

Efficacy and safety of local vs. systemic steroid therapy for patients with sudden deafness and diabetes mellitus: A systematic review and meta-analysis

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Abstract. The present study aimed to systematically evaluate the effects of local steroid injection (LSI) vs. systemic steroid therapy (SST) on glycemic control, clinical efficacy and safety in diabetic patients with sudden sensorineural hearing loss (SSNHL), and to compare different LSI routes [postauricular steroid injection (PSI) vs. intratympanic steroid injection (ITSI)] as well as combination LSI strategies. PubMed, Embase, Cochrane Library, Web of Science, Google Scholar, China National Knowledge Infrastructure and Wanfang Data databases were systematically searched from inception to February 2026. Studies comparing LSI (PSI or ITSI) with SST in diabetic patients with SSNHL were included. Two investigators independently screened the literature, extracted data and assessed methodological quality. Meta-analysis was conducted using RevMan 5.4 and Stata 14.0. A total of 18 studies involving 1,577 patients were included. The overall methodological quality of the included studies was moderate to high. Compared with SST, LSI was associated with markedly lower fasting blood glucose (FBG) levels [mean difference (MD), -1.09 mmol/l], lower 2-h postprandial blood glucose (PBG) levels (MD, -2.05 mmol/l) and a reduced incidence of hyperglycemic events [risk ratio (RR), 0.18]. In addition, LSI achieved a markedly higher overall response rate (ORR) (RR, 1.14) and greater hearing threshold improvement [MD, 3.14 dB hearing level (HL)]. No significant

difference was observed in the overall incidence of adverse events (AEs) between local and systemic therapy (RR, 0.49). However, subgroup analysis showed that PSI was associated with fewer AEs than SST (RR, 0.37), whereas no significant difference was observed between ITSI and SST. PSI and ITSI demonstrated comparable ORRs (RR, 1.00) and hearing threshold improvements (MD, 0.73 dB HL), although PSI was associated with fewer AEs (RR, 0.39) and slightly higher FBG levels (MD, 0.48 mmol/l). Furthermore, combination LSI achieved a higher ORR (RR, 1.25) and better hearing recovery than single-route LSI. Sensitivity analysis confirmed the robustness of the pooled results, and no substantial publication bias was detected. In conclusion, in diabetic patients with SSNHL, LSI provides better glycemic control and superior therapeutic efficacy compared with SST, while maintaining a comparable overall safety profile. PSI and ITSI demonstrate similar efficacy, although PSI appears to be associated with fewer AEs. Combination LSI may further improve clinical outcomes; however, additional high-quality studies are needed to confirm its benefits.

Introduction

Sudden sensorineural hearing loss (SSNHL) is a common otologic emergency that can result in permanent hearing impairment in severe cases, substantially reducing patients' quality of life. Epidemiological studies from China, South Korea, and America have reported an annual incidence of 5-30 cases per 100,000 population, with a rising trend in recent years (1-4). This increase has been attributed, at least in part, to greater occupational and psychological stress as well as the widespread use of multimedia audio devices (5). Despite extensive research, the exact etiology and pathogenesis of SSNHL remain incompletely understood. Current hypotheses primarily involve viral infection, cochlear microcirculatory disturbances and rupture of the membranous labyrinth (6,7). Notably, diabetes mellitus (DM) is closely associated with the occurrence and progression of SSNHL. Chronic hyperglycemia in diabetic patients can induce microangiopathy, increase blood viscosity and impair vascular endothelial

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function, thereby disrupting cochlear microcirculation and causing ischemic and hypoxic injury to sensory hair cells (8). Consequently, the risk of SSNHL is markedly elevated in this population. Previous studies have demonstrated that diabetic patients have a 1.5- to 2-fold higher risk of developing SSNHL than non-diabetic individuals, and hearing loss is often more severe once the disease occurs (9). Furthermore, diabetic patients frequently present with microvascular complications, including thickening of the capillary walls and basement membranes of the stria vascularis, which may further hinder drug delivery to the inner ear and complicate treatment (10). Of particular concern is that the global DM prevalence continues to rise. In 2021, an estimated 537 million adults worldwide were living with diabetes, and this number is projected to increase to 783 million by 2045 (11). As a result, the population of patients with diabetes complicated by SSNHL is expected to expand substantially, underscoring the urgent need to optimize therapeutic strategies for this high-risk patient group.

The current management of SSNHL primarily relies on steroid therapy, with systemic administration remaining the standard first-line treatment (12). The therapeutic effects of steroids are primarily mediated through anti-inflammatory and immunosuppressive actions, as well as the regulation of inner-ear ion homeostasis, thereby reducing cochlear edema, improving microcirculation, inhibiting hair cell apoptosis and ultimately facilitating hearing recovery (13). However, the use of steroids in patients with DM presents a major clinical dilemma. On the one hand, high-dose systemic steroid therapy (SST) remains a cornerstone of SSNHL management and plays a critical role in suppressing inflammatory responses and preserving auditory function. On the other hand, steroids can substantially elevate blood glucose levels by stimulating hepatic gluconeogenesis and impairing peripheral glucose uptake and utilization (14). In patients with pre-existing disorders of glucose metabolism, SST may precipitate severe hyperglycemic events, including hyperglycemic crises and even diabetic ketoacidosis, which can be life-threatening in extreme cases (15). Moreover, diabetic patients frequently have comorbid conditions such as hypertension and peptic ulcer disease, both of which may be exacerbated by SST (16). Therefore, identifying a steroid delivery strategy that minimizes the impact on glycemic control while maintaining therapeutic efficacy has become a critical clinical challenge in the management of diabetes complicated by SSNHL.

Given the limitations of SST in diabetic patients, local steroid injection (LSI), including postauricular (PSI) and intratympanic steroid injection (ITSI), has increasingly attracted attention as an alternative treatment strategy (17). Theoretically, local delivery can bypass the blood-labyrinth barrier, achieve higher drug concentrations within the inner ear and reduce systemic absorption, thereby minimizing adverse effects on glycemic control (18). However, the relative advantages and disadvantages of LSI vs. SST in terms of clinical efficacy, glycemic control and safety remain controversial in patients with diabetes complicated by SSNHL. Furthermore, the comparative effectiveness and safety of different LSI routes, particularly PSI vs. ITSI, have not been systematically evaluated. Although several studies and a previous meta-analysis have investigated the efficacy of LSI in diabetic patients

with SSNHL, important knowledge gaps remain (19,20). For example, the meta-analysis conducted by Wang *et al* (19) included 23 studies with 1,777 patients and demonstrated that LSI markedly improved the overall response rate (ORR) [risk ratio (RR), 1.17] and exhibited a greater hearing threshold improvement [mean difference (MD), 6.60 dB hearing level (HL)] compared with SST. However, the analysis has several notable limitations: It did not comprehensively assess the impact of different treatment routes on glycemic control, did not directly compare PSI and ITSI, and failed to systematically evaluate the clinical value of combination LSI. Furthermore, the literature search was conducted only up to October 2022, and a substantial body of new evidence has since become available. Therefore, the present meta-analysis aims to evaluate the effects of LSI on glycemic control, directly compare the efficacy and safety of PSI and ITSI, and systematically assess the benefits of combination LSI vs. single-route LSI. By incorporating the latest available evidence, this study seeks to provide a more comprehensive and updated evidence base for selecting the optimal steroid administration strategy in patients with diabetes complicated by SSNHL.

Materials and methods

Data sources and search strategy. The present meta-analysis followed the Preferred Reporting Items for Systematic Reviews (21) and Meta-analysis guidelines and was structured based on the Population, Intervention, Comparison, and Outcome framework (22). A systematic literature search was performed in PubMed (<https://pubmed.ncbi.nlm.nih.gov>), Embase ([embase.com](https://www.embase.com)), Cochrane Library (<https://www.cochranelibrary.com>), Web of Science (<https://www.webof-science.com>), Google Scholar (scholar.google.com), China National Knowledge Infrastructure (<https://www.cnki.net>) and Wanfang Data (<https://www.wanfangdata.com.cn>) databases from inception to February 2026. The main search terms included: ('sudden hearing loss' OR 'sudden deafness' OR 'sudden sensorineural hearing loss' OR 'SSNHL'), ('diabetes mellitus' OR 'type 2 diabetes' OR 'DM'), ('glucocorticoid' OR 'steroid' OR 'corticosteroid' OR 'methylprednisolone' OR 'dexamethasone' OR 'budesonide'), ('local injection' OR 'ITSI' OR 'postauricular injection' OR 'systemic administration' OR 'intravenous' OR 'oral'), and outcome-related terms, including ('blood glucose' OR 'fasting blood glucose' OR 'postprandial blood glucose' OR 'hyperglycemia'), ('response rate' OR 'treatment response' OR 'efficacy'), ('pure-tone average' OR 'hearing improvement'), and ('adverse reaction' OR 'adverse event' OR 'safety' OR 'side effect').

Inclusion criteria. Studies were considered eligible if they met the following criteria: i) Participants were patients with a confirmed diagnosis of SSNHL (7) complicated by DM, with SSNHL diagnosis confirmed by audiometry typically defined as sensorineural hearing loss of at least 20 dB HL at two contiguous frequencies occurring within 72 h; ii) the intervention group received LSI, including PSI and/or ITSI; iii) the control group received SST, including oral or intravenous administration; and iv) at least one of the following outcomes was reported: Glycemic control outcomes [fasting blood glucose (FBG), 2-h postprandial blood glucose (PBG),

or incidence of hyperglycemic events], efficacy outcomes (ORR or hearing threshold improvement) or safety outcomes.

Exclusion criteria. Studies were excluded if they met any of the following criteria: i) Participants had secondary SSNHL attributable to identifiable causes, such as trauma, tumors, Ménière's disease or otitis media; ii) participants had concomitant diseases that could substantially affect glucose metabolism or glycemic control, such as Cushing's syndrome or hyperthyroidism; iii) the intervention did not involve steroid therapy or included concomitant treatments that could confound the assessment of treatment efficacy; iv) the publication was a duplicate report, conference abstract, review article, animal study, single-arm study, case report or a study for which the full text was unavailable; or v) the reported data were incomplete or insufficient for effect size calculation, and the required information could not be obtained after contacting the study authors.

Data extraction. Study selection and data extraction were independently performed by two investigators. The extracted data were cross-checked, and any discrepancies were resolved through discussion and consensus. If disagreement persisted, a third investigator was consulted for adjudication. Initially, titles and abstracts were screened to exclude clearly irrelevant studies. The full texts of potentially eligible articles were subsequently retrieved and assessed in detail according to the predefined inclusion and exclusion criteria. The following data were extracted from each included study: First author, year of publication, study design, sample size, intervention characteristics (LSI or SST, steroid type, dosage, administration frequency and treatment duration) and outcome measures [FBG, 2h-PBG, incidence of hyperglycemic events, ORR, hearing threshold improvement and incidence of adverse events (AEs)]. For glycemic outcomes, FBG and 2h-PBG values were extracted as reported by the original authors; values were considered as post-treatment values regardless of whether they were measured during or after the steroid treatment course, as the specific timing of assessment was not uniformly reported across studies. For hyperglycemic events, data were extracted as reported by the original studies; in studies where a quantitative definition was not explicitly provided, events described as clinically significant hyperglycemia requiring medical intervention or treatment modification during the course of steroid therapy were included. For hearing threshold outcomes, the within-group improvement in hearing threshold for each study arm was extracted, defined as the pre-treatment hearing threshold minus the post-treatment hearing threshold, with a positive value indicating hearing improvement. For AEs, studies reporting a composite 'total AEs' endpoint were pooled directly; when a study reported multiple specific AE types without specifying whether events overlapped, each AE type was analyzed separately in subgroup analyses rather than summed into a composite endpoint. For studies with incomplete or missing data, attempts were made to contact the corresponding authors via email to obtain the original data. If the required information could not be retrieved, only the available extractable data were included in the quantitative analysis.

Quality assessment of included studies. The methodological quality of the included studies was independently assessed by two investigators, and the assessment results were cross-checked. Any disagreements were resolved through discussion and consensus, and when necessary, a third investigator was consulted for adjudication. The revised Cochrane Risk of Bias tool (RoB 2.0; <https://www.riskofbias.info/welcome/rob-2-0-tool>) was used to assess the risk of bias in randomized controlled trials (RCTs), while the Newcastle-Ottawa Scale (NOS) was applied to evaluate the methodological quality of cohort studies (23). Studies with a total NOS score of 7-9 were considered high quality, those with a score of 4-6 were considered moderate quality and those with a score of 0-3 were considered low quality.

Statistical analysis. Meta-analysis was performed using RevMan 5.4 (<https://revman.cochrane.org>) and Stata 14.0 (<https://www.stata.com>) software. For dichotomous outcomes, including ORR, hyperglycemic events and AEs, effect sizes were expressed as RRs with corresponding 95% confidence intervals (CIs). For continuous outcomes, including FBG, 2h-PBG and hearing threshold improvement, effect sizes were expressed as MDs with 95% CIs. Statistical heterogeneity was assessed using the χ^2 test ($\alpha=0.10$) and I^2 statistic. Given that clinical and methodological diversity is expected across studies conducted in different settings and populations, a random-effects model was applied to all meta-analyses to account for potential between-study heterogeneity, regardless of the I^2 value. Subgroup and sensitivity analysis were performed to explore heterogeneity sources. For multi-arm studies, shared comparator or intervention groups were split approximately equally between pairwise comparisons to avoid unit-of-analysis errors. For continuous outcomes, the sample size of the split arm was halved while the mean and standard deviation were kept unchanged. For AEs, when a study reported a composite 'total AEs' endpoint, these data were pooled directly. When multiple specific AE types were reported separately without information on whether events overlapped, each AE type was analyzed independently rather than combined into a composite endpoint. For studies in which numerical data were presented only graphically, data were extracted using GetData Graph Digitizer version 2.26 (GetData Pty Ltd.). For studies reporting hearing threshold improvements at individual frequencies without providing an overall hearing threshold improvement value, pooled means and standard deviations were recalculated based on the reported frequency-specific data and sample sizes. Publication bias was qualitatively assessed using funnel plots. For outcomes that included at least 10 studies, Egger's regression test was further conducted to quantitatively evaluate potential publication bias. Sensitivity analysis was performed using a leave-one-out approach to determine the influence of individual studies on the pooled effect estimates. Subgroup analysis were conducted according to the route of LSI (PSI vs. ITSI) to investigate potential sources of heterogeneity and differences in treatment effects between subgroups. All statistical tests were two-sided, and $P<0.05$ was considered to indicate a statistically significant difference.

Results

Literature search and study selection. A total of 1,247 potentially relevant studies were initially identified through database searches, including 609 Chinese-language articles and 638 English-language articles. After removing duplicates using EndNote, 892 records remained for screening. Following title and abstract review, 831 studies were excluded as they were unrelated to the research topic or were review articles, case reports, animal studies or conference abstracts. The remaining 61 articles underwent full-text assessment for eligibility. During full-text review, 22 studies were excluded as the study population did not consist of patients with diabetes complicated by SSNHL, 11 studies were excluded as the interventions did not involve LSI or SST as a comparator, 6 studies were excluded due to unavailable full texts or incomplete data and 4 single-arm studies were excluded. Ultimately, 18 studies met the inclusion criteria and were included in the meta-analysis (Fig. 1), comprising 12 Chinese-language studies and 6 English-language studies (24-41). Among these, 9 were RCTs, 5 were prospective cohort studies and 4 were retrospective cohort studies. Regarding diagnostic verification, 13 out of the 18 included studies explicitly adopted the 2015 Chinese guidelines for SSNHL diagnosis (7), and the remaining 5 provided detailed baseline pure-tone audiometry data confirming the audiological diagnosis. Therefore, the diagnosis of SSNHL was verified by objective audiometric testing rather than administrative medical records alone. The 18 included studies involved a total of 1,577 patients with DM complicated by SSNHL, including 958 patients in the LSI group, 496 patients in the SST group and 123 patients in the combination LSI group. LSI consisted of PSI in 5 studies and ITSI in 6 studies. In addition, 5 studies directly compared the efficacy of PSI and ITSI, while 2 studies evaluated combination local therapy (PSI plus ITSI) vs. single-route local treatment. Methylprednisolone was the most commonly used steroid (11 studies), followed by dexamethasone (6 studies) and budesonide (1 study). Most studies employed an LSI regimen consisting of 40 mg methylprednisolone per administration, given every other day for a total of four to five sessions. Treatment efficacy was generally assessed between 10 days and 1 month after completion of therapy. Regarding glycemic assessment, none of the included studies explicitly reported the specific day or the number of steroid doses administered before post-treatment blood glucose measurement; most studies stated that FBG and 2h-PBG were measured 'before and after treatment' without further specification, and no study provided long-term glycemic follow-up data beyond the acute treatment period. Detailed characteristics of the included studies are summarized in Tables I-III. The Results section is organized as follows: Glycemic outcomes are presented first, as glycemic control directly determines treatment eligibility and safety in diabetic patients with SSNHL, followed by clinical efficacy and other AEs. Within each domain, three comparisons are reported sequentially: LSI vs. SST, PSI vs. ITSI and combined LSI vs. single-route LSI.

Quality assessment of included studies. The methodological quality of included studies was assessed using RoB 2.0 for RCTs and the NOS for cohort studies. Among the 9 RCTs, 7

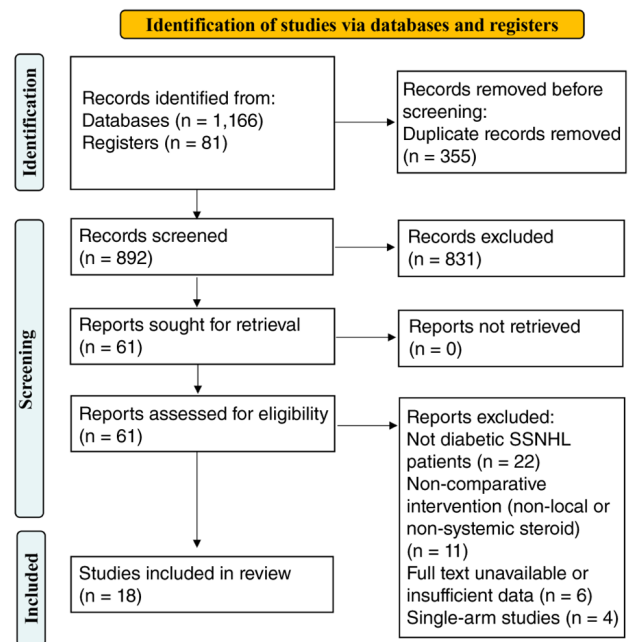


Figure 1. Flow chart for data retrieval.

had a low risk of bias, while 2 raised concerns due to unclear blinding procedures [Chen *et al* (31) and Ye *et al* (34)] (Fig. 2). Of the 9 cohort studies, 6 were of high quality (7-8 points) and 3 of moderate quality (6 points). Overall, the included studies were of moderate to high methodological quality and suitable for meta-analysis. Detailed quality assessment results are presented in Table IV.

LSI has a smaller impact on glycemic control than SST. FBG levels of patients in the LSI group were markedly lower than that in the SST group (MD, -1.09 mmol/l; 95% CI, -1.60 to -0.59; $P<0.0001$). Subgroup analysis showed that both PSI (MD, -0.93 mmol/l; 95% CI, -1.47 to -0.39; $P=0.0008$) and ITSI (MD, -1.68 mmol/l; 95% CI, -2.52 to -0.85; $P<0.0001$) were associated with markedly lower FBG levels compared with SST. Moderate to substantial heterogeneity was observed across studies (overall $I^2=80\%$; PSI subgroup $I^2=83\%$), with the results of the ITSI subgroup being highly consistent ($I^2=0\%$) (Fig. 3A). In addition, compared with SST, the LSI group showed markedly lower 2h-PBG levels (MD, -2.05 mmol/l; 95% CI, -3.17 to -0.94; $P=0.0003$), despite substantial heterogeneity among the included studies ($I^2=88\%$) (Fig. 3B). Regarding hyperglycemic events, the 2 included studies reporting this outcome [Takehata *et al* (25) and Han *et al* (27)] defined it based on clinical assessment during hospitalization, referring to worsening blood glucose levels that required additional medical intervention or treatment modification. The pooled analysis showed that the LSI group had a significantly lower risk of hyperglycemic events than the SST group (RR, 0.18; 95% CI, 0.04-0.93; $P=0.04$), with no significant heterogeneity across studies ($I^2=0\%$) (Fig. 3C). Overall, these findings suggest that LSI exerts a smaller impact on both fasting and postprandial blood glucose levels compared with SST, and overall, significantly reduces the risk of hyperglycemic events in diabetic patients with SSNHL.

Table I. Basic information and relevant efficacy indicators of included studies (LSI vs. SST).

First author, year	Study design	Patients, n		Therapeutic regimen		Fasting blood glucose, mmol/l ^a		2-h postprandial blood glucose, mmol/l ^a		Hyper glycemic events, n/total n		Overall response rate, n/total n		Hearing gain, dB HL ^a		Adverse events, n/total n	
		LSI	SST	LSI	SST	LSI	SST	LSI	SST	LSI	SST	LSI	SST	LSI	SST	LSI	SST
Lu <i>et al</i> , 2020	RCT	25	25	Postauricular methylpred- nisolone 40 mg/qod x5	IV methylpred- nisolone 40 mg/ qd tapering x10 days	4.98± 0.97	6.74± 1.08	8.24± 1.78	11.96± 1.87	NR	NR	24/25	19/25	NR	NR	NR	NR
Lu <i>et al</i> , 2023	RCT	64	64	Postauricular methylpred- nisolone 40 mg/ qd x5	IV methylpred- nisolone 40 mg/ qd tapering x10 days	7.82± 1.33	8.34± 1.24	11.19± 1.54	12.22± 1.61	NR	NR	62/64	55/64	36.46± 14.93	33.57± 13.73	4/64	7/64
Long and Zuo, 2025	RCS	66	62	Postauricular methylpred- nisolone 40 mg/ qd x5	IV methylpred- nisolone 40 mg/ qd tapering x10 days	7.83± 1.29	8.47± 1.35	11.31± 1.64	12.54± 1.94	NR	NR	60/66	47/62	38.07± 16.78	35.77± 14.01	5/66	14/62
Ye <i>et al</i> , 2025	RCT	41	20	Postauricular methylpred- nisolone 40 mg/ qd x4	IV methylpred- nisolone 60 → 40 → 20 mg/qd stepwise tapering	9.51± 3.12	12.10± 3.21	NR	NR	NR	NR	32/41	10/20	11.3± 2.69	10.8± 2.66	NR	NR
Cheng <i>et al</i> , 2019	RCT	45	20	Intratympanic methylpred- nisolone 40 mg/ qd x4	IV methylpred- nisolone 60 → 40 → 20 mg/qd stepwise tapering	9.77± 3.17	12.10± 3.21	NR	NR	NR	NR	31/45	11/20	12.0± 3.66	10.8± 2.66	NR	NR
Zhao and Jin, 2013	PCS	40	42	Intratympanic methylpred- nisolone 20 mg/ qd x10	IV dexamet- hasone 10 mg/ qd tapering	6.9± 0.8	7.3± 0.6	NR	NR	NR	NR	34/58	36/58	12.0± 1.3	11.0± 1.23	0/58	0/58
						8.01± 2.03	9.48± 2.40	8.81± 1.76	11.34± 3.17	NR	NR	32/40	28/42	42.8± 10.3	35.1± 12.4	0/40	12/42

(32)

(33)

(24)

(34)

(31)

(35)

Table I. Continued.

First author, year	Study design	Patients, n		Therapeutic regimen		Fasting blood glucose, mmol/l ^a		2-h postprandial blood glucose, mmol/l ^a		Hyper glycemic events, n/total n		Overall response rate, n/total n		Hearing gain, dB HL ^a		Adverse events, n/total n		(Refs.)
		LSI	SST	LSI	SST	LSI	SST	LSI	SST	LSI	SST	LSI	SST	LSI	SST	LSI	SST	
Han <i>et al</i> , 2008	PCS	19	17	Intratympanic dexamethasone 5 mg/ml x 0.5 ml, biw x4	IV prednisolone 100→80→ 55 mg/qd + oral prednisone tapering	14.68± 4.96	13.02± 4.89	NR	NR	0/19	2/17	16/19	10/17	25.1± 17.3	17.6± 27.8	0/19	2/17	(26)
Han <i>et al</i> , 2009	PCS	17	47	Intratympanic dexamethasone 5 mg/ml x 0.5 ml, biw x4	Oral prednisone 60 → 40 → 20 → 10 mg/qd tapering	NR	NR	NR	NR	0/17	1/47	13/17	34/47	25.8± 17.8	26.2± 19.2	0/17	6/47	(27)
		17	30	Intratympanic dexamethasone 5 mg/ml x 0.5 ml, biw x4	IV prednisolone 100→80→ 55 mg/qd + oral prednisone tapering	NR	NR	NR	NR	0/17	2/30	14/17	20/30	25.8±1 7.8	20.0± 21.6	0/17	6/30	
Kakehata <i>et al</i> , 2006	PCS	10	21	Intratympanic dexamethasone 4 mg/ml x 0.5 ml, qd x8	IV dexamethasone, methasone, 8 mg qd/ tapering, total 40 mg over 10 days	NR	NR	NR	NR	0/10	4/21	10/10	14/21	40.5± 4.9	25.1± 4.8	2/10	4/21	(25)
Jiang <i>et al</i> , 2015	RCT	42	42	Intratympanic budesonide suspension 0.3 ml/qod x5	Oral prednisone 1 mg/kg/day tapering	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	24/42	0/43	(41)

Table I. Continued.

First author, year	Study design	Patients, n		Therapeutic regimen		Fasting blood glucose, mmol/l ^a		2-h postprandial blood glucose, mmol/l ^a		Hyper glycemic events, n/total n		Overall response rate, n/total n		Hearing gain, dB HL ^a		Adverse events, n/total n	
		LSI	SST	LSI	SST	LSI	SST	LSI	SST	LSI	SST	LSI	SST	LSI	SST	LSI	SST
Kim <i>et al</i> , 2019	RCS	42	48	Intratympanic dexamethasone, 5 mg/ml, 3-7 days for a total of 3-5 injections	Oral methylpre dnisolone 48 → 32 → 16 → 8 mg/qd tapering over 10 days IV dexam- thasone 10 → 5 mg/qd over 7 days (total 60 mg), followed by oral methyl- prednisolone tapering	NR	NR	NR	NR	NR	NR	21/42	26/48	12.42±	15.42±	NR	NR
														17.53	22.66		(28)

^aData are presented as the mean ± SD. LSI, local steroid injection; SST, systemic steroid therapy; RCT, randomized controlled trial; RCS, retrospective cohort study; PCS, prospective cohort study; qod, quaque odie die; IV, intravenous; qd, quaque die; biw, bis in week; NR, not reported.

Table II. Basic information and relevant efficacy indicators of included studies (PSI vs. ITSI).

First author, year	Study design	Patients, n		Therapeutic regimen		Fasting blood glucose, mean $\pm$ SD, mmol/l		2-h postprandial blood glucose, mean $\pm$ SD, mmol/l		Hyper- glycemic events, n/total n		Overall response rate, n/total n		Hearing gain, mean $\pm$ SD, dB HL		Adverse events, n/total n		(Refs.)
		PSI	ITSI	PSI	ITSI	PSI	ITSI	PSI	ITSI	PSI	ITSI	PSI	ITSI	PSI	ITSI	PSI	ITSI	
Jia <i>et al</i> , 2018	RCT	39	39	Postauricular methylpred- nisolone 40 mg/ qod x 5	Intratympanic methylpred- nisolone 40 mg/ qod x 5	3.82 $\pm$ 0.50	3.30 $\pm$ 0.40	NR	NR	NR	NR	29/39	28/39	24.33 $\pm$ 3.19	23.98 $\pm$ 3.07	8/39 3/39 0/39 2/39	23/39 11/39 1/39 3/39	(38)
Wang and Ma, 2018	RCT	62	62	Postauricular dexamethasone 5 mg/qod x 5	Intratympanic dexamethasone, 2.5 mg/qod x 5	10.95 $\pm$ 2.45	11.02 $\pm$ 2.52	NR	NR	NR	NR	50/62	53/62	33.08 $\pm$ 5.93	32.04 $\pm$ 5.30	1/62 1/62 0/62 0/62	1/62 3/62 1/62 4/62	(40)
Zhu <i>et al</i> , 2020	RCS	40	48	Postauricular methylpred- nisolone 40 mg/ qod x 5	Intratympanic methylpred- nisolone 40 mg/ qod x 5	10.9 $\pm$ 1.9	10.5 $\pm$ 1.6	NR	NR	NR	NR	30/40	34/48	25.11 $\pm$ 2.93	24.22 $\pm$ 2.57	9/40 3/40 0/40 4/40	28/48 13/48 2/48 5/48	(39)
Ai <i>et al</i> , 2020	PCS	17	16	Postauricular dexamethasone (5 mg) plus lidocaine (0.5 ml), qod x5	Intratympanic dexamethasone, 5 mg/qod x 5	NR	NR	NR	NR	NR	NR	13/17	11/16	NR	NR	NR	NR	(37)
Li <i>et al</i> , 2019	RCT	30	30	Postauricular methylpred- nisolone 40 mg/ qod x 5	Intratympanic methylpred- nisolone 40 mg/ qod x 5	NR	NR	NR	NR	NR	NR	31/30	20/30	NR	NR	NR	NR	(36)

PSI, postauricular steroid injection; ITSI, intratympanic steroid injection; RCT, randomized controlled trial; RCS, retrospective cohort study; PCS, prospective cohort study; qod, quaque odie; NR, not reported.

Table III. Basic information and relevant efficacy indicators of included studies (combined LSI vs. single-route LSI).

First author, year	Study design	Patients, n		Therapeutic regimen		Fasting blood glucose, mean $\pm$ SD, mmol/l		2-h postprandial blood glucose, mean $\pm$ SD, mmol/l		Hyperglycemic events, n/total n		Overall response rate, n/total n		Hearing gain, mean $\pm$ SD, dB HL		Adverse events, n/total n	
		Combined LSI	Single-route LSI	Combined LSI	Single-route LSI	Combined LSI	Single-route LSI	Combined LSI	Single-route LSI	Combined LSI	Single-route LSI	Combined LSI	Single-route LSI	Combined LSI	Single-route LSI	Combined LSI	Single-route LSI
Li <i>et al.</i> , 2025	RCS	44	40	Intratympanic (day 1) then postauricular (day 2) methylpred-nisolone 40 mg each route, qod x 5	Intratympanic methylpred-nisolone alone, 40 mg/qod x 5	5.73 $\pm$ 0.99	7.23 $\pm$ 0.95	7.86 $\pm$ 1.08	9.15 $\pm$ 1.37	NR	NR	36/44	24/40	5.73 $\pm$ 0.99	7.23 $\pm$ 0.95	4/44	6/40
Li and Zhang, 2020	RCT	50	49	Intratympanic combined with postauricular methylpred-nisolone, 20 mg each route qod x 5	Postauricular methylpred-nisolone alone, 40 mg/qod x 5	7.60 $\pm$ 0.77	7.61 $\pm$ 0.86	NR	NR	NR	NR	44/50	35/49	NR	NR	NR	NR
Li <i>et al.</i> , 2019	RCT	14	30	Intratympanic combined with postauricular methylpred-nisolone, 20 mg each route, qod x 5	Intratympanic methylpred-nisolone alone, 40 mg/qod x 5	NR	NR	NR	NR	NR	NR	12/14	20/30	NR	NR	NR	NR
		15	30	Intratympanic combined with postauricular methylpred-nisolone, 20 mg each route, qod x 5	Postauricular methylpred-nisolone alone, 40 mg/qod x 5	NR	NR	NR	NR	NR	NR	12/15	21/30	NR	NR	NR	NR

LSI, local steroid injection; RCT, randomized controlled trial; RCS, retrospective cohort study; qod, quaque odie die; qd, quaque die; NR, not reported.

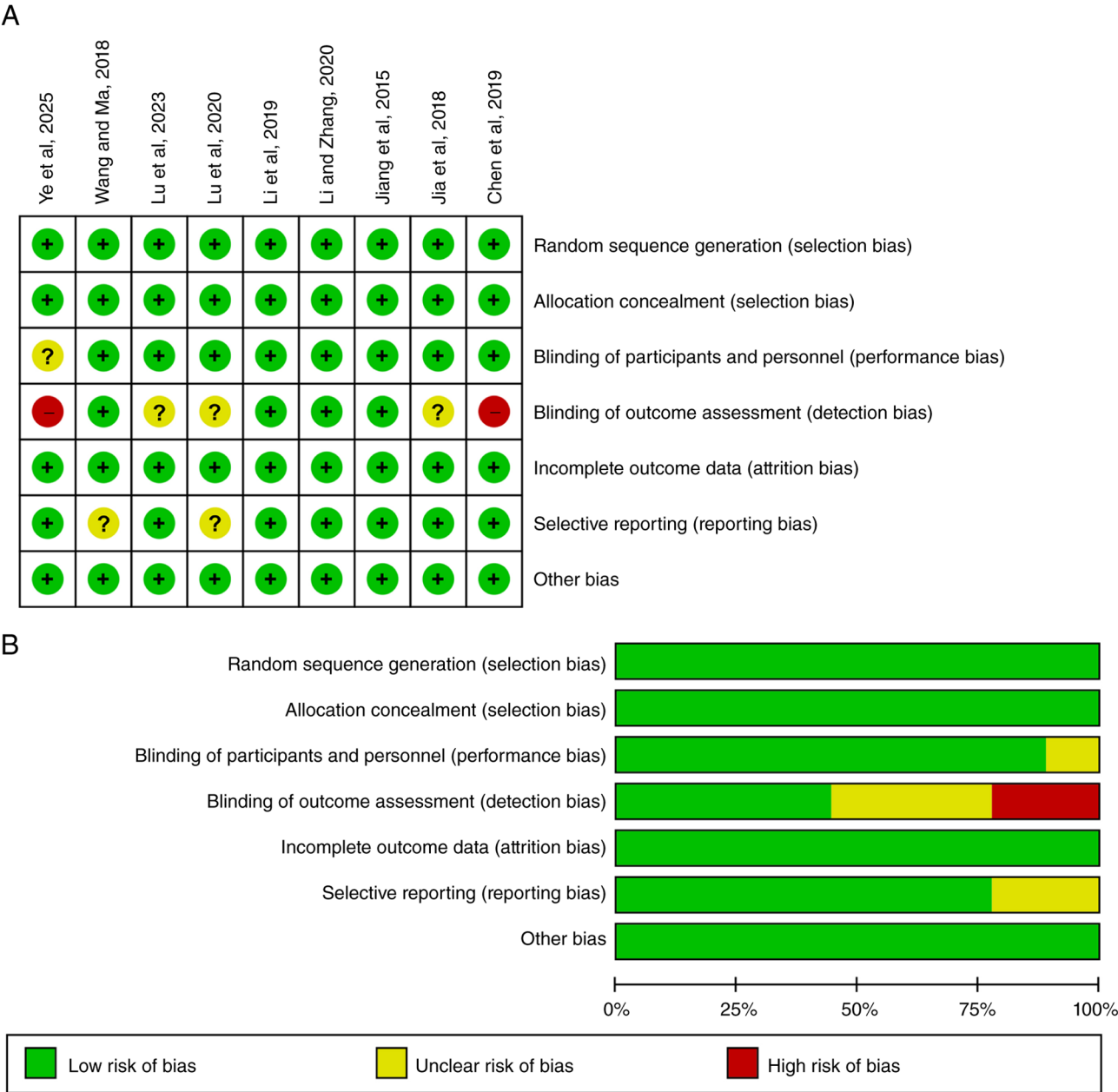


Figure 2. Risk of bias assessment of included studies. (A) Risk of bias summary and (B) risk of bias graph.

LSI demonstrates superior efficacy compared with SST. The pooled analysis showed that LSI was associated with a markedly higher ORR compared with SST (RR, 1.14; 95% CI, 1.04-1.24; P=0.006). Subgroup analysis showed that the PSI subgroup achieved a markedly higher ORR than the SST group (RR, 1.16; 95% CI, 1.06-1.26; P=0.0009), with low between-study heterogeneity ($I^2=8\%$). Similarly, the ITSI subgroup showed a higher ORR than the SST group; however, the difference did not reach statistical significance (RR, 1.13; 95% CI, 0.96-1.32; P=0.13). Moderate heterogeneity was observed among studies in this subgroup ($I^2=49\%$) (Fig. 4A). Meanwhile, LSI resulted in significantly greater hearing threshold improvement than SST (MD, 3.14 dB HL; 95% CI, 1.32-4.96; P=0.0007). In subgroup analysis, PSI was associated with markedly greater hearing threshold improvement than SST (MD, 1.08 dB HL; 95% CI, 0.56-1.59;

P<0.0001), with no evidence of heterogeneity across studies ($I^2=0\%$). By contrast, although the ITSI subgroup showed numerically greater hearing threshold improvement than the SST group, the difference was not statistically significant (MD, 5.10 dB HL; 95% CI, -1.01 to 11.21; P=0.10). Substantial heterogeneity was observed in this subgroup ($I^2=89\%$) (Fig. 4B). Overall, LSI demonstrated superior therapeutic efficacy compared with SST in diabetic patients with SSNHL, as reflected by a higher ORR (RR, 1.14) and greater hearing threshold improvement (MD, 3.14 dB HL). The PSI subgroup consistently showed significant advantages in both efficacy outcomes with minimal heterogeneity, whereas the ITSI subgroup exhibited favorable trends that did not reach statistical significance, likely owing to the considerable heterogeneity among the included studies. Notably, the study by Zhao and Jin (35) reported a within-group hearing

Table IV. Newcastle-Ottawa Scale for cohort studies.

Study	Selection				Comparability	Exposure			Scores	(Refs.)
	Is the case definition adequate?	Representa- tiveness of the cases	Selec- tion of controls	Defini- tion of controls	Compara- bility of cases and controls on the basis of the design or analysis	Ascertain- ment of exposure	Same method of ascertain- ment for cases and controls	Non- response rate		
Long and Zuo, 2025	*	*	*	*	*	*	*		7	(24)
Zhao and Jin, 2013	*	*	*	*	*	*		*	7	(35)
Han <i>et al</i> , 2008	*	*	*	*	*	*			6	(26)
Han <i>et al</i> , 2009	*	*	*	*	*	*	*		7	(27)
Kakehata <i>et al</i> , 2006	*	*	*	*	*	*	*	*	8	(25)
Kim <i>et al</i> , 2019	*	*	*	*	**		*		7	(28)
Zhu <i>et al</i> , 2020	*	*	*	*	*		*		6	(39)
Ai <i>et al</i> , 2020	*	*	*	*	*		*		6	(37)
Li <i>et al</i> , 2025	*	*	*	*	**	*		*	8	(29)

threshold improvement of 42.8 dB HL in the ITSI group and 35.1 dB HL in the SST group, yielding a between-group difference of 7.7 dB HL, which was the largest effect size contributed by any single study and may have contributed to the observed heterogeneity.

Safety outcomes: LSI vs. SST. The pooled analysis showed no statistically significant difference in the overall incidence of AEs between the LSI group and the SST group (RR, 0.49; 95% CI, 0.15-1.54; $P=0.22$). Subgroup analysis demonstrated that the incidence of AEs was significantly lower in the PSI subgroup than in the SST group (RR, 0.37; 95% CI, 0.18-0.74; $P=0.005$), with no evidence of heterogeneity among studies ($I^2=0\%$). By contrast, no significant difference in AE incidence was observed between the ITSI subgroup and the SST group (RR, 0.82; 95% CI, 0.05-12.32; $P=0.88$), with considerable heterogeneity detected within this subgroup ($I^2=80\%$) (Fig. 5). The types of AEs varied depending on the route of

steroid administration. In the PSI group, reported AEs were generally mild and transient, including dizziness and local pain at the injection site. Among the studies evaluating ITSI, Kakehata *et al* (25) reported delayed healing of tympanic membrane perforation (TMP), with an average healing time of 15 weeks. Jiang *et al* (41) reported post-injection pain ($n=13$), itching or burning sensations ($n=4$) and dizziness ($n=7$). In the SST group, AEs were predominantly systemic in nature, including poor glycemic control, gastrointestinal discomfort and insomnia. For example, both Han *et al* (26), Han *et al* (27) and Kakehata *et al* (25) documented failed glycemic control or hyperglycemic events in the systemic therapy group, and Zhao and Jin (35) reported 6 cases each of gastrointestinal discomfort and insomnia. Overall, PSI was associated with a significantly lower incidence of AEs than SST, whereas no significant difference was observed between ITSI and SST. Given the absence of heterogeneity in the PSI subgroup and the consistency of the findings across

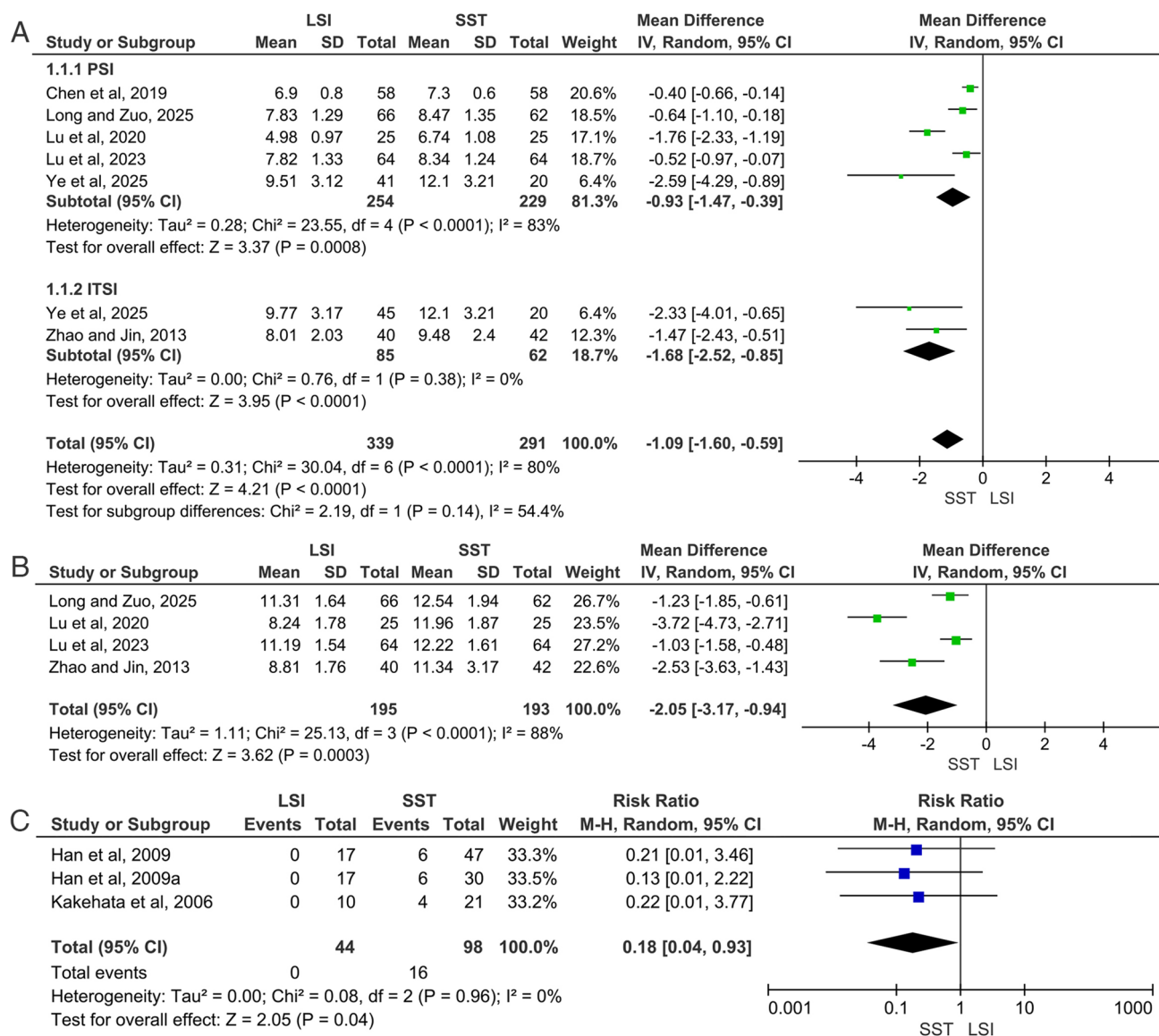


Figure 3. Forest plots for glycemic control outcomes comparing LSI vs. SST. (A) Fasting blood glucose; (B) 2-h postprandial blood glucose; (C) Hyperglycemic events. Subgroup analyses were performed for PSI and ITSI. LSI, local steroid injection; SST, systemic steroid therapy; PSI, postauricular steroid injection; ITSI, intratympanic steroid injection; SD, standard deviation; CI, confidence interval; df, degrees of freedom.

studies, the safety profile of PSI appears favorable. Notably, no severe or life-threatening AEs were reported in either the LSI or SST group.

PSI has a greater impact on FBG than ITSI. The pooled analysis showed that PSI was associated with higher post-treatment FBG levels than ITSI (MD, 0.48 mmol/l; 95% CI, 0.30-0.67; $P < 0.00001$), with no heterogeneity detected across studies ($I^2 = 0\%$), indicating excellent consistency and robustness of the results (Fig. 6). Specifically, Jia *et al* (38) reported significantly higher FBG levels in the PSI group compared with those in the ITSI group (MD, 0.52 mmol/l; 95% CI, 0.32-0.72). Zhu *et al* (39) also observed higher FBG levels in the PSI group; however, the difference was not statistically significant (MD, 0.40 mmol/l; 95% CI, -0.34 to 1.14). Overall, the pooled evidence suggests that PSI is associated with a modest but statistically significant increase in FBG levels compared with ITSI in diabetic patients with SSNHL.

Comparable efficacy of PSI and ITSI. The pooled analysis demonstrated no significant difference in ORR between the PSI and ITSI groups (RR, 1.00; 95% CI, 0.90-1.12; $P = 0.99$), with no heterogeneity across studies ($I^2 = 0\%$), indicating highly consistent findings (Fig. 7A). Meanwhile, PSI demonstrated no significant difference in hearing threshold improvement compared with ITSI (MD, 0.73 dB HL; 95% CI, -0.08 to 1.54; $P = 0.08$), with no heterogeneity detected across studies ($I^2 = 0\%$) (Fig. 7B). Overall, no significant differences were observed between PSI and ITSI in terms of ORR or hearing threshold improvement.

PSI is associated with fewer AEs than ITSI. The PSI group had a significantly lower incidence of AEs than the ITSI group (RR, 0.39; 95% CI, 0.27-0.56; $P < 0.00001$), and the results were consistent across studies ($I^2 = 0\%$) (Fig. 8). Subgroup analyses by AE type further confirmed this pattern, with the reduction in AEs primarily attributable to lower rates of local

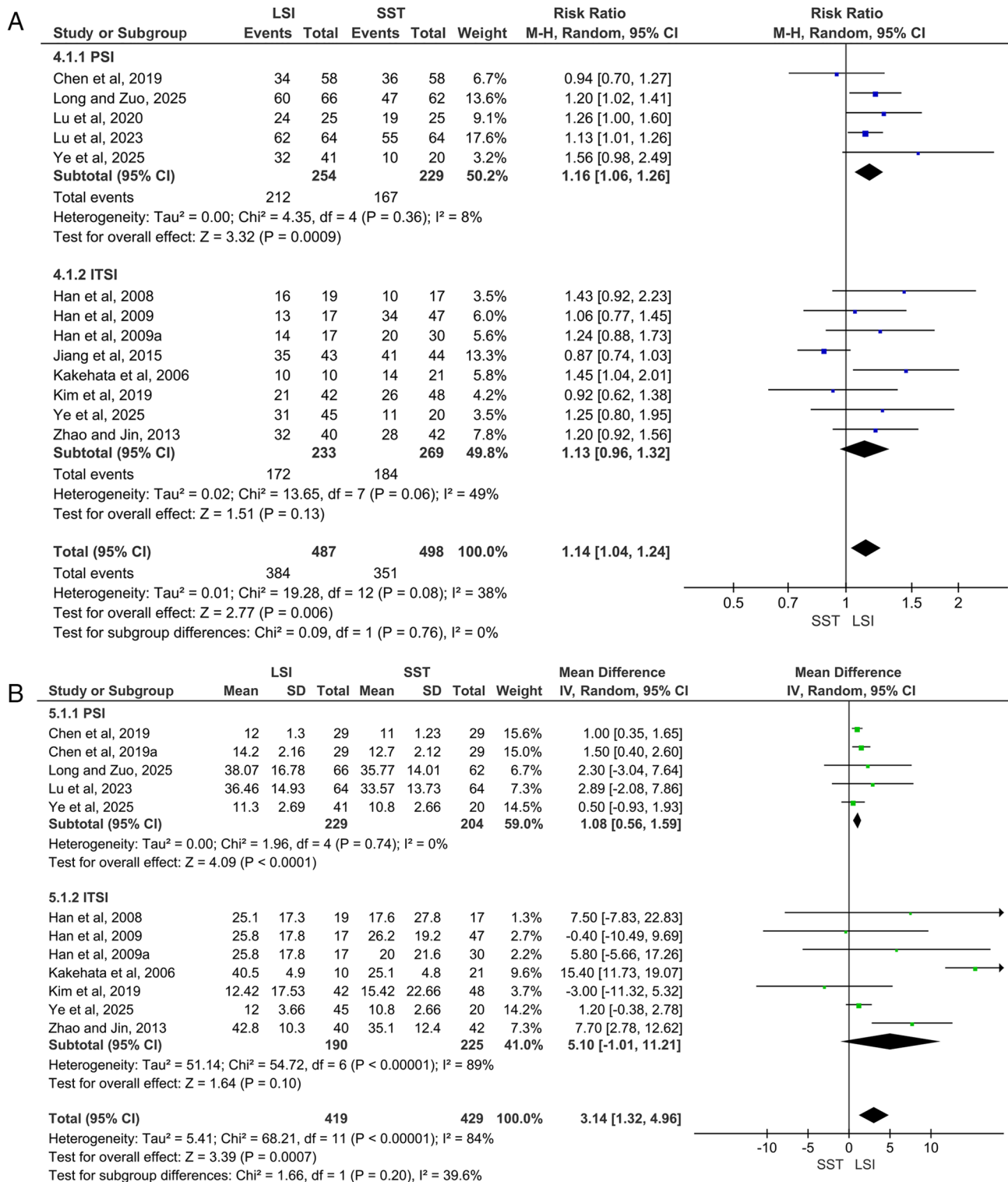


Figure 4. Forest plots for efficacy outcomes comparing LSI vs. SST (A) Overall response rate; (B) Hearing threshold improvement. Subgroup analyses were made for PSI and ITSI. LSI, local steroid injection; SST, systemic steroid therapy; PSI, postauricular steroid injection; ITSI, intratympanic steroid injection; SD, standard deviation; CI, confidence interval; df, degrees of freedom.

pain and vertigo. Specifically, the incidence of local pain was markedly lower in the PSI group (RR, 0.38; 95% CI, 0.24-0.59; $P < 0.0001$), and a similar reduction was observed for vertigo (RR, 0.28; 95% CI, 0.13-0.62; $P = 0.002$), both with no heterogeneity across studies ($I^2 = 0\%$). TMP occurred exclusively in the ITSI group (4 cases across 3 studies), whereas no cases were reported in the PSI group; however,

this difference did not reach statistical significance (RR, 0.30; 95% CI, 0.05-1.79; $P = 0.18$). Local bleeding was uncommon in both groups, with no significant difference observed (RR, 0.85; 95% CI, 0.31-2.33; $P = 0.75$). In addition, middle ear infection was reported only in the ITSI group in the study by Wang and Ma (40) (4 cases), with no cases in the PSI group; as the remaining studies did not report this outcome,

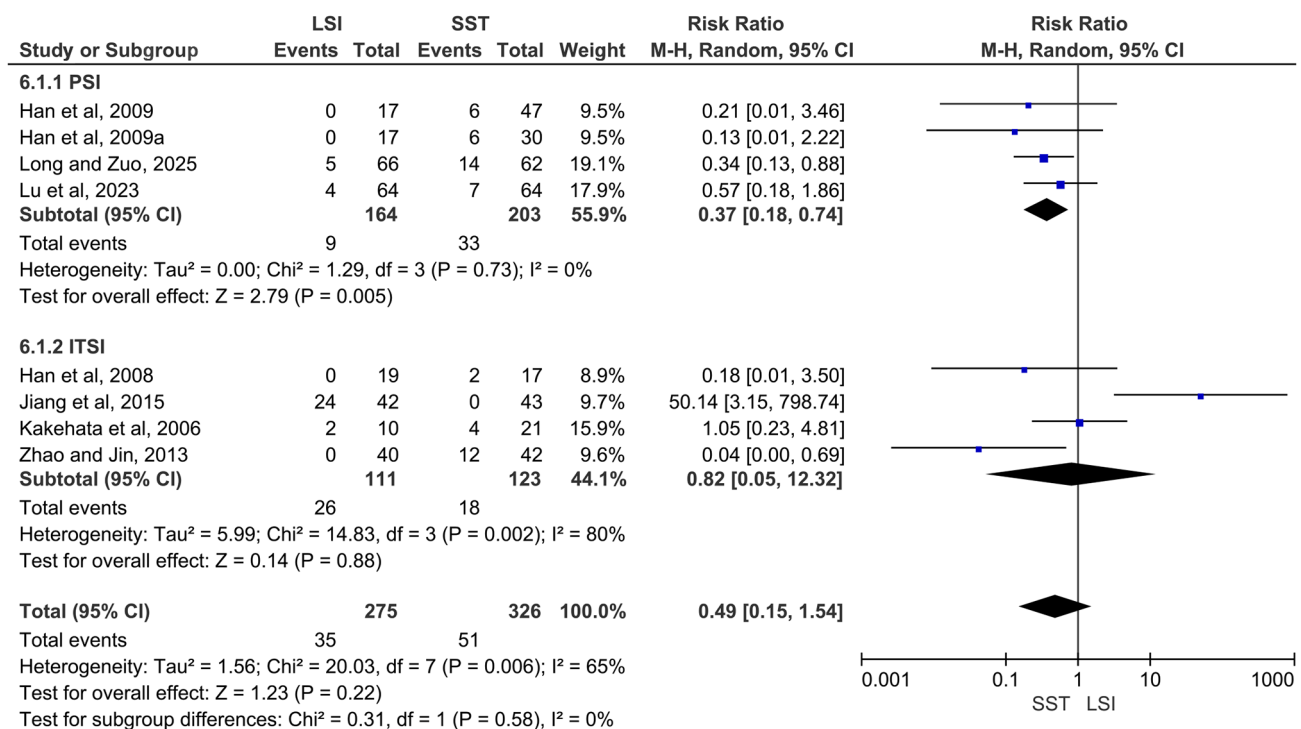


Figure 5. Forest plot for adverse events comparing LSI vs. SST. Subgroup analyses were made for PSI and ITSI. LSI, local steroid injection; SST, systemic steroid therapy; PSI, postauricular steroid injection; ITSI, intratympanic steroid injection; SD, standard deviation; CI, confidence interval; df, degrees of freedom.

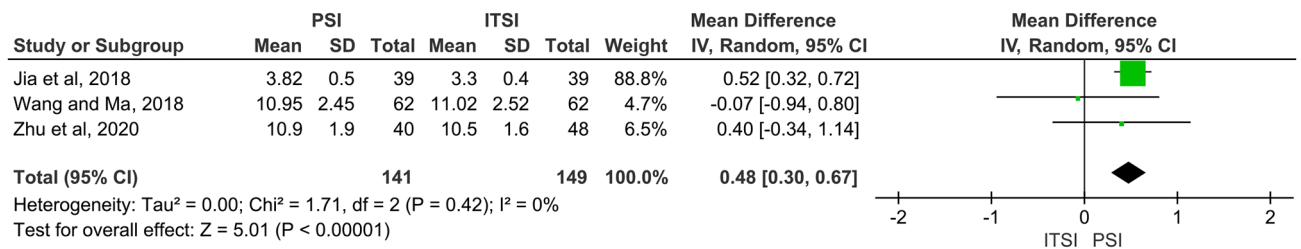


Figure 6. Forest plot for fasting blood glucose comparing PSI vs. ITSI. PSI, postauricular steroid injection; ITSI, intratympanic steroid injection; SD, standard deviation; CI, confidence interval; df, degrees of freedom.

it could not be included in the quantitative meta-analysis. Overall, PSI was associated with a significantly lower risk of AEs than ITSI in diabetic patients with SSNHL, primarily driven by lower rates of local pain and vertigo, while TMP occurred only with ITSI. No severe or life-threatening AEs were reported with either administration route.

Combination PSI and ITSI has a comparable impact on glycemic control to single-route LSI. The pooled analysis demonstrated no significant difference in post-treatment FBG levels between the combination therapy group and the single-route LSI group (MD, -0.75 mmol/l; 95% CI, -2.21 to 0.71; $P=0.31$), although substantial heterogeneity was noted across studies ($I^2=97\%$) (Fig. 9). The individual study results were inconsistent. Li *et al* (29) reported markedly lower post-treatment FBG levels in the combination therapy group than in the ITSI group (MD, -1.50 mmol/l; 95% CI, -1.92 to -1.08), whereas Li and Zhang (30) found no significant difference between combination therapy and PSI

alone (MD, -0.01 mmol/l; 95% CI, -0.33 to 0.31). Given the substantial heterogeneity and the use of different comparators across the 2 studies, these findings should be interpreted with caution. Regarding 2h-PBG, only Li *et al* (29) reported this outcome; therefore, no pooled analysis was performed, and the result is presented descriptively: Markedly lower 2h-PBG levels were observed in the combination therapy group than in the ITSI group (MD, -1.29 mmol/l; $P<0.0001$), suggesting a potential advantage of combination therapy in controlling PBG compared with ITSI alone. Overall, the pooled analysis did not demonstrate a significant difference in FBG levels between combination local therapy and single-route local treatment. Nevertheless, the available evidence suggests that combination PSI and ITSI exerts only a limited impact on glycemic control in diabetic patients with SSNHL. While 1 study indicated superior glycemic control with combination therapy compared with ITSI alone, no advantage was observed when compared with PSI alone.

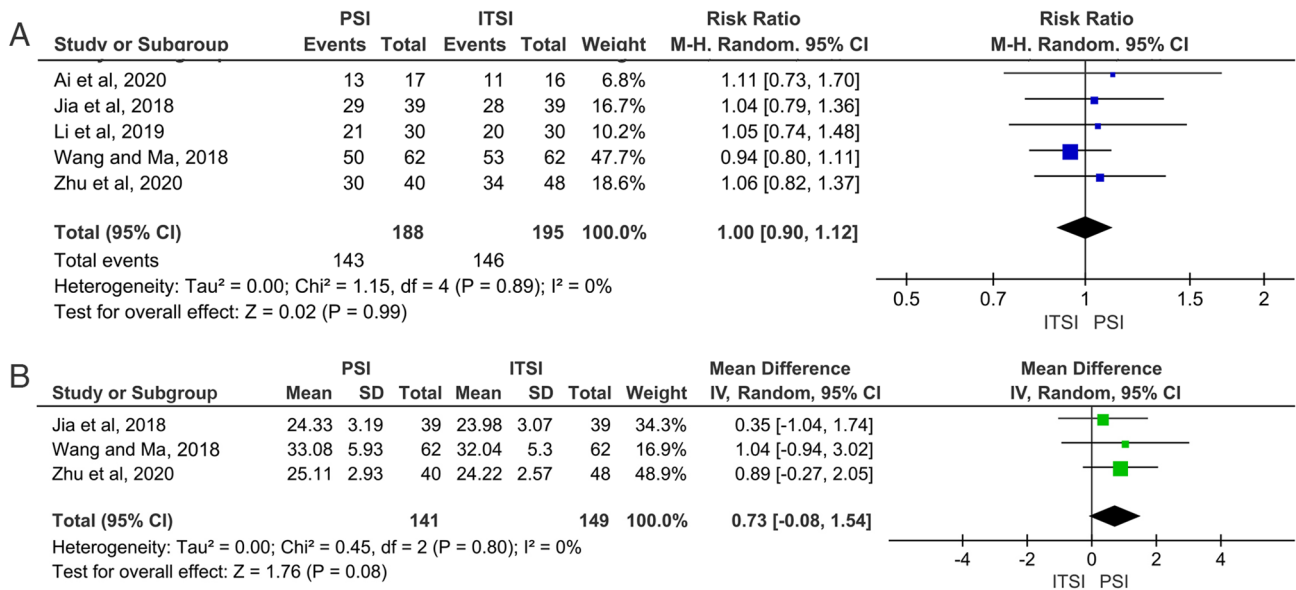


Figure 7. Forest plots for efficacy outcomes comparing PSI vs. ITSI. (A) Overall response rate; (B) Hearing threshold improvement. PSI, postauricular steroid injection; ITSI, intratympanic steroid injection; SD, standard deviation; CI, confidence interval; df, degrees of freedom.

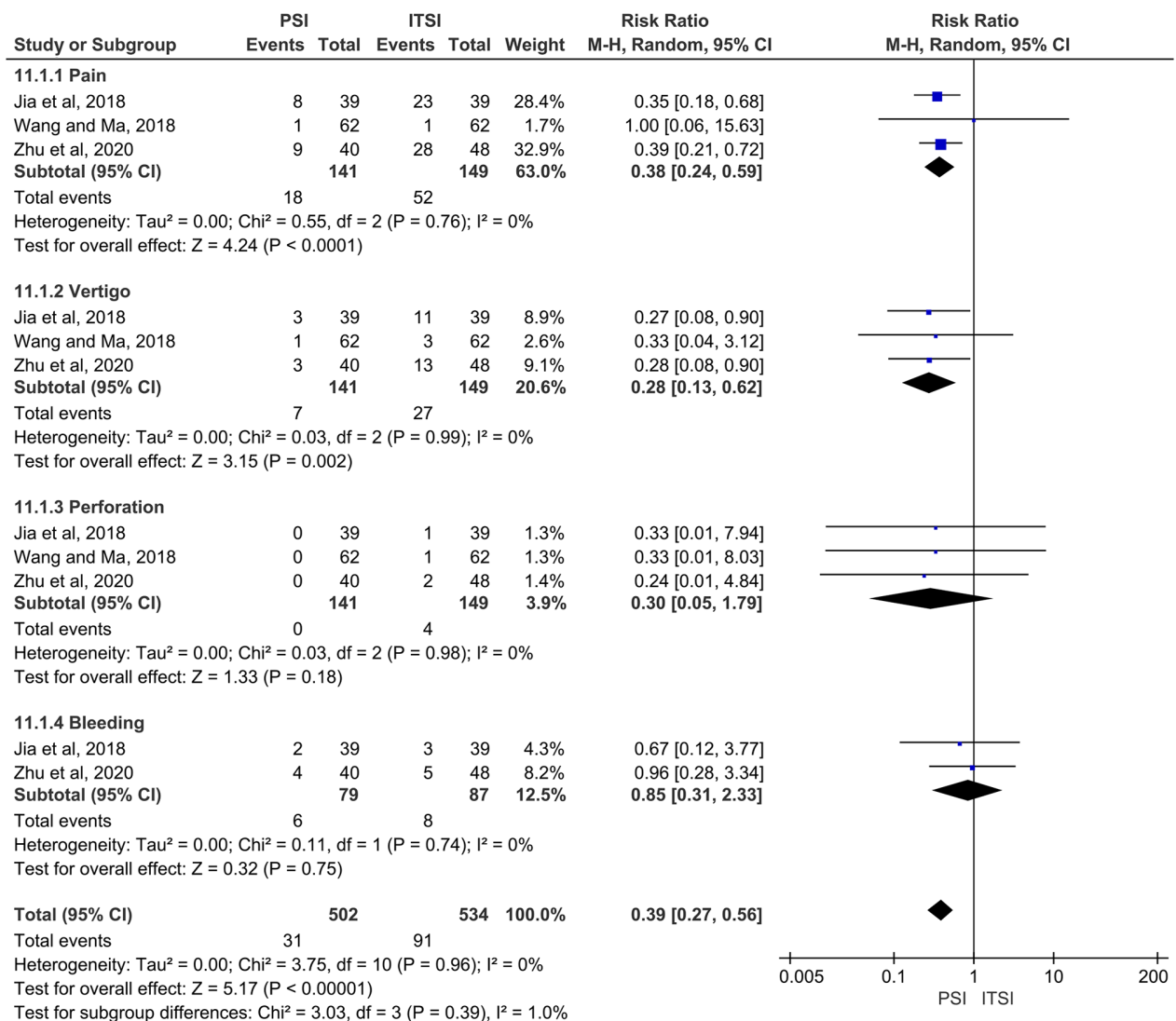


Figure 8. Forest plots for adverse events comparing PSI vs. ITSI. PSI, postauricular steroid injection; ITSI, intratympanic steroid injection; SD, standard deviation; CI, confidence interval; df, degrees of freedom.

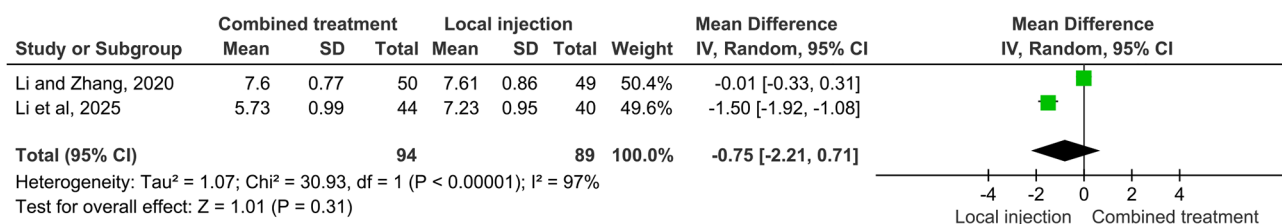


Figure 9. Forest plots for fasting blood glucose comparing combination therapy (PSI + ITSI) vs. single-route LSI. LSI, local steroid injection; PSI, postauricular steroid injection; ITSI, intratympanic steroid injection; SD, standard deviation; CI, confidence interval; df, degrees of freedom.

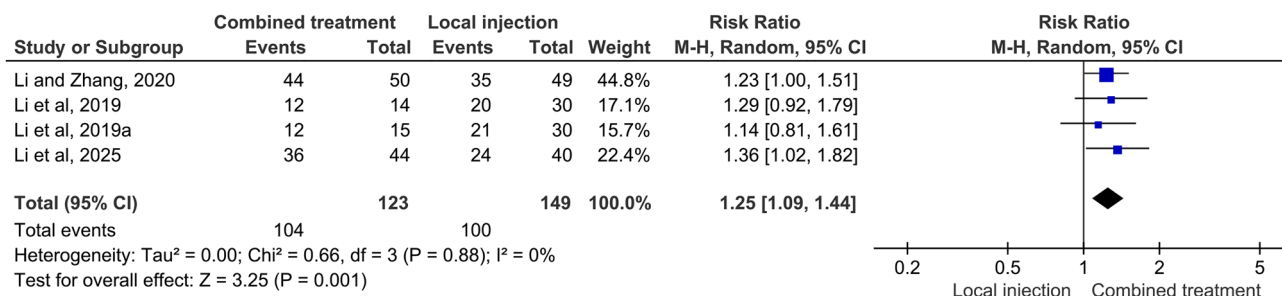


Figure 10. Forest plots for overall response rate comparing combination therapy (PSI + ITSI) vs. single-route LSI. LSI, local steroid injection; PSI, postauricular steroid injection; ITSI, intratympanic steroid injection; SD, standard deviation; CI, confidence interval; df, degrees of freedom.

Combination PSI and ITSI demonstrates superior efficacy compared with single-route LSI. The combination therapy group had a markedly higher ORR than the single-route LSI group (RR, 1.25; 95% CI, 1.09-1.44; P=0.001), with no heterogeneity detected (I²=0%), indicating robust and consistent results (Fig. 10). The study by Li *et al* (29) (2025), which included 84 patients (44 receiving combination therapy and 40 receiving ITSI alone), reported post-treatment hearing thresholds across different frequencies. Combination therapy achieved markedly lower thresholds than ITSI alone at 250 Hz (MD, -7.38 dB HL), 500 Hz (MD, -14.93 dB HL) and 1,000 Hz (MD, -12.06 dB HL) (all P<0.05), indicating better hearing recovery with the combined regimen. Overall, combination therapy was associated with a significantly higher ORR than single-route local treatment. Evidence regarding hearing outcomes was limited to a single study, which reported superior hearing recovery with combination therapy.

Safety outcomes: Combination PSI and ITSI vs. single-route LSI. Among the 3 studies comparing combination local therapy with single-route local therapy, only Li *et al* (29) reported AE data, while the remaining 2 studies [Li and Zhang (30) and Li *et al* (36)] did not, precluding a quantitative meta-analysis. In the study by Li *et al* (29), the overall AE incidence was 9.09% (4/44) in the combination group vs. 15.00% (6/40) in the single-route ITSI group, with no significant difference (P=0.404). The specific AEs in the combination therapy group included burning sensation (1 case), vertigo (2 cases) and tinnitus (1 case), with no cases of TMP or middle ear infection. In the single-route ITSI group, AEs included TMP (1 case), middle ear infection (1 case), burning sensation (2 cases), vertigo (1 case) and tinnitus (1 case). Notably, no severe or life-threatening AEs were reported in either the combination therapy or single-route local therapy group.

Sensitivity analysis. Sensitivity analysis was performed using a leave-one-out approach in RevMan, and the detailed results showed that exclusion of any single study did not materially alter the pooled effect estimates or the statistical significance of the results (data not shown). These findings indicate that the overall conclusions of the meta-analysis were robust. For the meta-analysis of post-treatment FBG comparing LSI with SST, the smallest pooled effect estimate was observed after exclusion of the study by Lu *et al* (32) (MD, -0.85 mmol/l; 95% CI, -1.29 to -0.41), whereas the largest pooled effect estimate was obtained after exclusion of the study by Chen *et al* (31) (MD, -1.30 mmol/l; 95% CI, -1.91 to -0.69). In all analyses, the pooled results consistently favored LSI. For the meta-analysis of ORR, the pooled RR ranged from 1.12 to 1.17 following sequential exclusion of individual studies. The lowest pooled RR was observed after removal of the study by Ye *et al* (34) (RR, 1.12), whereas the highest pooled RR was obtained after exclusion of the study by Jiang *et al* (41) (RR, 1.17). Nevertheless, the conclusion that LSI was associated with superior efficacy compared with SST remained unchanged. Similarly, the meta-analysis of hearing threshold improvement demonstrated good stability. The pooled MD varied between 1.21 and 3.67 dB HL. Exclusion of the study by Kakehata *et al* (25), resulted in the greatest reduction in the pooled effect estimate (MD, 1.21 dB HL), whereas exclusion of the study by Chen *et al* (31) yielded the largest pooled estimate (MD, 3.67 dB HL). In addition, for the comparison between PSI and ITSI, the pooled RR for ORR ranged from 0.99 to 1.06, and the corresponding 95% CIs consistently included unity. For the comparison between combination local therapy and single-route local treatment, the pooled RR for ORR varied from 1.22 to 1.29 following sequential study exclusion. Overall, the sensitivity analysis demonstrated that the pooled effect estimates were stable.

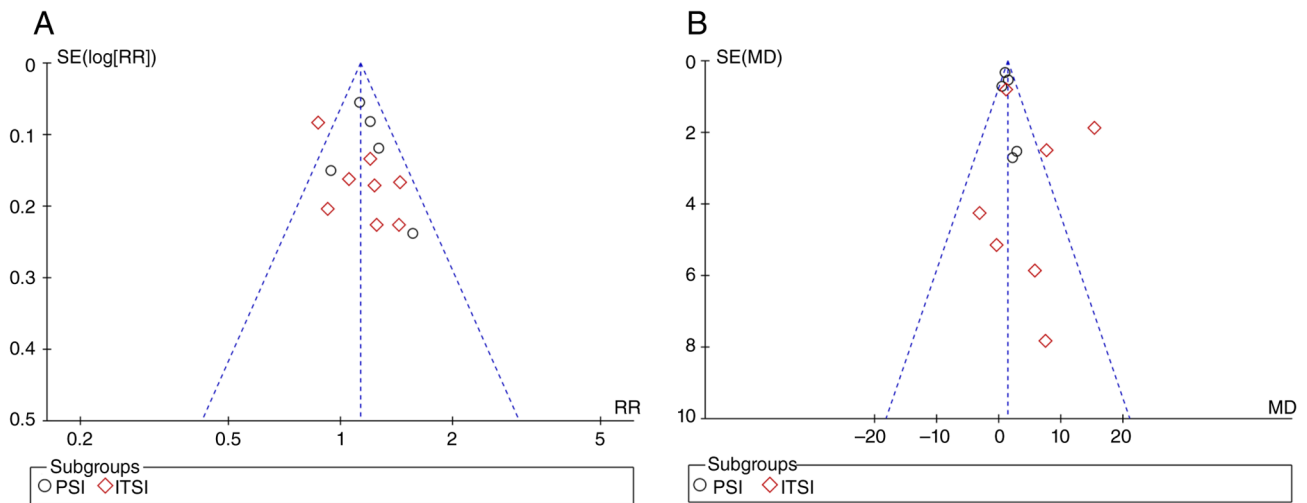


Figure 11. Funnel plots for publication bias assessment. (A) Overall response rate and (B) hearing threshold improvement. PSI, postauricular steroid injection; ITSI, intratympanic steroid injection; SE, standard error; RR, risk ratio; MD, mean difference.

and that no single study exerted a decisive influence on the overall conclusions of the meta-analysis.

Publication bias. Publication bias was assessed using funnel plots for outcomes that included a sufficient number of studies. The evaluated outcomes comprised ORR (11 studies, 13 datasets) and hearing threshold improvement (9 studies, 12 datasets) between LSI and SST groups. For ORR, the funnel plot showed that the included studies were generally symmetrically distributed around the pooled effect estimate (RR, 1.14), with most studies located near the top of the funnel, suggesting a limited influence of small-study effects (Fig. 11A). Egger's regression test did not indicate significant publication bias ($P=0.245$). Regarding hearing threshold improvement, the funnel plot appeared broadly symmetrical, although a relatively wider dispersion of studies was observed (Fig. 11B), which may be attributable to the substantial between-study heterogeneity ($I^2=84\%$). Some small-sample studies, including Kakehata *et al* (25), were located near the margins of the funnel plot; however, no obvious asymmetry was detected. Nevertheless, no apparent asymmetry was observed. Overall, visual inspection of the funnel plots and the results of Egger's regression tests did not reveal substantial evidence of publication bias, suggesting that the likelihood of significant publication bias in the present meta-analysis is low.

Discussion

DM complicated by SSNHL represents a challenging otologic emergency. In addition to the risk of permanent hearing impairment, these patients often face the dilemma of steroid-induced deterioration of glycemic control. Although steroids remain the cornerstone of SSNHL treatment, the optimal route of administration in diabetic patients remains controversial (24,29). To address this issue, a comprehensive meta-analysis evaluating the effects of different steroid administration strategies on glycemic control, therapeutic efficacy and safety in diabetic patients with SSNHL was conducted. The present study demonstrated that LSI was associated with markedly better

glycemic control than SST, as evidenced by lower FBG levels, lower 2h-PBG levels and a markedly reduced incidence of hyperglycemic events. At the same time, LSI achieved superior therapeutic outcomes, including a higher ORR and greater hearing threshold improvement. Regarding safety, although no significant difference was observed in the overall incidence of AEs between LSI and SST, subgroup analysis revealed that PSI was associated with markedly fewer AEs than systemic treatment. These findings suggest that LSI can effectively minimize systemic metabolic disturbances while maintaining or even improving hearing outcomes. Direct comparisons between different LSI routes further demonstrated that PSI and ITSI provided comparable therapeutic efficacy, with no significant differences in ORR or hearing threshold improvement. However, PSI was associated with a markedly lower incidence of AEs, whereas ITSI resulted in slightly lower post-treatment FBG levels. Taken together, these findings suggest that both LSI routes are effective treatment options for diabetic patients with SSNHL, although PSI may offer a more favorable balance between efficacy and safety. In addition, the present analysis showed that combination local therapy consisting of PSI and ITSI achieved a markedly higher ORR than single-route LSI. Limited evidence also suggested potential advantages of combination therapy in hearing recovery and glycemic control when compared with ITSI alone. Nevertheless, these findings were derived from a small number of studies and should therefore be interpreted cautiously. Further well-designed prospective studies are required to confirm the clinical value of combination local therapy in diabetic patients with refractory SSNHL. Compared with a previous meta-analysis (19), the present study provides a more comprehensive evaluation of steroid treatment strategies in diabetic patients with SSNHL. In addition to assessing therapeutic efficacy, glycemic outcomes were systematically examined, PSI and ITSI were directly compared and the potential role of combination local therapy was evaluated. Collectively, these findings provide updated evidence to support individualized treatment decisions in this special patient population. This approach is consistent with the contemporary framework of SSNHL management reviewed by

Lee and Chung (12), which emphasizes tailoring therapeutic strategies to patient comorbidities and prognostic factors.

Glycemic control is a major concern during the treatment of diabetic patients with SSNHL. Although steroids remain the cornerstone of SSNHL management, steroid-induced hyperglycemia may offset part of the therapeutic benefit and, in severe cases, lead to serious metabolic complications. Therefore, identifying an administration route that minimizes the impact on glucose metabolism while maintaining therapeutic efficacy is of considerable clinical importance. In the present meta-analysis, LSI was associated with markedly lower FBG levels, lower 2h-PBG levels and a reduced incidence of hyperglycemic events compared with SST. These findings are biologically plausible and may be explained by the distinct pharmacokinetic characteristics of local vs. systemic administration. During SST, high drug concentrations are required to achieve therapeutic levels within the inner ear since only a limited proportion of the administered drug can penetrate the blood-labyrinth barrier. Consequently, substantial systemic exposure may occur, promoting hepatic gluconeogenesis, glycogenolysis and peripheral insulin resistance, thereby contributing to hyperglycemia (15). Experimental evidence supports this explanation. By contrast, LSI can achieve substantially higher inner-ear drug concentrations while minimizing systemic exposure (17). Following ITSI, steroids diffuse directly across the round window membrane into the perilymph, with only a limited fraction entering the systemic circulation through absorption by the middle-ear mucosa (18). Miwa *et al* (42) demonstrated that intratympanic injection of high-concentration dexamethasone (50 mg/ml) achieved long-term drug retention in the inner ear for >2 months without damaging auditory or vestibular function, with drug levels maintained at therapeutic concentrations markedly longer than conventional concentrations. Furthermore, a randomized clinical trial by Dahm *et al* (43) involving 40 cochlear implant recipients reported median perilymph triamcinolone acetate concentrations of 796.0 ng/ml following intratympanic injection, while the drug was undetectable in plasma in 78% of patients, confirming that intratympanic administration achieves exceptionally high perilymph drug levels with minimal systemic absorption. PSI appears to share similar advantages. Pharmacokinetic studies have suggested that drugs administered via the postauricular route may preferentially distribute to structures surrounding the inner ear while producing relatively low systemic exposure. Chen *et al* (44) used an *in vivo* optical imaging system to compare the distribution of dexamethasone between postauricular and intramuscular injection in guinea pigs, demonstrating that postauricular injection achieved significantly higher inner-ear drug concentrations with sustained release and lower systemic exposure. Furthermore, Jin *et al* (45) compared the uptake of dexamethasone in the rat inner ear following different administration routes and found that the fluorescence intensity of dexamethasone in the cochlea after postauricular injection was significantly higher and more prolonged than after intravenous injection. These findings may explain why LSI exerts a smaller effect on glycemic control than SST. Notably, direct comparison of LSI routes in the present study revealed that post-treatment FBG levels were significantly higher in the PSI group than in the ITSI group. A possible explanation is that

the postauricular region is characterized by a richer vascular supply and a larger absorptive surface area than the tympanic cavity, allowing a greater proportion of the administered drug to enter the systemic circulation. Nevertheless, the absolute difference between the two approaches was modest (MD, 0.48 mmol/l), suggesting that both LSI routes exert only limited effects on glucose metabolism compared with SST. Taken together, these findings indicate that LSI can achieve effective inner-ear drug delivery while minimizing systemic metabolic disturbances. Among the available LSI strategies, ITSI may exert the smallest impact on glycemic control, although the clinical significance of the observed difference compared with PSI remains uncertain.

ORR and hearing threshold improvement are two key indicators of treatment efficacy, reflecting the proportion of patients achieving clinical improvement and the magnitude of hearing recovery, respectively. In the present meta-analysis, LSI was associated with a markedly higher ORR and greater hearing threshold improvement than SST. Several mechanisms may explain the observed advantages of LSI. First, systemic steroids must cross the blood-labyrinth barrier to reach the inner ear. As this barrier restricts the entry of numerous circulating substances, therapeutic concentrations within the cochlea often require high systemic doses, which may still result in relatively limited drug exposure at the target site. By contrast, local administration bypasses the blood-labyrinth barrier and delivers steroids directly to the vicinity of the inner ear, thereby achieving substantially higher local drug concentrations (17). Previous studies have demonstrated that intratympanic administration is an effective strategy for enhancing inner-ear drug delivery and maintaining therapeutic drug levels within the cochlea (42,46). Second, the therapeutic advantages of LSI may be particularly relevant in diabetic patients. Chronic hyperglycemia is associated with microvascular dysfunction, thickening of capillary basement membranes, endothelial injury and impaired cochlear blood flow (47,48). These pathological alterations not only contribute to hearing impairment but may also reduce the efficiency of drug transport from the systemic circulation into the inner ear. Consequently, the efficacy of SST may be diminished in diabetic individuals. By bypassing the compromised cochlear microcirculation and delivering drugs directly to the target tissues, LSI may overcome these limitations and provide more effective treatment. In addition, steroid receptors are widely distributed throughout the inner ear, including the stria vascularis, spiral ligament, organ of Corti and spiral ganglion neurons. Higher local drug concentrations achieved through LSI may promote more effective receptor activation and enhance downstream anti-inflammatory, anti-apoptotic and neuroprotective signaling pathways (49,50). Experimental studies have suggested that steroids may protect cochlear hair cells and auditory neurons through modulation of multiple intracellular signaling cascades, thereby facilitating hearing recovery (51-53). It should be noted that, in the present study, the between-group difference in hearing threshold improvement was modest (MD, 3.14 dB HL), which may be of limited clinical significance when considered in isolation. However, this represents the additional hearing gain achieved by LSI over SST rather than the absolute within-group improvement, which was substantially larger [for example, 42.8 dB HL in

the ITSI group and 35.1 dB HL in the SST group in the study by Zhao and Jin (35)]. Moreover, the clinical relevance of a given dB HL difference depends on the baseline hearing level and the specific frequencies affected; even a small additional gain may be meaningful for patients with severe-to-profound hearing loss, particularly in the mid-to-low frequency range critical for speech perception. Finally, the pooled estimate represents an average across heterogeneous studies, and the true effect may be larger in specific subgroups (for example, an MD of 5.10 dB HL in the ITSI subgroup). Notably, direct comparison between PSI and ITSI revealed no significant differences in either ORR or hearing threshold improvement. Although the two approaches utilize different delivery pathways, both are capable of achieving therapeutically effective steroid concentrations within the inner ear. ITSI provides rapid drug access through diffusion across the round window membrane, whereas PSI may allow sustained drug distribution to periauricular and inner-ear structures through local vascular and tissue pathways. Despite these pharmacokinetic differences, the clinical outcomes observed in the present study suggest that both techniques provide comparable therapeutic efficacy. Taken together, the present findings indicate that LSI is more effective than SST for diabetic patients with SSNHL. Furthermore, PSI and ITSI appear to provide similar hearing outcomes, suggesting that both LSI routes are clinically effective treatment options.

Safety is another critical consideration when selecting steroid treatment strategies for diabetic patients with SSNHL. In addition to well-recognized systemic AEs, local administration may also be associated with route-specific complications. Therefore, an optimal treatment approach should balance therapeutic efficacy with both systemic and local safety. In the present meta-analysis, no significant difference was observed in the overall incidence of AEs between LSI and SST. However, subgroup analysis revealed important differences among administration routes. PSI was associated with a markedly lower incidence of AEs than SST, whereas no significant difference was observed between ITSI and SST. The AEs associated with SST are well documented and are particularly relevant in diabetic patients. Systemic steroids may exacerbate hyperglycemia through increased gluconeogenesis and insulin resistance, while also contributing to gastrointestinal discomfort, sleep disturbances and other systemic complications (54). Several studies included in the present analysis reported treatment-related hyperglycemic events, poor glycemic control (25-27), gastrointestinal symptoms and insomnia (35) in patients receiving SST. These findings highlight the challenges associated with systemic steroid exposure in this vulnerable patient population. By contrast, LSI substantially reduces systemic drug exposure by delivering medication directly to the inner ear, thereby minimizing the risk of systemic AEs. Nevertheless, LSI is not entirely free of complications. Most AEs associated with LSI are procedure-related and vary according to the administration route. Notably, direct comparison between PSI and ITSI demonstrated a markedly lower incidence of AEs in the PSI group. The majority of complications reported following ITSI included transient pain (41), dizziness, TMP and delayed perforation healing (25,38,39). These AEs are largely attributable to the trans-tympanic nature of the procedure. Needle

penetration of the tympanic membrane may directly stimulate sensory nerve endings, resulting in pain, while middle-ear drug administration may provoke vestibular symptoms such as transient vertigo. In addition, TMP, although generally self-limiting, remains a recognized complication and may occasionally persist for prolonged periods. Kim *et al* (55) reported that intratympanic injection is associated with TMP in 2.5-11.5% of cases and vertigo in 10-30%, which broadly overlap with the ranges observed in the studies included in the present meta-analysis (TMP, 1.6-4.2%; vertigo, 4.8-28.2%). By contrast, PSI is performed within the soft tissues posterior to the auricle and does not require entry into the middle-ear cavity. Consequently, complications such as TMP and middle-ear infection are largely avoided. Furthermore, as the procedure does not directly stimulate vestibular structures, dizziness appears to occur less frequently. In the studies included in the present analysis, AEs associated with PSI were generally mild and transient, consisting primarily of local discomfort and occasional dizziness, with no reported cases of TMP or treatment-related glycemic deterioration. Importantly, no severe or life-threatening AEs were reported in any of the included studies, regardless of the steroid administration route. Taken together, these findings suggest that PSI may offer the most favorable safety profile among currently available steroid administration routes for diabetic patients with SSNHL. Given that PSI and ITSI demonstrated comparable efficacy in the analysis, the lower incidence of AEs associated with PSI may represent a clinically meaningful advantage when selecting an individualized treatment strategy.

Optimizing treatment strategies for diabetic patients with refractory SSNHL or those who respond inadequately to initial LSI remains a major clinical challenge. Combination local therapy, consisting of PSI and ITSI, has recently emerged as a potential therapeutic option. Theoretically, simultaneous utilization of two local delivery routes may enhance inner-ear drug exposure through complementary pharmacokinetic mechanisms. However, its clinical value has not been comprehensively evaluated. In the present meta-analysis, combination local therapy was associated with a markedly higher ORR than single-route LSI. In addition, limited evidence suggested potential benefits of combination therapy with respect to hearing recovery. These findings indicate that dual-route LSI may provide additional therapeutic advantages in selected patients. Several mechanisms may explain the observed benefits. Although both PSI and ITSI are classified as local steroid delivery methods, their drug transport pathways and pharmacokinetic characteristics differ substantially. ITSI delivers steroids directly into the middle-ear cavity, allowing rapid diffusion across the round window membrane into the perilymph and producing high local drug concentrations shortly after administration. However, this route is subject to several limitations, including drug loss through the Eustachian tube and substantial interindividual variability in round window membrane permeability (43,56,57). Previous studies have reported considerable variation in membrane permeability among individuals, potentially resulting in inconsistent inner-ear drug exposure (17,18). By contrast, PSI appears to provide a more sustained pattern of drug delivery and may be less dependent on round window membrane permeability. Although the onset of action may be slower, prolonged

drug retention around the inner ear may facilitate sustained therapeutic effects. Therefore, combining the two approaches may offer complementary advantages, with ITSI providing rapid initial drug delivery and PSI contributing to prolonged maintenance of therapeutic drug concentrations. The potential superiority of combination local therapy may be particularly relevant in diabetic patients, in whom chronic hyperglycemia contributes to microvascular dysfunction, oxidative stress and persistent inflammatory activation within the cochlea. Experimental and clinical studies have demonstrated that steroids suppress inflammatory signaling pathways and improve inner-ear microcirculation. Supporting this concept, Li *et al* (29) reported markedly lower levels of inflammatory markers (interleukin-6, C-reactive protein and procalcitonin) and improved hemorheological parameters following combination therapy compared with ITSI alone. These findings suggest that sustained and enhanced local steroid exposure may contribute to more effective suppression of inflammation and restoration of cochlear microcirculation. Importantly, combination local therapy did not appear to increase the risk of glycemic deterioration compared with single-route LSI. Although the available evidence remains limited, the current findings suggest that the addition of a second local delivery route does not substantially increase systemic steroid exposure. This observation is consistent with the pharmacokinetic characteristics of local administration, in which the majority of the drug remains concentrated within the middle ear, inner ear and adjacent tissues, with only limited absorption into the systemic circulation. Regarding safety, combination local therapy did not increase the overall incidence of AEs compared with single-route LSI in the only study reporting this outcome (9.09 vs. 15.00%), with no cases of TMP or middle ear infection (29). This finding is clinically plausible, as the addition of PSI does not involve a second puncture of the tympanic membrane or direct manipulation of the middle ear, and thus would not be expected to introduce additional otologic complications beyond those already associated with ITSI. Nevertheless, this evidence was derived from a single study, and the safety profile of combination local therapy remains inadequately characterized. Collectively, these findings should be interpreted cautiously. The evidence regarding combination local therapy was derived from a small number of studies, and hearing-related outcomes were reported by only a single study. Therefore, additional large-scale RCTs are required to confirm whether combination local therapy should be routinely recommended for diabetic patients with refractory SSNHL.

Moderate to substantial heterogeneity was observed in several pooled outcomes, including FBG ($I^2=80\%$), ORR ($I^2=58\%$), hearing threshold improvement ($I^2=84\%$) and AEs ($I^2=65\%$). Several clinical and methodological factors may have contributed to these findings. For FBG, heterogeneity was likely attributable to differences in baseline glycemic status among study populations. The included studies enrolled patients with varying degrees of diabetes control, with pretreatment FBG levels ranging from ~ 8.8 to >12 mmol/l (32,34). In addition, the duration of diabetes varied considerably across studies, and longer disease duration may be associated with greater susceptibility to steroid-induced hyperglycemia. Variations in steroid regimens may have further contributed to heterogeneity.

Although most PSI studies adopted a similar local methylprednisolone protocol (24,32-34), systemic control groups differed substantially in steroid type, dosage and tapering schedules. For example, some studies used methylprednisolone (32-34), whereas others used dexamethasone (31), which possesses a longer biological half-life and potentially more prolonged hyperglycemic effects. Differences in glycemic management strategies during treatment may also have influenced outcomes. While some studies explicitly reported maintaining preexisting antidiabetic regimens (32,33), others did not specify their glucose-control protocols. Furthermore, variations in postauricular injection techniques may have affected the extent of systemic drug absorption. Notably, subgroup analysis demonstrated minimal heterogeneity in the ITSI subgroup ($I^2=0\%$) but substantial heterogeneity in the PSI subgroup ($I^2=83\%$), suggesting that administration route may represent an important source of variability. The heterogeneity observed for clinical efficacy outcomes was likely related to differences in response criteria, baseline hearing severity, steroid administration protocols and follow-up duration. Definitions of treatment success varied across studies, with hearing gain thresholds ranging from 10 dB HL (26) to 30 dB HL (25). Baseline hearing levels also differed considerably. Studies enrolling predominantly severe-to-profound hearing loss cases (25) generally reported larger hearing improvements than those including milder cases (28). In addition, ITSI frequency varied substantially, ranging from daily administration to injections every other day. More intensive treatment schedules may have resulted in greater inner-ear drug accumulation and enhanced hearing recovery, which may directly explain why the hearing threshold improvements reported by Kakehata *et al* (25) (40.5 dB HL) and Zhao and Jin (35) (42.8 dB HL) were substantially higher than those in other studies (12-26 dB HL) (24,26-28,31,34). Follow-up duration also differed across studies, varying from 10 days (33) to 1 month after treatment (25-27,35), which may have influenced the degree of observed hearing recovery. Variations in steroid type may have further contributed to heterogeneity, as dexamethasone (25-27) and methylprednisolone (34,35) differ in terms of pharmacokinetic properties, tissue penetration and receptor-binding characteristics. Importantly, subgroup analysis demonstrated no heterogeneity in the PSI subgroup ($I^2=0\%$) but substantial heterogeneity in the ITSI subgroup ($I^2=89\%$), indicating that treatment outcomes following ITSI may be more sensitive to protocol-related differences. For AEs, heterogeneity was primarily attributable to differences in the types and definitions of reported complications. SST was mainly associated with systemic AEs, including gastrointestinal discomfort, insomnia and hyperglycemia (25,26,35), whereas ITSI predominantly resulted in local complications such as otalgia, vertigo and TMP (25,38,39,41). PSI was generally associated with mild injection-site reactions. Combining these clinically distinct AEs into a single pooled outcome inevitably introduced clinical heterogeneity. Furthermore, differences in injection techniques, complication reporting standards and sample sizes may have contributed to the variability observed among studies. Despite the presence of moderate-to-high heterogeneity in several outcomes, sensitivity analysis demonstrated that the pooled effect estimates remained stable after sequential exclusion of individual

studies. Therefore, although residual heterogeneity cannot be completely eliminated, the overall conclusions of the present meta-analysis appear robust and reliable.

Several limitations of the present study should be acknowledged. First, although RCTs were included, a considerable proportion of the available evidence was derived from prospective and retrospective cohort studies with relatively small sample sizes, which may have introduced selection bias and reduced the overall certainty of evidence. Second, substantial heterogeneity was observed in several outcomes, particularly FBG ($I^2=80\%$) and hearing threshold improvement ($I^2=84\%$). This heterogeneity likely resulted from variations in steroid type, administration frequency, treatment duration, outcome definitions, baseline hearing severity and follow-up periods across studies. Third, the timing of blood glucose assessment varied across studies, and none specified the exact day or cumulative steroid doses before post-treatment FBG and 2h-PBG measurement, potentially introducing heterogeneity. Moreover, hyperglycemic events lacked a standardized quantitative definition; the 2 reporting studies relied on clinical judgment rather than a specific glucose threshold, limiting comparability. Furthermore, no study provided glycemic follow-up beyond the acute treatment phase, precluding assessment of sustained metabolic effects. Fourth, the reporting criteria for AEs were not standardized, and minor complications may have been under-reported in some studies, potentially affecting the accuracy of safety assessments. Furthermore, the safety profile of combination local therapy remains inadequately characterized, as only 1 of the 3 studies evaluating combination LSI vs. single-route LSI reported AE data, precluding a quantitative meta-analysis. Fifth, most studies evaluating PSI were conducted exclusively in Chinese populations, which may limit the generalizability of the findings to other ethnic and geographic populations. Sixth, the majority of included studies had relatively short follow-up periods ranging from 10 days to 1 month, preventing comprehensive evaluation of long-term hearing outcomes, recurrence rates and delayed AEs. Finally, evidence regarding combination local therapy was derived from only a limited number of studies, and therefore its potential advantages should be interpreted cautiously. Future well-designed multicenter RCTs with larger sample sizes are needed to validate the present findings. Standardized protocols regarding steroid type, dosage, administration frequency, treatment duration, efficacy assessment criteria and AE reporting should be established to improve comparability among studies. In addition, longer follow-up periods of at least 6 months are warranted to comprehensively assess long-term efficacy, hearing recovery, recurrence, and safety outcomes.

In conclusion, this meta-analysis systematically compared the effects of LSI and SST in diabetic patients with SSNHL, with particular emphasis on glycemic control, clinical efficacy and safety. Based on the 18 included studies, LSI was associated with markedly lower FBG levels (MD, -1.09 mmol/l), 2h-PBG levels (MD, -2.05 mmol/l) and incidence of hyperglycemic events (RR, 0.18), while achieving superior ORRs (RR, 1.14) and greater hearing threshold improvement (MD, 3.14 dB HL) compared with SST. Direct comparison of local administration routes demonstrated comparable efficacy between PSI and ITSI in terms of ORR (RR, 1.00) and hearing

improvement (MD, 0.73 dB HL). However, PSI was associated with markedly fewer AEs (RR, 0.39), despite a slightly higher FBG level than ITSI (MD, 0.48 mmol/l). In addition, combination local therapy (PSI plus ITSI) showed a higher ORR than single-route local treatment (RR, 1.25) without a substantial increase in glycemic burden. Overall, the current evidence suggests that LSI offers important advantages over SST in diabetic patients with SSNHL by improving glycemic safety while maintaining or enhancing therapeutic efficacy. Among local treatment options, PSI appears to provide a favorable balance between efficacy and safety and may therefore be considered an attractive treatment strategy. Combination local therapy may represent a promising option for selected patients with refractory disease, although further high-quality studies are required to confirm its long-term benefits and safety.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

SP and XM contributed to the conception and design of the study. CW and SC performed the literature search and data analysis. SP and YL drafted the initial version of the manuscript. YL and CL contributed to data interpretation and critically revised the manuscript for important intellectual content. YL and CL confirm the authenticity of all the raw data. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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