Systematic Review
Iranian Journal of Otorhinolaryngology, Vol.38(3), Serial No.146, May-2026

Efficacy of Intratympanic versus Systemic Corticosteroids in Sudden Sensorineural Hearing Loss: A Systematic Review

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Abstract

Introduction:

Sudden sensorineural hearing loss (SSNHL) is an otologic emergency that typically requires prompt treatment with corticosteroids, administered either systemically or intratympanically. The optimal route for initial therapy remains uncertain due to heterogeneity in efficacy and safety profiles.

Materials and Methods:

We conducted a systematic review of randomized controlled trials (RCTs) published between 2011 and 2025, comparing intratympanic and systemic corticosteroids as primary treatment for SSNHL in adults. Following PRISMA 2020 and Cochrane Handbook guidelines, we screened studies without language restrictions. Two independent reviewers performed study selection, data extraction, and risk of bias assessment using the RoB 2.0 tool. Outcomes were synthesized narratively, focusing on changes in pure-tone average (PTA), complete/functional recovery, speech discrimination, and safety. Trials with combination/salvage strategies, adjuncts, or formulation comparisons were synthesized separately.

Results:

Seventeen RCTs were included. Efficacy results were heterogeneous; however, most studies indicated that intratympanic corticosteroids are at least as effective as systemic therapy. In severe hearing loss, intratympanic treatment achieved higher success rates (up to 70.6%) and greater PTA improvement compared to systemic administration. Adverse events differed by route: systemic corticosteroids were associated with metabolic disturbances, while intratympanic therapy caused localized, self-limiting events. Overall, 47.1% of studies had high risk of bias, and 52.9% showed some concerns.

Conclusion:

Intratympanic corticosteroids appear to be a non-inferior alternative to systemic steroids for initial SSNHL treatment, with potential advantages in cases of severe hearing loss or systemic contraindications. Nonetheless, methodological limitations across studies warrant cautious interpretation. Future high-quality trials should address efficacy, functional recovery, and safety more rigorously.

Keywords: Hearing Loss, Sudden; Injection, Intratympanic; Glucocorticoids; Dexamethasone; Methylprednisolone.

Received date: 01 Oct 2025
Accepted date: 28 Feb 2026

****Please cite this article;*** *Leal Capacho MA, León Suárez LT, Figueroa Márquez ML, Cuaspa Damian JL, Alzate Granado JP, Gómez Ballesta FJ. Efficacy of Intratympanic versus Systemic Corticosteroids in Sudden Sensorineural Hearing Loss: A Systematic Review. Iran J Otorhinolaryngol. 2026:38(2):137-148. Doi: 10.22038/ijorl.2026.91544.4050*

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Introduction

Sudden sensorineural hearing loss (SSNHL) is an otologic emergency characterized by a rapid onset of hearing loss (typically within ≤72 hours) that can significantly impact quality of life if not promptly treated.

Early management with corticosteroids is standard practice, administered either systemically or topically via intratympanic injections, aiming to reduce inflammation and improve cochlear perfusion.

The updated clinical guidelines from the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) emphasize the importance of initiating treatment within the first two weeks.

These guidelines recognize corticosteroids as a valid first-line therapy, without specifying a preferred route, and recommend intratympanic administration as a "salvage" therapy in patients who do not respond to initial systemic treatment (1,4). Recent systematic reviews have identified differences in safety profiles depending on the route of administration: systemic corticosteroids have been associated with hyperglycemia, insomnia, and psychiatric disturbances, while intratympanic steroids have been linked to transient pain, vertigo, or tympanic membrane perforation. These differences underscore the clinical relevance of defining the optimal initial route, considering both efficacy and safety.

Despite the widespread use of corticosteroids, uncertainty remains regarding their comparative efficacy when used as primary treatment. A classic randomized clinical trial demonstrated that intratympanic dexamethasone was not inferior to oral prednisone in hearing recovery at two months (1).

However, subsequent meta-analyses have yielded conflicting results: some found no superiority of the intratympanic route nor added benefit from combined therapy (2), while others suggest advantages of the intratympanic route, especially in patients with contraindications to systemic therapy (3).

The most recent Cochrane review concluded that intratympanic corticosteroids "may result in little to no difference" compared to systemic corticosteroids as a first-line treatment, although combination therapy may offer modest benefit, with clinical uncertainty regarding its magnitude (4,5). This methodological and outcome heterogeneity prevents a definitive recommendation on the optimal primary route of administration. Based on the above, we propose the following primary hypothesis: in adults with SSNHL treated within the first 14 days, intratympanic corticosteroid administration is not inferior to systemic administration in short-term improvement of hearing thresholds (e.g., change in pure-tone average), and presents a distinct adverse event profile, with lower systemic burden but greater local reactogenicity. This hypothesis is based on the pharmacokinetic possibility of achieving high cochlear concentrations through the intratympanic route, while limiting systemic exposure compared to oral or intravenous routes.

The research question guiding this systematic review was: What is the comparative efficacy and safety of corticosteroids administered intratympanically versus systemically when used as primary treatment for SSNHL?

Our objective was to estimate the relative effect on patient-centered outcomes, such as average improvement in pure-tone threshold and rates of complete/functional recovery, and to characterize route-specific adverse events.

As a secondary aim, we explored plausible clinical effect modifiers, including baseline audiometric severity, time to treatment initiation, type and dose of corticosteroid, and concomitant use of hyperbaric oxygen therapy.

We also summarized evidence on sequential/ salvage and combined (systemic plus intratympanic) strategies separately from the primary first-line route-only comparison. To address this question, we conducted a systematic review in accordance with PRISMA 2020 guidelines.

Randomized controlled trials evaluating intratympanic versus systemic corticosteroid administration as first-line treatment for idiopathic SSNHL were included; trials assessing sequential/salvage or combined strategies were considered and reported separately.

The search covered major biomedical databases and clinical trial registries. Risk of bias was assessed using RoB 2. Where appropriate, meta-analysis was planned; however, quantitative pooling was not undertaken due to methodological heterogeneity. This approach aimed to provide an updated and clinically useful synthesis to inform the choice of initial corticosteroid route in SSNHL.

Materials and Methods

Study Design

A systematic review of the literature was conducted, focusing exclusively on randomized controlled trials (RCTs), without performing a meta-analysis. Methodological and reporting guidelines from the *Cochrane Handbook* were followed to define eligibility criteria, search strategy, study selection, data extraction, risk of bias assessment, and to present results transparently.

Eligibility Criteria

Types of Studies

Included studies were randomized controlled trials (RCTs). For the primary question, we prioritized RCTs that directly compared intratympanic versus systemic corticosteroids as first-line treatment for SSNHL. RCTs evaluating combination therapy, sequential/salvage intratympanic therapy after systemic failure, adjunctive interventions (e.g., hyperbaric oxygen therapy), placebo-controlled intratympanic strategies, or formulation comparisons were also included but were synthesized in separate strata and were not used to infer the primary first-line route effect. Non-randomized studies, observational designs, cohort studies, case-control studies, and case reports were excluded.

Types of Participants

Included participants were adults with idiopathic SSNHL, operationally defined as a ≥30 dB hearing loss in ≥3 contiguous frequencies occurring within ≤72 hours (standard definition in clinical otology). Excluded were cases with identifiable etiologies (e.g., confirmed autoimmune, retrocochlear, traumatic), conductive hearing loss, and pediatric cases unless they could be analyzed separately.

Types of Interventions/Exposures

- Intervention 1 (Intratympanic): Corticosteroids administered into the middle ear (e.g., dexamethasone or methylprednisolone), specifying the drug, concentration, volume, number of applications, interval, and timing in relation to SSNHL onset.
- Intervention 2 (Systemic): Corticosteroids administered orally or intravenously (e.g., prednisone/ prednisolone or methylprednisolone), with details on initial dose, tapering schedule, and duration.
- **Co-interventions and complex trial designs (decision rules):** Trials were eligible for the primary question only when the randomized comparison isolated the route of steroid delivery (intratympanic monotherapy vs systemic monotherapy) or included these arms as direct comparators.

Studies in which both groups received the same co-interventions (e.g., antivirals, vasodilators) were retained. Trials evaluating combination therapy (systemic plus intratympanic), sequential/ salvage intratympanic therapy after systemic failure, adjunctive interventions (e.g., hyperbaric oxygen therapy), placebo-controlled intratympanic strategies, or formulation comparisons were included but synthesized in separate strata and were not used to infer the primary first-line route effect.

Types of Outcomes

Primary Outcomes

- Clinically significant hearing recovery at 4–12 weeks (as defined in each study; ideally according to AAO-HNS criteria).
- Change in Pure Tone Average (PTA, dB) (0.5–1–2–4 kHz) at 4–12 weeks.

Secondary Outcomes

- Speech discrimination (%).
- Time to recovery.
- Improvement in tinnitus and vertigo.
- Adverse events (e.g., tympanic membrane perforation, otitis media, pain, hyperglycemia, or other systemic effects).
- Need for salvage therapy, relapse, and quality of life (e.g., HHIA).

Outcomes were defined and prioritized a priori to include both clinically relevant benefits and harms.

Search Methods for Identifying Studies

Electronic Searches

We searched MEDLINE (PubMed), Embase, LILACS, Cochrane CENTRAL, Web of Science Core Collection, and Scopus from 1 January 2011 to 20 September 2025, without language restrictions.

Searches were conducted between 15 August 2025 and 20 September 2025; the last search date was 20 September 2025. We restricted

inclusion to 2011 onwards to provide an updated synthesis aligned with contemporary steroid regimens and reporting standards.

Pubmed

("Hearing Loss, Sensorineural"[Mesh] OR "Sudden Hearing Loss"[Mesh] OR "sensorineural hearing loss"[tiab] OR "sudden hearing loss"[tiab] OR "SSNHL"[tiab]) AND (corticosteroids [Mesh] OR steroid*[tiab] OR glucocorticoid*[tiab] OR prednisone[tiab] OR prednisolone[tiab] OR dexamethasone[tiab]) AND (intratympanic[tiab] OR "middle ear"[tiab] OR transtympanic[tiab]) AND (systemic[tiab] OR oral[tiab] OR intravenous [tiab] OR intramuscular[tiab] OR parenteral [tiab]) AND (adults [Mesh] OR adult*[tiab]).

Another boolean search:Embase

('sensorineural hearing loss'/exp OR 'sudden hearing loss'/exp OR "sensorineural hearing loss":ti,ab OR "sudden hearing loss":ti,ab OR SSNHL:ti,ab) AND ('corticosteroid'/ exp OR steroid*:ti,ab OR glucocorticoid*:ti,ab OR prednisone:ti,ab OR dexamethasone: ti,ab) AND (intratympanic:ti,ab OR 'middle ear':ti,ab OR transtympanic:ti,ab) AND (systemic:ti,ab OR oral:ti,ab OR intravenous:ti,ab OR intramuscular:ti,ab OR parenteral:ti,ab) AND ('adult'/ exp OR adult*:ti,ab).

LILACS

("Hipoacusia neurosensorial súbita"[decs] OR "hipoacusia súbita"[decs] OR "sudden sensorineural hearing loss":ti,ab OR "SSNHL": ti,ab) AND ("corticosteroides"[decs] OR corticosteroid*:ti,ab OR steroid*:ti,ab OR dexamethasone:ti,ab OR prednisone:ti,ab) AND (intratimpánico:ti,ab OR intratympanic: ti,ab OR transtimpanic:ti,ab) AND (sistémico: ti,ab OR systemic:ti,ab OR oral:ti,ab OR intramuscular: ti,ab OR parenteral:ti,ab) AND (adulto:ti,ab OR adults:ti,ab).

Cochrane

(SSNHL OR "sudden sensorineural hearing loss" OR "sudden hearing loss") AND (intratympanic OR transtympanic OR "middle ear" OR tympan*) AND (corticosteroid* OR steroid* OR dexamethasone OR methyl-prednisolone OR prednisone OR prednisolone) Limits: Publication year 2011–2025; no language restrictions

Scopus

((SSNHL OR ("sudden" W/3 "sensorineural" W/3 "hearing" W/3 "loss") OR ("sudden" W/3 "hearing" W/3 "loss")) AND (intratympanic OR transtympanic OR "middle ear" OR tympan* OR transtympan*) AND (corticosteroid* OR glucocorticoid* OR steroid* OR dexamethasone OR methylpre dnisolone OR prednisone OR prednisolone))

Web of science

("sudden sensorineural hearing loss" OR SSNHL OR "sudden hearing loss") AND (intratympanic OR transtympanic OR "middle ear" OR tympan*) AND (dexamethasone OR methylprednisolone OR prednisone OR prednisolone OR steroid OR corticosteroid)

Search for Other Sources

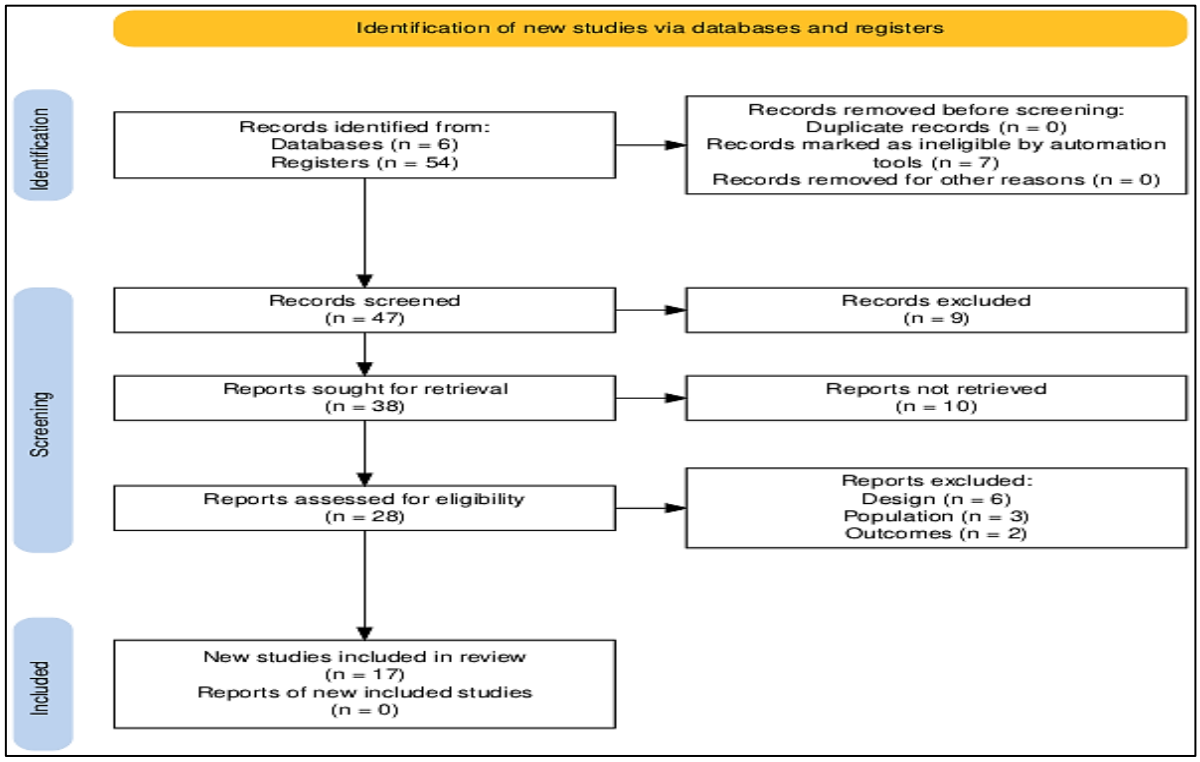
Other sources. We searched ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (WHO-ICTRP) and screened reference lists of included studies and relevant reviews. When key information was missing, study authors were contacted.

Record management and duplicates

Record management and duplicates. All records were imported into Zotero. Duplicates were identified using Zotero's Duplicate Items function (matching title/author/year/identifiers such as DOI/PMID when available) and resolved by merging records; this was followed by manual verification prior to screening. The number of duplicates removed is reported in the PRISMA flow diagram.

Data Collection and Analysis:Study Selection

Two reviewers independently and in duplicate screened titles/abstracts and assessed full texts based on predefined criteria. Discrepancies were resolved by consensus or by consulting a third reviewer. Reasons for exclusion were recorded. A PRISMA flow diagram is provided (Figure 1).



Note: PRISMA 2020 flow diagram of the selection process. Searches were conducted across six databases and trial registers, identifying 54 records. No duplicate records were found (n=0), Seven records were removed before screening due to ineligibility (e.g., non-RCT design/publication type). A total of 47 records were screened by title and abstract, and 9 were excluded. Full-text retrieval was sought for 38 reports, of which 10 could not be retrieved. Twenty-eight reports were assessed for eligibility, and 11 were excluded due to study design (n=6), population (n=3), or outcomes (n=2). Ultimately, 17 studies were included in the review.

Fig 1. PRISMA Flow Diagram**.** Flowchart of the selection process for included studies in the systematic review, adapted from PRISMA 2020 guidelines.

Data Extraction and Management

Two reviewers independently extracted data using piloted forms (study/participant characteristics, intervention details, outcomes, follow-up times, analysis, and handling of missing data). Duplicate extraction was used to minimize errors and bias.

Forms were piloted prior to final use and adjusted as necessary. When multiple publications existed for a single trial, information was consolidated at the study level.

Critical Appraisal of Studies

Risk of bias was assessed using the RoB 2.0 tool (Risk of Bias 2.0, Cochrane Collaboration). The following RoB 2.0 domains were evaluated: bias arising from the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result.

Each domain was rated as low risk, some concerns, or high risk, with justifications provided via direct quotes from the studies. Where appropriate, assessments were conducted per outcome.

Bias Management

Handling of Missing Data

For each outcome and time point, we extracted the number randomized, the number analyzed, and reasons for attrition by group. When key outcome data (e.g., denominators, SD/SE, event counts) were missing or unclear, we contacted study authors.

Primary approach. We used an available-case analysis (participants with observed outcome data), and we transparently reported the extent of missingness by arm.Decision rules and sensitivity approach. If missing outcome data exceeded 10% overall or were imbalanced between groups (>5% absolute difference), we flagged the finding as at increased risk of bias and reflected this in the RoB 2 “missing outcome data” domain and in the certainty/interpretation of the result. For continuous outcomes with missing dispersion, we derived SDs from SEs, confidence intervals, p-values, or interquartile ranges when reported; if not derivable, the study contributed narratively without quantitative calculation.

For dichotomous outcomes with incomplete denominators, we avoided unverifiable imputations; where feasible, we explored the qualitative impact of best/worst-case assumptions on the direction of effect and noted whether conclusions changed.

Assessment of Reporting Bias

Publication bias and selective reporting were explored by comparing pre-specified outcomes from protocols/registries with those published. Due to the absence of meta-analysis, funnel plots were not constructed, but small-study effects were discussed in the context of available evidence. Additionally, bias at the review level was mitigated through a broad and reproducible search strategy across multiple sources, avoiding reliance on MEDLINE alone, and by thoroughly documenting the search process.

Plan for Quantitative and Qualitative Synthesis of the Review

No meta-analysis was conducted due to substantial clinical and methodological heterogeneity across trials (differences in steroid type and regimen, timing from onset, outcome definitions, follow-up time points, and co-interventions). A structured narrative approach was followed. Studies were synthesized in pre-specified strata: (1) primary first-line route comparisons isolating intratympanic monotherapy versus systemic monotherapy (or including these arms as direct comparators); (2) combination therapy (systemic plus intratympanic) versus monotherapy; (3) sequential/salvage intratympanic therapy after systemic failure; and (4) adjuncts/placebo-controlled intratympanic strategies/formulation comparisons. Within each stratum, studies were categorized by drug type, dosage/regimen, time from onset (<14 vs ≥14 days), baseline severity, and follow-up duration. For each outcome, effects per study were presented (e.g., mean differences for PTA, recovery rates), including 95% confidence intervals when available, and the direction, magnitude, and consistency of findings were evaluated despite the lack of statistical pooling. "Characteristics of included studies" tables and outcome-focused summary tables were used for critical outcomes, without aggregate statistical synthesis. Risk of bias informed interpretation, and heterogeneity was discussed as a plausible explanation for inter-study differences.

Results

A total of seventeen randomized controlled trials (RCTs) were included in this systematic review. Table 1 summarizes eleven RCTs that included intratympanic (IT) and systemic corticosteroid arms (first-line route comparisons, combination strategies, and sequential/salvage designs), whereas Table 2 summarizes six additional RCTs evaluating intratympanic strategies beyond the primary first-line route comparison (placebo-controlled IT, adjuncts such as hyperbaric oxygen therapy, and formulation/concentration comparisons). For the primary question (first-line route choice), we focused on trials where randomization isolated intratympanic versus systemic monotherapy (or included these as direct comparator arms).

Trials evaluating combination therapy, sequential/salvage intratympanic treatment after systemic failure, adjuncts (e.g., hyperbaric oxygen), placebo-controlled IT strategies, or formulation comparisons were retained but interpreted within their respective strata and were not used to infer the primary first-line route effect. Across the eleven RCTs summarized in Table 1, most studies included young and middle-aged adults, with homogeneous inclusion criteria (onset ≤72 hours to 14 days, ≥30 dB loss in ≥3 consecutive frequencies, and no identifiable secondary etiology). Comparators varied: IT monotherapy, systemic monotherapy, simultaneous or sequential combinations, and in some cases, adjunctive interventions such as hyperbaric oxygen therapy (HBO).

In terms of efficacy, results were heterogeneous. Some studies reported advantages for the intratympanic approach: for example, (6) showed a higher success rate with IT (50%) compared to oral (33.3%) and intravenous (30%) administration, with significant differences in severe hearing loss (70.6% IT vs. 41–50% systemic). Others, such as (7), described better trends for IT (71.9% response) versus systemic (60%), though not statistically significant. Trials like (8,9) found no differences between arms, while (10,11) reported comparable recovery rates between groups (Table 1).

Table 1. Randomized controlled trials including intratympanic and systemic corticosteroid arms (first-line route comparisons, combination strategies, and sequential/salvage designs).

Author	Population	Intervention	Comparator	Numerical
Jie Huang, 2021	104 unilateral SSNHL patients, onset ≤72 h, ≥30 dB loss in ≥3 consecutive frequencies, age 18–65. Exclusions: severe systemic disease, uncontrolled diabetes/hypertension, active ulcer, epilepsy, psychosis, identifiable causes (Ménière, otitis, retrocochlear, etc.)	Group A: intratympanic dexamethasone alone, every 48 h for 24 days (5 mg/ml, 1.5 mg/0.3 ml)	Group B: IV dexamethasone for 12 days (10→5 mg/day), followed by IT dexamethasone every 48 h for 12 days	- Overall hearing gain (D90): IT 31.0 ± 9.64 dB vs IV+IT 29.4 ± 9.18 dB (p>0.05).- Complete/partial recovery: IT 87.8% vs IV+IT 85.7% (p>0.05).- Difference at low frequencies on D7 (favoring IT), not sustained.- Adverse effects: fewer systemic AEs in IT; 1 mild Cushing's case in IV+IT. Pain and injection refusal in both groups.
Busheng Tong, 2020	96 unilateral ISSNHL patients, age 18–70, onset ≤3 days, >20 dB loss in ≥3 frequencies. Final n=90. Exclusions: retrocochlear, chronic otitis, congenital malformations, ototoxics, pregnancy, trauma.	Group I: oral methylprednisolone (0.8 mg/kg/day ×5 days, then 8 mg/day ×5 days).Group II: IV methylprednisolone, same dose.Group III: IT methylprednisolone (40 mg/ml, 0.6 ml), every 48 h, 5 doses.	Direct comparison: oral vs IV vs IT	- Success rate: oral 33.3%, IV 30%, IT 50% (p<0.05).- Mean PTA gain: oral 16.1 ± 15.3 dB, IV 14.3 ± 12.7 dB, IT 21.6 ± 20.4 dB (p<0.05 for IT).- In severe cases: IT 27.2 ± 23.5 dB vs oral 14.4 and IV 15.1 (p<0.05).- Efficacy in severe loss: IT 70.6%, oral 50%, IV 41.2%.
Michael Tsounis, 2018	102 ISSNHL patients, mean age 54.4, onset ≤14 days, ≥30 dB loss in ≥3 frequencies. Exclusions: prior treatment, >14 days onset, contraindications to steroids. Follow-up: 90 days.	A: IV prednisolone 1 mg/kg ×7 days → taper + oral methylprednisolone.B: IT methylprednisolone 62.5 mg/ml, 0.4–0.6 ml on days 1, 3, 5, 10.C: combination of both.	Direct comparison: systemic vs IT vs combined	- PTA gain: A 29.0 dB, B 27.0 dB, C 29.8 dB (p>0.05).- Complete recovery: A 40%, B 17.6%, C 36.4%.- Partial: A 11.4%, B 29.4%, C 21.2%.- No improvement: A 22.9%, B 29.4%, C 21.2%.- Better outcomes in <60 yrs (p=0.02). Onset time/severity not predictive.
Khorsandi Ashtiani, 2018	147 ISSNHL patients, onset ≤10 days, 112 completed: 32 IT, 45 systemic, 35 combined. Severity: mild-moderate 23%, severe 21%, profound 44%.	1: IT (0.6 ml methylprednisolone, days 1, 5, 9, 13) + oral placebo.2: Oral prednisolone 75 mg/day ×10 days + IT placebo.3: Combined. All received acyclovir + omeprazole.	Direct comparison: IT vs systemic vs combined	- Response rate: IT 71.9%, systemic 60%, combined 68.6% (p=0.5).- Mean SDS: IT 34.6%, systemic 18.9%, combined 27.9% (p>0.2).- Mean SRT: IT −36 dB, systemic −27 dB, combined −34 dB.- Worse prognosis: tinnitus + vertigo (p=0.002), family history (p=0.01). Severity did not affect outcome.
Ilyoung Cho, 2018	60 patients with severe-profound ISSNHL (≥70 dB), onset ≤10 days, 58 completed.	Study: oral methylprednisolone + IT dexamethasone + 10 HBO sessions (100% O_2, 2.5 ATA, 60 min/day).Control: same without HBO.	Systemic + IT with or without HBO	- No significant PTA difference at 3 months.- 500 Hz improved earlier in HBO group (p<0.05).- 1 kHz better in HBO at 3 months (p=0.043).- WDS: study 66.4% vs control 56.7% (p=0.029).- Recovery (complete/partial): 60.7% vs 33.3% (p=0.037).
Gülce Ermutlu, 2017	41 unilateral SSNHL patients, onset ≤7 days, 35 completed: 16 oral, 19 IT. Mean age: 45.7.	IT: dexamethasone 0.5–0.7 ml (8 mg/2 ml), 3 injections on alternate days, transtympanic under microscopy.	Oral: prednisolone 1 mg/kg/day (max 80 mg), taper 10 mg every 3 days	- 3-month recovery: overall 85.7%; oral 87.5%, IT 84.2% (p>0.99).- Complete recovery: oral 75%, IT 63.2%.- Severe HL (≥50 dB): poorer recovery (p=0.038).- Vertigo trend toward worse outcome.
Kavita Swachia, 2016	42 SSNHL patients, onset ≤14 days. 83.3% unilateral.	I: Oral prednisone 1 mg/kg ×10 days → taper over 4 days.II: IT methylprednisolone 40 mg/ml, 1 ml, twice/week ×2 weeks.	IT vs oral	- PTA gain: oral 18.24 ± 8.72 dB, IT 14.68 ± 12.88 dB (not significant).- Furuhashi recovery: oral 86.4%, IT 80%.- Complete recovery: oral 18.2%, IT 25%.- Severe HL, vertigo = worse outcomes.
Moo Kyun Park, 2011	92 unilateral ISSNHL patients, onset ≤7 days, age 18–65.	Simultaneous: IV + IT dexamethasone (6 injections/2 weeks).Sequential: same systemic therapy, IT started on day 7 only if no recovery.	Simultaneous vs delayed IT	- Recovery: 63.6% vs 56.8% (p=0.183).- PTA gain: 34.7 vs 32.6 dB (p=0.898).- Early recovery: 50% vs 47.7%.- AEs: IT otalgia 12.5%, vertigo 10.2%, transient perforation 2.3%.
Francesco Dispenza, 2011	46 idiopathic ISSNHL patients, onset ≤10 days. Mean PTA 59 dB.	A: IT dexamethasone 4 mg/ml, 0.4–0.5 ml, 1/week ×4.B: Oral prednisone 60 mg/day, taper ×14 days.	IT vs oral	- ≥10 dB gain: IT 80%, oral 81%.- PTA gain: IT 41.2%, oral 44.7% (p=0.61).- Recovery time: IT 15.9 days, oral 21.1 (NS).
Hung-Pin Wu, 2011	60 idiopathic ISSNHL patients, non-responders to initial systemic therapy (PTA gain ≤10 dB).	ITSI: 4 IT dexamethasone injections (0.5 ml, 8 mg/2 ml) over 2 weeks.ITNI: placebo (saline) IT injections.	IT (post-systemic) vs placebo IT	- PTA gain: ITSI +9.7 dB vs ITNI +4.5 dB (p<0.05).- ≥10 dB response: 44.4% vs 10.7% (p=0.005).- ≥15 dB: 29.6% vs 7.1% (p=0.032).
Jong Bin Lee, 2011	46 SSNHL patients, non-responders to systemic steroids (≤10 dB gain). Mean age ~44 years.	ITDI: 4 IT dexamethasone injections (0.3–0.4 ml, 5 mg/ml), twice/week ×2 weeks after systemic therapy.	Control: no additional treatment after systemic therapy	- ≥10 dB improvement: ITDI 47.6% vs control 16% (p=0.027).- Mean PTA gain: ITDI 11.4 dB vs control 1.7 dB (p=0.004).- More benefit in PTA ≥70 dB (p=0.038).

Note: Only trials in which the randomized comparison isolated the initial route (intratympanic monotherapy vs systemic monotherapy) were used to infer the primary first-line route effect; combination and sequential/salvage designs are summarized separately.

In patients refractory to initial systemic therapy, studies (12,13) confirmed additional benefit from intratympanic administration: (12) reported a mean PTA improvement of +9.7 dB with IT versus +4.5 dB with placebo ($p<0.05$), and (13) showed a ≥10 dB response in 47.6% with IT compared to 16% in controls ($p=0.027$). Regarding safety, systemic administration was associated with metabolic disturbances (hyperglycemia, fluid retention, insomnia), whereas the intratympanic route was mainly linked to local pain, transient vertigo, or self-limiting tympanic membrane perforations (Tables 1 and 2).

Table 2. Randomized trials evaluating intratympanic strategies beyond the primary first-line route comparison (placebo-controlled IT, adjuncts such as HBO, and formulation/concentration comparisons).

Author	Population	Intervention	Comparator	Numerical
Maryam Amizadeh, 2025	96 adults with SSNHL (43.8% male, 56.3% female). Inclusion: ≥30 dB loss in ≥3 frequencies within ≤72 h, onset ≤14 days. Exclusions: otitis, prior surgery, Ménière, acoustic/barotrauma, genetic or retrocochlear causes, severe comorbidities.	IT nanogel MPA: 4 doses of 20 mg over 8 days (every other day), under microscopy + oral prednisolone 1 mg/kg/day (max 60 mg) ×14 days.	Conventional IT MPA: 4 doses of 4 mg + same oral prednisolone.	- Complete recovery: 37.5% (nano) vs 12.5% (control); partial: 47.5% vs 66%; no recovery: 15% vs 21.5% (p=0.016).- Tinnitus at 2 months: 2.5% vs 18% (p=0.02).- Vertigo: no difference (p>0.4).- PTA/WRS improved significantly in both (p<0.0001), but not between groups.
Shi-yi Wang, 2025	203 unilateral ISSNHL patients (18–65 y), onset ≤7 days, no prior treatment. Exclusions: prior HL, ear lesions, severe hypertension/diabetes, GI/hematologic disorders, pregnancy/lactation, psychiatric conditions.	IT dexamethasone at 3 concentrations: 5, 10, 20 mg/ml. Dose: 0.5–1 ml every 2 days for 10 days under local anesthesia + standard systemic therapy (oral prednisone + IV ginkgo biloba + IV gastrodin).	Standard systemic therapy only.	- Global efficacy: control 57.4%, IT 67.3% (NS). Subgroup efficacy: 5 mg/ml 62.0%, 10 mg/ml 69.1%, 20 mg/ml 70.6%.- Hearing gain: control 11.25 ± 10.0 dB, IT 12.5 ± 10.9 dB.- In severe/profound HL: 20 mg/ml group had greater gain than control (16.25 vs 10.0 dB; p<0.05).- AEs: 35 cases of transient vertigo, 8 of transient otalgia; no serious complications.
Markus Suckfuell, 2014	210 patients (18–61 y), SSNHL or acute acoustic trauma ≤48 h, ≥30 dB loss in 3 frequencies. Exclusions: Ménière, autoimmune, radiation-induced HL, endolymphatic hydrops, perilymph fistula, retrocochlear pathology, otic infections, pregnancy.	Single IT injection of AM-111 (0.4 or 2.0 mg/ml). Rescue: oral prednisolone if <10 dB gain at D7.	Placebo IT injection (identical appearance). Rescue if <10 dB gain at D7.	- Overall: no significant differences (D7 PTA: placebo 24.0 dB, AM-111 0.4 mg/ml 27.9 dB, AM-111 2.0 mg/ml 22.5 dB; p=0.208).- Severe/profound subgroup (≥60 dB, n=92): AM-111 0.4 mg/ml superior to placebo: • PTA gain: +12.1 dB (p=0.017) • Relative gain: +19.5% (p=0.021) • Complete recovery: +17.7% (OR=5.5, p=0.044)- SDS improved: +21.5% (60 dB), +18.3% (80 dB) over placebo.- Tinnitus remission: 56% (AM-111) vs 26.1% (placebo) (p=0.045).- Safety: well tolerated, only mild/moderate local AEs, no significant differences vs placebo.
Roberto Filipo, 2013	50 patients with moderate ISSNHL (flat audiogram 250–8000 Hz), mean age 50.4 (range 15–85), onset ≤3 days. Exclusions: uncontrolled hypertension/diabetes, ischemia, Ménière, retrocochlear, autoimmune, trauma, fluctuating, noise/radiation-induced HL.	IT prednisolone 62.5 mg/ml, 0.3 ml/day ×3 consecutive days.	IT placebo (saline), 0.3 ml/day ×3 days.	- Complete recovery at T1: 76% IT vs 20% placebo (p=0.0002).- Marked: 8% IT vs 0% placebo.- Mild: 12% IT vs 0% placebo.- No recovery: 4% IT vs 80% placebo.- After systemic rescue: T3 recovery: IT 76% vs placebo 72% (NS).- PTA significantly better in IT group at T1 (p<0.0001).- Mild AEs: local pain (4), transient vertigo (6); no major complications.
Ljiljana Cvorovic, 2013	50 ISSNHL patients with <10 dB gain after systemic steroids. Age 14–72 (mean: HBO 53.6, IT 47.3). Idiopathic confirmed (MRI, CT negative). Exclusion: >4 weeks since onset.	HBO group (n=25): 20 sessions (2 ATA, 100% O_2, 60 min/day, 5 days/week).	IT dexamethasone (n=25): 4 injections (0.3–0.5 ml, 4 mg/ml) over 13 days.	- Both groups had significant PTA improvements (p<0.05).- No global differences IT vs HBO, except 2 kHz (HBO better, p<0.05).- In PTA >81 dB: IT better than HBO.- HBO more effective in <60 years (40.2 ± 16.4 dB vs 21.2 ± 10.3 dB in ≥60).
Peng Li, 2011	65 SSNHL patients non-responsive to IV prednisolone (1 mg/kg ×5 days + taper). Inclusion: onset ≤14 days, ≥30 dB loss in 3 frequencies. Exclusions: bilateral HL, otitis media, cochlear malformation, neoplasms, pregnancy, ototoxics, hepatic/renal failure.	IT methylprednisolone (40 mg/ml, 1 ml buffered), 4 doses every 3 days over 15 days.	Otic drops: methylprednisolone on tympanic membrane.Control: no additional treatment.	- IT: PTA improved from 60.7 dB to 52.9 dB (gain 7.8 dB; p<0.01).- ≥10 dB improvement: 37% in IT group.- Drops & control: no significant changes (~0.9 dB).- Subgroups with higher response (NS): male (40%), <60 yrs (50%), early onset (50%), ascending curve (62.5%), no vertigo (45.5%).

Note: SSNHL = sudden sensorineural hearing loss; ISSNHL = idiopathic SSNHL; IT = intratympanic; IV = intravenous; MPA = methylprednisolone acetate; DEX = dexamethasone; AM-111 = brimapitide (JNK inhibitor peptide); HBO = hyperbaric oxygen therapy; ATA = atmospheres absolute; PTA = pure-tone average; WRS = word recognition score; SDS = speech discrimination score; MRI = magnetic resonance imaging; CT = computed tomography; AEs = adverse events; dB = decibels; kHz = kilohertz; ml = milliliters.

Overall, synthesis of the trials indicates that intratympanic administration is at least equivalent to systemic use as initial therapy and may offer advantages in patients with severe hearing loss or those who fail conventional treatment, with a more favorable safety profile regarding systemic side effects. Six additional studies evaluated both novel formulations and comparative interventions against placebo or other treatments for SSNHL. First, (14) explored an intratympanic methylprednisolone nanogel combined with oral prednisolone, showing a higher rate of complete recovery (37.5% vs. 12.5%) and less persistent tinnitus (2.5% vs. 18%) compared to the conventional formulation, with statistically significant differences. In a larger trial with over 200 patients, (15) found no overall differences between standard systemic therapy and the addition of intratympanic dexamethasone, although in subgroups with severe/profound hearing loss, the higher-concentration IT regimen (20 mg/ml) was associated with greater hearing gain (16.2 vs. 10.0 dB; $p<0.05$) (Table 1). Among placebo-controlled trials, (16) evaluated AM-111, an apoptosis antagonist, showing no global differences but a significant benefit in patients with ≥60 dB loss, improving PTA (+12.1 dB) and tinnitus remission (56% vs. 26% placebo). Similarly, (17) demonstrated that intratympanic prednisolone achieved early complete recovery in 76% versus 20% with placebo ($p=0.0002$), although after systemic rescue, final differences were not significant. In systemic-refractory scenarios, (18) compared intratympanic dexamethasone with hyperbaric oxygen therapy, showing similar overall PTA efficacy, with a slight advantage for IT in profound losses (>81 dB) and for HBO in younger patients (<60 years).

Finally, (19) reported that intratympanic methylprednisolone led to a mean gain of 7.8 dB ($p<0.01$) after systemic treatment failure, significantly superior to otic drops or no treatment (Table 2).Collectively, these trials reinforce that intratympanic therapy represents an effective alternative, especially in patients with severe/profound hearing loss or those refractory to systemic steroids. It also shows a favorable safety profile and differential effects in specific clinical subgroups.The methodological assessment of the seventeen included RCTs revealed significant limitations. Overall, 8 out of 17 studies (47.1%) were classified as having high overall risk of bias, including studies (3,6,8,10,11,14,15,20). These ratings were mainly due to shortcomings in allocation concealment, lack of blinding, and incomplete outcome reporting (Table 3).

The remaining 9 studies (52.9%) were rated as having "some concerns," including (7,9,12,13,16–19,21). These concerns were related to insufficient reporting of randomization procedures, loss to follow-up, or possible selective reporting bias (Table 3).

Table 3. Overall risk of bias.

Author	Overall Risk
Maryam Amizadeh, 2025	High
Shi-yi Wang, 2025	High
Jie Huang, 2021	High
Busheng Tong, 2020	High
Michael Tsounis, 2018	High
Mohammadtaghi Khorsandi Ashtiani, 2018	Some concerns
Ilyoung Cho, 2018	High
Gülce Ermutlu, 2017	High
Kavita Swachia, 2016	High
Markus Suckfuell, 2014	Some concerns
Roberto Filipo, 2013	Some concerns
Ljiljana Cvorovic, 2013	Some concerns
Peng Li, 2011	Some concerns
Moo Kyun Park, 2011	Some concerns
Francesco Dispenza, 2011	Some concerns
Hung-Pin Wu, 2011	Some concerns
Jong Bin Lee, 2011	Some concerns

The risk of bias assessment was conducted using the RoB 2.0 tool (Risk of Bias 2.0, Cochrane Collaboration). High: high risk of bias; Some concerns: presence of concerns that may partially affect internal validity but do not constitute a high risk.

Although all trials contribute data on the comparative efficacy of intratympanic versus systemic corticosteroids in SSNHL, overall confidence in the findings is low to moderate, given that nearly half of the studies present high risk of bias and the rest have relevant methodological uncertainties.

Discussion

This systematic review of 17 randomized controlled trials evaluates the comparative efficacy of corticosteroids administered via the intratympanic versus systemic route as primary treatment for sudden sensorineural hearing loss (SSNHL). Overall, the findings support that the intratympanic route is at least non-inferior to the systemic route in terms of average hearing recovery (improvement in PTA) and rates of complete/partial recovery, particularly in patients with severe or profound hearing loss. Additionally, the intratympanic route demonstrated a more favorable safety profile, with fewer systemic adverse events, although it was associated with self-limiting local effects.

Several included trials corroborate previous findings showing intratympanic corticosteroids to be equivalent or superior to systemic steroids in selected subgroups.

For instance, (6) demonstrated a significantly higher success rate with intratympanic administration (50%) compared to oral (33.3%) and intravenous (30%) routes, with greater benefit in severe hearing loss (70.6% vs. 41–50%). Similarly, (20) reported significant differences in functional recovery (60.7% vs. 33.3%) when hyperbaric oxygen therapy was added to combined steroid therapy, suggesting possible clinical synergy.

In salvage therapy studies, (12,13) showed significant benefits of sequential intratympanic administration following systemic treatment failure ($p=0.027$ and $p<0.05$, respectively), supporting its use in refractory cases.

However, other studies did not report clinically significant differences between the two routes. For example, (8–10) observed similar recovery rates ($p>0.05$) between intratympanic and systemic groups. Study (15), with a sample of 203 patients, found no overall differences when adding intratympanic dexamethasone, except in subgroups with severe hearing loss, highlighting the importance of stratifying by severity. This heterogeneity may be explained by variations in treatment initiation timing, dosages used, definitions of recovery, and the use of co-interventions such as hyperbaric oxygen. Furthermore, the high risk of bias in over 47% of studies—particularly due to lack of blinding and allocation concealment—limits confidence in the magnitude of the observed effects.

Among the methodological strengths of this review are the exclusive inclusion of randomized controlled trials, rigorous risk of bias assessment (RoB 2.0), and a comprehensive, language-unrestricted search across multiple databases. Nonetheless, no meta-analysis was conducted, preventing a pooled quantitative estimate of effect. There was considerable heterogeneity in study designs, therapeutic regimens, and outcomes, and the overall quality of evidence was mostly low to moderate. Moreover, many studies had limited sample sizes, and few reported patient-centered outcomes such as quality of life or symptom duration.

The findings suggest that intratympanic corticosteroids may be considered a valid initial treatment option in SSNHL, particularly for patients with contraindications to systemic steroids or with severe/profound hearing loss. From a safety perspective, intratympanic use may reduce the burden of systemic adverse events without compromising efficacy. However, current evidence does not establish definitive superiority, and higher-quality trials with greater statistical power and subgroup analyses—including clinical phenotypes, timing of intervention, and audiometric profiles—are needed. Additionally, future studies should prioritize functional outcomes and quality of life measures. Although no meta-analysis was performed, this structured synthesis provides an updated qualitative appraisal of randomized trials comparing intratympanic versus systemic corticosteroids in SSNHL. The absence of statistical pooling is justified by methodological heterogeneity, and future studies should ensure better standardization-including consistent reporting of patient-centered symptoms-to allow meaningful quantitative synthesis.

Beyond audiometric recovery, SSNHL frequently presents with tinnitus and vestibular symptoms, and improvement in these domains may strongly influence patient-perceived

benefit. In the included trials, reporting of tinnitus/vertigo outcomes was inconsistent, limiting direct comparisons by route; however, some studies suggested symptom improvement alongside hearing gains (e.g., lower rates of persistent tinnitus in intervention arms). In addition, recent clinical evidence supports the relevance of these endpoints: in a 2025 clinical study evaluating simultaneous systemic plus intratympanic corticosteroids, 24% of tinnitus cases resolved completely and 51% improved partially within one month, while vertigo resolved completely in 67% and improved partially in 33%, underscoring the need for more consistent symptom measurement in future trials.

Conclusion

In summary, intratympanic corticosteroid administration appears to be at least as effective as systemic therapy for the initial treatment of sudden sensorineural hearing loss, with a distinct safety profile. Although the results support its use in specific subgroups, the evidence remains heterogeneous and of limited certainty. Until further studies resolve these uncertainties, treatment decisions should be individualized, taking into account hearing severity, comorbidities, and patient preferences.

Acknowledgements

The authors declare no conflict of interest. No funding was received for this study.

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