Journal of Otology 21 (2026) 259 – 271

Journal of Otology

journal homepage: www.sciopen.com/journal/1672-2930

Evaluation of Transtympanic Steroid Injection Dosage in Treatment of Sensorineural Hearing Loss: A Systematic Review

Sanjana Nallapaneni[1], Naveen S. Raj[1], Margaret P. Byars[1], Alexander M. Belardo[1] and Anita S. Jeyakumar[1,2] ✉

[1] *Northeast Ohio Medical University, College of Medicine, Ohio, United States*

[2] *HEARS, LLC, United States*

ABSTRACT

Objectives: In sensorineural hearing loss treatment, transtympanic membrane (TTM) steroid injections help in recovery. However, steroid dosage distribution and patient recovery rates remains underexplored. Our systematic review compiles steroid regimens and their hearing recovery rates. Data Sources: PubMed, OVID, and Google Scholar. Review Methods: Search terms included TTM steroid and hearing loss. Inclusion criteria were measurements for human hearing recovery, full-text articles, and studies published on or before 1/20/2025. Exclusion criteria included reviews. Primary outcomes were hearing and patient recovery rates. For analysis, we focused on dose levels and simultaneous systemic steroids, and employed descriptive and exploratory study-level analysesResults: 29 articles were included. Of studies reporting gender, the distribution was 54.6% (635) male and 45.4% (528) female. 1,294 total patients received TTM steroids with distributions being: 26.0% (n = 336) received 4 mg/mL dexamethasone, 25.2% (n = 326) received 5 mg/mL dexamethasone, 2.7% (n = 35) received 8 mg/mL dexamethasone, 3.5% (n = 45) used 10 mg/mL dexamethasone, 3.1% (n = 40) received 24 mg/mL dexamethasone, 31.8% (n = 411) received 40 mg/mL methylprednisolone, 2.6% (n = 34) received 62.5 mg/mL methylprednisolone, and 5.2% (n = 67) received 125 mg/mL methylprednisolone. Hearing recovery ranged from 6.4-41 decibels (dB). The exploratory analysis did not identify significant differences in hearing recovery; however, methodological variance limits direct cross-study comparison and limits dose equivalence. Conclusion: Variability exists in regimen and outcomes reported. The findings of this study-level exploratory analysis should not be interpreted as evidence that a dose-response relationship does not exist. Therefore, this study provides a framework for researchers and clinicians to understand steroid regimens used to date.

KEYWORDS

Sudden sensorineural hearing loss (SSNHL), transtympanic steroid injection (TTM), intratympanic steroid, dexamethasone, methylprednisolone, hearing recovery, systematic review, steroid dosage, combination therapy.

ABBREVIATIONS

SSNHL (sudden sensorineural hearing loss), TTM (transtympanic membrane), PTA (pure tone average), IV (intravenous), dB (decibels), RCT (randomized controlled trial), PRISMA (preferred reporting items for systematic reviews and meta-Analyses) (ITM (intratympanic membrane), mg/mL (milligrams per millilite)

1 Introduction

In sudden sensorineural hearing loss treatment, transtympanic (TTM) membrane steroid injections are commonly used as a treatment option. Sudden sensorineural hearing loss (SSNHL) is an otologic emergency defined as sensorineural hearing loss of 30 decibels dB or greater over at least three contiguous audiometric frequencies occurring within a 72-hour period (Tripathi et al., 2022). SSNHL affects between 5 to 20 out of 100,000 people each year (Shemirani et al., 2009). SSNHL can be idiopathic or can arise from a variety of conditions such as metabolic, vascular, autoimmune, neurologic, infection, and traumatic conditions (Kuhn et al, 2011). TTM steroid injections, which involve injection of dexamethasone or methylprednisolone steroid through the tympanic membrane into the middle ear space, are commonly used as a treatment option (Plontke et al, 2022).

The presumed mechanism of action of corticosteroids to affect improvement in SNHL is unknown but presumed to be the reduction of edema and inflammation in the cochlea (Kuhn et al, 2011). Concentrations for dexamethasone and methylprednisolone used by clinicians across

international research are reported as 4-24 mg/mL and 40-125 mg/mL, respectively (Chandrasekar et al., 2019). There may be a dose-response relationship when examining steroid concentration and hearing recovery (Alexander et al., 2015; Sang et al., 2019; Shewel et al., 2020; Nelson et al., 2023). With the heterogeneous data reported, there is no clear conclusion on best practices for

Peer review under responsibility of PLA General Hospital Department of Otolaryngology Head and Neck Surgery.

* Corresponding author Anita Jeyakumar, ajeyakumar@neomed.edu

https://doi.org/10.26599/JOTO.2026.9540082

Received 5 May 2026; Revised 11 October 2026; Accepted 13 October 2026

©2026 PLA General Hospital Department of Otolaryngology Head and Neck Surgery. Publishing services by Tsinghua University Press. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

TTM (Roebuck et al., 2006; Inoue et al., 2012).

Objective

Our systematic review aims to review, compare, and summarize the steroid dosing

that have been used for treatment in the context of hearing recovery.

2 Methods

2.1 Literature Search

IRB approval was obtained. A systematic review was conducted according to PRISMA guidelines. Search terms used included "sensorineural hearing loss" and "transtympanic steroid injection" or "intratympanic steroid injection." Inclusion criteria were measurements for

hearing recovery (either improvement in pure tone average [PTA] or percent patient recovery), full-text articles, patients with unilateral or bilateral SNHL, and one TTM steroid dosage treatment. Both idiopathic and non-idiopathic cases of SNHL were included. Dates of studies included were published on or before January 20, 2025. Exclusion criteria included systematic reviews, meta-analyses, review articles, case reports, and articles with more than one

TTM steroid dosage. Articles related to Meniere's disease and ear infections were excluded due to the possibility of heterogeneity of the study populations. Primary outcomes were measured as hearing recovery (in decibels), percentage of patients who reported any degree of hearing recovery, and speech intelligibility (through speech discrimination score and word recognition score). Steroid regimen (type and dosage) was primarily considered with age, gender, simultaneous non-TTM systemic steroids, time to onset, primary versus salvage therapy, and injection schedule additionally considered. The age of the TTM steroid treatment group

was included. If this was not provided, the overall age of the participants or grouped ages (including the study's treatment and control group) were reported. PubMed, Google Scholar, and OVID were searched.

These three databases were selected to provide broad coverage of the relevant biomedical, medical, and otolaryngology literature. The search strategy incorporated terminology related to sensorineural hearing loss and transtympanic/intratympanic steroid therapy. Although three databases were searched, the selected sources provided overlapping coverage of the relevant literature; however, additional specialty-specific databases or trial registries, such as the Cochrane ENT Trials Register, may have identified supplementary studies. The absence of searches of additional specialty-specific sources is acknowledged as a limitation of the search strategy. The search was limited to studies published in English due to the authors' ability to accurately evaluate the methodology, extract data, and interpret the clinical outcomes reported in the included studies. We recognize that this language restriction may have introduced language bias and potentially resulted in the omission of relevant studies published in other languages; this is acknowledged as a limitation of the review.

Studies that compared multiple dosages of TTM steroid injections were excluded due to the

risk of double-counting. Inclusion of such studies could introduce bias through disproportionate weighting of studies with multiple arms and complicate aggregation of outcomes across studies as studies with multiple dosages of TTM may be weighed more heavily than those with a single dosage. A flowchart of inclusion and exclusion criteria in a PRISMA format is outlined in Figure 1.

Population:

Human patients with sensorineural hearing loss; Intervention:

transtympanic/intratympanic corticosteroid treatment; Comparison: transtympanic

steroid doses, concentrations, or treatment regimens; Outcomes: hearing

recovery measured by change in pure-tone average (PTA), percentage of patients with

hearing recovery, and speech intelligibility.

Data Analysis

Data were separated into tables based on steroid dosage, steroid regimen, etiology, study authors, participant characteristics, treatment regimens, steroid type and dosage, SNHL comorbidities, whether SNHL was idiopathic, hearing recovery, patient recovery, total injection volume (mL), and injection schedule. SN screened, reviewed, and extracted every article. NR and MB provided secondary screening, article review, and extraction where the articles were split in half for their review. Disagreements were resolved by the NR and MB depending on which reviewer was

not originally assigned to the article.

Mean Hearing Recovery Calculation

Mean hearing recovery (dB) was calculated for each treatment group, considering steroid type (dexamethasone or methylprednisolone) and dosage (mg/mL). For each treatment group, mean hearing recovery values (improvement in PTA) were recorded directly from the studies and averaged with those from the same treatment group; studies that did not state mean recovery values were excluded. Mean hearing recovery was then computed for all treatment groups. Since individual participant-level data, standardized variance estimates, outcome definitions, and treatment protocols, were not consistently available, this calculation represents a treatment-group-level descriptive summary rather than a pooled individual-level effect estimate.

Analysis of Doses and Hearing Recovery

All studies that defined their TTM injection protocol and reported average patient hearing recovery in dB were reviewed. To compare the effectiveness of different doses, a standardized measure of total drug given per week was found by multiplying concentration by average volume administered, then multiplied again by average doses per week. Because validated dose-equivalence relationships between transtympanic dexamethasone and methylprednisolone have not been established, dexamethasone amounts were then converted to the equivalent in Methylprednisolone by multiplying by a factor of 5.3, per a standardized dose efficacy ratio of IV administration assuming similar dose ratio relationship for TTM steroid administration.[24] The amounts of steroids given per week were then divided into three categories. Group 1 is "low dose" of <40mg total per week; Group 2 is "intermediate dose" of 40-70mg per week; Group 3 is "high dose" of >70mg per week. A Kruskal-Wallis test was performed to evaluate the data, given that the average hearing recovery between studies is not assumed to be normally distributed.

The process was performed again with a smaller subset of studies that reported systemic steroid use along with TTM injections. The groups were divided using the same criteria, and a Kruskal-Wallis test was run again.

Risk of Bias Assessment

Risk of bias was generated via the Joanna Briggs Institute criteria which employed criteria for RCTs and quasi-randomized studies,

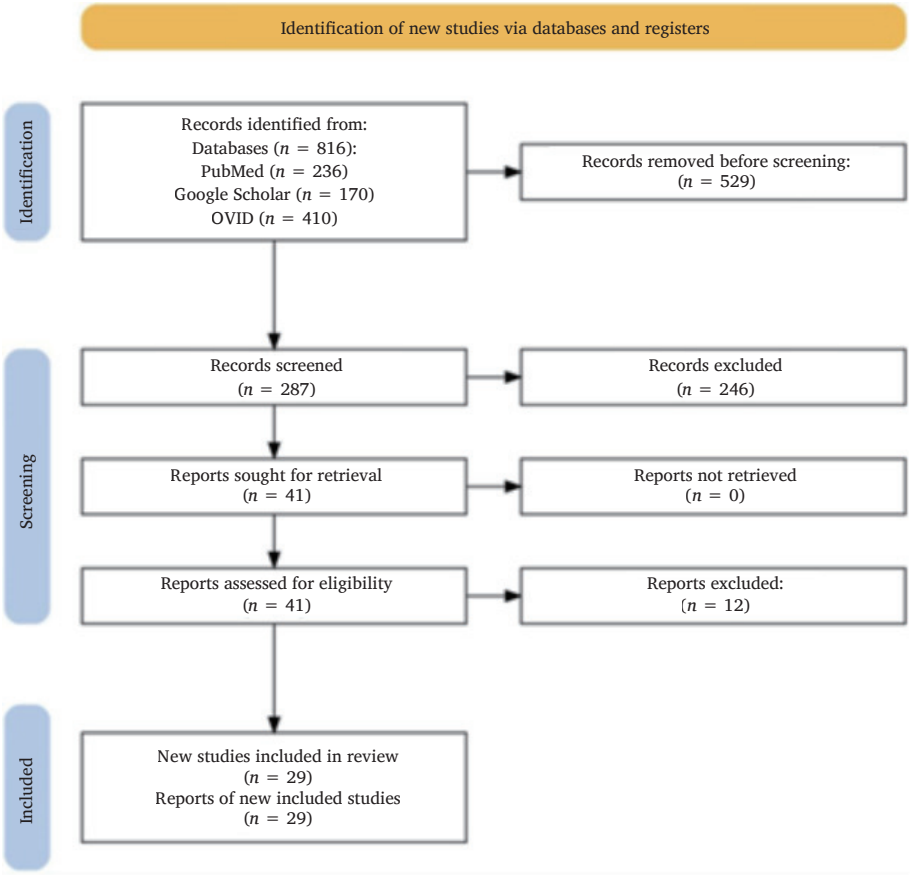


Figure 1 Flow Chart of Literature Search and Screening

retrospective observational studies, and case series studies. The corresponding criteria was used to appraise each study with answers of yes, no, and unclear if it was not specified in the text. Because the included studies varied in design, risk-of-bias assessment was performed using design-specific criteria rather than applying a single appraisal tool across all studies, with overall appraisal depending on patterns of answers.

3 Results

816 articles populated across the search. The 529 review articles were excluded. 287 articles were screened. 258 articles were excluded. 29 articles met final inclusion criteria with a total of 2,386 human subjects (Table 5). Of the patients with dose-specific data, 1,294 patients received TTM steroids.

Out of the studies that reported gender (23/29 studies including 1,163 subjects), 54.6% (635) were male and 45.4% (528) were female. 26/29 articles investigated primary steroid treatments while 3/29 investigated salvage steroid treatments. Of the patients receiving TTM steroids (1,294 total patients), 26.0% (n=336) received 4 mg/mL dexamethasone, 25.2% (n=326) received 5 mg/mL dexamethasone, 2.7% (n=35) received 8 mg/mL dexamethasone, 3.5% (n=45) used 10 mg/mL dexamethasone, 3.1% (n=40) received 24 mg/mL dexamethasone, 31.8% (n=411) received 40 mg/mL methylprednisolone, 2.6% (n=34) received 62.5 mg/mL methylprednisolone, and 5.2% (n=67) received 125 mg/mL methylprednisolone.

Of the 29 studies reviewed, 23 studies reported hearing recovery in PTA decibels, that ranged from 6.4-41 dB, and 7 studies reported speech intelligibility outcomes. The highest recovery for dexamethasone was 41 dB from a comparative study on diabetic patients in Japan (Kakehata et al., 2006) using a dosage of 4mg/mL (n=10). The highest recovery for methylprednisolone was 38.4 dB from an Italian clinical trial on patients with unilateral SSNHL (Filipo et al., 2010) using a dosage of 62.5 mg/mL (n=34) (Tables 1-8). Injection schedules (Table 9), time to onset and primary versus salvage nature of treatment (Table 10), PTA range definitions and influence of baseline PTA on recovery (Supplemental Table 1), speech intelligibility outcomes (Table 11) are outlined.

There were no significant differences in hearing recovery across groups ($\chi^2(2) = 1.86$, $p = 0.394$). The post hoc Dunn-Bonferroni test yielded no significant differences in pairwise post-correction ($p \geq 0.51$). No significant differences were observed amongst groups in the combination therapy analysis when comparing hearing recovery across intensity (magnitude of steroid dosage) across groups ($\chi^2(2) = 0.28$, $p = 0.87$).

The post hoc Dunn-Bonferroni test for this analysis yielded no significant differences in pairwise post-correction ($p \geq 0.64$) (Figures 2A-2B).Risk-of-bias assessment demonstrated variability across study designs. For RCTs and quasi-randomized studies, categories with the highest numbers of No/Unclear ratings were blinding of treatment providers (10/12), analysis according to randomized treatment assignment (9/12), and participant blinding (8/12). For retrospective observational studies, categories with the most No/Unclear ratings were follow-up completeness (7/9), strategies to address confounding (6/9), and exposure measurement consistency (3/9). For case series studies, categories with the most No/Unclear ratings were statistical analysis (4/8), comparability of groups where applicable (3/8), and strategies to address con-

Table 1 Distribution of Dosage, Hearing Recovery, and Patient Recovery

Type & Dosage of Steroid	Hearing Recovery (Mean dB)	Patient Recovery (% PTA Improvement
4 mg/mL Dexamethasone (n = 336)	9.9–41 dB	37%–100% (depending on study criteria)
5 mg/mL Dexamethasone (n = 326)	8.6–30.84 dB	34.8%–79.4% (depending on study criteria)
8 mg/mL Dexamethasone (n = 35)	20.9 dB	48.60% (depending on study criteria)
10 mg/mL Dexamethasone (n = 45)	12.2 dB	-
24 mg/mL Dexamethasone (n = 40)	15 dB	37.5% (depending on study criteria)
40 mg/mL Methylprednisolone (n = 411)	14.68–28.7 dB	46%–73% (depending on study criteria)
62.5 mg/mL Methylprednisolone (n = 34)	38.4 dB	77% (≥10 dB PTA decrease)
125 mg/mL Methylprednisolone (n = 67)	6.4 dB	66% (any improvement in PTA)

Table 2 Comparison of Hearing Recovery TTM Steroid Only versus Combination

Group	Steroid Type	Avg dB Recovery	Avg % Recovery (≥10 dB)	# of Studies
TTM Only	Dexamethasone	~17.5 dB	About 56%	9
Combination (TTM + systemic)	Dexamethasone	~26.8 dB	About 72%	10
TTM Only	Methylprednisolone	~21.4 dB	About 55%	8
Combination (TTM + systemic)	Methylprednisolone	~25.2 dB	About 67%	2

Table 3 Statistical Analysis of Steroid Dosage: where dexamethasone is converted to methylprednisolone equivalents and Group 1 is <40mg per week, Group 2 is 40-70mg per week, Group 3 is >70mg per week.

Kruskal-Wallis Ranks					
Group	n	Median	Mean Rank		
1	7	27	12		
2	8	17.15	9.69		
3	8	22.25	14.31		
Total	23	—	19.78		
Kruskal-Wallis Test					
Statistic	df	p-value			
1.86	2	0.394			
Dunn-Bonferroni Post-Hoc Tests					
Comparison	Test Statistic	Std. Error	Std. Test Statistic	p-value	Adjusted p-value
1-2	2.31	3.51	0.66	0.51	1
1-3	-2.31	3.51	-0.66	0.51	1
2-3	-4.62	3.39	-1.36	0.172	0.517

Table 4 Statistical Analysis: Combined Regimen Intensity and Duration: where dexamethasone is converted to methylprednisolone equivalents and Group 1 is <40mg per week, Group 2 is 40-70mg per week, Group 3 is >70mg per week

Kruskal-Wallis Ranks					
Group	n	Median	Mean Rank		
1	4	20.2	4.75		
2	3	19.78	5.67		
3	2	16.55	4.5		
Total	9	—	19.78		
Kruskal-Wallis Test					
Statistic	df	p-value			
0.28	2	0.87			
Dunn-Bonferroni Post-Hoc Tests					
Comparison	Test Statistic	Std. Error	Std. Test Statistic	p-value	Adjusted p-value
1-2	-0.92	2.09	-0.44	0.661	1
1-3	0.25	2.37	0.11	0.916	1
2-3	1.17	2.5	0.47	0.641	1

Table 5 Participant Characteristics and Study Design

Study	Participant characteristics (total population): total number, ethnicity, and sex; study design	Average Age (years)	Study Type
Arastou et al., 2013	77 patients from Iran (21 females, 56 males)	45.4 +/- 14.8 SD	Clinical trial
Hara et al., 2018	53 patients from the United States (24 females, 29 males)	Combined: 61.9 +/- 10.9; TTM: 66.7 +/- 13.5	Retrospective review
Yang et al., 2015	220 patients from China (132 females, 88 males); retrospective case–control study	47.4 +/- 16.2	Retrospective case-control study.
Suzuki et al., 2012	276 patients from Japan (146 females, 130 males)	57.0 +/- 19.4	Randomized clinical trial
Choung et al., 2006	66 patients from South Korea (39 females, 27 males)	39.3	Case-control study
Kakehata et al., 2006	32 patients from Japan (9 females, 23 males)	57.7 +/- 3.3	Comparative study
Zhou et al., 2011	86 patients from China (30 females, 56 males)	53.84 +/-14.9	Randomized control trial
Ermutlu et al., 2017	35 patients from Turkey (12 females, 23 males)	49.68 (range 24–80 years)	Prospective randomized case-controlled clinical trial
Zhou et al., 2013	62 patients from China (9 females, 53 males)	28.62 +/- 18.4	Randomized control trial
Dispenza et al., 2011	46 patients from Italy (18 females, 28 males)	Overall: <39: n=12, 39-59: n=19; <59: n=15	Randomized control trial
Dallan et al., 2006	12 patients from Italy (7 females, 5 males)	Overall: 59 +/- 19 SD (26-81 range)	Prospective, non-randomized study
Wang et al., 2012	87 patients from China (35 females, 52 males)	46.2 +/- 13.3	Controlled Clinical Trial
Ho et al., 2004	29 patients from Taiwan (13 females, 16 males)	46.1 +/- 19.9	Clinical Trial
Khadav et al., 2022	45 patients from India (17 females, 28 males)	Combined: 37.93; TTM: 47.66	Prospective case control study
Kovács et al., 2024	78 patients from Hungary (42 females, 36 males)	52.3 (25.7% cohort above age of 60)	Randomized control trial
Wu et al., 2011	55 patients from China (37 females, 18 males)	49.1 +/- 4.250.9	Randomized control trial
Tsai et al., 2011	128 patients from Taiwan (59 females, 69 males)	Responsive patients: 56.1+/-12.2; Unresponsive patients: 58.9+/-17.4	Retrospective chart review
Xenellis et al., 2006	37 patients from Greece (20 females, 17 males)	50.9	Randomized control trial
Rauch et al., 2011	250 patients from the United States (99 females, 151 males)	51.3 (48.3-53.9)	Randomized control trial
Haynes et al., 2007	40 patients from the United States (26 females, 14 males)	Overall: 54.8 (range 17-84)	Retrospective review
Swachia et al., 2016	42 patients from India (16 females, 26 males)	Overall: range 18-65	Randomized control trial
Filipo et al., 2010	34 patients from Italy (17 females, 17 males)	Overall: 51 +/- 17.8	Clinical trial
Deenadayal et al., 2016	67 patients from India (24 females, 43 males)	Overall: 44 (range 13-75)	Retrospective study
Swaminatha et al., 2019	44 patients from India (13 females, 31 males)	Overall: 47.43 +/- 14.358 (range: 18-77)	Non-randomized control trial
Jia et al., 2019	212 patients from China (116 females, 96 males)	Combined: 53.4 +/- 12.8; TTM: 54.7 +/- 13.42	Retrospective analysis
Joshi et al., 2011	27 patients from India		Prospective study
Han et al., 2009	114 patients from South Korea	56.5 +/- 12.8	Prospective non-randomized multicenter clinical trial
Jung et al., 2016	105 patients from South Korea	47.6 +/- 15.7	Retrospective case control
Dallan et al., 2010	27 participants from Italy	56.5 +/- 15.6	Prospective case series

founding where applicable (2/8) (Supplemental Table 2-4).

4 Discussion

Substantial variability exists within regimen and hearing outcomes. The most commonly cited concentrations of TTM steroids are dexamethasone at 4-24 mg/mL and methylprednisolone at 30 or 40 mg/mL, but other studies have used other dosages (Chandrasekar et al., 2019). A dose-response relationship may exist when examining steroid concentration and hearing recovery, but our review did not substantiate a dose-response relationship. Specifically, one retrospective case series study suggests that patients administered 24 mg/mL yielded double the hearing improvement rate as those administered 10 mg/mL (Alexander et al., 2015). A prospective randomized control trial (RCT) study using 10 mg/mL yielded higher hearing recovery rates than those administered 4 mg/mL (Shewel et al., 2020). Conversely, a retrospective cohort study has suggested that there was no significant difference between 10 mg/mL and 24 mg/mL dosage and recovery rates for SNHL (Nelson et al., 2022). Moreover, while 4-24 mg/mL dexamethasone is commonly used, one prospective study has suggested that 125 mg/mL methylprednisolone may yield higher hearing recovery rates (Sang et al., 2019).

4.1 Steroid Dosage

4-5 mg/mL dexamethasone was the most common dosage among the 29 studies reviewed and was used in 16 studies across 662 participants (51.2% of the patients undergoing TTM therapy). Despite previous research suggesting higher doses of TTM steroids are associated with higher hearing recovery rates

Table 6 Intervention and Comorbidities

Study	Total receiving intervention with transtympanic membrane TTM steroid: total number, ethnicity, sex	Comorbidities and Idiopathic Diagnosis (Amongst TTM Treated Participants)
Arastou et al., 2013	36 participants received TTM steroid (25 males and 11 females)	
Hara et al., 2018	45 participants received TTM steroid (26 males and 19 females): 39 received combined oral + IT therapy (21 males and 18 females), and 6 received IT therapy alone (5 males and 1 female).	45 idiopathic cases
Yang et al., 2015	55 participants received TTM steroid (33 male and 22 female)	7 had diabetes; 14 had hypertension
Suzuki et al., 2012	102 participants received TTM steroid (49 males and 53 females)	28 diabetes; 102 idiopathic cases
Choung et al., 2006	33 participants received TTM steroid (13 males and 20 females)	
Kakehata et al., 2006	10 participants received TTM steroid	10 had diabetes
Zhou et al., 2011	37 participants received TTM steroid (24 males and 13 females)	
Ermutlu et al., 2017	19 participants received TTM steroid (14 males and 5 females)	
Zhou et al., 2013	27 participants received TTM steroid (22 males and 5 females)	27 were idiopathic cases
Dispenza et al., 2011	25 participants received TTM steroid	
Dallan et al., 2006	8 participants received TTM (4 males and 4 females)	
Wang et al., 2012	23 participants received TTM steroid (15 males and 8 females)	
Ho et al., 2004	15 participants received TTM steroid	2 had diabetes
Khadav et al., 2022	30 participants received TTM steroid (15 TTM steroid only (8 male and 7 female) and 15 combined TTM and systemic steroid (10 male and 5 female))	
Kovács et al., 2024	35 participants received TTM steroid (17 males and 18 females)	3 had diabetes; 16 had cardiovascular disease; 35 idiopathic cases
Wu et al., 2011	28 participants received TTM steroid (9 males and 19 females)	7 had diabetes
Tsai et al., 2011	128 participants received TTM steroid (69 males and 59 females)	17 had diabetes and 18 had hypertension
Xenellis et al., 2006	19 participants received TTM steroid (9 males and 10 females)	19 idiopathic cases
Rauch et al., 2011	113 participants received TTM steroid (68 males and 45 females)	113 idiopathic cases
Haynes et al., 2007	40 participants received TTM steroid (14 males and 26 females)	5 had diabetes
Swachia et al., 2016	20 participants received TTM steroid	3 patients had diabetes; unspecified number of participants with hypertension
Filipo et al., 2010	34 participants (17 males and 17 females) participants received TTM steroid	
Deenadayal et al., 2016	67 participants received TTM steroid (43 males and 24 females)	67 idiopathic cases
Swaminatha et al., 2019	44 participants received TTM (31 males and 13 females) (23 TTM steroid only; 21 combination IV and TTM steroid)	15 had diabetes and 10 had hypertension
Jia et al., 2019	160 participants received TTM steroid (82 TTM steroid only [43 males and 39 females] and 78 combined TTM steroid and intravenous batroxobin [35 males and 43 females]).	212 total had diabetes; 160 total patients received TTM; not specified how many of the TTM patients have diabetes.
Joshi et al., 2011	27 participants received TTM steroid	27 idiopathic cases
Han et al., 2009	34 participants received TTM steroid	34 had diabetes
Jung et al., 2016	53 participants received TTM steroid (28 males and 25 females)	53 idiopathic cases
Dallan et al., 2010	27 participants received TTM steroid (9 males and 18 females)	

(Alexander et al., 2015; Arastou et al., 2013; Chandrasekar et al., 2019), these findings were not replicated in this work. When a Kruskal-Wallis statistical analysis was used to compare low, medium, and high-dose TTM steroid use, no significant differences were observed ($\chi^2(2) = 1.86$, $p = 0.394$). Even after adjusting through Post-hoc Dunn-Bonferroni tests, statistically significant differences were still not observed ($p \geq 0.51$). It cannot be concluded that higher TTM steroid dosage yielded higher hearing recovery. These findings did not demonstrate a statistically significant association between higher TTM steroid dosage and hearing recovery; however, they do not establish that higher doses are ineffective.

The highest reported hearing recoveries within the 4-5 mg/mL TTM dexamethasone range were from Kakehata et al. (2006) at 41 dB. Their study of Japanese patients used 4 mg/mL dexamethasone. The next highest hearing recovery was reported by Yang et al. (2015). They reported a retrospective, case-control study on South Korean patients that showed an average 30.84 dB recovery rate at a with treatment using 5mg/mL of dexamethasone combined with 80mg of oral methylprednisolone. However, while 4-5 mg/mL TTM dexamethasone can result in significant hearing recovery, the systematic review also indicates low hearing recovery rates with similar dosages. Specifically, the lowest hearing recovery rates within the 4-5 mg/mL dexamethasone range were 8.6 dB (Wang et al., 2012) from a controlled clinical trial using 5 mg/mL of dexamethasone performed on patients of Chinese descent and 9.1 dB which is a case control study using a 5 mg/mL dexamethasone dosage on Chinese patients (Choung et al., 2006). In essence,

Table 7 Steroid Dosage and Regimen

Author	Dosage	Treatment Regimen
Arastou et al., 2013	4 mg/mL Dexamethasone	Combination therapy with systemic intravenous (IV) steroid prednisolone 1 mg/kg
Choung et al., 2006	5 mg/mL Dexamethasone	
Deenadayal et al., 2016	125 mg/mL Methylprednisolone	
Dispenza et al., 2011	4 mg/mL Dexamethasone	
Ermutlu et al., 2017	4 mg/mL Dexamethasone	
Filipo et al., 2010	62.5 mg/mL Methylprednisolone	
Hara et al., 2018	10 mg/mL Dexamethasone	Combination therapy with oral steroids 60 mg prednisone
Han et al., 2009	5 mg/mL Dexamethasone	
Ho et al., 2004	4 mg/mL Dexamethasone	Combination therapy with Methylprednisolone 1 mg/kg per day divided in 2 doses for 5 days tapering to 10 mg for another 5 days
Jia et al., 2019	40 mg/mL Methylprednisolone	
Joshi et al., 2011	4 mg/mL Dexamethasone	
Jung et al., 2016	5 mg/mL Dexamethasone	Combination 10 mg IV Dexamethasone for 5 days then 5 days reduced to lower dosage of 5 mg
Kakehata et al., 2006	4 mg/mL Dexamethasone	
Khadav et al., 2022	4 mg/mL Dexamethasone	Combination therapy with 1 mg/kg oral Methylprednisolone
Kovács et al., 2024	8 mg/mL Dexamethasone	Combination therapy with IV methylprednisolone-natrium-succinate 250 mg three days then 125 mg for 2 days, then tapering oral corticosteroid with 8 mg maximum
Rauch et al., 2011	40 mg/mL Methylprednisolone	
Swachia et al., 2016	40 mg/mL Methylprednisolone	
Swaminatha et al., 2019	4 mg/mL Dexamethasone	Combination IV methylprednisolone day 1 1g, day 2 500 mg and day 3 250 mg
Suzuki et al., 2012	4 mg/mL Dexamethasone	Combination therapy with IV Hydrocortisone (400 mg per day)
Tsai et al., 2011	5 mg/mL Dexamethasone	
Wang et al., 2012	5 mg/mL Dexamethasone	
Xenellis et al., 2006	40 mg/mL Methylprednisolone	
Yang et al., 2015	5 mg/mL Dexamethasone	Combination therapy with 80 mg of oral methylprednisolone for four days, then 60 mg of oral methylprednisolone for two days, tapering for six days
Zhou et al., 2011	40 mg/mL Methylprednisolone	Combination therapy with Methylprednisolone IV: 125 mg on day 1, then 32 mg for 5 days, then 16 mg for 2 days, then 8 mg for 2 days
Zhou et al., 2013	40 mg/mL Methylprednisolone	Combination therapy with Methylprednisolone IV: 125 mg on day 1, then 32 mg for 5 days, then 16 mg for 2 days, then 8 mg for 2 days
Dallan et al., 2006	40 mg/mL Methylprednisolone	
Dallan et al., 2010	40 mg/mL Methylprednisolone	
Haynes et al., 2007	24 mg/mL Dexamethasone	
Wu et al., 2011	4 mg/mL Dexamethasone	Combination - Initial therapy with IV steroids for 5 days and tapers off of steroids with oral prednisolone for 5 days; Dexamethasone given in 4 injections of 0.5 mL within a 2 week period (4 days apart)

the most common dosage of 4-5 mg/mL dexamethasone yields a variety of hearing recovery and has been tested with a variety of treatment regimens, such as those that incorporate additional oral or IV steroids. Given the results in hearing recovery using 4-5 mg/mL dexamethasone considerable hearing recovery has still been reported with lower steroid dosage.

Steroid Type

The two types of TTM steroids reviewed in our study were (1) dexamethasone and (2) methylprednisolone. Previous research suggests that 125 mg/mL methylprednisolone may yield higher hearing recovery rates than 24 mg/mL dexamethasone.[29] Dexamethasone was the most common steroid used in the study with 19 of the 29 (782 total patients and 60.4% of TTM patients) using dexamethasone and 10 out of 29 (512 total patients and 39.6% of TTM patients) using methylprednisolone. The highest hearing recovery was 41 dB recovery using a 4 mg/mL dosage (Kakehata et al., 2006) while the lowest dosage of dexamethasone was 8.6 dB using a 5 mg/mL dexamethasone dosage (Wang et al., 2012). The highest hearing recovery of methylprednisolone of 38.4 dB was reported by Filipo et al. (2010) using a dosage of 62.5 mg/mL methylprednisolone, and the lowest was 6.4 dB which was reported by a retrospective study on patients in India using 125 mg/mL methylprednisolone (Deenadayal et al., 2016). It is unclear whether dexamethasone or methylprednisolone yields higher recovery, and further experimental study is warranted.

TTM Only versus Combined (TTM and Systemic Steroid) Regimens

The 12 studies using combination regimens included 507 TTM-treated participants, while the remaining studies included 787 TTM-treated participants receiving TTM steroid therapy without an additional systemic steroid regimen. Previous research suggests the effectiveness of combining TTM steroid with systemic steroids

Table 8 Hearing Outcomes and Recovery

Author	Hearing Recovery (dB)	Patient Recovery (Improvement of PTA)
Deenadayal et al., 2016	6.4 dB	66% recovery (more than 0 dB decreased PTA threshold)
Wang et al., 2012	8.6 dB	34.8% recovery (16-54 dB decreased PTA threshold)
Choung et al., 2006	9.1 dB	39.4% recovery (at least 10 dB decreased PTA threshold)
Wu et al., 2011	9.9 dB	44.4% (at least 10 dB decreased PTA threshold)
Suzuki et al., 2012	12 dB	79.4% recovery (at least 10 dB decreased PTA threshold)
Hara et al., 2018	12.2 dB	Combination therapy / Recovery
Swachia et al., 2016	14.68 dB	
Xenellis et al., 2006	14.9 dB	47% (at least 10 dB decreased PTA threshold)
Haynes et al., 2007	15 dB	37.50% recovery (at least 20 dB decreased PTA threshold or at least 20% improved SDS)
Zhou et al., 2013	15 dB	52% recovery (at least 15 dB decreased PTA threshold)
Dallan et al., 2010	19.3 dB	55.6% recovery rate (at least 18 dB relative gain for PTA)
Swaminatha et al., 2019	19.78 dB	52% recovery (at 15 dB decreased PTA threshold)
Kovács et al., 2023	20.9 dB	45.6% recovery for systemic only; 48.6% for combined (at least 15 dB decreased PTA threshold)
Dallan et al., 2006	22.4 dB	53% recovery (at least 15 dB decreased PTA threshold)
Jia et al., 2019	23.6 dB	73% any recovery (at least 15 dB decreased PTA threshold)
Dispenza et al., 2011	27 dB	80% recovery (at least 10 dB decreased PTA threshold)
Tsai et al., 2011	27 dB	69% recovery (at least 10 dB decreased PTA threshold)
Ho et al., 2004	28.4 dB	53.3% recovery (over 30 dB decreased PTA threshold)
Rauch et al., 2011	28.7 dB	61% (at least 10 dB decreased PTA threshold)
Jung et al., 2016	29.5 dB	69.8% recovery rate (at least 15 dB decreased PTA threshold)
Yang et al., 2015	30.84 dB	60% recovery (more than 10 dB in PTA)
Kakehata et al., 2006	41 dB	70% recovery (improvement of at least 30 dB); 100% (improvement of at least 10 dB)
Filipo et al., 2010	38.4 dB	77% recovery (at least 10 dB decreased PTA threshold)
Zhou et al., 2011		46% recovery (significant improvement in at least 15 dB decreased PTA threshold)
Arastou et al., 2013		75% recovery rate (at least 15 dB decreased PTA threshold)
Ermutlu et al., 2017		84.2% recovery (based on 15 dB PTA decreased PTA threshold or WRS)
Han et al., 2009		79.4% recovery rate (at least 15 dB decreased PTA threshold)
Khadav et al., 2022		66.67% recovery: Combined oral and ITD; 33.33% recovery: ITD only group (at least 10 dB decreased PTA threshold)
Joshi et al., 2011		37% recovery (at least 10 dB decreased PTA threshold)

for treatment of SNHL when compared with TTM steroid only (Inoure et al., 2012; Roebuck et al., 2006).

Most studies using a combined regimens sought to test whether combined versus single yields higher hearing recovery. No significant differences were observed in hearing outcomes among groups who received different concentrations of steroids. Specifically, when Kruskal-Wallis tests were performed, statistically significant differences were not found across longer and higher dosage systemic regimens ($\chi^2(2) = 0.28$, $p = 0.87$). Even after the Dunn-Bonferroni correction, higher hearing recovery rates were not seen with longer and higher dose systemic steroids ($p \geq 0.64$). The highest hearing recovery rates in the combined regimen studies were for (1) a study using 5 mg/mL dexamethasone dosage combined with 80 mg oral methylprednisolone that yielded a 30.84 dB hearing recovery (Yang et al., 2015) and (2) a retrospective case-control study using 5 mg/mL dexamethasone dosage combined with 10 mg/mL IV dexamethasone that yielded a 29.5 dB (Jung Jung et al., 2016). Studies in the review that used TTM steroid therapy only appeared to also report substantial recovery rates. Further experimental study could test TTM therapy versus TTM with additional systemic therapy.

Injection Schedules

TTM steroid protocols varied, with injection volumes ranging from 0.2-1.0 mL and treatment schedules varying from single injections to daily dosing over several weeks. Most studies administered around 0.3-0.5 mL per injection, commonly given as 3-4 injections over 1-2 weeks. Follow-up timing was not uniform across studies, and injection volume and schedules ranged from single injections to repeated treatments over several weeks (Table 7). This variability highlights the lack of standardization in dosing protocol and may explain outcomes heterogeneity.

4.2 *Time to Onset and Primary versus Salvage Treatment*

Twenty-six of the 29 studies investigated TTM steroid regimens as primary treatments, while 3 of the 29 studies investigated TTM regimens as salvage treatment. Most studies investigated treatment within seven days, but some investigated two weeks or more. Studies with patients earlier and within 7-10 days, such as Ermutlu et al. (2017) and Jia et al. (2019), displayed greater than or equal to

Table 9 Total Injection Volume and Injection Schedules

Study	Total Injection Volume (mL)	Dose Schedule
Deenadayal et al., 2016	0.3	4 injections in 20 days
Choung et al., 2006	0.3 to 0.4	4 injections in 2 weeks (twice per week same dosage)
Yang et al., 2015	0.3–0.4	6 injections in 2 weeks (every 2–3 days same dosage)
Joshi et al., 2011	0.3–0.5	3 injections in 3 weeks
Haynes et al., 2007	0.3 to 0.5	Up to 3 injections in 1 day
Suzuki et al., 2012	0.2 to 0.4	4 injections in 4 weeks (every week same injection)
Filipo et al., 2010	0.4	3 injections in 3 days
Arastou et al., 2013	0.4	4 injections in 20 days
Zhou et al., 2013	0.4	4 injections in 8 days (one injection of same dosage every other day)
Ho et al., 2004	0.4 to 0.7	3 injections in 3 weeks
Khadav et al., 2022	0.5 ml	4 injections in 4 weeks
Wu et al., 2011	0.5	4 injections in 2 weeks
Tsai et al., 2011	0.5	4 injections in 2 weeks
Han et al., 2009	0.5	4 injections in 2 weeks
Xenellis et al., 2006	0.5	4 injections in 15 days
Wang et al., 2012	0.5	4 injections in 8 days (one injection of same dosage every other day)
Kakehata et al., 2006	0.5	8 injections in 8 days (each day same dosage)
Ermutlu et al., 2017	0.5–0.7	3 injections in 6 days (3 times same dosage every other day)
Jung et al., 2016	0.3 and 0.7	5 injections in 10 days
Jia et al., 2019	0.6–0.8	5 injections in 10 days
Dallan et al., 2006	1	1 injection
Dallan et al., 2010	1	1 injection
Rauch et al., 2011	1	4 injections in 2 weeks
Swachia et al., 2016	1	4 injections in 2 weeks
Swaminatha et al., 2019	0.5–1	3 injections in 5 days
Hara et al., 2018	Not stated	3 injections in 7-10 days
Dispenza et al., 2011	0.4–0.5	4 injections in 4 weeks
Kovács et al., 2024	0.3–0.5	5 injections in 5 days

15 dB recovery while delayed and salvage treatments displayed more variable and/or lower dB recovery, such as Dallan et al. (2006) and Haynes et al. (2007).

4.3 PTA Definition and Baseline PTA Considerations

Most studies used four to six frequencies, ranging from 250 Hz and 8 kHz. PTA was a strong prognostic factor in some studies where higher baseline PTA was associated with worse recovery (Filipo et al., 2010; Haynes et al., 2007; Swachia et al., 2016). It is important to note that there was prominent variance in outcome definition, especially for PTA across studies. PTA was calculated using different sets of frequencies, and recovery thresholds ranged from any PTA improvement to specified thresholds such as ≥10, ≥15, ≥20, or ≥30 dB; some studies also incorporated speech discrimination or word-recognition

measures. However, PTA was not explicitly considered a prognostic factor for hearing recovery in the rest of the study. Overall, PTA was measured in a variety of ways, with baseline PTA

being useful, but not a universal predictive factor for hearing prognosis. These differences in PTA definition also reduce the ability to draw quantitative comparisons between groups.

4.4 Comorbidities: Idiopathic Versus Non-Idiopathic SNHL

Several studies (12 of 29) reported diabetes and hypertension within their study participants. Of those treated with TTM steroids, 124 had diabetes and 58 had hypertension and/or cardiovascular disease. These aggregate counts include only studies that had confirmed TTM participants with each comorbidity. Jia et al. (2019) reported that 212 patients in the overall study population had diabetes, but did not specify how many of the 160 TTM patients had diabetes while Swachia et al. (2016) reported that 3 TTM patients had diabetes but did not specify the number of TTM participants with hypertension.

A total of 488 participants had SNHL pathologies labeled as idiopathic. For the 12 studies that included patients with comorbidities (diabetes and/or hypertension), the hearing recovery averages ranged from 9.9 to 41 dB, and 6 out of the 12 studies used combined regimens. Several studies (8 studies out of 29) also reported SNHL as idiopathic. The hearing recovery rates of these studies ranged from 12-29.5 dB with 2 out of 8 studies using combined TTM and systemic steroid regimens. It is unclear whether idiopathic SNHL has different responsiveness to TTM steroid therapy and combined TTM and systemic steroid therapy than

Table 10 Time to Onset and Primary Versus Salvage Treatment

Study	Time to Onset	Primary or Salvage
Yang et al., 2015	TTM (d): 5.4 +/-10.5; control: 4.8 +/-6.5; p= 0.450	Primary.
Suzuki et al., 2012	TTM (d): 5.5 +/- 4.6; HBO (d): 6.1 +/- 5.5; p=0.358	Primary
Choung et al., 2006	TTM (d): 5.2; control (d): 6.5; p=0.831	Primary
Kakehata et al., 2006	TTM (d): 5.5 +/- 1.1; IV Steroid: 4.7 +/- 1.0; p = NS	Primary
Zhou et al., 2011	control (d): 11.2 +/- 6.2; TTM: 9.6 +/- 8.3 days. The differences of these datawas not significant	Primary
Ermutlu et al., 2017	Not discussed	Primary
Zhou et al., 2013	The time from onset to initial treatment was 3 days to 2 weeks.	Primary
Dispenza et al., 2011	Days before beginning treatment <3: 15 (32.6%); 3-10: 23 (50%) >10: 8 (17.4%)	Primary
Dallan et al., 2006	21.5 +/- 9.6 SD days with a range of 11–39 days	Salvage
Wang et al., 2012	Not discussed	Primary
Ho et al., 2004	Not discussed	Primary
Khadav et al., 2022	<3 days of presentation: 13 patients; From 3 to 14 days of presentation; 18 patients; From 8 to 14 days of presentation; 14 patients	Primary
Kovács et al., 2024	Onset of symptoms (4 days, %): TTM:6.4: systemic only: 8.4; p = 0.063 Onset of symptoms (7 days, %): TTM: 65.7: systemic: 69.8: p = 0.703	Primary
Wu et al., 2011	TTM (d): 4.4. +/- 1.6; control (d): 4.7 +/- 1.9, p= 0.613	Salvage
Tsai et al., 2011	92 patients were treated in less than or equal to seven days; 36 patients were treated in greater than seven days	Primary
Xenellis et al., 2006	Time to onset was 30 days or less	Primary
Rauch et al., 2011	Oral <7 day: 61; TTM <7 day: 62; Oral greater than or equal to 7 day: 60; TTM greater than or equal to 7 day: 67	Primary
Haynes et al., 2007	10 d or less: 4 patients; 11–20 d: 10 patients; 21–30 d: 7 patients >30: 19 patients	Primary
Swachia et al., 2016	Less than 14 days	Primary
Filipo et al., 2010	Less than or equal to 15 days	Primary
Deenadayal et al., 2016	Mean of 10.8 days	Primary
Swaminatha et al., 2019	within 10 days	Primary
Jia et al., 2019	TTM: 6.7 ± 6.4; control: 7.6 ± 6.8	Primary
Joshi et al., 2011	time lapse of 6 weeks or less between onset of hearing loss and time of initial presentation	primary
Han et al., 2009	14 days after the initial systemic treatment	Salvage
Jung et al., 2016	Within 10 days from onset of hearing loss	Primary
Dallan et al., 2010	20.5 +/- 29.8 SD days (range, 7Y150)	Primary
Arastou et al., 2013	Delay to treatment (d): Treatment: Average: 18.97(SD:23.6); Control: Average 15.5(SD: 22.6)	Primary
Hara et al., 2018	21.3622.9 (1–90)	Primary

Table 11 Speech Intelligibility Outcomes

Study	Speech Intelligibility (Speech Discrimination Score (SDS)/Word Recognition Score (WRS))
Zhou et al., 2011	43.2% improvement (significant at least 15% improvement in SDS)
Ermutlu et al., 2017	84.2% recovery (based on at least 10 dB decreased PTA threshold or at least 10% WRS)
Zhou et al., 2013	67% improvement (based on improvement at least 15% SDS)
Rauch et al., 2011	Increase of speech discrimination of 16.3% (41.7% to 58%)
Haynes et al., 2007	37.50% recovery (at least 20 dB decreased PTA threshold or at least 20% improved SDS)
Deenadayal et al., 2016	Improvement of 5.7 (49.6% to 55.3%)
Jung et al., 2016	No significant improvement

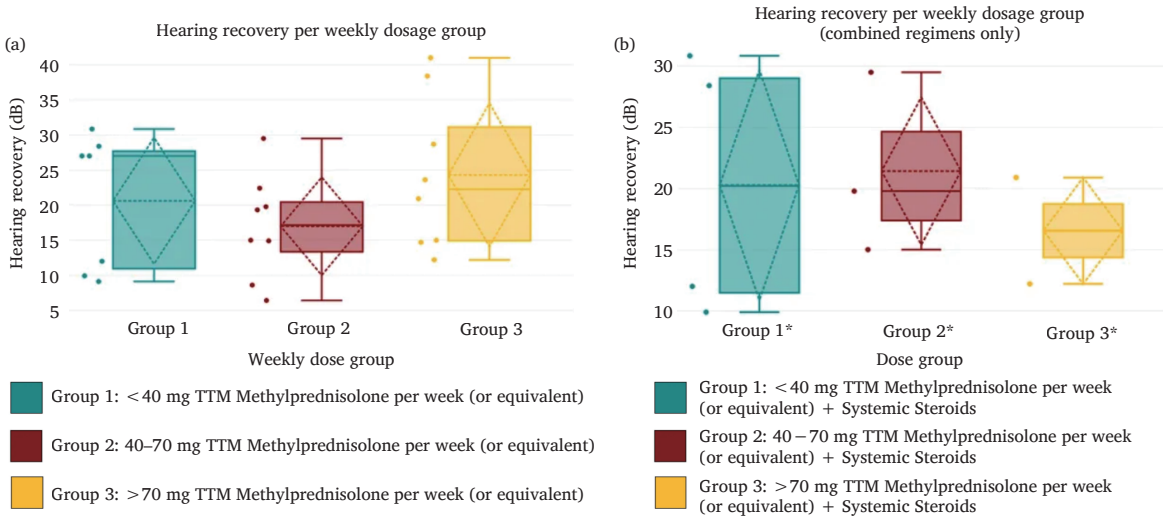


Figure 2 Statistical Analysis for Transtympanic Steroid Dosage Level: where dexamethasone is converted to methylprednisolone equivalents and Group 1 is <40mg per week, Group 2 is 40-70mg per week, Group 3 is >70mg per week. Figure 2B: Statistical Analysis for Combination Steroid Dosage Level: where dexamethasone is converted to methylprednisolone equivalents and Group 1 is <40mg per week, Group 2 is 40-70mg per week, Group 3 is >70mg per week.

non-idiopathic SNHL. Given the heterogeneity of the study, conclusions cannot be drawn about which doses and regimens are the most effective for idiopathic SNHL patients. Accordingly, the findings of this review should be interpreted as applying broadly to the heterogeneous population of SNHL represented in the included literature rather than exclusively to idiopathic SNHL.

Speech Intelligibility

In addition to PTA measurements, an assessment of speech intelligibility may be used to help assess hearing recovery. However, only seven out of the 29 total studies included speech intelligibility in their outcomes data. Only four studies reported speech intelligibility as a separate outcome from PTA. Additional research is needed concerning the impact of treatment on speech intelligibility. We recommend that future studies report it.

4.5 *Mechanistic Considerations for TTM Steroids*

The specific mechanism by which TTM steroids treat SNHL remains incompletely understood. After middle ear administration, steroids are believed to reach the inner ear via diffusing across the round window membrane. Passage through the oval window or alternative anatomic pathways have been proposed. There is variance within steroid permeability which influences susceptibility to treatment. Heterogeneity within the round window mucosal folds, fibrosis, and inflammatory composition may also mediate responses to TTM steroid.

Variance in TTM formulation, such as dexamethasone versus dexamethasone phosphate's molecular weight differences, may influence round window permeability and intracochlear pharmacokinetics. As described in previous research, drug properties may affect intratympanic delivery, such as round window membrane diffusion as well as cochlear clearance and distribution (Salt et al., 2018). Future studies should investigate formulation-specific pharmacokinetics and treatment efficacy.

Drug-delivery strategies, such as sustained-release formulation, biodegradable hydrogels, nanoparticles, and catheter-based or micro-pump delivery systems, which seek to drug delivery to the round window may reduce steroid delivery.

Emerging data suggests that SNHL may involve both peripheral cochlea damage and inflammation of central auditory pathways triggering microglial and astrocytic activation in cochlear nuclei and superior olivary complex. TTM steroids may help target cochlear inflammation while the systemic steroids may mediate central auditory inflammation (Kim, 2022). Future research should elucidate the TTM's effect on SNHL.

Limitations

Limitations of the study include heterogeneity in terms of dosage, regimen, and demographics. Additionally, there were substantial inconsistencies in the reporting of hearing recovery, patient recovery, and speech intelligibility reporting, making it difficult to compare studies, consider confounders, and assess the certainty of the reported findings. Not all studies reported hearing recovery in decibels, and patient recovery rates had varying definitions. Variability in study design and lack of uniform reporting standards may further affect the overall strength of the evidence base and limit the confidence ratings. Furthermore, methodological limitations reflected in the risk of bias assessment and critical appraisal may reduce confidence in attributing observed differences in hearing outcomes specifically to transtympanic or intratympanic steroid therapy or dosage. In particular, limitations in treatment allocation, blinding, follow-up, and control of confounding highlight the heterogeneity in methodological rigor across the available evidence, suggesting potential bias may be included in the articles reviewed. The heterogeneity in PTA definitions, recovery criteria, follow-up intervals, injection volumes, dosing frequency, treatment timing, and use of concomitant systemic steroids precluded a valid pooled effect estimate. Accordingly, we did not perform a formal meta-analysis. The Kruskal–Wallis analyses should be regarded as descriptive, exploratory study-level comparisons rather than estimates of comparative treatment efficacy. The absence of searches of additional specialty-specific sources and use of three databases is acknowledged as a limitation of the search strategy. Three databases were selected given the overlap in articles across databases. The three particular databases, PubMed, OVID, and Google Scholar, were with the intention to provide broad coverage of the relevant biomedical, medical, and otolaryngology literature. Limiting the study search to texts English was done to preserve authors' ability to accurately evaluate the methodology, extract data, and interpret the clinical outcomes reported in the included studies; however, this language restriction may have introduced language bias and potentially resulted in the omission of relevant

studies published and is a limitation of our study.

The use of grouped analysis of steroid ranges instead of a continuous analysis for statistical analysis is a limitation. Differences in dosage calculation and reporting may as well as bias concerning the time to initiate treatment introduce misclassification bias in grouping and comparison and confounding factors influencing confounding variables. Our study is also limited by the quality of the studies reviewed. Specifically, publication and selection biases may be present in the studies included as positive and significant findings are more likely to be published. Lastly, while a comprehensive search strategy was used across multiple databases, the possibility of missed studies cannot be fully excluded. Because PTA definitions, recovery criteria, follow-up, injection schedules, treatment timing, and patient populations varied substantially, these recovery values should not be interpreted as directly comparable estimates of treatment efficacy, and these findings should not be interpreted as evidence against a dose-response relationship.

5 Conclusion

The systematic review summarizes SNHL regimens to date along with measurable outcomes of these regimens, serving as a guide for assessing what regimens have been reported to date. A wide heterogeneity of regimens was studied with a wide range of hearing improvements reported from 6.4-41 dB.

Although individual studies have reported greater hearing recovery with higher intratympanic steroid doses or combined intratympanic and systemic steroid regimens, no statistically significant association was identified between categorized steroid exposure and reported hearing recovery. However, this finding should not be interpreted as evidence of equivalent efficacy between dose groups because substantial clinical and methodological heterogeneity limited quantitative comparison. This does not establish that there is no dose-response relationship, nor does it establish equivalence among dose groups; rather, the observed association is uncertain in the setting of substantial clinical and methodological heterogeneity.

Despite the variety of regimens studied and substantial hearing recovery rates, standardized, universal protocols for TTM therapy to treat SNHL have yet to be achieved. Future research could benefit from quantitative testing of TTM and of combined regimens and performing controlled trials to evaluate TTM steroid dose-response relationships. Through such research and continued study, our hope is that a standardized treatment regimen for SNHL can be found that results in optimum, long-term hearing outcomes for our patients.

Data availability statement

All data generated or analyzed during this study are included in this manuscript and its supplementary materials.

Ethical approval

IRB approval was obtained for this study.

Informed consent

Not applicable.

Acknowledgements

The team for this study would like to thank all authors on the paper.

Author Contributions

Sanjana Nallapaneni: Developed inclusion and exclusion criteria and search strategy, screened articles, performed data extraction, conducted literature review, performed statistical data analysis, and contributed to manuscript drafting. Naveen S. Raj: Screened articles, performed data extraction, conducted literature review, performed statistical data analysis, and contributed to manuscript drafting. Margaret P. Byars: Screened articles, performed data extraction, conducted literature review, performed statistical data analysis, and contributed to manuscript drafting. Alexander M. Belardo: Performed data extraction, conducted literature review, performed statistical data analysis, and contributed to manuscript drafting. Anita S. Jeyakumar: Conceived the study concept and methodology; provided expert oversight, critical revisions, and final approval of the manuscript.

References

Alexander, T.H., Harris, J.P., Nguyen, Q.T., et al., 2015. Dose effect of intratympanic dexamethasone for idiopathic sudden sensorineural hearing loss: 24 mg/mL is superior to 10 mg/mL. *Otol. Neurotol.* 36(8), 1321–1327.

Arastou, S., Tajedini, A., Borghei, P., 2013. Combined intratympanic and systemic steroid therapy for poor-prognosis sudden sensorineural hearing loss. *Iran. J. Otorhinolaryngol.* 25(1), 23–28.

Chandrasekhar, S.S., Tsai Do, B.S., Schwartz, S.R., et al., 2019. Clinical practice guideline: Sudden hearing loss (update). *Otolaryngol. Head Neck Surg.* 161(1_suppl), S1–S45.

Choung, Y.H., Park, K., Shin, Y.R., et al., 2006. Intratympanic dexamethasone injection for refractory sudden sensorineural hearing loss. *Laryngoscope* 116(5), 747–752.

Dallan, I., Bruschini, L., Nacci, A., et al., 2006. Transtympanic steroids as a salvage therapy in sudden hearing loss: Preliminary results. *ORL J. Otorhinolaryngol. Relat. Spec.* 68(5), 247–252.

Dallan, I., De Vito, A., Fattori, B., et al., 2010. Intratympanic methylprednisolone in refractory sudden hearing loss: A 27-patient case series with univariate and multivariate analysis. *Otol. Neurotol.* 31(1), 25–30.

Deenadayal, D.S., Vidyasagar, D., Bommakanti, V., et al., 2016. Role of intratympanic steroids in the management of idiopathic sudden sensori neural hearing loss —Our experience of 67 cases. *Int. J. Otolaryngol. Head Neck Surg.* 5(4), 174–180.

Dispenza, F., Amodio, E., De Stefano, A., et al., 2011. Treatment of sudden sensorineural hearing loss with transtympanic injection of steroids as single therapy: A randomized clinical study. *Eur. Arch. Otorhinolaryngol.* 268(9), 1273–1278.

Ermutlu, G., Süslü, N., Yılmaz, T., et al., 2017. Sudden hearing loss: An effectivity comparison of intratympanic and systemic steroid treatments. *Eur. Arch. Otorhinolaryngol.* 274(10), 3585–3591.

Filipo, R., Covelli, E., Balsamo, G., et al., 2010. Intratympanic prednisolone therapy for sudden sensorineural hearing loss: A new protocol. *Acta Otolaryngol.* 130(11), 1209–1213.

Han, C.S., Park, J.R., Boo, S.H., et al., 2009. Clinical efficacy of initial intratympanic steroid treatment on sudden sensorineural hearing loss with diabetes. *Otolaryngol. Head Neck Surg.* 141(5), 572–578.

Hara, J.H., Zhang, J.A., Gandhi, K.R., et al., 2018. Oral and intratympanic steroid therapy for idiopathic sudden sensorineural hearing loss. *Laryngoscope Investig. Otolaryngol.* 3(2), 73–77.

Haynes, D.S., O'Malley, M., Cohen, S., et al., 2007. Intratympanic dexamethasone for sudden sensorineural hearing loss after failure of systemic therapy. *Laryngoscope*

117(1), 3–15.

Ho, H.G., Lin, H.C., Shu, M.T., et al., 2004. Effectiveness of intratympanic dexamethasone injection in sudden-deafness patients as salvage treatment. *Laryngoscope* 114(7), 1184–1189.

Inoue, D.P., Bogaz, E.A., Barros, F., et al., 2012. Comparison of hearing recovery criteria in sudden sensorineural hearing loss. *Braz. J. Otorhinolaryngol.* 78(3), 42–48.

Jia, H.G., Yu, Z., Li, X.P., et al., 2019. Efficacy of intratympanic corticosteroid, intravenous batroxobin and combined treatment for sudden sensorineural hearing loss with type-2 diabetes. *Acta Otolaryngol.* 139(6), 522–528.

Joshi, A.A., Shewale, S.S., Shah, K.D., Bradoo, R.A., 2011. Intratympanic dexamethasone injection in refractory cases of idiopathic sudden sensorineural hearing loss. *Bombay Hospital Journal* 53(1), 7–10.

Jung, D.J., Park, J.H., Jang, J.H., et al., 2016. The efficacy of combination therapy for idiopathic sudden sensorineural hearing loss. *Laryngoscope* 126(8), 1871–1876.

Kakehata, S., Sasaki, A., Oji, K., et al., 2006. Comparison of intratympanic and intravenous dexamethasone treatment on sudden sensorineural hearing loss with diabetes. *Otol. Neurotol.* 27(5), 604–608.

Khadav, S., Arya, P., Gupta, G., et al., 2022. Combined intratympanic and systemic steroid therapy in sudden sensorineural hearing loss. Indian J. Otolaryngol. Head Neck Surg. 74(Suppl 1), 293–298. https://doi.org/10.1007/s12070-020-02056-9.

Kovács, M., Uzsaly, J., Bodzai, G., et al., 2024. Efficacy of high dose systemic versus combined (systemic and intratympanic) corticosteroid therapy in idiopathic sudden sensorineural hearing loss: A prospective randomized trial and risk factor analysis. *Am. J. Otolaryngol.* 45(1), 104099.

Kuhn, M., Heman-Ackah, S.E., Shaikh, J.A., et al., 2011. Sudden sensorineural hearing loss: A review of diagnosis, treatment, and prognosis. *Trends Amplif.* 15(3), 91–105.

Nelson, L., Swanson, D., Borowiec, E., et al., 2023. The impact of intratympanic steroid dosage on hearing recovery in sudden sensorineural hearing loss. *Ann. Otol. Rhinol. Laryngol.* 132(8), 879–887.

Neurotology Eastern Region Virtual Education, 2022. Rationale of steroid use for idiopathic SSNHL-Dr. Ana Kim, MD-University of Columbia. Available at https://www.youtube.com/watch?v=d6SpGRKR5F0.

Plontke, S.K., Meisner, C., Agrawal, S., et al., 2022. Intratympanic corticosteroids for sudden sensorineural hearing loss. *Cochrane Database Syst. Rev.* 7(7), CD008080.

Rauch, S.D., Halpin, C.F., Antonelli, P.J., et al., 2011. Oral vs intratympanic corticosteroid therapy for idiopathic sudden sensorineural hearing loss: A randomized trial. *JAMA* 305(20), 2071–2079.

Roebuck, J., Chang, C.Y.J., 2006. Efficacy of steroid injection on idiopathic sudden sensorineural hearing loss. *Otolaryngol. Head Neck Surg.* 135(2), 276–279.

Salt, A.N., Plontke, S.K., 2018. Pharmacokinetic principles in the inner ear: Influence of drug properties on intratympanic applications. *Hear. Res.* 368, 28–40.

Sang, C.C.Y.L.S., Zhen, E., Shaw, C.K.L., 2019. Evaluating and comparing the efficacy of intratympanic high dose dexamethasone (24 mg/mL) and high dose methylprednisolone (125 mg/mL) as a primary and salvage treatment for idiopathic sudden sensorineural hearing loss. *Aust. J. Otolaryngol.* 2, 26.

Shemirani, N.L., Schmidt, M., Friedland, D.R., et al., 2009. Sudden sensorineural hearing loss: An evaluation of treatment and management approaches by referring physicians. *Otolaryngol. Head Neck Surg.* 140(1), 86–91.

Shewel, Y., Asal, S.I., 2020. Intratympanic injection of dexamethasone 4 mg/mL versus 10 mg/mL for management of idiopathic sudden sensorineural hearing loss. *Egypt. J. Otolaryngol.* 36(1), 3.

Suzuki, H., Hashida, K., Nguyen, K.H., et al., 2012. Efficacy of intratympanic steroid administration on idiopathic sudden sensorineural hearing loss in comparison with hyperbaric oxygen therapy. *Laryngoscope* 122(5), 1154–1157.

Swachia, K., Sharma, D., Singh, J., 2016. Efficacy of oral vs. *intratympanic corticosteroids in sudden sensorineural hearing loss. J. Basic Clin. Physiol. Pharmacol.* 27(4), 371–377.

Swaminathan, G., Ramalingam, R., Kumarappa Gounder, R.K., 2019. Steroid therapy in the management of sudden sensorineural hearing loss: A nonrandomized clinical trial. *Ann. Otol. Neurotol.* 2(2), 59–65.

Tripathi, P., Deshmukh, P., 2022. Sudden sensorineural hearing loss: A review. *Cureus* 14(9), e29458.

Tsai, Y.J., Liang, J.G., Wu, W.B., et al., 2011. Intratympanic injection with dexamethasone for sudden sensorineural hearing loss. *J. Laryngol. Otol.* 125(2), 133–137.

Wang, Y.W., Ren, J.H., Lu, Y.D., et al., 2012. Evaluation of intratympanic dexamethasone for treatment of refractory sudden sensorineural hearing loss. *J. Zhejiang Univ. Sci. B* 13(3), 203–208.

Wu, H.P., Chou, Y.F., Yu, S.H., et al., 2011. Intratympanic steroid injections as a salvage treatment for sudden sensorineural hearing loss: A randomized, double-blind, placebo-controlled study. *Otol. Neurotol.* 32(5), 774–779.

Xenellis, J., Papadimitriou, N., Nikolopoulos, T., et al., 2006. Intratympanic steroid treatment in idiopathic sudden sensorineural hearing loss: A control study. *Otolaryngol. Head Neck Surg.* 134(6), 940–945.

Yang, H.C., Cho, Y.B., Jang, C.H., et al., 2015. Efficacy of concomitant intratympanic steroid injection for sudden deafness according to initial hearing loss. *Otol. Neurotol.* 36(10), 1604–1609.

Zhou, Y.D., Zheng, H.L., Zhang, Q., et al., 2011. Early transtympanic steroid injection in patients with 'poor prognosis' idiopathic sensorineural sudden hearing loss. *ORL J. Otorhinolaryngol. Relat. Spec.* 73(1), 31–37.

Zhou, Y.D., Zheng, G.L., Zheng, H.L., et al., 2013. Primary observation of early transtympanic steroid injection in patients with delayed treatment of noise-induced hearing loss. *Audiol. Neurotol.* 18(2), 89–94.