao et al.'s (2013) study, the anticonvulsant drugs and the glucocorticoids were administered after the noise exposure as well to assess whether the drugs had any therapeutic effect after noise-induced trauma. The researchers found that anticonvulsant and glucocorticoid drugs could have both a prophylactic and therapeutic effect, and that there was a synergistic prophylactic effect when the drug families were used together (Bao et al., 2013). Further studies are necessary to ascertain whether the drugs would have the same effect in preventing and treating NIHL in humans.

Vitamins and minerals are also being tested in the prevention and treatment of NIHL. Studies show that magnesium has both a prophylactic and therapeutic effect on noise-induced injuries. In the cochlea, levels of magnesium are essential for preventing disruption in cochlear microcirculation and oxygenation and for protecting against free radicals. Clinical trials are ongoing to assess whether application of magnesium to the inner ear, together with the administration of an antioxidant, can prevent and reduce hearing damage after a noise-related trauma (Rajguru, 2012).

Tziridis et al (2014) conducted a study on the use of ginkgo biloba extract EGb 761 to prophylactically treat NIHL and tinnitus in the Mongolian gerbil. Their study results demonstrate the neuroplastic effects of EGb 761 on central and peripheral levels of auditory processing when given prophylactically to gerbils exposed to noise. The researchers posit that the antioxidant effect of EGb 761 provides protection against NIHL. Additionally, EGb 761 was shown to increase blood flow, so it provides a protective effect against noise exposure, which can decrease blood flow in the cochlea. While EGb 761 has not yet been tested on humans, the results of the gerbil study are promising (Tziridis et al., 2014).

Another agent being tested in the prevention and treatment of NIHL is vitamin B12. Vitamin B12 is an essential cofactor in methylation of myelin basic protein and cell membrane phospholipids and also important in methionine synthesis from homocysteine. There have been studies that have shown that individuals who have low levels of vitamin B12 and folic acid are more susceptible to hearing loss caused by noise exposure. When there is a B12 deficiency, there can be axon degeneration and neuronal loss. Kibar et al. (2013) theorize that supplementary B12 can decrease

homocysteine synthesis in the cochlea, increase concentration of nitric oxide, and thus cause the blood vessels to dilate. As such, the B12 may be able to induce increased vascular perfusion and cellular metabolism within the cochlea. In a study Kibar et al. (2013) conducted with guinea pigs, they were not able to show a significant decrease in hearing loss when the guinea pigs were treated with B12. However, studies are ongoing to determine the efficacy of B12 treatments in preventing and minimizing the damage of NIHL (Kibar et al., 2013).

Hyperbaric oxygen therapy (HBOT) is also being considered for its use in treating NIHL. HBOT can be used to improve oxygenation in the inner ear, and thus improve microcirculation and attenuate injured cochlear hair cells. HBOT can infuse hypoxic areas of the cochlea with oxygen, which can work to speed up cellular mechanisms necessary for recovery. There are ongoing studies that are evaluating the impact of HBOT on NIHL, as well as the combined use of HBOT and glucocorticoids (Rajguru, 2013).

Conclusion

Though the effects of noise exposure have been known within the medical community since the 1960s, the general public remains largely unaware of the long-term effects of both sudden and gradual noise trauma. In a study conducted with American respondents, only 16% of those surveyed reported that they had read about or heard about NIHL in newspapers or other media forums. In another American-based study, 72% of respondents admitted that they never wear hearing protection when they are exposed to loud noises, even though they are aware that noise exposure can be harmful (Ramma, 2011).

It has been said that an ounce of prevention is worth a pound of cure, and this maxim is especially relevant in regards to NIHL. It is essential that the general public is made aware of the damaging effects of noise exposure, both on the job and during recreational activities. While studies related to the prophylactic and therapeutic intervention for NIHL are promising, there is currently no widely-accepted treatment protocol and no known cure. As such, it is imperative that OSHA and EPA guidelines are adhered to in all areas of work, and that HPDs are employed during occupational hazards and leisure activities. Moreover, it is essential that people recognize that their ears are vulnerable to injury, and they should be protected from unnecessary – and often irreversible – damage.

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