# Adverse Effects of Steroid Therapy in Sudden Sensorineural Hearing Loss: A Scoping Review

# Abstract

Objective  
Sudden sensorineural hearing loss (SSNHL) is an otologic emergency and treated with steroid therapy. Despite adverse events (AEs) associated with long term steroid use being well evidenced, there is sparsity of literature regarding the AEs of short-course prescriptions in the SSNHL cohort, which limits the quality of patient counselling and informed consent.

Method  
A literature search was performed on the Medline and Embase databases for studies assessing AEs in adults with SSNHL managed with oral (OST), intratympanic (ITS) and intravenous steroid therapy (IVS). Two authors screened titles, abstracts, and full-text articles, with conflicts resolved by a third reviewer. Forty-three papers were included.

Results  
In systemic steroid therapies, hyperglycaemia and hypertension are reported in up to 29.8% and 37.9% of patients respectively. Patients with medication-dependent diabetes and hypertension are at higher risk. Gastric and mood disturbances affected up to 27.9% and 44.6% of patients respectively. ITS carried risks of otalgia (up to 54.3%), dizziness (up to 27.1%), perforations (up to 11.5%), and otitis media (up to 4.7%).

Conclusion  
Comprehensive counselling is key in obtaining informed consent, especially in cohorts with diabetes mellitus (DM) and hypertension where monitoring of glucose and blood pressure is recommended. Gastroprotection should be considered. Future focus is required to study short-term steroid AEs and raise awareness amongst prescribing clinicians and patients.

*Keywords: Sensorineural Hearing Loss, Pharmacology, Communication, Informed Consent, Medico-legal*

Key Points:

1. Medication-dependent diabetic and hypertensive patients are at increased risk of hyperglycaemia and hypertension with systemic steroids.
2. Diabetic and hypertensive patients should be monitored whilst taking systemic steroids. GPs and community diabetic teams should be involved in titrating medications accordingly.
3. ITS as first-line SSNHL management in diabetic and hypertensive cohorts requires further investigation.
4. PPI should be considered in patients at risk of gastrointestinal bleeding or dyspepsia.
5. Information leaflets should be developed to and supplied alongside urgent prescriptions.

# Introduction

SSNHL is an otologic emergency typically characterised by sensorineural hearing loss over three consecutive audiometric frequencies developing over a period of up to 72 hours. (1) Most cases (estimated to be 90%) do not have a known causal event, and given the broad demographic affected, are likely to be the manifestation of multiple aetiologies with similar clinical presentations. Theories include viral inflammation or ischaemic insult to the cochlea. The intention is to improve function through anti-inflammatory and immune-modulatory effects, thus reducing inflammation in the vestibulocochlear nerve and cochlea. (2,3) SSNHL affects 5 to 20 people per 100,000, though under-reporting, under-investigation and delayed presentation mean that its epidemiology is difficult to ascertain. (4)

Patients usually present to primary care or to the emergency department. As per ENT UK, first-line treatment is OST of 1mg/kg up to 60mg for 7 days. This may then be tapered by 10mg daily. (1) ITS is an alternative route of steroid administration, and several papers demonstrate equivocal benefit when compared to OST. (5,6) The SeaSHeL national prospective cohort study recently examined SSNHL patients’ demographics, management regimes and clinical pathways, and revealed more understanding on risk factors such as cardiovascular disease and concurrent vertigo. (7) The STARFISH Trial, which started patient recruitment in January 2023, aims to compare hearing outcomes in SSNHL patients managed with OST versus ITS. (8)

The side-effect profile of long-course steroids is well understood with reports of hyperglycaemia, hypertension, mood and sleep disturbance, thinning of skin, and easy bruising. (9) However, the risks of shorter courses are poorly captured by clinicians and perhaps under-reported by patients. Studies are often too heterogenous to the SSNHL patient base, both with respect to duration and intensity of steroids and their co-morbidities, to draw valid comparisons. Xie *et al* (2003) found an increased incidence of hypertension, diabetes and hyperlipidaemia in SSNHL patients. The incidence of hypertension ranged from 21.1-39.2% of SSNHL patients, and that the prevalence of SSNHL in diabetic patients is 1.54 times that of their non-diabetic counterparts. (10)

With steroid usage being commonplace in ENT, a thorough understanding of their AEs is also necessary for general practitioners and emergency medicine clinicians. By synthesising the available data, we hope to provide clinicians with a better understanding of the associated risks, enabling them to make informed decisions and conduct more robust counselling when managing SSNHL. Our recommendations have been formed in collaboration with pharmacist colleagues.

## Objectives of this scoping review

In performing this scoping review, we aim to establish the documented adverse effects of systemic and intra-tympanic steroid therapy in the management of SSNHL.

Objectives:

1. Detail the AEs of steroid therapy in SSNHL management.
2. Compare the AEs of systemic and ITS for SSNHL.
3. Provide recommendations for clinicians prescribing steroids for SSNHL.

# Methods

## Search strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidance was followed. A literature search of the MedLine and Embase databases was performed in July 2024 to include articles up to July 2024. Subject headings were utilised to explore synonyms.

## Inclusion criteria:

1. Papers exploring management of SSNHL with OST, IVST or ITS, and reported AE rates.
2. Adult patients (≥18 years)
3. Human studies.
4. English language.

## Exclusion criteria:

1. Papers where AEs were not attributed to steroid therapy (i.e. AEs grouped with non-steroid comparison arms).
2. Case reports.
3. Alternative middle-ear steroid delivery (e.g. eustachian tube catheterisation).
4. Refractory SSNHL.
5. SSNHL management of patients with renal or hepatic impairment.

## Selection of sources of evidence

Reports were exported to Covidence (Veritas Health Innovation Ltd.), a systematic review management software. Duplicate studies were manually and automatically identified and removed. Titles and abstracts were screened by two authors (M.A. and P.K.) and conflicts were resolved by a third author (T.R.).

Data relating to study design, steroid administration and AEs were extracted according to a template. Studies were grouped according to route of steroid administration. Steroids were converted using an online medical calculator (MDCalc Ltd.) to prednisolone. (Table 1) Where doses were given per-kilogram and tapers were left undefined, the average weight was estimated to be 70kg and tapers were estimated to allow for analysis. A formal meta-analysis on the data was not possible due to heterogeneity.

# Results

*Figure 1* illustrates the PRISMA flowchart. 853 studies were identified, and 203 were duplicates. 650 studies were screened, and 155 full texts were evaluated. 43 studies were included.

The most common design was randomised-controlled trials (n = 17), followed by non- or quasi-randomised trials (n = 10). 32 papers collected prospective data. The median number of study participants was 68 (range: 6-908), and mean age was 50.6 ± 8.7. AE monitoring methodology was specified in 18 papers. 16 papers reported participants’ co-morbidities.

We identified 22 ITS, 19 OST, 13 IVST, 7 combined OST and ITS, and 7 combined IVST and ITS study arms. (Table 2)

## Oral steroid therapy

18 OST reports were identified. (Table 3) 20 study arms are included, as one report compares high- and regular-dose OST (11) and another compares steroid types. (12)

Most studies (n = 11) used prednisolone. One paper did not report the steroid nor regime. (2) The average daily dose of prednisolone was 63.0mg (range 22.5-400.0mg) and the average duration of therapy is 11.6 days (range 5-19 days). Seven papers specified dosages per weight, and three did not specify tapers.

Hyperglycaemia and hypertension are the most reported AEs with a range of 2.1-29.8% and 4.2-37.9% respectively. Severe hyperglycaemia occurred in one participant, who was removed from analysis. (13) Gastric disturbance and psychological disturbances including altered mood and sleep range from 4.2-27.9% and 8.4-44.6% respectively. (Table 4)

Halevy (2022) found there was a relative risk of 0.59 vs 0.13 (P <0.001) of hyperglycaemia in DM versus non-DM patients. This applied to patients who used insulin or oral anti-hyperglycaemic agents, and not to diet-controlled DM patients. The same applied to hypertensive patients, who were at a higher risk of hypertension (0.54 vs 0.29, P = 0.004). Dosing regimens are not detailed, but there is a reference to a guideline to manage SSNHL patients with 1 mg/kg daily of OST for 7-10 days. (2)

10 papers reported no AEs. (10,14–22) These are italicised in *Table 3*. In these papers, the average daily dose of prednisolone is 42.5mg, compared to 82.9mg in papers reporting AEs (p = 0.33). Four papers reporting no AEs excluded diabetic patients, and one excluded any patients with contraindications to OST.

## Intratympanic Steroid Therapy

20 ITS reports were identified. (Table 5)

A 25-gauge spinal needle was the most common choice and used in six papers. Postero-inferior injections were the most common (n = 9), followed by antero-inferior and antero-superior (n = 3 each). One paper described injections in either the antero-inferior or postero-inferior quadrants, but rates were not detailed. Eight papers did not report needle size, and five did not report injection site.

The median number of doses was four (range 3-12), and median time in which they were given is 14 days (range 3-28).

Dexamethasone was the most popular intratympanic drug. (n = 13) Methylprednisolone was second. (n = 6) Betamethasone and prednisolone were each used in one treatment arm.

Five papers performed secondary punctures to allow air in the middle ear to escape as the steroid solution was instilled. Two papers (18,23) performed an antero-inferior puncture, and two performed an antero-superior puncture. (19,24) One paper performed a secondary myringotomy, but it was not detailed as to where this was. (25)

Three papers documented that they warmed their steroid solutions. (22,26,27) Jia (2019) and Wang (2024) warmed them to body temperature, while Tong (2021) rolled the vial between hands.

The commonest AEs were temporary dizziness and otalgia. These were reported in nine and six papers respectively. The range of patients experiencing dizziness was 5.5-27.1%. Dizziness was still present in studies which warmed their steroid solutions. 5.5% (n = 4 out of 73) of patients in Jia (2009) experienced vertigo, as did 20.0% (n = 6 out of 30) of patients in Tong (2021). The range of patients experiencing otalgia was 2.8-54.3%. (Table 6)

Perforations were divided into those which healed spontaneously and those which persisted beyond follow-up. Several tympanoplasty methods are detailed, but there were patients who elected not to have further procedures. Healing perforations were noted in two papers in 1.3% and 4.7% of participants. (23,27) Persistent perforations are described in 3.9-11.5% of studies. We were unable to correlate the gauge of needle used to the frequency of temporary and persistent perforations.

Seven studies report no AEs with ITS. (4,13,18,21,24,25,28) Most studies used dexamethasone except Fitzgerald (2007), who used methylprednisolone. Five studies used topical anaesthetic (lidocaine, phenol, and one unspecified) and none warmed the steroid. Dispenza (2011) excluded any patients with a history of ear pathology and contraindication to steroids, and Hong (2009) excludes any DM patients. AE reporting methods were unreported in five papers. Han (2009) measured capillary blood glucose four times daily, and Dispenza (2011) captured AEs with an online patient questionnaire. The median number of injections for these papers was 3 (range: 3-8 doses) and the median period of administration was 14 days (range: 8-28 days), which are not significantly different to the wider cohort.

## Intravenous Steroid Therapy

We identified 14 IVST study arms. (Table 7)

Studies preferred dexamethasone (n = 5) or prednisolone (n = 4). The median length of therapy (including oral tapers) was 10 days (range: 5-15 days). 10 studies included an oral taper and the average cumulative dose was 758.4mg (range 266.7-2365mg). The average daily dose was 84.6mg (range 26.7-236.5mg). Doses were given per weight in four papers and tapers were left undisclosed in two.

Hyperglycaemia was the most reported AE, and rates ranged from 11.9-48.0%. Lan (2018) examined a cohort of DM patients and likely monitored blood glucose levels closer than other studies. Uncontrolled hyperglycaemia occurred in 6.5% of one study, and one of these patients was subsequently removed from analysis. Insomnia was reported in 16.1-41.3% of participants, and gastric disturbance in 2.2-21.4%. (Table 8)

Six papers reported no AEs, which are italicised in *Table 7*. Among these, the average length of therapy was 10.5 days, and the average dose of prednisolone was 818.3 mg. One paper (29) disclosed participants’ co-morbidities, and no papers disclosed AEs reporting methodology. Two papers (30,31) excluded diabetic and hypertensive patients. Two papers did not report exclusion criteria. Four papers detailed therapies including a low salt diet (n = 3) and smoking cessation (n = 2).

## Combination Therapies (Intratympanic plus systemic therapies)

12 study arms used a combination of systemic steroid and ITS. This comprised six OST and ITS, and six IVST and ITS arms. (Table 9)

Studies most frequently used prednisolone or methylprednisolone (n = 3 each) as OST, dexamethasone (n = 3) for IVST, and dexamethasone for ITS (n = 10). Systemic therapy was given for 10.3 days on average in OST, and 10.8 days on average in IVST. Average daily doses were 53.0mg and 51.9mg respectively. The mean number of IT injections was 4.8 delivered over 11.2 days on average.

Vertigo and otalgia were the most reported AEs, with rates of 8.1-28.3% and 3.8-13.5% respectively. Perforations occurred transiently in 5.4% and persisted in 4.0% of patients. There was one case of otitis media (2.2%). One paper (32) reported on systemic AEs. (*Table 11*). Tapers were estimated in 5 papers. (33–37)

5 papers noted no AEs, which are italicised in *Table 9*. (4,29,30,37,38) Three papers append qualifiers- Arslan (2011) states no ‘important’ complications, Battaglia (2008) states no ‘long-term’ complications, and Fu (2011) states no ‘severe’ complications. Among these papers, the average daily dose of prednisolone was 54.5mg, which is similar to the average of 51.2mg among papers reporting AEs.

## Steroids in Pregnancy

We included papers related to pregnancy as this is an important demographic for clinicians to be aware of. (Table 12) (24,28,39) These papers used dexamethasone ITS and topical anaesthesia pre-injection. All patients in one study received intravenous Dextran-40. (28) No complications were noted in two papers. (24,28) 42.9% (n = 3) and 14.3% (n = 1) of seven patients enrolled in Lyu (2020) experienced post-injection otalgia and vertigo respectively. No systematic AEs were reported, though it is difficult to draw conclusions due to the limited number of participants.

# Discussion

This review has identified several risks to consider when starting steroid therapy to manage SSNHL. The incidence varies depending on the route of administration and can be divided into local and systemic AEs. Ranges are summarised in *Table 13*. While a proportion of studies reported no AEs, drawing conclusions is difficult due to variation in follow up, reporting measures, definitions of AEs and additional therapies.

Long-term steroids are used in the management of myriad inflammatory and auto-immune conditions. In a survey of 2446 patients using long-term glucocorticoids, Curtis *et al* (2006) found that 90% of patients reported at least one AE, with 55% classifying it as ‘very bothersome’. These included weight gain (70%), cataracts (15%) and easy bruising (12%) and have a linear relationship with steroid dose and duration. (9) Sequelae such as bruising, osteoporosis, and avascular necrosis were not identified in our review and suggests that risk rises with long-term usage or co-morbidity. While the latter is a very rare AE, it carries significant impacts on a patient’s life and requires operative intervention. Co-morbid and immunosuppressed individuals are at greater risk, and should be counselled accordingly. (40)

The Royal College of Physicians suggests courses of ≥40mg of prednisolone for longer than one week are at risk of adrenal suppression, and patients should be given an NHS Steroid Emergency Card. This resource details the steroid therapy and contains guidance on management of adrenal crisis. (41) NICE guidelines suggest that proton-pump inhibitors (PPI) need not be prescribed routinely but “considered for those at risk of gastrointestinal bleeding or dyspepsia” for long-term prescriptions. (42) A review by Narum *et al* (2014) suggests outpatient OST is not associated with an increased risk of gastrointestinal bleeding. (43)

# Conclusion and Recommendations:

1. Closer ambulatory monitoring of diabetic and hypertensive patients. Blood pressure and glucose measurements can be monitored at home and discussed with general practitioners and local diabetic teams to titrate medications appropriately.
2. ITS as first-line therapy requires further investigation in diabetic and hypertensive cohorts.
3. Gastroprotective measures should be considered in patients predisposed to gastrointestinal bleeding or dyspepsia.
4. Further well-designed studies examining AEs and at-risk cohorts are required to establish our clinical evidence base and improve counselling.
5. Development of patient information leaflets to include in patient letters regarding known side-effects of steroid therapy, to include with urgent prescriptions.
6. Consider providing patients with the NHS steroid emergency card when prescribed a course of OST ≥40mg daily for over one week.

The evidence base which clinicians can draw on to counsel their patients on the risk profile of short-course steroids is limited. To effectively counsel our patients, further research is required.

# Limitations

The greatest limitation to the conclusions made by this study is the considerable heterogeneity between papers. To allow for analysis, we estimated steroid tapers and an average weight of 70 kg where taper data was omitted, or doses were presented in mg per kg.

We assumed the length of follow up based on the date of the final audiology appointment unless specified.

Many papers excluded patients with diagnoses of diabetes or hypertension, or with unspecified contra-indications to steroids. AE profiles may therefore be positively skewed. Some reports terminated steroid therapy following hearing recovery, but patients remained enrolled without completing the full course. This also potentially positively skews AE rates.

Different systolic blood pressure or blood glucose thresholds triggered AE recording. Immediately apparent events such as vertigo and otalgia are more easily captured compared to AEs such as hypertension or hyperglycaemia, which require additional equipment. In the ITS cohort, limited data made it difficult to correlate the gauge of spinal needle and perforation rates.

We converted all steroids to prednisolone-equivalent doses. It is unclear whether the severity of AEs translates linearly. Some studies employed measures including dietary modification, hyperbaric oxygen, gingko biloba, and Dextran- it is unclear whether these conferred any therapeutic effect.

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