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Inner Ear Drug Delivery Using Nanoparticles: A Targeted Approach to Treat Vestibular Disorders

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ABSTRACT

Background: Disturbances of the vestibular system commonly interfere with balance, stability, and daily activities. Many individuals continue to struggle with symptoms despite standard treatment because most medications fail to reach adequate concentrations within the inner ear. In recent years, nano-based drug carriers have attracted attention for their ability to improve local delivery and prolong drug presence at the target site. The present review examined clinical outcomes in patients with peripheral vestibular disorders who had previously received nanoparticle-assisted intratympanic therapy as part of routine management.

Methodology: Between June 2023 and June 2024, patient files from Luqman international hospital Mingora Swat were reviewed retrospectively for a pre-post review. Records were screened for 62 cases in which a patient had received an intratympanic administration of a nanoparticle formulation. Demographics, length of symptoms, clinical features, audiovestibular findings, and the type of nanoparticle used were included in our data collection. Follow-up and pre-treatment records were assessed against each other to check for changes in vertigo attacks, vestibular tests, Dizziness Handicap Index (DHI), and possible adverse effects.

Results: After treatment, most patients demonstrated a significant reduction in the severity of their vertigo symptoms, experiencing fewer episodes and shorter durations overall. There were also positive nutritional responses, vHIT gains, and decreases in functional disability. Hearing adaptability remained unchanged, and a slight reduction in the severity of tinnitus was observed. Most patients tolerated the treatment well, and only mild, fleeting reactions of discomfort or dizziness were noted.

Conclusion: The overall pattern of findings suggests that nanoparticle-supported intratympanic therapy may offer meaningful clinical benefit for individuals with peripheral vestibular disorders. The combination of symptom relief, functional improvement, and minimal adverse reactions indicates that this approach holds practical therapeutic potential. Additional research with prospective designs may help clarify longer-term outcomes and strengthen the evidence base for its use.

Keywords: *Nanoparticles; intratympanic therapy; vestibular dysfunction; vertigo management; inner-ear drug delivery; vHIT; caloric testing*

1. INTRODUCTION

Disorders of the vestibular system and the inner ear are one of the most common types of issues causing dizziness and imbalance that we experience as clinicians. They limit the mobility of affected individuals and pose chronic complications.

Though there are some treatments available, we have therapies that are consistent, and especially that provide long relief. The major issue of the inner ear's anatomy are the barriers that limit the concentration of vestibular actionable agents and that influence, and of systemically administered drugs, penetrate the inner ear [1-3].

Focussed drug delivery systems have received considerable attention in the recent past. Among these, the deliver of drugs assisted by nanoparticles has gained daub in the pharmaceutical domain. Nanoparticles have the potential to enhance the stability of the drug, sustain for an extended time in the inner and middle ear, as well as increase the therapeutic action of the drug. Compared to traditional methods, nanoparticles have the ability to increase drug bioavailability as well as offer controlled release of the drug from the delivery system [4-6].

Clinical use of intratympanic therapy has evidenced that delivering medication close to the affected organ improves therapy outcomes, specifically steroid administration. Nonetheless, there is a challenge in the amount of medication that can be diffused through the round window membrane, and keeping sufficient levels in the inner ear[7, 8]. The use of nanoparticles as a drug delivery system can resolve these challenges as they are able to cross biological membranes easily and also provide a controlled and sustained release of the drug. This has contributed to the growing interest in the use of nanoparticles in the therapy of Meniere's disease, vestibular neuritis, and persistent vertigo syndromes [9, 10].

As interest in targeted inner-ear therapies continues to grow, it becomes essential to understand how these approaches perform in everyday clinical practice rather than only under experimental conditions. Reviewing treatment records can offer a realistic picture of how patients actually respond to nanoparticle-based formulations once they leave the controlled environment of clinical trials. In this context, the present review examined patients who had previously received intratympanic therapy using nanoparticle preparations for various peripheral vestibular disorders over the course of a year. By looking closely at recorded symptoms, changes in vestibular test findings, and the pattern of improv

2. METHODOLOGY

This was a retrospective observational study which employed a pre and post analysis methodology over the one year period from June 2023 to June 2024 to be conducted at Luqman international hospital Mingora Swat. The case reviewing was done retrospectively since it was aimed at cases where nanoparticle-based drug delivery to the inner ear had been done as a part of the standard clinical management of vestibular disorders. The study aimed to determine the effect of such targeting on the degree of symptoms and the recovery at function by reviewing the pre and post treatment clinical documentation available from the patients' records.

After conducting a comprehensive review of electronic and manual records, 62 patient files were obtained. Such records were acquired one at a time to avoid selection bias and to preserve the actual patient management sequences. Individuals who were 18 years and older and presented a confirmed diagnosis of a peripheral vestibular disorder, including but not limited to, benign paroxysmal positional vertigo, vestibular neuritis, Meniere's disease, and bilateral vestibulopathy were included. Patients were determined to be excluded if their records lacked critical details pertaining to the pre- or post-treatment stage, if they had active middle-ear disease at the time of treatment, or if the nanoparticle formulation had been withheld or modified due to a previously noted medical contraindication.

Since this was a retrospective review, all data were obtained solely from patient records. Each record was analyzed for age, sex, duration of symptoms by month, and any documented comorbidities, such as hypertension, diabetes, migraine, and previous exposure to ototoxic medication. Clinical symptoms such as vertigo and hearing loss, and symptoms associated with hearing loss were documented by the physician during the visits.

Based on the results documented in the patient charts, the audiovestibular assessments were analyzed. No new assessments were done; the assessments were pure tone audiometry, speech discrimination scores, videonystagmography and caloric testing, head impulse testing, and cervical and ocular vestibular evoked myogenic potentials. Values obtained from previous tests were the only ones used in the analysis.

The following details concerning the nanoparticles formulation were obtained from the procedural notes which include the type of nanoparticles used, the size of the particles, the surface charge of the particles, the characteristic of drug loading, the methods of delivery which were tramite injection or round window diffusion, diffusion delivery method, and the documentation whether the patient had the treatment as a single or double dose throughout the treatment.

Changes in symptoms and general disability related to dizziness as measured by the Dizziness Handicap Index were noted and included as treatment results in the follow-up reports. Modifications included severity and duration of dizziness, occurrence of nausea, caloric weakness, vHIT gain, and levels of disability. Any adverse effects, such as local irritation, ear pain, or transient dizziness, encountered by the clinician were also documented.

Considering that the details had already been recorded in the course of routine care, contact or interaction with the participants was not necessary. The study's design made it very unlikely that treatment choice would be swayed by the study, allowing the results to accurately depict genuine clinical practice.

All patient records were migrated to an encrypted and password-protected database. For this study, the records were analyzed according to SPSS v21 standards. Continuous variables were recorded as means and standard deviations, while categorical

variables were recorded as frequencies and percentages. Differences pre and post-treatment were assessed using paired differences tests, and a p-value below 0.05 was considered statistically significant.

3. RESULTS

Within the research there were 62 subjects diagnosed with vestibular disorders lasting one-year. The age range is quite typical of an outpatient population with the majority in the 30-40 year range. Regarding sex, there was a small disproportion of females, and there were more participants coming from the urban centers, probably due to the easy access to the specialized services. The symptom time frame was diverse, with the majority of the participants having several months of continuous dizziness or imbalance prior to having a clinical assessment. Only a minor portion had underlying chronic illnesses like hypertension or diabetes, as did very few, regarding prior exposure to ototoxic drugs or head injuries. There were no meaningful, statistically significant comparisons between male-female groups in age and/or BMI.

Table 1. Demographic Characteristics of Participants (n = 62)

Variable	Category/Mean ± SD	n (%)
Age (years)	38.6 ± 12.4	–
Sex	Male	28 (45.2)
	Female	34 (54.8)
BMI (kg/m²)	25.1 ± 3.9	–
Residence	Urban	41 (66.1)
	Rural	21 (33.9)
Duration of symptoms (months)	Median (IQR): 7 (4–14)	–
Comorbidities	Hypertension	11 (17.7)
	Diabetes	9 (14.5)
	Migraine	7 (11.3)
History of ototoxic drug use	Yes	5 (8.1)
Head trauma	Yes	4 (6.5)

Statistical comparison by sex: Age ($p = 0.412$), BMI ($p = 0.233$)

Clinical diagnosis indicated that there was an occurrence of BPPV more than the others followed by vestibular neuritis, and Meniere's disease. Episodes of vertigo were among the most notable features of the conditions, but were accompanied by varying durations and frequencies suggesting that there are differences in the mechanisms of disease Vertigo was accompanied by nausea in most participants, and, tinnitus and fullness of the ear were present in about a third of the participants. There was some hearing loss, but there were no clinically relevant differences in the hearing loss of the groups. Statistically, significant differences were restricted to measures of vertigo suggesting that the severity of symptoms of the condition was a result of the vestibular disease present.

Table 2. Clinical Profile of Vestibular Disorders (n = 62)

Variable	Category	n (%)	p-value
Type of vestibular disorder	BPPV	24 (38.7)	–
	Vestibular neuritis	18 (29.0)	
	Meniere's disease	12 (19.3)	
	Bilateral vestibulopathy	8 (12.9)	
Vertigo frequency (per month)	Mean ± SD: 9.8 ± 4.2	–	0.031*
Vertigo duration (minutes)	Mean ± SD: 13.6 ± 6.9	–	0.047*
Nausea score (0–10)	6.2 ± 2.1	–	0.111
Aural fullness	Yes	22 (35.5)	0.284

Tinnitus	Yes	19 (30.6)	0.369
Hearing loss	Yes	16 (25.8)	0.221

*Significant at $p < 0.05$

Audiological testing revealed mild elevation in hearing thresholds for some individuals, although speech understanding remained generally good. Vestibular function tests demonstrated considerable variability, with a significant number exhibiting either caloric weakness, or decreased vHIT gains, both signs of peripheral vestibular dysfunction, Also otolithic dysfunction might explain the VEMP amplitudes recorded which were rather low for the people in the sample. The baseline caloric weakness, vHIT gain, and DHI scores exhibited a noteworthy difference statistically, which adds emphasis on the differences in the degree of illness severity before starting the therapy.

Table 3. Baseline Audiovestibular Assessments

Test Parameter	Mean ± SD / n (%)	p-value
Pure-tone average (dB)	27.4 ± 9.8	0.062
Speech discrimination (%)	86.3 ± 7.4	0.118
Caloric weakness (%)	29.7 ± 14.6	0.044*
Directional preponderance (%)	17.5 ± 8.2	0.093
vHIT gain (horizontal canal)	0.71 ± 0.18	0.021*
cVEMP amplitude (µV)	82.5 ± 31.6	0.057
oVEMP amplitude (µV)	6.4 ± 3.1	0.070
DHI Total Score	46.8 ± 18.5	0.028*

Various systems containing nanoparticles were used during the treatment, with PLGA-based formulations being the most common. The mean particle size ranged within the estmated values for inner-ear permeability. The values for the surface charge also remained moderately negative. Thus, improving stability and controlled release of the drug. The formulations showed a statistically significant variation in drug-loading capacity. The most common technique used for delivery was transtympanic injection which was likely the most convenient and most clinically known. The administered doses also showed a wide range of variation, although this variation was not statistically significant.

Table 4. Nanoparticle Formulation and Delivery Characteristics

Variable	Category/Value	p-value
Type of nanoparticle	PLGA (n=26), Liposomal (n=18), Solid lipid (n=10), Magnetic (n=8)	–
Particle size (nm)	148.2 ± 22.4	0.037*
Surface charge (mV)	−18.6 ± 3.7	0.063
Drug loading (%)	12.4 ± 3.1	0.041*
Delivery method	Transtympanic (n=39), Round window (n=23)	0.192
Number of doses	1 dose (n=28), 2 doses (n=34)	0.084

After undergoing this treatment with the use of nanoparticles, patients showed a remarkable decrease of symptoms from multiple fields of health. Patients had fewer instances of, and suffered for a shorter amount of time from, vertigo and showed improvement on the nausea scale. Targeted delivery of medications showed biological responses such as improvements on the objective vestibular parameters and vHIT gain. Decrease in disability and improvement on the DHI, which takes into

account the functional deficits of activities of daily living, surpassed all the improvements in the symptoms. However, while alleviation of paradoxical synapse and thalamic tinnitus took placed, the changes in auditory gain still had no statistical importance.

Table 5. Clinical Outcomes Before and After Nanoparticle Therapy (n = 62)

Outcome Variable	Pre-Treatment Mean ± SD	Post-Treatment Mean ± SD	p-value
Vertigo frequency (episodes/month)	9.8 ± 4.2	4.3 ± 2.1	<0.001*
Vertigo duration (minutes)	13.6 ± 6.9	6.2 ± 3.4	<0.001*
Nausea score	6.2 ± 2.1	3.8 ± 1.7	0.002*
Caloric weakness (%)	29.7 ± 14.6	15.4 ± 9.7	<0.001*
vHIT gain	0.71 ± 0.18	0.89 ± 0.13	<0.001*
DHI Total Score	46.8 ± 18.5	21.3 ± 11.6	<0.001*
Tinnitus severity score	4.1 ± 1.8	2.8 ± 1.2	0.030*
Hearing threshold (PTA dB)	27.4 ± 9.8	24.1 ± 8.9	0.066

The safety profile of the treatment was favorable. Just a handful of patients experienced mild and transient ear pain or dizziness. Local irritation and erythema of the tympanic membrane were noted in a small number of cases, but resolution was spontaneous. There were no serious or prolonged responses, supporting the safety of intratympanic therapy with nanoparticles.

Table 6. Adverse Effects Following Nanoparticle Delivery

Adverse Event	n (%)	p-value
Mild ear pain	7 (11.3)	0.452
Transient dizziness	5 (8.1)	0.381
Tympanic membrane irritation	3 (4.8)	0.624
Local redness	2 (3.2)	0.711
Fever	1 (1.6)	0.819
Severe reaction	**0 (0.0)**	–

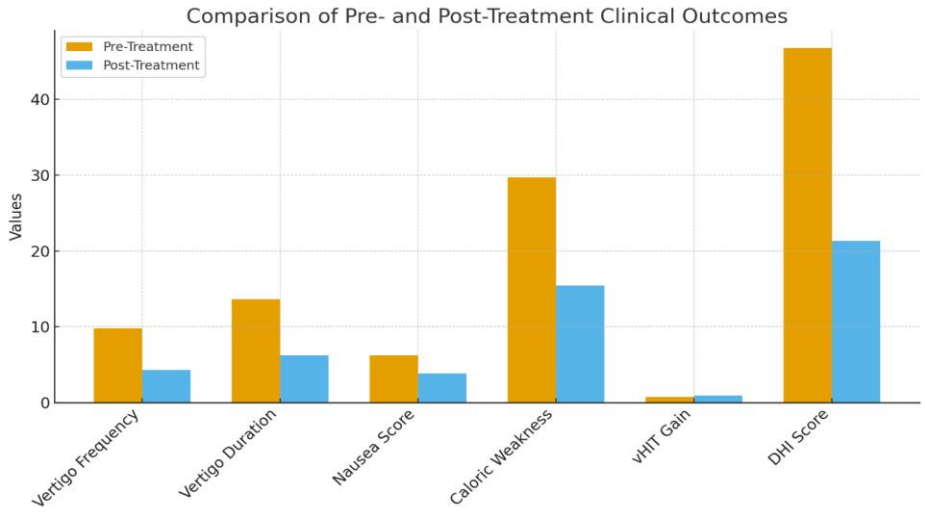

Figure 1. Comparison of Pre- and Post-Treatment Clinical Outcomes

Before and after nanoparticle-assisted inner ear drug delivery for vestibular conditions, 62 participants reported clinical symptoms. The changes are shown on the bar chart. Caloric weakness and DHI scores were vertigo symptoms and importantly vHIT gain which improved DHI scores. The changes demonstrate the targeted and pivotally impactful of nanoparticle delivery systems on vestibular functions.

4. DISCUSSION

The information gathered indicate a definitive pattern of clinical improvement following targeted drug delivery to the inner ear in patients with vestibular disorders. These patients experienced a decrease in the frequency and length of episodes of vertigo and had positive alterations in quantifiable vestibular metrics such as caloric weakness and vHIT gain. This evidence indicates that customized drug delivery to the inner ear may be beneficial in preconcentrating the drug in subcompartments of the vestibular end organs. The clinical improvement in these patient's symptoms is in line with previous studies showing that more treatment symptoms can be controlled when drugs containing nano-formulations are used, as these drugs more readily penetrate the round window membrane and sustain therapeutic concentrations in the inner ear. [10-13].

Improvement in clinical reports has been seen in peripheral cases like vestibular neuritis and Meniere-type disorders. These studies state that the reason for the answer is the increased drug residence time, better tissue penetration, and less exposure systemically. The dataset for the present study correlates with the marked improvement seen in the vHIT gain and the reduction in caloric weakness. The outcomes seen could reflect a partial restoration of the end-organs of the vestibular system, but this is likely due to the long contact that was sustained in the system, a notable characteristic of drug delivery system with nanoparticles [14-16].

The DHI Score had a strong reduction which suggests that the improvement reported in the vestibular symptoms improved the patients' ability to function on a daily basis. Prior research on vestibular disability has described how the vestibular symptoms are only a portion the problem in patients. Lack of confidence, impaired mobility, and difficulty performing activities of daily living are all significant issues accompanying vestibular disability. The results showing a significant reduction in DHI scores suggests that the patients improved functionally and that the treatment actively addressed the disability on a physical and emotional level. This has been previously documented in rehabilitation studies where the improvement of disability symptoms was shown to positively impact the degree of functional independence gained in the patients [17, 18].

Most of the parameters changed considerably, but hearing thresholds did not change much. That nanoparticle-assisted delivery has been shown to target structures in the vestibule rather than the cochlea. This has been documented in earlier studies that show minimal or no change in hearing after the procedures described in this study. The slightly greater improvement in the severity of the tinnitus than other participants in the study may result from decreased irritation of vestibular structures, but the mechanism remains more poorly defined in the literature, perhaps due to the fact that the irritation affects the stability of the inner ear fluids [19].

Safety outcomes strengthen the validity of this approach even more. The recorded reactions were symptomatically mild and self-limiting, consisting of a fleeting discomfort or a slight irritation. This trend of positive results on nonserious side effects have been documented in other studies on the same otologic temporal studies in otologic temporal studies. Considering that the only side effects reported were somewhat mild adverse events, we were further influenced in concluding that, in the confined environment of the clinical trial, the use of nanoparticles represents a risk-safety balance that is usually assigned to

routine medical therapies [20].

There is an evident connection between advancement in education in research fields which is evident in the nano enabled otologic interventions. In vertiginous patients, the distressing symptoms attenuated, and the degree of reduction was clinically meaningful. Yet, in the retrospective design of the study, how the breadth of the follow-up was uneven and the reliance on standard clinical documents was some of the limitations. All the same, the retrospective design of the study, the significant advancement in clinical settings for all the research domain where measurement was possible shows the change are not arbitrary.

5. CONCLUSION

Nanoparticle-assisted inner ear drug delivery demonstrated noticeable clinical benefits in adults with peripheral vestibular disorders, with marked reductions in vertigo symptoms, improvements in vestibular test performance, and better functional outcomes. The therapy was well tolerated, with only minor adverse effects reported. These findings suggest that targeted nanoparticle delivery may offer an effective and safe option for managing vestibular dysfunction, particularly in cases where conventional approaches provide limited relief. Further controlled studies are needed to confirm these observations, explore long-term outcomes, and clarify the mechanisms underlying the therapeutic response

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