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Research Article

Evaluating Efficacy of Localized Drug Delivery Techniques for Cochlear Protection and Regeneration

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Abstract

Background: Sensorineural hearing loss (SNHL) affects hundreds of millions globally, often due to irreversible damage to cochlear hair cells or auditory nerve fibers. Systemic drug delivery is limited by poor intracochlear penetration and systemic side effects, prompting the development of localized delivery strategies.

Objective: This preclinical study evaluates and compares the efficacy of three localized drug delivery techniques—intratympanic dexamethasone (IT-Dex), cochlear implant-mediated sustained BDNF release (CI-Drug), and biodegradable gelatin hydrogel loaded with GDNF (Hydrogel-GDNF)—in preserving auditory function and promoting cochlear regeneration in a noise-induced hearing loss (NIHL) model in guinea pigs.

Methods: Sixty guinea pigs were randomly assigned to six groups (n = 10/group): IT-Dex, CI-Drug, Hydrogel-GDNF, systemic steroids, placebo, and untreated control. NIHL was induced via 110 dB SPL noise exposure for 2 hours. Auditory function was assessed using auditory brainstem response (ABR) at baseline and days 7, 14, and 03. Cochlear histology, inflammatory markers (IL-6, TNF-α), and tissue integrity were analyzed post-mortem.

Results: At 30 days post-treatment, CI-Drug showed the lowest ABR thresholds (28 ± 5 dB SPL) and highest hair cell survival (82%), followed by Hydrogel-GDNF (30 ± 4 dB SPL; 75%). Both localized neurotropic-based therapies significantly outperformed IT-Dex, systemic steroids, and placebo ($p < 0.05$). Systemic steroids showed minimal benefit over placebo. Localized delivery methods also reduced inflammation and tissue damage compared to systemic and placebo controls.

Conclusion: Localized drug delivery techniques, particularly sustained-release systems incorporating neurotrophic factors, offer superior cochlear protection and regenerative potential compared to systemic administration. These findings support further translational research into implantable and biodegradable delivery platforms for treating SNHL.

Keywords: Noise-Induced Hearing Loss (NIHL); Sensorineural Hearing Loss (SNHL)

Introduction

Hearing loss affects over 430 million people globally, with sensorineural hearing loss (SNHL) accounting for the majority of cases [1]. SNHL often arises from damage to the sensory hair cells within the cochlea or degeneration of auditory nerve fibers, commonly due to noise exposure, aging, ototoxic drugs, or genetic factors [6]. Despite advances in diagnostics and therapeutics, treatment options remain limited, particularly once structural damage has occurred.

Systemic drug delivery faces significant challenges in treating inner ear disorders due to the presence of the blood-labyrinth barrier, which restricts drug entry into the cochlea [2]. Additionally,

systemic administration often leads to suboptimal intracochlear concentrations and potential off-target effects, including immunosuppression and metabolic disturbances [1]. These limitations have driven the development of localized drug delivery strategies, such as intratympanic injections, cochlear implants with integrated drug release systems, and biodegradable hydrogel carriers, which aim to bypass anatomical barriers and deliver therapeutic agents directly to the cochlea [3]. Emerging research highlights the regenerative potential of neurotrophic factors, including brain-derived neurotrophic factor (BDNF) and glial cell line-derived neurotrophic factor (GDNF), in promoting survival and regeneration of hair cells and spiral ganglion neurons [5].

CI-Drug (Cochlear Implant + Sustained Release of BDNF) A novel cochlear implant system has been developed with an integrated sustained-release reservoir or coating that delivers BDNF (Brain-Derived Neurotrophic Factor) directly to the cochlea over a 30-day period [4].

This approach aims to:

- Enhance spiral ganglion neuron survival after implantation, preserving neural integrity and improving responsiveness to electrical stimulation [5,7].
- Improve neural-electrode interface by promoting neurite outgrowth and reducing neural degeneration, thereby enhancing signal transmission [3,5].
- Potentially extend cochlear implant candidacy to patients with limited neural survival and optimize auditory outcomes in both early and delayed implantation scenarios [1,7].
- This approach aims to enhance spiral ganglion neuron survival after implantation, preserving neural integrity and improving responsiveness to electrical stimulation [5,7], with emerging clinical evidence supporting its translational potential [8].

Mechanism

- Drug delivery is achieved via biodegradable polymer matrices, nanochannel membranes, or microsphere depots integrated within or alongside the electrode array, enabling localized and controlled release of BDNF [3,4].
- The sustained neurotrophic support is synchronized with the critical post-implantation window, supporting neural adaptation and integration with the implant [5,7].

Applications

- Patients with residual neural degeneration due to prolonged deafness or disease.
- Enhancing outcomes in cases of delayed cochlear implantation, where neural survival may be compromised.
- As an adjunct to neural regeneration therapies, potentially synergizing with stem cell-based or gene therapy approaches [5,7].

This preclinical study evaluates the hypothesis that localized drug delivery techniques significantly enhance cochlear protection and regeneration, offering superior outcomes compared to systemic therapy.

Objectives

Primary objective

To compare the efficacy of three localized drug delivery methods—intratympanic dexamethasone injection, cochlear implant-mediated sustained BDNF release, and biodegradable gelatin hydrogel loaded with GDNF —in preserving auditory function and cochlear morphology in a noise-induced hearing loss (NIHL) model in guinea pigs.

Secondary objectives

- To assess the regenerative capacity of neurotropic-based therapies in terms of hair cell survival and neural preservation.
- To evaluate the safety profile (e.g., inflammation, tissue toxicity) of each delivery method.
- To determine whether localized delivery improves drug bioavailability and reduces systemic side effects compared to oral steroid treatment.

Methodology

Study design

A preclinical, randomized controlled trial using a guinea pig model of NIHL was conducted.

Subjects

Sixty adult albino guinea pigs were randomly assigned to six experimental groups (n = 10 per group):

- **Intratympanic Dexamethasone (IT-Dex):** Single post-noise exposure injection.
- **Cochlear Implant + Sustained BDNF Release (CI-Drug):** Electrode-integrated reservoir releasing BDNF over 30 days.
- **Biodegradable Hydrogel + GDNF (Hydrogel-GDNF):** Gelatin-based hydrogel applied near the round window membrane.
- **Systemic Steroids (Control 1):** Daily oral prednisolone for 14 days.
- **Placebo (Control 2):** Intratympanic saline injection.
- **Untreated Control (Control 3):** No intervention post-NIHL.

Intervention protocol

All animals underwent standardized noise trauma (110 dB SPL for 2 hours).

Treatments were administered immediately post-exposure (or at day 1 for CI-Drug).

Outcome measures

Primary outcomes

- **Auditory Function:** Auditory Brainstem Response (ABR) thresholds measured at baseline, 7, 14, and 30 days post-treatment across frequencies (2, 4, 8, 16 kHz).
- **Hair Cell Survival:** Quantified via confocal microscopy following immunostaining (e.g., myosin VIIa).

Secondary outcomes

- **Inflammatory Response:** Serum and cochlear IL-6 and TNF-α levels.
- **Histopathological Assessment:** Tissue integrity scored by blinded observers using a 0–3 scale (0 = normal, 3 = severe damage).
- **Drug Distribution:** Fluorescent labeling used to track BDNF/GDNF distribution in select animals.

Statistical analysis

- One-way ANOVA with Turkey's post-hoc test for intergroup comparisons.
- Repeated-measures ANOVA for longitudinal ABR data.
- Significance threshold: $p < 0.05$.
- Data expressed as mean ± standard deviation (SD).

Results

IT-Dex	35 ± 6	<0.001	0.002
CI-Drug (BDNF)	28 ± 5	<0.001	<0.001
Hydrogel-GDNF	30 ± 4	<0.001	<0.001
Systemic Steroids	45 ± 8	0.12	—
Placebo	58 ± 10	—	—

Table 1: ABR Thresholds (dB SPL) at Day 30 Post-Treatment.

IT-Dex	68 ± 12	18 ± 4	1.2 ± 0.3
CI-Drug (BDNF)	82 ± 9	12 ± 3	0.8 ± 0.2
Hydrogel-GDNF	75 ± 11	15 ± 5	1.0 ± 0.4
Systemic Steroids	40 ± 15	25 ± 6	2.5 ± 0.6
Placebo	22 ± 8	30 ± 7	3.0 ± 0.0

Table 2: Hair Cell Survival (%) and Safety Outcomes.

Key findings

- CI-Drug (BDNF) showed the greatest improvement in ABR thresholds and hair cell survival, outperforming all other groups ($p < 0.05$).
- Hydrogel-GDNF demonstrated comparable efficacy to IT-Dex, with reduced inflammation and no observed toxicity.
- Systemic steroids showed minimal benefit over placebo in both functional and histological outcomes.
- All localized delivery methods significantly reduced inflammatory cytokines and tissue damage scores compared to systemic/placebo controls.

Discussion

The findings of this study support the hypothesis that localized drug delivery offers superior cochlear protection and regenerative potential compared to systemic administration. The sustained-release CI-Drug system provided the most consistent auditory recovery and maximal hair cell survival, likely due to prolonged neurotropic support and direct access to the cochlear fluids [5]. These results are consistent with prior work demonstrating the critical role of neurotrophins in auditory nerve and hair cell maintenance [5,7]. The hydrogel-based delivery system also showed

promising outcomes, suggesting its utility in chronic conditions where repeated injections may be impractical [3,4]. Compared to IT-Dex, which remains a common clinical approach for sudden sensorineural hearing loss (SSNHL), the CI-Drug and Hydrogel-GDNF groups exhibited not only improved hearing but also greater cellular preservation, indicating regenerative rather than merely protective effects [1,2].

However, several limitations must be acknowledged:

- The short-term nature of the animal model limits extrapolation to long-term human use.
- Species differences between guinea pigs and humans may affect translatability of dosing and kinetics.
- Lack of behavioral or electrophysiological correlates beyond ABR may limit full understanding of functional recovery.

Nonetheless, these findings align with emerging clinical evidence supporting targeted, sustained-release therapies for inner ear disease [6-8].

Future studies should focus on scaling up models, human cadaver trials, and eventually phase me /II clinical trials to validate safety and efficacy in humans.

Conclusion

Localized drug delivery techniques, particularly those incorporating sustained-release systems and neurotrophic factors, demonstrate significant advantages over systemic therapy in protecting and potentially regenerating cochlear structures. Among the tested approaches, BDNF-releasing cochlear implants and GDNF-loaded biodegradable hydrogels show particular promise for future translation into clinical practice.

Further research is needed to optimize delivery kinetics, dosage regimens, and long-term safety profiles, especially for chronic applications. These findings underscore the importance of precision medicine approaches in the management of sensorineural hearing loss.

Bibliography

1. Plontke SK., *et al. Frontiers in Neurology* 8 (2017): 86.
2. Salt A N., *et al. Hearing Research* 341 (2016): 155-164.
3. Farahmand Ghavi F., *et al. Biomaterials ,* 243 (2020): 119931.
4. Shi X., *et al. Acta Biomaterialia* 88 (2019): 1-13.
5. Wan G., *et al. Journal of Neuroscience* 34.22 (2014): 7513-7521.
6. Bas E., *et al. Journal of Controlled Release* 297 (2019): 24-35.
7. Liu Y., *et al. Nature Communications* 12.1 (2021): 1-13.
8. Hessler R., *et al. Otology and Neurotology* 43.2 (2022): e210-e218.