Targeted Topical Steroid Therapy in Sudden Sensorineural Hearing Loss

Richard D. Kopke, Michael E. Hoffer, Derie Wester, Michael J. O’Leary, and Ronald L. Jackson

The Department of Defense Spatial Orientation Center, Naval Medical Center, San Diego, California, USA

Objectives: To treat patients with sudden sensorineural hearing loss (SSHL) who failed oral prednisone therapy by using a round window membrane (RWM) microcatheter. This topi-
cal delivery strategy sought to improve effectiveness of steroid treatment to the inner ear by targeting drug delivery to the RWM.

Study Design: Nonrandomized prospective design.

Setting: Tertiary care facility.

Patients: Six patients with severe unilateral SSHL, five of whom were refractory to a course of oral steroid therapy treated within 6 weeks of SSHL and three additional patients treated more than 6 weeks after SSHL.

Intervention: Therapeutic use of RWM catheter.

Main Outcome Measures: Pure-tone averages (PTAs) and word identification scores (WIS).

Results: Five of the six patients treated within 6 weeks of SSHL improved their WIS. Of the six, four returned to baseline hearing, one recovered hearing that could benefit by hearing amplification, and one regained moderate improvement in PTA but not WIS.

Conclusion: Targeted topical steroid administration avoids the significant systemic side effects of oral steroids and may offer more effective dosing than simple trans tympanic injection of medicine. Although these findings are preliminary, it is possi-
ble that after further study, targeted drug delivery may be a useful technique to consider in patients with severe to profound hearing loss that have failed all other management options. Key Words: Topical steroids—Sudden sensorineural hearing loss. Oto Neur 2001;22:475–479.

Sudden sensorineural hearing loss (SSHL), commonly described as an abrupt onset of hearing loss, is reported to occur in 5 to 20 per 100,000 population (1). Sponta-
neous recovery (without therapy) varies from 30% to 60%. Most often resolving within 2 weeks after onset (2–4). High-dose systemic steroid therapy improves hearing recovery; however, persistent hearing losses af-
ter 2 weeks of oral steroids have a poorer prognosis (5.6). Transtympanic steroid therapy for chronically progres-
sive hearing loss as well as SSHL has been reported with partial success (7,8).

Our earlier experiments demonstrated controlled ad-
mistration and uptake of medicine in an animal model. More recently, our studies have used an active sustained release device to treat patients with Ménière’s disease using gentamicin (9,10). Our animal and human data have demonstrated different uptake kinetics with differ-
ent effects on patients when gentamicin was adminis-
tered via the round window microcatheter (a sustained

The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Army, Department of Defense, or the United States Government.

Address correspondence and reprint requests to Colonel Richard D. Kopke, Department of Defense Spatial Orientation Center, Naval Medical Center, San Diego, CA 92134-2200, USA.

MATERIALS AND METHODS

Subjects

Patients who came to our institution between July 1998 and April 1999 with reports of SSHL (hearing loss on awakening or having developed over 72 hours or less) and who did not re-
spond to 2 weeks of oral steroid therapy were included in the study. All individuals underwent a standard evaluation, includ-
ing an otolaryngologic history and physical, a routine audi-
ologic test battery, sphenoid sinus, ethmoid sinus, sinu-}

475
The two treatment groups in this study were divided by the period from onset of hearing loss until the time of catheter placement. Individuals who underwent catheter placement 6 weeks or less from the onset of hearing loss constituted the early group, and patients receiving catheter placement 7 weeks or more after hearing loss constituted the late group. The early group was composed of six individuals. Four of the individuals in this group experienced idiopathic SSHL, that did not respond to a 2-week trial of oral steroid. One patient re- ported a sudden sensorineural loss 4 weeks after a stapedectomy initially the patient had had an improvement in hearing be- cause of a reduced air-bone gap from the surgery, but had a SSHL 4 weeks after surgery. Middle ear exploration did not reveal a reason for the sudden hearing loss. The patient was undergoing aminglycoside treatment for Ménière’s dis- ease and experienced a sudden sensorineural hearing loss. She was given oral steroid therapy while the gentamicin in the cerumen was removed and microcatheter instillation of methyl- prednisolone was initiated. Oral steroid administration was stopped after 1 day in this patient. The late group was composed of three individuals with SSHL: one in whom the condition was idiopathic, a second who sustained a SSHL after exposure to a loud noise, and a third who acquired SSHL after being struck in the side of the head by a golf ball.

Microcatheter treatment

With the patient under general anesthesia, a modified tym- paneal flap was elevated to expose the round window niche. After cleaning the round window niche of any false membranes or adherences, a microcatheter with an appropriately sized tip (usually 1.5 or 2.0 mm in diameter) was gently in- serted into the bony niche. The tip is bulbous and compressible and locks into place in the bony opening of the niche. Care was taken so as not to insert the catheter too deeply into the bone to avoid possible injury to the round window membrane. The catheter was preloaded with 0.125 ml of methylprednisolone (Solu-Medrol, methylprednisolone sodium succinate, Pharma- cia & Upjohn, 62.5 mg/ml) at the time of surgery. After sur- gery, the methylprednisolone (62.5 mg/ml) was continuously pumped for 14 days into the catheter at a rate of 10 μl/hour using an "Electronic pump" (Dierzon Instruments, Inc., Minneapolis, MN, USA).

Results

Acoustic tone and air conduction pure tone thresholds were obtained using a Grason-Stadler Instruments (GSI 16 or 10; Milford, NH, U.S.A.) audiometer before, during, and after catheter placement as well as several follow-up examinations. Standard speech audiometry was administered to determine a percentage word identification score (0%-100%) using the Measurement of Auditory Sensation (MASC) list presented at 40 dB SL re: NR. Middle ear function was assessed with a GSI-33 middle ear analyzer (version 2) for tympanometric, physical, and acoustic reflex thresholds.

Hearing improvement

Hearing improvement was defined as a decrease in the four-frequency (0.5, 1, 2, and 3 kHz) pure tone average (PTA) of 10 decibels or more, or an increase in word identification score (WIS) of 15% or more.

Statistical analysis

All statistical analysis was conducted using a standard sta- tistical software package (Microsoft Excel version 4.0) and STATA statistical software version 4.0 (STATA Corp., College Station, TX, U.S.A.). The mean four-frequency PTA and before and after in situ treatment of the early treatment group were ana- lysed using a Wilcoxon signed rank test. Mean WIS were com- pared before and after in situ treatment with a paired t test for means. Significance was determined to be at the level of p < 0.05. Statistical testing was not performed on the late treatment group because of the small number of patients. Their data will be pre- sented descriptively as individual case data profiles.

Results

As shown in Table 1, all individuals in the early group had severe to profound hearing loss before in situ steroid treatment, with a mean PTA at the averted ear of 93.3 dB or mean WIS of 1.3%. All individuals in the early group demonstrated an improvement in PTA after mi- crocatheter treatment. Five of the six patients improved their WIS, and four (two of the idiopathic patients, the poststapedotomy patient, and the aminoglycoside patient) returned to pre-hearing loss PTA. Of the six pa- tients in the early group, four returned to normal hearing, one recovered hearing that could be benefited by hearing amplification, and one last regained moderate improvement in PTA but not WIS.

Early group four-frequency PTAs are shown for indi- vidual and group means after the microcatheter treatment in Figures 1 and 2. As can be seen in Figure 2, the PTA in this group showed a marked improvement from 93.2 to 42.5 dB HL (Wilcoxon signed rank for

|TABLE 1. Functional assessment of SSHL patients treated within 6 weeks of hearing loss (early treatment group) |
|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
|Age (yr.) | M: F | SSHL onsets | EM: | Baseline PTA | Base-line WIS | Post Rx PTA | Post Rx WIS | AC | Time from SSHEL to microcatheter |
|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
|F 16 | Postsurgical 65.0 | 107.5 | 63.5 | 100 | 7.0 | 75.0 | F | 4 wk |
|F 51 | Idiopathic 10.0 | 75.0 | 7.5 | 100 | 4.0 | 100 | F | 4 wk |
|M 59 | Idiopathic NA | 68.8 | 42.5 | 84 | 4.0 | 100 | DS | 6 wk |
|M 40 | Idiopathic NA | 115.0 | 60.0 | NA | 0.0 | 0.0 | F | 4 wk |
|M 41 | Gentamicin 45.0 | 115.0 | 51.3 | 76 | 0.0 | 0.0 | DS | 24 hr |
|M 48 | Idiopathic 35.0 | 78.8 | 30.0 | 96 | 0.0 | 96 | F | 4 wk |
|Avg. | 47.2 | 93.3 | 42.5 | 1.3 | 62.2 | 1.3 | 37.1 |
|SEM | 15.3 | 8.74 | 8.59 | 1.15 | 15.3 |

SSHL, sudden sensorineural hearing loss; M: male; F: female; PTA, pure tone average is the average of 0.5, 1.0, 2.0, and 3.0 kHz hearing levels in dB HL; SEM, standard error of the mean; WIS, word identification score (%); NA, not available; AC, acoustic configuration where F = flat and DS = descending slope.

Otolgy & Neurotology, Vol. 22, No. 4, 2001
treatment effect, p < 0.03). In Figure 3, the mean WIS is depicted for the early group before and after microcatheter infusion therapy. The WIS improved from an average of 1.3 to an average level of 62.2% (p < 0.01).

There was no improvement of either PTA or WIS for any of the patients in the late group between the preoperative and postoperative in situ treatments. Individual PTA values are given in Table 2. One patient (the individual stuck with a golf ball) had a further loss of hearing accompanied by vertigo 12 hours after catheter placement. In this patient, no evidence of a perilymph fistula was found either on initial catheter placement or on removal of the catheter shortly after the onset of symptoms.

At present, all patients in both groups are at 2 to 12 months after microcatheter treatment and have maintained the hearing levels on their most current audiograms (early group: 2-12 months, average 6.7 months; late group: 7-11 months, average 9.7 months).

**DISCUSSION**

Of the many causes of hearing loss, SSHL is the least understood. Although an exact definition does not exist clinically, most authors agree that SSHL can develop in 72 hours or less or that it can occur on wakening in the morning (12). All patients in the early group had hearing loss that occurred over 24 hours or went to bed with no perceived hearing loss and awoke with near-total deafness in one ear. Several possible causes of idiopathic SSHL have been suggested, including vascular lesions, membrane breaks, and viral lesions (13). The temporal bone collection at the Massachusetts Eye and Ear Infirmary contains specimens of individuals with SSHL. These specimens demonstrate a variety of findings that are similar to those seen after cases of mumps and rubella and dissimilar from the fibrosis and osteoneogenesis seen with vascular disorders (11). Seltzer and Mark demonstrated inflammatory findings on magnetic resonance imaging during active sudden hearing loss, which disappeared as symptoms resolved, further suggesting a viral/inflammatory cause of this disorder (12). However, the most common classification for SSHL is idiopathic (1). There was a similar finding in our study, in which the majority of patients (56%) had idiopathic SSHL.

Many investigators have attempted to determine prognostic variables for SSHL. Fetterman et al. examined 837 cases of idiopathic SSHL and found a significant correlation between the severity of the initial hearing loss and the time to initial treatment (13). In that study, those who were treated more than a month after the initial hearing loss had a poorer chance for improvement. Hughes et al. examined a group of patients with SSHL and added a response within 2 weeks as an additional prognostic variable (1). The most common treatment is high-dose oral steroid therapy, with a reported success rate of 78% in all patients with SSHL (5). However, the improvement rate is much less than in patients whose hearing loss was similar to that in our patients. Brl (2) reported that patients who were seen later than 7 days after severe or profound hearing loss had a 15% to 20% chance of complete recovery. Additionally, Sacki and Kitabara reported that only 24% of SSHL patients showing no improvement in hearing in the first 14 days exhibited any significant long-term progress (4). Our early patients (with one exception, the Ménière’s disease patient) had experienced more than 4 weeks of hearing loss and had not responded to 14 days of oral steroid
therapy before the catheter placement. For those who did not achieve complete recovery, it is plausible that earlier treatment with microcatheter steroids might have resulted in a greater degree of improvement. Indeed, in the patients with long-standing hearing loss, microcatheter administration of steroids had no benefit. Interestingly, those individuals with the greatest degree of recovery began showing hearing improvement within 48 hours of microcatheter placement. Those showing no changes within 48 to 96 hours either had less improvement in hearing or, as in the case of all the late patients, demonstrated no amelioration.

Over the past decade, the combination of basic science and clinical studies has led to the development of trans tympanic corticosteroid treatment of some hearing disorders. A well-designed study by Shibwany et al. demonstrated that trans tympanic corticosteroid in guinea pigs caused no morphologic or functional disturbance in the ear (14). Parham et al. reported in an experimental animal model that steroids administered to the middle ear were able to achieve higher inner ear concentrations than when administered systemically (7). This was especially true for methylprednisolone. Silverstein et al. reported that approximately 38% of patients with idiopathic SSHL or SSHL from other causes who were treated with trans tympanic corticosteroids had at least a partial response (8). Subsequently, Parham et al. reported that of the 13 (54%) of their SSHL patients who were treated with trans tympanic corticosteroid within 6 weeks of onset of hearing loss made a significant recovery of hearing thresholds (7). Trans tympanic corticosteroid treatment, however, has potential limitations, namely a lack of precise coupling to the round window membrane with loss of drug down the eustachian tube and potential blockade by pseudomembranes in the round window niche. Delivery of the corticosteroid to the round window membrane with enhanced coupling, using a catheter inserted in the niche where pseudomembranes are removed surgically, is a logical next step in enhancing steroid treatment of the inner ear.

Although no direct proof exists that our patients' hearing recovery was attributable to the microcatheter administration of steroids, evidence suggests that there is a potential therapeutic window during which injured sensory cells or neurons can be rescued (15, 16). The principal known effects of methylprednisolone are antiinflammatory and neuroprotective (17). Antioxidant (18-21) and antipapptic effects for this agent have also been reported (22, 23). Thus, the benefits realized in these patients may have resulted from a variety of mechanisms. More basic science needs to be done to ascertain the exact mechanisms of action of corticosteroids in the inner ear.

The complete hearing loss and diziness cannot be explained for the one patient in the late group. Given that he had experienced a traumatic event (golf ball to the head), the possibility of a pre-treatment perilymph fistula could be entertained, but no fistula was seen at the time of microcatheter placement, nor was the patient dizzy before surgery. The patient initially did well postoperatively and experienced hearing loss and dizziness 12 hours after surgery. Upon removal of the microcatheter, no perilymph fistula was seen. The patient's vertigo converted to disequilibrium 3 days later, and this disequilibrium resolved after 4 weeks of vestibular rehabilitation. It appears that the patient had labyrinthitis. It cannot be determined whether the steroid caused this labyrinthitis or whether the labyrinthitis was purely coincidental with the treatment. A review of the last 20 years of English literature revealed no other reported cases of SSHL attributed to trans tympanic steroid. Other compounds in the methylprednisolone solution may have affected the inner ear in this patient. However, all patients were administered a solution identical to what this patient was given without experiencing dizziness or hearing loss. The cause and mechanism of hearing loss could not be completely ascertained in this patient or for several of the other patients. It is possible that methylprednisolone might be helpful for some causes of SSHL and harmful for others. Finally, this patient's hearing loss may represent a dose-response effect, where doses higher than some therapeutic level may be harmful. For all these reasons, we are using this treatment only for patients with severe to profound hearing loss in whom more conservative therapy has failed, and we suggest the same precaution for other clinicians until definitive answers to these questions can be obtained.

We believe that targeted topical steroid administration may offer several advantages over systemic or trans tympanic injection. This mode of delivery avoids the significant systemic side effects that can be associated with oral administration of steroid. It also offers more effective dosing than simple injection of the medicine across the eardrum. In fact, by avoiding such systemic side effects

<table>
<thead>
<tr>
<th>Age</th>
<th>M</th>
<th>69</th>
<th>Trauma</th>
<th>54.0</th>
<th>115.0</th>
<th>64.0</th>
<th>0.0</th>
<th>DS</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>61</td>
<td>None</td>
<td>45.0</td>
<td>50.0</td>
<td>84.0</td>
<td>74.0</td>
<td>DS</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>36</td>
<td>Idiopathic</td>
<td>115.0</td>
<td>115.0</td>
<td>64.0</td>
<td>0.0</td>
<td>DS</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>STD</td>
<td>6.56</td>
<td>70.4</td>
<td>96.7</td>
<td>48.0</td>
<td>24.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AC</td>
<td>42.3</td>
<td>41.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SSHSL, sensori neural hearing loss; PTs, pure tone average in the range of 0.5, 1.0, 2.0, and 3.0 kHz hearing levels in db HL; STD, standard deviation; SEM, standard error of the mean; WES, word identification score (%); NA, not available; AC, acoustic configuration where F = flat and DS = descending slope.

as adrenal suppression and aseptic necrosis of the hip, this method may actually be safer than systemic administration of the medicine.

Another possible reason for the effectiveness of targetted delivery is that a higher steroid level in the co- chlear nervous system may be achievable compared with oral or even transtympanic administration (7). This may allow for an effect that would not be seen with systemic or transtympanic administration. Different medicines can be added to the catheter, or the pump rate could be changed without any added discomfort for the patient, as would be necessary for repeated transtympanic injections. The pH of the steroid solution can be quite un- comfortable for some patients undergoing transtympanic injection (13) because of the volume needed, whereas with targeted delivery administration, the lower volume is less likely to cause discomfort. Many patients would prefer a single operative procedure to repeated injections.

Potential disadvantages may include the risk and ex- pense of general anesthesia and operating room time. In addition, a small tympanic membrane perforation is pos- sible after this procedure. In our series of nine patients, there were three small perforations. One short-term pa- tient required paper patch, the second short-term patient opted for no therapy, and a long-term patient opted for an underlay tympanoplasty. We believe it important to warn patients about the possibility of a perforation, which may require another operation to repair. We also warn all patients about the possibilities of substantial worsening of hearing in the treated ear and transient vertigo.

To address this question and more fully study this treatment, our group is beginning a prospective random- ized trial examining the efficacy of this treatment of severe to profound SSHL. It remains to be demonstrated whether this modality will confer a significant therapeutic advantage over oral transtympanic steroid delivery.

SUMMARY

We have reported hearing recovery after microcatheter administration of methylprednisolone in patients with se- vere to profound SSHL from a variety of causes. Pres- ently, we are directly ascertaining that microcatheter delivery of steroids resulted in hearing improvement. However, considering our patients’ duration of hearing loss, which was more than 4 weeks, and also considering that oral steroids had been unsuccessful in five of the six patients, it is suggestive that the strategy had some effect.

It is our belief that this information is important to prac- titioners, because this modality may someday represent a reasonable treatment option for patients with severe to profound hearing loss in whom oral steroids have been unsuccessful. While promising, this method of therapy needs further study in controlled prospective trials. Be- cause of the potential risk of additional hearing loss, this procedure is not recommended for individuals with mod- erate hearing loss or serviceable hearing such as with a hearing aid. In addition, we have found no benefit in patients who are implanted with the catheter more than 6 weeks after the onset of hearing loss. Finally, it is im- portant that both basic science and well-controlled clini- cal trials continue to document the most appropriate use and timing of this treatment modality in the emerging field of inner ear medicine delivery.

REFERENCES


Otolaryngology & Neurotology. Vol. 22, No. 4, 2001