Corticosteroids in the Treatment of Vestibular Neuritis: A Systematic Review and Meta-Analysis


*1st Department of Otorhinolaryngology–Head and Neck Surgery, ENT Department, AHEPA University Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece; and †Department of Otolaryngology and Skull Base Surgery, Pellegrin University Hospital, University of Victor Segalen Bordeaux 2, Bordeaux, France

Objective: To systematically review and meta-analyze the results of all randomized controlled trials comparing corticosteroids with placebo for the treatment of patients with vestibular neuritis.

Data Sources: An electronic search was performed in MEDLINE, EMBASE, Cochrane Library, and CENTRAL databases, and then extensive hand-searching was performed for the identification of relevant studies. No time and language limitations were applied.

Study Selection: Prospective randomized controlled trials comparing corticosteroids with placebo for the treatment of patients with vestibular neuritis.

Data Extraction: Odds ratios (ORs), weighted mean differences (WMD), 95% confidence intervals (CIs), and tests for heterogeneity were reported.

Data Synthesis: Four studies were eventually identified and systematically reviewed. Meta-analysis was feasible for 3 studies. Regarding the recovery of clinical symptoms, the proportion of patients with clinical recovery at 1 month after the initiation of therapy did not differ significantly between the corticosteroids and placebo groups (OR, 1.45; 95% CI, 0.26–8.01; p = 0.67). The proportion of patients with caloric complete recovery was significantly different between the corticosteroids and placebo groups both at 1 (OR, 12.64; 95% CI, 2.6–61.52; p = 0.002; heterogeneity, p = 0.53; fixed effects model) and 12 months (OR, 3.35; 95% CI, 1.45–7.76; p = 0.005; heterogeneity, p = 0.03; random effects model) after the initiation of therapy. The caloric extent of canal paresis at 12 months after the initiation of therapy seemed to differ significantly between patients who received corticosteroids and those who received placebo (WMD, −12.15; 95% CI, −19.85 to −4.46; p < 0.05; heterogeneity, p < 0.05; random effects model).

Conclusion: The present systematic review and meta-analysis, based on the currently available evidence, suggests that corticosteroids improve only the caloric extent and recovery of canal paresis of patients with vestibular neuritis. At present, clinical recovery does not seem to be better in patients receiving corticosteroids. Key Words: Corticosteroids—Meta-analysis—Neuritis—Randomized—Vestibular. Otol Neurotol 31:183–189, 2010.

Vestibular neuritis (VN) is 1 of the 3 most common causes of peripheral vestibulopathy, with its incidence reported to reach 3.5 per 100,000 (1,2). The symptoms of VN include an acute or subacute onset of sustained rotatory vertigo, gait and postural imbalance with tendency to fall, nausea, and vomiting.

The cause of the disease remains unsettled. Initially, inflammation of the vestibular nerve and labyrinth ischemia had been proposed as the possible underlying cause (3–5). Recently, the theory of virus infection has been postulated (2,6). Furthermore, atrophy of the vestibular nerve and sensory epithelium, being similar to the histopathological findings in herpes zoster oticus, has been reported (7). The detection of DNA of herpes simplex virus 1 in human vestibular ganglia, using the methods of polymerase chain reaction, remains an additional sign of virus involvement in the pathogenesis of VN (8–10).

The natural course of VN is characterized by an incomplete recovery. Clinical recovery is achieved via proprioceptive and visual substitution for the unilateral vestibular deficit combined with central vestibular compensation of the imbalance in vestibular tone (11). Several studies have reported continuous or episodic vertigo or unsteadiness in 43 to 53% of patients (12,13). In 1993, Okinaka et al. (14) supported that horizontal semicircular canal paresis occurred in approximately 90% of patients approximately 1 month after the onset of symptoms and in 80% approximately 6 months after the onset
of symptoms, whereas the caloric responses were normalized in only 42% of them. However, it should be noted that the vestibular impairment, deriving from the results of bedside and laboratory tests, does not reflect the subjective clinical complaints and the level of incapacity (15).

Nowadays, the therapeutic choices for VN include (a) corticosteroids, (b) antiviral therapy (acyclovir or valacyclovir), and (c) combination of corticosteroids and antiviral agent. In the acute phase of VN, patients are mostly treated by short-term vestibular suppression. The rationale for treatment of patients with VN with corticosteroids is based on the reports of positive effects of steroid therapy to patients experiencing acute cranial nerves neuroptathies, such as optic neuritis, facial nerve paresis, and idiopathic hearing loss (16–19). In addition, the activation of glucocorticoid receptor was reported to enhance vestibular compensation after acute peripheral vestibular insults in various animal models (20,21).

The purpose of this systematic review was to address the following question: Among patients with VN, is the improvement of clinical symptoms and of the extent of caloric paresis significantly different between patients receiving corticosteroids and those not receiving any drug agent (placebo group)?

PATIENTS AND METHODS

Search Strategy

A computer literature search in MEDLINE, EMBASE, the Cochrane Library (Issue 1, 2008), and CENTRAL electronic databases was performed by the 2 reviewers (J.G. and K.M.) from October 10 to November 10, 2008, to identify studies that answered the question of interest. For this purpose, the following free-text terms were used: “vestibular neuritis/neuronitis” or “idiopathic acute vestibular loss” or “unilateral vestibular loss” combined with “drug therapy” or “steroids/corticosteroids/cortisone/prednisolone/presolone/methylprednisolone/dexamethasone/glucocorticoids” or “treatment” or “therapy” and limited to “human.” In addition, extensive hand-searching of the references of all relevant studies was performed. No time and language limitations were applied.

Selection of Studies

All criteria for inclusion/exclusion of studies in the present systematic review were specified before the literature search. In order for a study to be eligible the following criteria should be met: (a) The study should be a randomized controlled trial and compare any type of corticosteroid therapy with placebo treatment regardless of the route (oral or parenteral), the dose, and the duration of administration. Vestibular sedatives should have been administered in all patients for symptomatic relief regardless of the subsequent therapy with either corticosteroids or placebo. (b) The study should include patients who started therapy in the acute or subacute (within 3 or 5 d from the onset of the disease, respectively) period of the disease. (c) The follow-up protocol should include assessments of patients’ clinical status at least 1 month after the onset of the disease.

The following exclusion criteria were also established: (a) any study including patients with uncontrolled diabetes, severe hypertension, contraindications to receive steroids, and vestibular or cochlear symptoms before recruitment to the study; and (b) any study including pregnant or breastfeeding women.

In case the published articles did not provide all the necessary information for the assessment of potential eligibility, the authors were contacted and asked to provide the missing data.

Studies Identified

The electronic search resulted in the initial identification of 157 publications. Subsequently, the titles of these articles were examined to exclude irrelevant studies, resulting in 34 potentially eligible articles. The abstracts of these articles were examined, and 14 articles that could provide data to answer the research question of interest were identified (Fig. 1). The full texts of these studies were examined thoroughly, resulting in the exclusion of 10 publications.

The references of all the studies in which the full text was retrieved were hand-searched. However, no additional studies that could provide data to answer the research question were identified. Eventually, 4 studies, comparing corticosteroids with placebo agents in patients with VN, were identified (Table 1).

Eligibility of these studies for the present systematic review was assessed independently by 2 of the reviewers (J.G. and K.M.). Any disagreement was resolved unanimously by discussion.

FIG. 1. Flow diagram for study selection.
Data Extraction

Data extraction was performed by 2 of the reviewers (J.G. and K.M.). The following data were recorded from each of the eligible studies: general characteristics (type of study, citation data, number of patients included, and their baseline characteristics), procedures (type of randomization, inclusion criteria, protocol of follow-up, protocol of corticosteroid therapy or placebo, and number of patients who dropped out of the study), and outcome data (vestibular clinical signs, the improvement, or recovery of unilateral vestibular loss according to the caloric test findings).

Outcomes

The outcome measures chosen for this systematic review and meta-analysis were as follows: (i) Clinical recovery of patients from vestibular symptoms at 1, 3, and 6 months after the initiation of therapy. Assessment of clinical symptoms was conducted either after the examination of patients (vertigo, spontaneous nystagmus, or tendency to fall) or after the report of their subjective handicap, using specific questionnaires, such as Dizziness Handicap Inventory (DHI). (ii) Caloric complete recovery of unilateral vestibular loss at 1 and 12 months after the initiation of therapy according to the findings of electronystagmography (ENG) after caloric irrigation. The magnitude of canal paresis was calculated using Jongkee’s formula (22). The rate of Jongkee’s formula less than 25% was considered as normal, indicating the complete recovery of canal paresis. (iii) And lateralization in ENG caloric test 1 and 12 months after the initiation of therapy.

Quantitative Data Synthesis

The dichotomous data results for each of the eligible studies for meta-analysis were expressed as an odds ratio (OR) with 95% confidence intervals (CI). These results were combined for meta-analysis using the Mantel/Haenszel model, when using the fixed effects method, and the DerSimonian and Laird model, when using the random effects method. When the outcome measure of interest was a continuous variable, the difference was calculated using Jongkee’s formula (22). The rate of Jongkee’s formula less than 25% was considered as normal, indicating the complete recovery of canal paresis. (iii) And lateralization in ENG caloric test 1 and 12 months after the initiation of therapy.

TABLE 1. Demographic data of the studies included in the systematic review

<table>
<thead>
<tr>
<th>Study number</th>
<th>Authors, publication year, journal</th>
<th>Design</th>
<th>Sample size</th>
<th>Sample size of steroids group</th>
<th>Sample size of placebo group</th>
<th>Randomization—patient allocation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Strupp et al., 2004, N Engl J Med</td>
<td>Randomized</td>
<td>73</td>
<td>35</td>
<td>38</td>
<td>Computer-generated block</td>
</tr>
<tr>
<td>2</td>
<td>Shupak et al., 2008, Arch Neurol</td>
<td>Quasi-randomized</td>
<td>30</td>
<td>15</td>
<td>15</td>
<td>Pseudorandomization</td>
</tr>
<tr>
<td>3</td>
<td>Ariyasu et al., 1990, Arch Neurol</td>
<td>Randomized</td>
<td>20</td>
<td>10</td>
<td>10</td>
<td>NR</td>
</tr>
<tr>
<td>4</td>
<td>Kitahara et al., 2003, Otol Res</td>
<td>Quasi-randomized</td>
<td>36</td>
<td>18</td>
<td>18</td>
<td>Pseudorandomization</td>
</tr>
</tbody>
</table>

NR indicates not reported.

RESULTS

Four studies fulfilled the inclusion criteria. Characteristics of the eligible studies are listed in Tables 1 and 2.

Systematic Review

The eligible studies were published between 1990 and 2008. Two studies used a truly randomization method for allocation of patients to groups, and 2 studies used quasirandomization methods. Study size ranged from 20 to 73 patients, whereas 159 patients were reviewed in total (corticosteroids group = 78, placebo group = 81; Table 1).

Regarding the type of corticosteroid used, in 3 studies, the patients received methylprednisolone, whereas the patients of the remaining study received prednisone. Details about the daily dose and the length of regimen used in each study group are provided in Table 2.

In all the eligible studies, the follow-up procedure included assessments of the patients for at least 1 month (Table 2). In 1 study, patient’s recovery was evaluated only at 1 month after the initiation of therapy (23). Two studies included only long-term follow-up of patients (24,25).

In 1 study, the researchers selected the occurrence of vestibular clinical signs at 1 month after the initiation of therapy as their main outcome measure (26). Recovery, according to the findings of caloric irrigation, at 1 and 12 months after the onset of therapy was used as the main outcome measure in 3 studies (23,24,26). Improvement of caloric paresis at 1 and 12 months after
the initiation of treatment was assessed in 2 studies (24,26). The initial severity of canal paresis of patients with VN, based on caloric findings of ENG, was reported in 2 studies (Table 2).

Two studies supported that corticosteroids improves the long-term recovery of peripheral vestibular function in patients with VN (24,25). The other 2 studies reported that therapy with corticosteroids provides earlier improvement, regarding the recovery of peripheral vestibular function, but does not improve the long-term prognosis of patients with VN (23,26).

**Meta-Analysis**

Of 4 studies, 3 provided relevant data for quantitative synthesis being eligible for our meta-analysis.

**Recovery of Clinical Symptoms**

Only 1 study provided data regarding the clinical recovery, and for this reason, meta-analysis was not feasible (26). In this study, the proportion of patients with recovery of clinical symptoms (defined as lack of signs and symptoms) at 1 month after the initiation of therapy did not differ significantly between the corticosteroids and placebo groups (OR, 1.45; 95% CI, 0.26–8.01; p = 0.67). The same was true at 3 (OR, 1.71; 95% CI, 0.40–7.29; p = 0.47) and 6 months (OR, 1.75; 95% CI, 0.40–7.66; p = 0.46) after the initiation of therapy.

The lack of significant difference between the corticosteroids and placebo groups at the first month of assessment was also revealed based on the results of DHI (WMD, 5.10; 95% CI, 17.52 to 17.72; p = 0.43).

**Caloric Complete Recovery**

The proportion of patients with caloric complete recovery at 1 month after the initiation of therapy was significantly different between corticosteroids group and placebo group according to the results from 2 studies (OR, 12.64; 95% CI, 2.6–61.52; p = 0.002; heterogeneity, p = 0.53; fixed effects model; Fig. 2) (23,26).

Regarding the assessments of caloric paresis 12 months after the initiation of therapy, the proportion of patients with caloric compete recovery was significantly different between the corticosteroids and placebo groups (OR, 3.35; 95% CI, 1.45–7.76; p = 0.005; heterogeneity, p = 0.03; random effects model; Fig. 3).

When only the studies that reported a detailed analysis of the randomization procedure and patient allocation were analyzed, caloric complete recovery of canal paresis at 12 months after the initiation of therapy differed significantly between the corticosteroids and placebo groups (OR, 6.35; 95% CI, 2.25–17.39; p < 0.05).

**Lateralization in ENG Caloric Test**

A meta-analysis regarding the findings of lateralization in caloric test at 1 month after the initiation of therapy was not feasible because results from only 1 study are available.

However, the lateralization in the caloric test at 12 months after the initiation of therapy seemed to differ

---

**Table 2. Characteristics of the studies included in the systematic review**

<table>
<thead>
<tr>
<th>Study number</th>
<th>Study</th>
<th>Percent canal paresis at presentation (corticosteroids/placebo, %)</th>
<th>Days of onset of palsy to start of treatment (corticosteroids/placebo, mean ± SD)</th>
<th>Corticosteroids group</th>
<th>Placebo group</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Strupp et al.</td>
<td>78.7 ± 15.8 / 78.9 ± 24</td>
<td>183 ± 11.1 / 177 ± 11</td>
<td>Methylprednisolone (100 mg 1 d, 40 mg 2 d, 20 mg 3 d, 10 mg 4 d, 5 mg 5 d)</td>
<td>Lactose Dimenhydrinate</td>
</tr>
<tr>
<td>2.</td>
<td>Shupak et al.</td>
<td>59 ± 27 / 58 ± 30</td>
<td>NR</td>
<td>Prednisone (1 mg/kg body weight, tapering down for 15 d)</td>
<td>Lactose Promethazine</td>
</tr>
<tr>
<td>3.</td>
<td>Ariyasu et al.</td>
<td>NR</td>
<td>NR</td>
<td>Methylprednisolone (32 mg 4 d, tapering down for 8 d)</td>
<td>Lactose Sodium bicarbonate</td>
</tr>
<tr>
<td>4.</td>
<td>Kitahara et al.</td>
<td>NR</td>
<td>NR</td>
<td>Methylprednisolone (500 mg, tapering down for 7 d)</td>
<td>SR</td>
</tr>
</tbody>
</table>

---

*According to Jonkee’s formula.

*Only slow-phase eye velocity was calculated.

---

*Copyright © 2010 Otology & Neurotology, Inc. Unauthorized reproduction of this article is prohibited.*
significantly between patients who received corticosteroids and those who received placebo (WMD, 12.15; 95% CI, −19.85 to −4.46; p < 0.05; heterogeneity, p < 0.05; random effects model; Fig. 4).

**DISCUSSION**

The current systematic review and meta-analysis supports that the administration of corticosteroids to patients with VN seems to provide benefit only to the caloric recovery of canal paresis and not to the recovery of clinical symptoms.

In this systematic review and meta-analysis, the recovery of vestibular signs was chosen as the main efficacy measure because the primary goal of medical practice remains the improvement of patient’s clinical symptoms. However, only one of the eligible studies included recovery of clinical symptoms (defined by lack of symptoms and signs) of patients among their outcomes. The results for this study do not support the presence of a benefit from administering corticosteroids to patients with VN compared with placebo after 1, 3, and 6 months from presentation (26). However, as the previously mentioned conclusion derives from the results of a single study, it should be interpreted with caution.

It should be noted that in the aforementioned study by Shupak et al. (26), the authors report a significant increase in the “complete resolution” of patients receiving corticosteroids 3 and 6 months after presentation compared with those receiving placebo. This outcome, however, is different from the outcome “clinical recovery” that was used in the present meta-analysis because in addition to the absence of clinical symptoms, it also includes a normal otoneurologic examination, DHI score less than 6, caloric test lateralization less than 25%, and normal ENG findings. Nevertheless, it should be stressed that in that same study the authors report that this difference in favor of corticosteroids in complete resolution was still not present 12 months after presentation.

It should be noted that proper evaluation of the rehabilitation of patients with VN requires both the assessment of “static” symptoms (without head movement), such as spontaneous nystagmus, vertigo, tendency to fall, and “dynamic” dysfunction. This last dysfunction manifests in the form of a retinal slip of images of the visual scene with oscillopsia during rapid, high-frequency head movements, walking, and running because of the insufficiency of the vestibular ocular reflex (VOR) (27,28). Electronystagmography caloric test is one of the assessment methods of VOR, indicating the improvement of canal paresis of patients with VN.

In the present systematic review and meta-analysis, patients who received corticosteroids had significantly higher probability of caloric complete recovery compared with those who received placebo, both at the 1st and 12th month of assessment after the initiation of therapy. The benefit from administering corticosteroids to
patients with VN was also revealed at the assessment of the extent of caloric paresis 12 months after the initiation of therapy.

A plausible explanation regarding the beneficial effect of corticosteroids on the complete recovery of caloric paresis might be the reduction of the swelling of the vestibular nerve (that causes a mechanical compression of the nerve within the temporal bone) through the anti-inflammatory action of the corticosteroids. Moreover, in animal experiments, corticosteroids reported to have an effect not only on the inflammatory process but also on the central compensation of the unilateral labyrinthine deficit (29,30).

Considering the natural course of VN, the present systematic review confirms the previously reported lack of correlation between recovery of clinical symptoms and of caloric lateralization regardless of the treatment strategy (corticosteroids or placebo) (12). Most patients feel symptom-free 1 to 6 weeks after onset of disease, but the functional restitution of the vestibular nerve demands long-term central compensation.

It should be noted, however, that the results of the present systematic review are liable to certain limitations. Revealing the statistical significance of treatment benefit in studies of VN requires a large number of patients because of the variable spontaneous recovery profile of patients. The long-term prognosis of patients with VN was assessed mainly by the ENG caloric test, which includes inherent limitations. The caloric test assesses only the horizontal semicircular canal or the portion of the superior vestibular nerve that innervates this canal. However, approximately one-third of patients with VN have loss of function in the inferior vestibular nerve as well; the persistent dysfunction of which may be responsible for the lack of recovery from the clinical symptoms (31–33). Moreover, caloric response is dependent on the morphology of the ear, the pneumatization of mastoid cells, and the patient’s alertness (34–36). Finally, it should be noted that the caloric test assesses only the low-frequency VOR (up to 0.003 Hz), being unable to evaluate the high-frequency function of the peripheral vestibular system (37). The dynamic tone imbalance can be assessed clinically by provoking a directional head-shaking nystagmus or testing of the high-frequency VOR with head-impulse test (37–39). Thus, the reported long-term handicap of patients with VN might be justifiable, despite normal ENG caloric findings (37,40).

CONCLUSION
The present systematic review and meta-analysis, based on the currently available evidence, suggests that corticosteroids improve only the caloric extent and recovery of canal paresis of patients with VN. At present, clinical recovery does not seem to be better in patients receiving corticosteroids. Further well-designed randomized controlled trials are needed to assess with more confidence the potential contribution of corticosteroids to the complete resolution of VN.

Acknowledgments: The authors thank the following persons for their support in this work: Strupp M. (Germany), Shupak A. (Israel), Ariyasu L. (United States), and Kiaihara T. (Japan).

REFERENCES
CORTICOSTEROIDS IN VESTIBULAR NEURITIS


34. Davis RJ, Mann RC. The effects of alerting tasks on caloric induced vestibular nystagmus. Ear Hear 1987;8:58–60.


