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Cochlear Mechanisms in Noise Induced Hearing Loss

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Abstract

One of the most common causes of hearing loss depends on noise overexposure. Noise is a stress factor that has auditory, psychological and physiological effects. Noise causes overproduction of stress hormones, sleep disturbances and impairment of cellular immunity. The effect of noise that inflicts organic damage on the human hearing system varies depending on intensity, and duration of the noise and individual susceptibility. There are several anatomical and physiologic abnormalities caused by noise overexposure. These abnormalities vary from the minimal loss of metabolic activities of hair cells and stiffness of stereocilia to total loss of organ of corti and the auditory nerve. The opportunity to treat and prevent noise induced hearing loss may increase with the clarification of the mechanism of cochlear damage in noise. Understanding of these mechanisms is important for development of new agents for treatment or prevention of noise induced hearing loss. In this report, we reviewed the pathological changes of the cochlea in noise induced hearing loss in the light of the literature.

Keywords: Hearing loss, noise-induced cochlea, mechanism of action

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Introduction

One of the most common causes of hearing loss is noise overexposure. Noise is a stress factor that has auditory, psychological and physiologic effects. Noise causes overproduction of stress hormones, sleep disturbances and impairment of cellular immunity [1]. The interest in noise induced hearing loss (NIHL) increased with the increase of awareness about the effects of sudden, loud or chronic noise exposed in social and work environment. NIHL is a preventable health problem in which both genetic and environmental factor acts together. The intensity and frequency of the noise and the type of noise exposure (sudden, continuous) determines the level and duration (temporary, permanent) of hearing loss, and the affected frequencies [2]. The effect of noise that inflicts organic damage on the human hearing system varies depending on intensity and duration of the noise and individual susceptibility. The first remarkable audiological sign after noise overexposure is high frequency hearing loss which typically occurs at frequencies 3000 Hz, 4000 Hz and 6000 Hz. With the increase in hearing loss, other frequencies may be involved. The highest loss occurs in 4000 Hz. There are several anatomical and physiologic abnormalities caused by noise overexposure. These abnormalities vary from the minimal loss of metabolic activities of hair cells and stiffness of stereocilia to total loss of organ of corti and the auditory nerve. The main abnormalities include metabolic tiring of hair cells, structural changes and degenerations of hair cells, morphological changes of cilia, ruptures of cell membranes, and complete degenerations and loss of hair cells, neural cells and supporting cells. The cochlear injuries caused by noise overexposure may be divided into two groups as primary and secondary injuries. The primary histological changes include degeneration of hair cells, especially outer hair cells. Secondary changes follow primary ones. The progressive degenerations of supporting cells are followed by degeneration of afferent neuron fibers. The best solution of blocking primary damage is preventing from loud noise [3]. In this manuscript, we aimed to discuss the cochlear pathological changes in noise induced hearing loss.

Material and Methods

Studies over years suggested that noise may cause important physical changes in cochlea, which may led to temporary threshold shift (TTS) or permanent threshold shift (PTS). After noise overexposure, the ability of stereocilias to transform mechanical energy to electrical

energy decreases due to loss of permeability of protein channels located at the cell membrane [4]. The stereocilias and their tips may be broken or may attach each other [5]. The tips of stereocilias of outer hair cells may separate from tectorial membrane, which causes loss of sensitivity [6]. These changes in stereocilias led to TTS. If the noise can be prevented or blocked at this stage, these changes are reversible. If the noise continues, irreversible changes including loss of supporting cells and afferent nerve fibers occur, which is called as PTS. The most important structural change in PTS is damage and loss of stereocilias [7].

Noise overexposure causes swelling and rupture of dendritic terminals of afferent nerve fiber via the mechanism of glutamate excitotoxicity. Glutamate is an excitatory neurotransmitter working in the synapse between the inner hair cells and auditory nerve fibers. In the situation of noise overexposure, the over stimulated inner hair cells produce more glutamate to the synapse, which tends to overstimulation of postsynaptic glutamate receptors. This is called excitotoxicity and is characterized by swelling of the postsynaptic cells and dendrites [8]. The swelling is caused by postsynaptic ion flow to auditory nerve terminal due to glutamate overstimulation [9].

Noise causes decrease in cochlear blood flow due to damage of blood vessels located in spiral limbus and stria vascularis. This decrease is associated with the duration and intensity of the noise [10]. A decrease in cochlear blood flow, even if temporary, increases the threshold shift and damages the cochlear vital tissues.

Noise overexposure can damage lots of cells in the cochlea but the main target is outer hair cells. The outer hair cells located at the basal end of cochlea are more susceptible to noise and they get lost in the first step after noise. When noise continues, the pathology includes death of inner hair cells, loss of auditory nerve fibers and damage of stria vascularis [11].

Studies about NIHL suggested that it may be an ischemia/reperfusion injury. In a review reported by Nuttall, the important role of ischemia/reperfusion injury in NIHL was explained [12]. Chen et al concluded that hypoxia aggravates the hearing loss after noise [13]. Although the effect of hypoxia on NIHL is not clear yet, the most focused factors are oxidative stress and free radicals. The studies showed that, the amount of free radicals increases after noise [11]. A free radical is a molecule containing an unpaired electron. This property gives them the capability to transfer electrons with stable molecules. Reactive oxygen particles (ROP) are

molecules which act like free radicals or capable to produce free radicals [11]. Superoxide, hydroxyl, peroxynitrite, hydrogen peroxide and ozone are some examples of ROP but the most suspected agent for NIHL is superoxide. In studies performed by Clerici et al and Bielefeld et al, it was suggested that superoxide increases permanent threshold shifts and causes hearing loss due to hair cell death [14, 15]. Superoxide is a metabolite of oxygen metabolism of outer hair cells which have to move. According to the higher amounts of energy requirement in noise overexposure, oxygen metabolism remains incapable and amount of superoxide increases [11]. Yamane et al determined another reason for increase of superoxide as ischemia / reperfusion injury [16]. Lots of studies showed decrease in cochlear blood flow after noise exposure [10,17]. Another theory suggests that ROP are the reason of decrease of blood flow, not the result [11].

Even if the reason or results of decrease of cochlear blood flow, ROP cause cell death by damaging the DNA, lipids and proteins. The cell death after noise exposure is associated with necrosis or apoptosis. Blowing up of the cell is a characteristic sign of necrotic cell death, which can be observed at outer hair cells after noise. Conversely, the cells are wrinkled in apoptotic cell death. Hu et al showed both blown up and wrinkled death cells in hair cells after trauma and suggested that both type of cell death is apparent in hair cells after noise [18].

Along the effect of ROP, the effect of reactive nitrogen species is another subject of recent studies about NIHL. Han et al investigated the changes in nitrogen mechanism and its effect on death of outer hair cells after noise exposure in guinea pigs. They showed both apoptotic and necrotic cell death mechanisms in the outer hair cells of noise exposed animals. Also, they found an increase in the amount of nitrotirozine in outer hair cells, inside the nucleus of apoptotic outer hair cells, lateral wall of cochlea, and strias. They concluded that, the increase of amount of nitrotirozine is associated with death of outer hair cells and reactive nitrogen species play an important role on pathophysiology of NIHL [19].

Another pathophysiologic change in NIHL is the level of prestin. Prestin, the motor protein of outer hair cells, is necessary for cochlear amplification and electromotility. Xia et al investigated the effect of noise overexposure in prestin levels and they found that the amount of prestin in residual outer hair cells increases for 32-58% after noise. It was thought that, this

increase depends on the overproduction of prestin in residual outer hair cells to compensate the loss of outer hair cells. The residual outer hair cells are capable of producing enough levels of prestin to provide hearing threshold and cochlear frequency sharpness [20].

Islet1 is a transcription factor expressed from young outer hair cells and supporting cells in otosistin prosensor region. It cannot be expressed at postnatal period. Huang et al focused on Islet1 gene to discover the genetic base of NIHL. They investigated the effect of Islet1 on outer hair cells in a mice model in which expression of Islet1 continues at postnatal period. They found that, both age related hearing loss and NIHL are lesser in Islet1 expressed group [21]. In another genetic study, Wang et al found that, people who carry some special genes are more susceptible to NIHL [22]. Similarly, Zhang et al found protocadherin-15 gene effective on susceptibility to NIHL [23].

Proinflammatory cytokines may be effective on noise induced damage to cochlea. Fujioka et al investigated the levels of cytokines in cochlea after noise trauma and they found that the levels of interleukin-1 beta, interleukin-6 and tumor necrosis factor are higher in cochlea after noise trauma. Especially, the expression of interleukin-6 was higher in spiral ligament, stria vascularis and spiral ganglion. It was suggested that, these cytokines are produced by cochlea against noise trauma; they caused an inflammatory response and played an important role on cochlear damage [25].

Cochlear nucleus complex is the entrance point of auditory stimulus into central auditory system. The changes in GABA levels in cochlear nucleus complex are suspected in pathogenesis of hearing losses. However, the role of protein kinase-C (PKC) in NIHL is unclear. Zhen et al investigated the effect of glutamic acid decarboxylase (a chemical receptor for neurons including GABA), receptor of GABA and activity of PKC. They found an increase in PKC and decrease in receptors of GABA after trauma. They reported the changes of activity of PKC and levels of receptors of GABA are associated with NIHL [26].

Brain derived neurotropic factor (BDNF) is a growth factor which has a critical role on development of central neuronal system. While BDNF is important for development of several systems, changes in the regulation of BDNF may be pathologic. BDNF has a critical role in the complexity of synapses of inner hair cells and afferent neurons in healthy auditory systems. In the manner of acoustic trauma, BDNF may be harmful. Zuccotti et al found that,

the lesser levels of BDNF causes physiologic malfunctions but may have a protective effect against noise trauma [27].

Conclusion

The possibility to prevent or treat NIHL increases with the increase in knowledge of mechanisms of cochlear damage after noise. The main effects of noise are production of ROP due to decrease of cochlear blood flow, followed by cell death with necrosis and apoptosis. The knowledge of these mechanisms is important to develop new agents for prevention and treatment of NIHL.

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