Sudden Sensorineural Hearing Loss and Intratympanic Steroids

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Sudden Sensorineural Hearing Loss

- First described in 1944 by DeKleyn
- Incidence: 5-20 per 100,000
- 4,000 new cases/year in US
- Idiopathic
- Hearing loss in 3 contiguous frequencies of at least 30 dB
  - Some authors use at least 20 dB loss
- Onset of hearing loss occurs in less than 72 hours
- Recovery rate without treatment 32% - 79%
  - Usually within 2 weeks of onset
  - Only 36% with complete recovery
- No middle ear disease
- Otologic emergency!
Sudden Sensorineural Hearing Loss

- Clinical Presentation
  - Sudden onset hearing loss
    - Less than 3 days
  - Usually unilateral
    - Left side possibly more common (55%)
    - Bilateral 2%
  - Median age 40-54
  - Equal among males and females
  - Awakening from sleep
  - Hearing a “popping” prior to hearing loss
  - Aural fullness
  - Tinnitus
  - Vertigo
Sudden Sensorineural Hearing Loss

- Differential Diagnosis
  - Infectious
    - Bacterial: meningitis, labyrinthitis, syphilis
    - Viral: Mumps, CMV
  - Inflammatory
    - Autoimmune, Cogan syndrome, Lupus, MS
  - Traumatic
    - Temporal bone fracture, acoustic trauma, perilymph fistula
  - Neoplastic
    - CPA tumor, temporal bone metastasis
  - Toxic
    - Aminoglycosides, aspirin
  - Vascular
    - Thromboembolism, macroglobulinemia, sickle cell disease, cerebral infarct, TIA
  - Congenital
    - Mondini malformation, enlarged vestibular aqueduct
Sudden Sensorineural Hearing Loss

- Theories
  - Viral infection
    - Temporal association of SSNHL with viral URI in 25% - 63%
    - Serology confirming active viral infection
      - HSV, VZV, CMV, influenza, parainfluenza, rubeola, mumps, rubella
      - Immunoreactivity against virus
    - Histopathology of human temporal bones
      - Atrophy of organ of Corti, spiral ganglion, tectorial membrane
      - Hair cell loss
      - Unraveling of myelin
    - Animal experiments confirm viral penetration of the inner ear
Sudden Sensorineural Hearing Loss

- Theories:
  - Vascular injury
    - Sudden onset suggesting infarction
      - Perlman (1959) demonstrated loss of cochlear microphonic 60 seconds after occlusion of labyrinthine artery in guinea pig
      - Buerger’s, macroglobulinemia, sickle cell, fat embolism
    - Histopathologic changes in cochlea caused by vascular occlusion in animal models
      - In guinea pigs, labyrinthine vessel occlusion lead to loss of spiral ganglion cells, mild to moderate damage to organ of Corti, cochlear duct fibrosis
  - Controversial
Sudden Sensorineural Hearing Loss

- Theories:
  - Intracochlear membrane rupture
    - Loss of endocochlear potential due to mixing of endolymph and perilymph
    - Gussen (1981) histologic evidence
    - Fallen out of favor
  - Likely combination of viral cause and vascular insult
Sudden Sensorineural Hearing Loss

- Challenges
  - True incidence is not known
  - Patients with spontaneous recovery usually do not present to an otolaryngologist
  - Patients may present beyond what is considered to be therapeutic window
  - Etiology still unclear
  - Relative paucity of studies examining treatments based on prospective, double-blind, randomized, controlled trials
Sudden Sensorineural Hearing Loss

- Clinical Evaluation
  - History
  - Complete head and neck exam
    - Pneumatototoscopy to evaluate for fistula sign
  - Audiogram including pure-tone audiometry (PTA), speech reception threshold (SRT), and speech discrimination scores (SDS)
  - Tympanometry
  - +/- Auditory brainstem response (ABR) and otoacoustic emission (OAE)
  - ENG if vestibular symptoms and/or signs are present
Sudden Sensorineural Hearing Loss

- Radiography
  - MRI with gadolinium
    - 0.8%-2% of patients with SSNHL have been diagnosed with IAC/CPA tumors
  - Non-contrasted CT of temporal bones in younger patients
    - Mondini malformation
    - Enlarged vestibular aqueduct
Sudden Sensorineural Hearing Loss

- Laboratory Evaluation
  - CBC with diff
    - Polycythemia, leukemia, thrombocytosis
  - Electrolytes
  - Erythrocyte sedimentation rate (ESR)
    - Nonspecific, autoimmune or inflammatory marker
    - Antinuclear antibody or 68 kD antibody
  - Rheumatoid factor (RF)
  - FTA-Abs (Syphilis)
  - Coagulation profile
  - Thyroid function testing
  - Lipid profile
Sudden Sensorineural Hearing Loss

- **Treatment**

  - **Systemic Steroids**
    - Historical perspective: Reduce inner ear inflammation
    - Nonspecific
    - Dependent on time to therapy
    - Oral, IV
    - Variable to poor response for profound SSNHL
    - Cannot be used for all patients
      - Diabetics, ulcers, TB, glaucoma
      - Intratympanic steroids
  
  - Antivirals
  - Volume expanders
  - Vasodilators
  - Anticoagulants
  - Carbogen inhalation
Sudden Sensorineural Hearing Loss

- Cochrane Database of Systematic Reviews
  - Wei (2003, Updated 2006): Steroids for idiopathic sudden sensorineural hearing loss
  - Only 2 prospective, double-blind, randomized, controlled trials evaluating therapy of SSNHL
Wilson (1980)

- Prospective, double-blind, randomized, controlled study to examine the effectiveness of steroid therapy for SSNHL
- Parameters strictly defined
- Kaiser Permanante and MEEI combined
- Inclusion: 30 dB loss over at least 3 contiguous frequencies in less than 3 days and presentation within 10 days of onset with normal laboratory studies
- 33 treated with steroids
  - KP Decadron 10 days tapered
  - MEEI Medrol 12 days tapered
- 34 placebo treated controls
- 52 untreated controlled
Wilson (1980)

- Patients stratified by type of audiogram
  - Mid-frequency loss
  - Loss at 4 kHz greater/equal to loss at 8 kHz
  - Loss at 8 kHz greater than loss at 4 kHz
  - Profound loss greater than 90 dB PTA
  - Unaffected ear used as reference

- Recovery
  - Complete: within 10 dB of reference SRT or PTA if HF
  - Partial: > 50% of reference SRT or PTA if HF
  - None: < 50% recovery
Wilson (1980)

- Results
  - All with midfrequency loss had complete recovery
    - 14% had vertigo
  - 76% with profound loss had no recovery, and 24% with partial recovery
    - No improvement in steroid treated group
    - 79% had vertigo
  - 4 kHz loss and 8 kHz groups were combined
    - Recovery with steroids 78%
    - Recovery in placebo group 33%
  - No adverse side effects
Wilson (1980)

- Prognostic factors
  - Vertigo not statistically significant
  - Age less than 40 years favorable for recovery
  - Type of audiogram
    - Midfrequency loss with best recovery
    - Profound loss less likely to have recovery
    - Loss between 40 dB – 85 dB more likely to respond to steroid therapy

Wilson (1980)
Wilson (1980)

**Fig 2.** Categories of sudden hearing loss as determined by spontaneous recovery rate and response to steroid therapy.
Wilson (1980)

- Relative Odds for recovery
  - Steroids vs Placebo 4.95:1
  - Steroids vs untreated controls 4.06:1
  - Untreated controls vs Placebo 1.22:1
  - Steroids vs all control 4.39:1
Cinamon (2001)

- Prospective, double-blind, randomized, controlled trial to evaluate the effectiveness of carbogen and steroids for SSNHL
- Hearing loss at least 20 dB over 3 frequencies
- 41 patients stratified by type of audiogram
  - Flat, midfrequency loss, low frequency loss, and high frequency loss
- Improvement: at least 15 dB change of PTA
- Four treatment groups for 5 days of therapy
  - Prednisone (1mg/kg/day)
  - Placebo
  - Carbogen (95% oxygen, 5% CO2) inhalation (30 min six times daily)
  - Room air inhalation
Results

- Overall improvement in PTA at follow-up (73%)
  - Steroid 80%
  - Placebo 81%
  - Carbogen 55%
  - Placebo inhalation 77%
  - Not statistically significant

Trends:

- Low frequency loss improved more
- High frequency loss improved less
- Patients without vertigo have better outcome
Barany (1935): used lidocaine for tinnitus
Schuknecht (1956): used streptomycin for Meniere’s disease
Bryan (1973): used steroids for a patient with facial paralysis
Intratympanic Steroids

- Administration of steroids to middle ear round window niche/membrane directly targeting the inner ear
- Very little systemic absorption
  - May benefit patients for whom systemic steroids are contraindicated
- Higher concentration to end organ
- May salvage hearing loss when non-responsive to systemic steroids
- Only one prospective, double-blind, randomized, controlled trial of IT Dex vs placebo (for treatment of Meniere’s)
Examined the effects of transtympanic injection of steroids on cochlear blood flow, auditory sensitivity and histology in guinea pigs

- Dexamethasone 4 mg/mL vs saline
- 30 gauge needle through AI TM
Shirwany (1998)

Results

- 29% increase in cochlear blood flow within 30 sec without change in auditory sensitivity measured by ABR
- Increase in cochlear blood flow was sustained for at least 1 hour
- No histologic changes
In a guinea pig model, the concentrations of hydrocortisone, dexamethasone, and methylprednisolone in plasma, endolymph, perilymph, and CSF were compared when administered orally, intravenously, and IT.

- Dexamethasone 26.7 times more potent than hydrocortisone
- Methylprednisolone 5.3 times more potent than hydrocortisone

Also designed IT steroid treatment routines for a variety of inner ear disorders.
Potency corrected levels in perilymph after IT administration

Parnes (1999)
Potency corrected levels in endolymph after IT administration

Parnes (1999)
Parnes (1999)

- 12 patients not previously treated for SSNHL (onset within 6 weeks of treatment) given IT methylprednisolone or dexamethasone
- 27 gauge needle
- 8 with Methylprednisolone 40 mg/mL
  - 1 full recovery
  - 3 partial recovery
  - 4 no recovery
- 4 with Dexamethasone 2 mg/mL
  - 2 partial recovery
  - 2 no recovery
- 50% with some recovery
- ?
- 3 developed otitis media, which resolved with Abx
Chandrasekhar (2001)

- Guinea pig model
- Greater concentration of dexamethasone in perilymph via intratympanic route vs IV
- IT-Dex with histamine significantly increased perilymph concentration compared to hyaluronic acid, dimethylsulfoxide, or dex alone
Prospective trial of intratympanic steroid therapy for patients with SSNHL when oral steroids failed or patients were unable to tolerate systemic steroids

SSNHL: > 20 dB loss in at least 3 contiguous frequencies within 3 days

Improvement: decrease of PTA or SRT of at least 10 dB or 10% increase in speech discrimination

Gianoli (2001)
Delivery:
- Posteroinferior tympanotomy and round window examined endoscopically with removal of adhesions of niche
- PET placed
- Methylprednisolone (62.5 mg/mL) or dexamethasone (25 mg/mL) placed through tube
- 4 applications (0.4 – 0.6 mL) over 10 - 14 day period
Gianoli (2001)

- Results (23 patients)
  - 44% had improvement in PTA
    - 15.2 dB
  - 48% had improvement in SRT
    - 15 dB
  - 35% had improvement in speech discrimination
    - 21%
  - 4% had worsening of speech discrim by 16%
Gianoli (2001)

- Stratified by time of onset to therapy
  - <6 weeks, >6 weeks
  - Range 0-520 weeks
  - No statistical significance in improvement

- Stratified by Age (<60, >60 years)
  - No statistical significance
  - Trend: younger patients with favorable results

- Stratified by type of steroid
  - No statistical significance
  - Trend: methylprednisolone group had greater improvement than dexamethasone group
Gianoli (2001)

- 1 (4%) adverse event: otitis media, resolved

Disadvantages/Advantages
- No control group, not blinded, not randomized
- Small sample size
- Not used as primary treatment for SSNHL in all
- Improvement may not be noted by patients
  - Profound loss
- Systematic approach
- IT steroids may be an option for patients unable to take systemic steroids or as salvage
Kopke (2001)

- Prospective trial using round window microcatheter for delivery of methylprednisolone in patients with SSNHL refractory to oral prednisone therapy
- Patients stratified by time of onset to catheter placement
  - 6 patients in six week or less group
    - 4 with SSNHL
    - 1 with hearing loss after stapedotomy
    - 1 with Meniere’s with hearing loss while undergoing aminoglycoside therapy
  - 3 in late group
    - 1 with SSNHL
    - 1 following acoustic trauma
    - 1 following closed head injury
- Improvement: decrease in PTA of 10 dB or increase in SDS by 15%
IT Delivery via Microcatheter

- GETA
- Tympanomeatal flap elevated
- Round window niche cleared of adhesions
- 1.5 mm to 2.0 mm microcatheter placed into niche
- Methylprednisolone (62.5 mg/mL) delivered continuously for 14 days at rate of 10 µL/hour using pump

Kopke (2001)
Kopke (2001)

- Results
  - 100% in group treated in 6 weeks had improved PTA scores
  - 83% with improved SDS
  - 66% to normal hearing
  - No improvement in late group

- Lefebvre (2002)
  - Similar results in 6 patients using continuous infusion with round window microcatheter

- Microcatheter removed from market by FDA
Silverstein (2002)

- Examined patients (48) with refractory hearing loss after systemic steroids for SSNHL using inner ear perfusion of dexamethasone 4-24 mg/mL with MicroWick
- 23% had improvement of PTA of at least 10 dB
- 35% had improved SDS of at least 15%
Silverstein (2002)

- MicroWick
  - Topical anesthetic
  - Posteroinferior myringotomy
  - Round window niche identified and adhesions removed
  - MicroWick (1 mm by 9 mm) placed
  - PET placed into myringotomy with Microwick through lumen
  - Drops instilled into ear
Guan-Min (2004)

- Prospective, randomized, controlled trial to study the effectiveness of IT Dex in patients with severe to profound SSNHL
- PTA, SRT, ABR, OAE, tympanometry, viral serology, MRI/CT if indicated
- 39 patients initially treated (18 severe, 21 profound)
  - Methylprednisolone for 10 days (except 3 with DM)
  - Nicametate (vasodilator), Vitamin B-complex, Benzodiazepine for 10 days
  - Carbogen for 5 days
- Patients divided by response
  - Normal hearing or improvement > 30 dB (10, 8 severe, 2 profound)
  - Improvement < 30 dB, no improvement, and worsening (29)
    - Control group (14) treated with above except steroids and carbogen
    - Treatment group (15)
- IT Dex applied 10 days after initial therapy if there was no or only partial response
  - Myringotomy with 22 gauge needle at posterior TM and 0.4 – 0.7 mL of Dex (4 mg/mL)
  - Once weekly for 3 weeks
Guan-Min (2004)

- Results
  - 53% (8/15) in IT-Dex group with improvement
    - 50% (4/8) with normal hearing
      - 1 with DM
    - 50% with > 30 dB improvement
  - 7% (1/14) improvement in control
  - Recovery for Severe SSNHL 44%
  - Recovery for Profound SSNHL 9.5%
  - No statistical significance:
    - Age (<50, >50 years)
    - Sex
    - Treatment delay time (<7 days, ≥7 days)
  - Side effects of IT-Dex: acne (1), vertigo (1)
Prospective study examining IT dex concurrent with oral steroids for profound SSNHL

25 adult patients
- SSNHL within 24 hours
- Range of time to presentation/treatment: 2-180 days
- Initial PTA at least 90 dB
- No otologic history
- Negative MRI

Treatment
- Methylprednisolone (64 mg/day, tapered over 11 days)
- Dexamethasone injections (24 mg/mL)
  - 27 gauge needle
  - 4 injections of 0.3 cc
  - 14 days
Battista (2005)

- Results
  - 8% with complete hearing recovery
  - 12% with partial recovery
  - Those with some recovery had treatment within 14 days of onset
  - 1 TM perforation repaired with paper patch

- Oral or IT steroids?
Xenellis (2006)

- Examined effectiveness of IT steroids for SSNHL patients who failed to improve with initial therapy
  - Prednisolone IV (1 mg/kg/day, tapered)
  - Acyclovir (4 g/day, 5 days)
  - Buflomedil (300 mg/day, 10 days)
  - Ranitidine

- Days to admission: 1-20
- Complete workup
- IT Methylprednisolone (40 mg/cc) vs no IT
  - Injection with 21 gauge needle
  - 4 times in 15 days
Xenellis (2006)

- Results
  - 47% treated with IT steroids improved > 10 dB
  - No controls improved
  - No adverse outcomes
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<td>Prospective</td>
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<td>Microcatheter</td>
<td>100%, ≤6wk(PTA/SDS) 0% &gt;6wk</td>
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</table>
Sudden Sensorineural Hearing Loss

- Advantages to IT steroids
  - May be used when systemic steroids are contraindicated or refused
  - Greater concentration achieved at target end organ
  - May be performed in outpatient setting
  - Possible use for salvage of hearing
  - Relatively low complication rate
Sudden Sensorineural Hearing Loss

- Challenges for IT steroids
  - Not well established as primary treatment strategy
  - Dosing?
  - Best delivery technique?
  - Long term effects?
  - Why does it work? .... Sometimes
Sudden Sensorineural Hearing Loss

- Take Home Messages:
  - SSNHL is an otologic emergency
  - Systemic steroids are mainstay of therapy
    - Prednisone 60 mg/day for 3-5 days, tapered 5-7 days
  - Better prognosis if treatment started early (within 4 weeks of onset)
  - IT steroids may be an alternative when systemic steroids are contraindicated
  - IT steroids is another option when oral steroids fail to restore hearing