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Innovative Strategies for Hearing Loss Treatment

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ABSTRACT

Introduction: Hearing loss significantly impacts patients' quality of life, making it an increasingly common issue, particularly among the elderly. Hearing loss is assessed based on the sound intensity threshold in decibels, ranging from mild (21–40 dB) to profound (above 90 dB). It is categorized into three types: conductive, sensorineural, and mixed. Various rehabilitation and treatment methods are applied depending on the type and degree of hearing impairment.

The aim of this paper is to review the current state of knowledge regarding the existing methods for treating hearing loss.

Materials and methods: A literature review covering studies from 2019 to 2024 was conducted, utilizing the PubMed and Google Scholar databases.

Summary of current knowledge: There are various methods to enhance hearing, including hearing aids, cochlear implants, and bone-anchored devices, which improve audibility and speech comprehension. While these methods are effective, they do not fully address all challenges faced by individuals with hearing loss, such as clear hearing in noisy environments. These therapies are continuously improved through technological advancements, such as smartphone integration, increasing patient satisfaction. Promising prospects include gene therapy, which potentially repairs genetic defects causing congenital deafness, and cell-based

therapies enabling the regeneration of damaged auditory cells. Future research on hearing protection focuses on antioxidant, anti-inflammatory, and gene-supporting drugs, employing nanotechnology to enhance therapy effectiveness.

Conclusions: Modern hearing technologies and biological therapies offer increasingly advanced methods for hearing rehabilitation. Each discussed method has its specific advantages, limitations, and applications. Continued research in this field may significantly transform the future of hearing loss treatment.

Keywords: hearing loss, hearing aids, stem cells, genetic therapy, cochlear implants

Hearing loss

Hearing loss is now a common issue affecting approximately 5% of the global population significantly, with even more individuals experiencing milder forms of the condition. It has a substantial impact on quality of life, often leading to isolation, depression, and cognitive decline. The prevalence of hearing loss increases with age—it affects about 1 in 3 people over the age of 65 and is slightly more common in men than women [1]. Hearing loss is defined based on the level of sound intensity required for an individual to barely hear sounds within the frequency range critical for speech understanding (typically 250–8000 Hz). Hearing thresholds are measured in decibels (dB), a logarithmic scale representing sound intensity:

Normal hearing - adults with normal hearing detect sounds between 0–20 dB, akin to the sound of human breathing.
Mild loss - individuals with mild hearing loss have thresholds between 21–40 dB and may struggle to hear whispers.
Moderate loss - thresholds of 41–55 dB make understanding normal conversation challenging.
Moderate to severe loss - thresholds of 56–70 dB create difficulties in hearing speech with background noise.
Severe loss - thresholds of 71–90 dB make hearing sounds like lawnmowers problematic.
Profound loss - thresholds above 90 dB can cause discomfort or pain at high sound levels [2].

Hearing loss can be classified as conductive, sensorineural, or mixed. Conductive issues involve the eardrum and middle ear, disrupting the transmission and mechanical vibration of sound [3].

Location	Condition	Typical clinical history	Findings on physical exam	Management
Middle ear	Cholesteatoma	Chronic ear infection, perforation, gradual hearing loss, otorrhea, late-stage ear pain	Tympanic membrane retraction, white mass behind the eardrum	Non-contrast CT, surgical removal often with mastoidectomy and ossicular chain reconstruction
	Ossicular chain injury	Trauma or chronic middle ear infection	Usually normal tympanic membrane, sometimes abnormal ossicle positioning	Non-contrast CT, surgical ossicular chain reconstruction
	Otitis media with effusion	Fever, ear pain	Red tympanic membrane, lack of movement on pneumatic otoscopy	Antibiotics, conservative management, myringotomy for persistent effusion
	Otosclerosis	Gradual bilateral hearing loss, better speech understanding in noise	Usually normal tympanic membrane	Hearing aids, consider stapedotomy or other surgical procedures
External	Cerumen	Gradual	Presence of	Wax removal via

auditory canal	impaction	hearing loss, no pain	cerumen blocking the canal	irrigation or curettage
	Exostoses ("Surfer's ear")	Gradual hearing loss, no pain	Abnormal canal shape, bony mass in the canal	Surgical removal of exostoses
	Foreign body in canal	Gradual hearing loss, no pain	Foreign body in the canal	Foreign body removal
	Otitis externa	Inflamed canal, presence of discharge	Inflamed canal, presence of discharge	Topical antibacterial and anti-inflammatory agents
Tympanic membrane	Perforation, tympanosclerosis	Barotrauma, head/ear injury, recurrent infections	Visible perforation or scarring	Antibiotics, tympanoplasty if perforation does not heal within 2 months

Table 1. Causes and selected clinical features of conductive hearing loss in adults [3].

Sensorineural problems affect the conversion of mechanical sound into neuro-electrical signals in the inner ear or auditory nerve, leading to sensorineural hearing loss [3].

Cause	Characteristic history	Findings on physical exam	Management
Autoimmune diseases	Progressive bilateral hearing loss, ataxia, vertigo, symptoms of autoimmune disease	Usually no abnormalities	Immunological tests, immunosuppressive drugs, corticosteroids
Cerebellopontine angle tumor	Slow, unilateral hearing loss, sometimes headache,	Sometimes ataxia, facial muscle weakness	Contrast-enhanced MRI, surgical removal of the tumor

	tinnitus, vertigo.		
Infections (e.g., meningitis, labyrinthitis)	Sudden hearing loss, often with fever, neurological symptoms, vertigo	Symptoms of ear infection, neck stiffness, nystagmus	Antibiotics, vestibular rehabilitation, specialist consultation
Ménière's disease	Episodic hearing loss with ear fullness, vertigo	Nystagmus, heightened sound perception (recruitment)	Symptomatic treatment (diuretics, antihistamines), surgical procedures
Noise exposure	Sudden or chronic noise exposure (e.g., above 85 dB), tinnitus	No changes	Hearing protection, audiological consultation, hearing aids
Exposure to ototoxic drugs	Hearing loss developing over weeks, associated with medications or industrial toxins	No changes	Audiological consultation, hearing protection
Presbycusis (age-related hearing loss)	Older age, family history	No changes	Hearing aids, cochlear implants for severe hearing loss
Trauma	Hearing loss after head or neck injury	Signs of trauma (e.g., hematoma, tympanic membrane perforation)	Imaging, otolaryngological consultation

Table 2. Causes and selected clinical features of sensorineural hearing loss in adults [3].

Hearing aids

Hearing aids (HAs) are designed to improve the audibility of speech and other sounds for individuals with hearing impairments. However, they alter the natural flow of sound to the ear canals, which can distort spatial signals crucial for accurately localizing sound sources [4].

Studies indicate that patients with asymmetric hearing loss experience greater challenges in sound localization and speech comprehension compared to those with symmetric hearing loss. Consequently, the use of bilateral hearing aids is recommended for more effective and natural restoration of hearing functions. Nonetheless, many patients, particularly older individuals, prefer using a single hearing aid due to a perceived lack of benefit or even negative auditory experiences with two devices [5]. Users increasingly report improved quality of life with hearing aids, likely due to technological advancements such as rechargeable batteries, mobile applications, and wireless sound transmission. Additionally, hearing aids enhance the ability to hear in challenging situations, such as conversations in noisy environments or watching television. However, phone calls remain problematic, with about 25% of users still facing difficulties in speech clarity and volume. Technologies like telecoils and wireless sound streaming can enhance these experiences, boosting patient satisfaction with hearing aids [6]. Furthermore, hearing aids provide significant relief for symptoms associated with hearing loss, such as tinnitus, leading to a considerable improvement in patients' quality of life [7]. A study by Gomez et al. revealed that hearing aids integrated with smartphones were positively rated by users, as they enhanced the sense of control and allowed for self-management of hearing loss. The study suggests that audiologists should consider such devices for all patients with smartphone access, as this approach shifts the responsibility of managing hearing loss from the clinician to the patient, enabling personalized adjustments based on current needs [8].

Cochlear implants

Cochlear implants (CIs) consist of an external device that receives and processes sounds and an internal component that stimulates the cochlear nerve. Although the concept is straightforward, developing effective implants required overcoming challenges in biocompatibility and advanced technologies. CIs include a microphone, speech processor, receiver, and electrode array that transmits sound signals to the cochlea. These devices have become a benchmark for other neural stimulators used in otolaryngology, enabling treatment for various sensory and functional disorders [9]. CIs bypass the mechanical structures of the inner ear, directly stimulating auditory neurons, which allows patients to regain speech perception. Implantation, however, can lead to a two-phase residual hearing loss: an immediate effect from surgical trauma and a delayed phase often associated with inflammation and fibrosis. Advances in implant design and surgical techniques have made it possible to preserve residual hearing, enabling the use of electroacoustic stimulation. This

approach improves speech comprehension in noisy environments, sound localization, and music perception. Research on hearing preservation in CI therapy focuses on minimizing cochlear trauma and inflammation through modifications in surgical techniques, novel electrode designs, and anti-inflammatory therapies [10]. A retrospective analysis of adult patients with severe to profound hearing loss who underwent cochlear implantation between 2008 and 2015 demonstrated significant improvements in speech perception. Patients with severe hearing loss achieved better outcomes than those with profound hearing loss [11]. A study by Firszt et al. evaluated the benefits of cochlear implants for adults with asymmetric hearing loss (AHL). In this analysis, 40 patients showed significant improvements in speech perception and sound localization in bimodal mode (CI + hearing aid in the better ear) three months post-implantation. The results suggest that CIs are an effective option for AHL patients, particularly when hearing loss in the poorer ear exceeds 70 dB [12]. Similarly, cochlear implants have proven to be one of the most effective solutions for treating hearing loss in children, particularly in cases of profound hearing loss or total deafness where traditional hearing aids provide insufficient benefits. They support auditory and speech development, especially when implemented early and bilaterally. Factors such as the age of implantation, socioeconomic status, parental education, and comorbidities significantly influence therapy outcomes. Early implantation and access to educational and therapeutic support promote better results, although challenges may arise from social and health-related barriers [13].

Bone-Anchored Hearing Devices (BAHD)

Bone-Anchored Hearing Devices (BAHD) utilize bone conduction to amplify sound and are affixed to the head via a flexible band or a surgically implanted component. BAHD is designed for individuals unable to use conventional hearing aids due to ear deformities or profound unilateral hearing loss. There are two main types of BAHD: percutaneous (a titanium abutment with a sound processor) and subcutaneous (magnetic attachment) systems [14,15]. A retrospective study by Bruschini et al. showed that bone conduction systems improve both auditory outcomes and subjective perceptions in patients with asymmetric hearing loss compared to their preoperative state. Treatment for asymmetric hearing loss (AHL) should be selected based on the hearing threshold in the worse ear and the type of hearing loss. For hearing thresholds above 70 dB in the worse ear, the best option is bimodal stimulation, which combines a cochlear implant in the worse ear with a hearing aid in the

better ear. If the threshold is below 70 dB, bilateral hearing aids are optimal, or if not possible, BAHD for the worse ear [16]. Another study by Gurses et al. compared 17 BAHD users with 29 individuals with normal hearing using temporal processing tests (frequency pattern, duration pattern, and speech-in-noise tests). The study revealed that using unilateral BAHD does not significantly affect the localization of auditory stimuli at the cortical level. While BAHD users achieve near-normal auditory thresholds and temporal ordering abilities, they still struggle with spatial aspects of speech perception, particularly in noisy environments or when listening to multiple sound sources simultaneously [17]. BAHD is also a safe rehabilitation method for children, provided appropriate indications are followed, particularly for conductive or mixed hearing loss. This approach is especially beneficial for younger patients unable to use traditional hearing aids due to conditions such as anotia, microtia, atresia of the auditory canal, or recurrent infections. Despite some limitations, results from newer surgical techniques and implant designs in pediatric populations appear promising. Larger implant diameters provide better implant survival, and single-stage surgeries with soft tissue preservation do not increase the risk of implant loss or skin reactions [18].

Gene therapy

Gene therapy, through genetic repair or modification, holds immense potential for treating genetic disorders. Hereditary Hearing Loss (HHL), affecting 1–3 in 1,000 newborns, is caused by genetic mutations in 60% of cases. Current therapies, such as cochlear implants and hearing aids, do not restore the intrinsic functions of inner ear cells or eliminate mutant genes. Thus, the inner ear is an ideal site for gene therapy, which can restore cellular functions and improve hearing. Key strategies—gene replacement, gene suppression, and gene editing—have shown promising results in preclinical HHL studies, particularly with CRISPR-Cas technology [19]. Viral vectors, especially Adeno-Associated Viruses (AAV), dominate gene therapy due to their excellent diffusion and compatibility with inner ear cells. However, they have drawbacks, such as immunogenicity and limited transgene size. The inner ear's enclosed structure, surrounded by bone, allows three primary AAV delivery methods: through the round window (which may cause hearing loss), the posterior semicircular canal (lower risk to hearing function but may disrupt vestibular function), and cochleostomy (requiring high precision and carrying a risk of hearing damage). Effective AAV delivery demands high virus concentration (10^9–10^{10} genome copies) in minimal volumes (~1 µL) to avoid pressure-induced damage to perilymph [20, 21]. Non-viral vectors, like nanoparticles or cationic lipids,

offer greater gene capacity and lower immunogenicity but are less efficient [22, 23]. Preclinical data over the past decade highlight the potential to restore high-quality hearing in moderate hearing loss cases, including the most common forms of congenital deafness. The most promising results involve gene therapy targeting OTOF-dependent hearing loss, as demonstrated in mouse models. OTOF mutations lead to defective synaptic transmission between inner hair cells (IHC) and cochlear neurons, causing deafness. Despite the lack of OTOF protein, inner ear development and structure remain intact, making this loss amenable to effective gene therapy. Studies in mice showed that delivering the OTOF gene to IHC using a dual-AAV strategy restored auditory function [24].

Stem cell therapy

Stem cell therapy is a promising approach to treating hearing loss by regenerating damaged auditory cells. Three types of stem cells are distinguished: embryonic (ESC), adult (ASC), and induced pluripotent stem cells (iPSC). ESCs can differentiate into various cell types but face ethical limitations. ASCs, though less plastic, show potential for regenerating inner ear neurons. iPSCs, derived from patient cells, hold great promise for treating sensorineural hearing loss and regenerating hair cells that convert sound waves into nerve signals in the inner ear. iPSCs minimize rejection risk and can be genetically modified, making them a potentially safe source for hearing loss therapies [25]. Lgr5-marked inner ear stem cells have potential for regenerating hair cells, especially after damage, making them an essential focus for hearing loss treatments. However, their regenerative capacity decreases postnatally, necessitating methods to restore their plasticity for clinical applications [26]. Research into endogenous and exogenous neural cells in hearing loss treatment has made significant progress. Neural cells can be implanted in the inner ear to replace or support hair cells and spiral ganglion cells, promoting cellular regeneration and neural network reconstruction to improve auditory functions. Despite promising results, challenges remain, including risks of tumor formation, immune rejection, and suboptimal restoration of hearing functions [27]. Currently, stem cell therapy is in the early research and preclinical stages, showing potential to restore hearing. Future studies should focus on understanding differentiation mechanisms, simulating the inner ear microenvironment, and ensuring comprehensive safety evaluations [28].

Cryotherapy

Another promising therapeutic method is otoprotective cryotherapy, with various in vivo experiments demonstrating its protective effects on hearing. Most research focuses on systemic hypothermia, which is challenging to apply clinically. While cryotherapy methods show promise, they yield inconsistent data, and the underlying mechanisms remain unclear. Positive effects observed include increased ischemic tolerance, reduced acoustic trauma, and decreased hearing loss caused by cochlear implants. Potential mechanisms, such as reduced blood flow, oxidative stress, and activation of cold-shock proteins, may enhance hearing recovery. Current studies are mainly limited to simple animal models and isolated human trials (e.g., neck cooling for idiopathic sudden hearing loss), precluding clinically significant conclusions [29].

Pharmacological treatment

Future hearing protection research focuses on antioxidant, anti-inflammatory drugs, gene-supportive approaches, and innovative nanotechnology. Synthetic coenzyme Q10 analog Qter has shown promise in reducing hearing damage in noise-exposed mice, supporting hair cell survival and maintaining redox balance. GV1001, a telomerase-derived peptide, prevents noise- and antibiotic-induced hearing loss. Anti-inflammatory agents, such as Avenanthramide-C, a flavonoid from oats, exhibit antioxidant and anti-inflammatory properties, reducing noise-induced hearing damage [30]. Metformin and probucol show therapeutic potential in protecting against age-related hearing loss (ARHL). Metformin has antioxidant, anti-inflammatory, and anti-apoptotic effects, reducing reactive oxygen species (ROS) and preventing cellular degeneration. Probucol promotes the activity of NRF2, a transcription factor, recruiting potent antioxidants to support auditory cell protection. Both drugs have ARHL prevention potential but require further research to fully understand their mechanisms and safety for hearing loss therapy [31]. Nanotechnology using nanopreparations offers promising advancements in delivering steroid drugs more effectively to the inner ear but requires further studies to ensure its safety [30].

Conclusions

Hearing loss is a global issue, especially prevalent in older populations, significantly affecting daily life. Hearing loss treatments rely on devices like hearing aids, which improve quality of life and alleviate associated symptoms such as tinnitus. Advances in mobile applications,

wireless sound transmission, and rechargeable batteries make hearing aids more user-friendly and accessible. Cochlear implants effectively restore speech perception in severe hearing loss cases where hearing aids fall short, while BAHD offers an alternative for individuals with ear deformities who cannot use traditional treatments. Intensive research into future hearing loss treatments is ongoing. Gene therapy shows the most promise for restoring natural hearing functions, particularly for congenital genetic mutations. Stem cell therapy leverages the regenerative potential of stem cells to rebuild hair cells and inner ear neurons, offering substantial possibilities for hearing loss treatment. Pharmacological therapies with antioxidants, anti-inflammatory drugs, and nanotechnology protect auditory cells and may prevent hearing loss. Each of these methods has advantages and limitations, with many still in the experimental phase. Continued research focusing on safety and minimizing risks of side effects remains a priority for the future of hearing loss treatment.

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Author's contribution:

Conceptualization: Krystian Żuk; methodology: Krystian Żuk, Alicja Góral, Michał Czachajda, Kamila Duszyńska, Karol Dolepski, software: Krystian Żuk, Alicja Góral, check: Alicja Góral, Kamila Duszyńska, Karol Dolepski; formal analysis: Alicja Góral, Krystian Żuk; investigation: Alicja Góral, Michał Czachajda, Krystian Żuk, Kamila Duszyńska, Karol Dolepski; resources: Alicja Góral, Krystian Żuk, Michał Czachajda, Karol Dolepski; data curation: Krystian Żuk, Kamila Duszyńska; writing – rough preparation: Krystian Żuk; writing – review and editing: Michał Czachajda, Alicja Góral, Kamila Duszyńska, Karol Dolepski; visualization: Alicja Góral, Krystian Żuk; supervision: Kamila Duszyńska, Karol Dolepski; project administration: Alicja Góral, Krystian Żuk.

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