Endolymphatic Hydrops (Meniere's Disease) Tests

Number: 0571

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.

Aetna considers dehydration testing with glycerol, urea, or other osmotic diuretics to verify the suspicion of endolymphatic hydrops (Meniere's disease) medically necessary only in members with atypical presentations of this disease.

Aetna considers dehydration testing experimental and investigational for other indications because its effectiveness has not been established.

Aetna considers genetic testing of KCNE1, KCNE3, SIK1, SLC8A1, and SLC26A4 gene mutation for the diagnosis of endolymphatic hydrops (Meniere's disease) experimental and investigational because its effectiveness has not been established.

Aetna considers testing for antibodies against inner ear antigens for the diagnosis of Meniere's disease experimental and investigational because its effectiveness has not been established.

Aetna considers vestibular evoked myogenic potential (VEMP) for the diagnosis of Meniere disease and monitoring of disease

Policy History

Last Review  06/08/2017
Effective: 11/09/2001
Next Review: 06/07/2018

Definitions

Additional Information

Clinical Policy Bulletin Notes
progression experimental and investigational because its effectiveness for these indications has not been established.

See also CPB 0238 - Chronic Vertigo (../200_299/0238.html), CPB 0467 - Vestibular Autorotation Test (VAT) (../400_499/0467.html), CPB 0514 - Meniere's Disease Surgery (0514.html), and CPB 0564 - Electrocochleogram and Perilymphatic Pressure Measurement (../500_599/0564.html).

Background

Dehydration Testing:

Osmotic diuretics are able to reduce endolymphatic pressure and volume, and hence improve peripheral auditory and vestibular function. After baseline audiometric testing, a glycerol, urea or other osmotic diuretic is administered. Repeat audiometric testing is performed at 3 hours (and sometimes at 1 and 2 hours) post-ingestion. The test is considered positive if: (i) there is a 10 dB or more improvement at 2 or more frequencies (250 to 2,000 Hz), or (ii) there is a 12 % or greater improvement in speech discrimination scores. The test is associated with a number of unpleasant side effects, including headache, nausea, thirst, diarrhea, emesis, diuresis, and dizziness.

Because dehydration tests are relatively specific for endolymphatic hydrops, they may be useful in confirming the presence of disease in patients with atypical presentations. However, because the tests are relatively insensitive, they are not useful to rule out endolymphatic hydrops or as screening tests for the disease.

Although the tests appear relatively specific for endolymphatic hydrops, they are relatively insensitive. Snyder (1974) reported the experience using the glycerol test in 122 patients with a combination of sensorineural hearing loss and tinnitus or vestibular symptoms, in whom endolymphatic hydrops was considered a diagnostic possibility. Fifty percent of patients ultimately found to have endolymphatic hydrops had positive tests. One false-positive was found among the positive tests. In a series of 95 patients with Meniere's disease, Akioka et al (1990) found 47 % to have a positive glycerol dehydration test. Stahle
and Klockhoff (1986) reported 60% of patients with Meniere's disease were found to have positive tests, and that positive tests were only found in ears with Meniere's disease.

Dehydration tests have not been proven to be useful in selecting patients with endolymphatic hydrops who are most likely to respond to surgery. Some authors have suggested that patients with positive glycerol tests are more likely to have beneficial responses to endolymphatic sac decompression, but statistical proof of such a relationship is lacking.

Whether a Meniere's disease patient will have a positive test or not seems to depend in part on the phase of the disease. Tests are more likely negative very early and very late in the course of disease, although the stage of the disease is not predictable from the results of the dehydration testing.

Critics of dehydration testing note that the test is unpleasant, not adequately sensitive, impractical, and subject to significant placebo effects. According to Fagan (1999), dehydration studies are little used these days because they are unpleasant and time consuming. There is only anecdotal evidence that positive responders to dehydration tests may be more likely to respond to endolymphatic sac decompression. Some investigators have found that the results of dehydration testing are highly affected by suggestion to the patients as to what they should expect. These investigators suggest that the use of the dehydration test to select patients for surgery risks induces a bias toward more placebo responders.

In a critical review of diagnostic testing in endolymphatic hydrops, Arts et al (1997) concluded: "At this point, the clinical use of dehydration testing is unclear at best. Despite many legitimate questions with regard to its practicality and sensitivity, there is considerable evidence that a real phenomenon, specific for endolymphatic hydrops, underlies this test. Given this, the test may be helpful in verifying the suspicion of endolymphatic hydrops in patients with atypical presentations. It is unlikely, however, that the choice of therapy will be altered by the results of this test in many instances".
An UpToDate review on “Meniere disease” (Dinces and Rauch, 2014) does not mention the use of dehydration testing as a diagnostic tool.

**Note:** Osmotic diuretics such as urea and isosorbide that can be taken orally have also been used as treatment for endolymphatic hydrops.

**Genetic Testing:**

In a case-report, Yoshida et al (2015) reported magnetic resonance imaging (MRI) findings in a 13-year old girl with an SLC26A4 gene mutation who had low-frequency sensori-neural hearing loss (SNHL). The patient exhibited bilateral and symmetric low-frequency SNHL. Upon genetic testing, a heterozygous c.1105A > G (p.K369E) mutation of the SLC26A4 gene was detected. Mild endolymphatic hydrops in the right cochlea and marked endolymphatic hydrops in the left vestibulum were seen by MRI 4 hours after an intravenous gadolinium injection. The authors concluded that this was the first reported case of a patient with the SLC26A4 gene mutation c.1105A > G (p.K369E) who had low-frequency SNHL. They stated that co-occurrence of cochlear and vestibular endolymphatic hydrops suggested an association with that pathology. These preliminary findings need to be validated by well-designed studies.

Lee and co-workers (2015) examined the prevalence, inheritance patterns, and clinical characteristics of familial Meniere's disease (MD) in a South Korean population. Direct and telephone interviews were performed for 286 definite MD patients and their family members who were suspected of having MD. The diagnosis of MD in family members was made by obtaining a detailed history, performing basic neurotological examinations and reviewing hearing test results. The clinical characteristics as well as the prevalence and inheritance patterns of familial MD were analyzed. The prevalence of familial Meniere-like syndrome (at least 1 family member with definite MD and other members with probable MD) and definite familial MD (2 or more family members with definite Meniere's disease) were 9.8 % and 6.3 %, respectively, and the most common inheritance pattern was
autosomal dominant with incomplete penetrance. The significant clinical characteristics of familial cases were an early disease onset and a higher prevalence of migraines. The authors concluded that this was the first report describing the genetic aspects of MD in a single large Asian population. The prevalence of definite familial MD was 6.3% with an incomplete autosomal dominant inheritance pattern in most cases. Early-onset age and a high prevalence of migraines were significant clinical features of familial MD in this South Korean population. They stated that these data could provide a basis for the analysis of the genetic mechanism of familial MD in Asian populations.

Li and colleagues (2016) noted that MD is defined as an idiopathic disorder of the inner ear characterized by the triad of tinnitus, vertigo, and sensorineural hearing loss. Although many studies have evaluated the association between variants in the KCNE1 or KCNE3 gene and MD risk, debates still exist. These researchers evaluated the association between KCNE gene variants, including KCNE1 rs1805127 and KCNE3 rs2270676, and the risk of MD by a systematic review. They searched the literature in PubMed, SCOPUS and Embase through May 2015, and calculated pooled OR and 95% CIs using a fixed-effects model or a random-effects model for the risk to MD associated with different KCNE gene variants. The heterogeneity assumption decided the effect model. A total of 3 relevant studies, with 302 MD cases and 515 controls, were included in this meta-analysis. The results indicated that neither the KCNE1 rs1805127 variant (for G versus A: OR = 0.724, 95% CI: 0.320 to 1.638, p = 0.438), nor the KCNE3 rs2270676 variant (for T versus C: OR = 0.714, 95% CI: 0.327 to 1.559, p = 0.398) was associated with MD risk. The authors concluded that based on current evidence from published studies, neither of the 2 variants from KCNE was significantly associated with the risk of MD. They stated that larger studies with mixed ethnicity subjects and stratified by clinical and subclinical characteristics are needed to validate these findings.

Teggi and associates (2017) examined the role of polymorphisms belonging to genes involved in the regulation of ionic homeostasis in Caucasian patients with MD. These investigators recruited 155 patients with definite MD and 186 controls (Control
Group 1) without a lifetime history of vertigo, overlapping with patients for age and rate of hypertension. These researchers validated the positive results on 413 Caucasian subjects selected from a European general population (Control Group 2). The clinical history for migraine and hypertension was collected; genomic DNA was characterized for a panel of 33 SNPs encoding proteins involved in ionic transport. They found a higher rate of migraineurs in MD subjects compared to Group 1 (46.8 versus 15.5 %, p = 0.00005); 4 SNPs displayed differences in MD patients compared to Group 1 controls: rs3746951 and rs2838301 in SIK1 gene, rs434082 and rs487119 in SLC8A1; the p values of Chi-squared test for genotype frequencies are 0.009, 0.023, 0.009 and 0.048, respectively. SLC8A1 gene encodes for Na+-Ca++ exchanger, while SIK1 gene encodes for Salt Inducible Kinase 1, an enzyme associated with Na+-K+ ATPase function. The validation with Control Group 2 displayed that only rs3746951 and rs487119 are strongly associated to MD (p = 0.001 and p = 0.0004, respectively). The authors concluded that these findings support the hypothesis that a genetically induced dysfunction of ionic transport may act as a predisposing factors to develop MD.

**Vestibular Evoked Myogenic Potentials:**

An UpToDate review on “Meniere disease” (Dinces, 2015) states that “Laboratory testing -- Tests for antibodies against inner ear antigens have been described, but are not considered to be clinically useful and are not part of a routine evaluation for Meniere disease .... Tests for endolymphatic hydrops -- The vestibular evoked myogenic potential (VEMP) is a newer test that shows promise for diagnosis and monitoring. Cervical VEMP (cVEMP) is an inhibitory sacculocollic reflex test that shows characteristic changes in symptomatic ears of Meniere patients, and may detect early saccular hydrops before the onset of classic Meniere symptoms. Ocular VEMP (oVEMP) engages both utricular and saccular afferent nerve fibers and may also be useful in assessment of Meniere patients. In addition to diagnosis, VEMP may be useful for monitoring patients for disease progression, and to identify the active ear in patients with bilateral disease. VEMP is an emerging technology that has not yet been standardized or fully validated clinically”.


Zhang and colleagues (2015) evaluated the clinical diagnostic value of VEMPs for endolymphatic hydrops (EH) by systematic review and meta-analysis. The pooled sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio (OR) and area under summary receiver operating characteristic curves (AUC) were calculated. Subgroup analysis and publication bias assessment were also conducted. The pooled sensitivity and the specificity were 49 % (95 % confidence interval [CI]: 46 % to 51 %) and 95 % (95 % CI: 94 % to 96 %), respectively. The pooled positive likelihood ratio was 18.01 (95 % CI: 9.45 to 34.29) and the pooled negative likelihood ratio was 1.54 (95 % CI: 0.47 to 0.61); AUC was 0.78 and the pooled diagnostic OR of VEMPs was 39.89 (95 % CI: 20.13 to 79.03). The authors conclude that the findings of this meta-analysis demonstrated that VEMPs test alone is insufficient for MD or delayed EH diagnosis, but that it might be an important component of a test battery for diagnosing MD or delayed EH. Moreover, VEMPs, due to its high specificity and non-invasive nature, might be used as a screening tool for EH.

Johnson and associates (2016) measured ocular VEMPs (oVEMPs) and cervical VEMPs (cVEMPS) in MD patients with confirmed cochlear hydrops and in the normal ears of volunteers. oVEMPs and cVEMPs were measured in 18 patients with a symptomatic diagnosis of MD and tone burst electrocochleographic confirmation of hydrops, and in the ears of 22 volunteers. Threshold measures: For cVEMP: no significant differences between Meniere's ears and controls; for oVEMP: significantly elevated thresholds in affected ears of Meniere's ears compared with their unaffected ears, but not with controls. Latency measures: cVEMP N1 peaks were significantly prolonged compared with the left and right ears of controls, but not with the non-affected ear. Amplitude measures: cVEMP P1N1 and N1P2 measures were significantly reduced compared with the right ear of controls, but not with the non-affected ear. For oVEMP, N2P2 amplitudes were significantly reduced compared with both ears of controls but not with the non-affected ear. The authors concluded that abnormalities of oVEMPs and cVEMPs were found in 18 MD patients who had an independent confirmation of cochlear hydrops. They noted that the overlap of the results from
MD patients compared with normal controls limited the use of VEMP abnormalities as a sole reliable diagnostic test for MD.

Maxwell and colleagues (2017) examined the effect of increased intracranial pressure on oVEMP amplitudes and frequency tuning in patients with MD to elucidate whether oVEMPS recorded under such conditions could provide a simple and accurate diagnostic test for MD. A total of 10 patients with certain unilateral MD (mean age of 48.2 years, range of 25 to 75, 6 males and 4 females) as confirmed by a locally enhanced inner ear MRI (LEIM) were enrolled in this study. Air-conducted tone-burst oVEMP amplitudes were measured in response to 500-Hz and 1,000-Hz in the horizontal plane (0 degree), a 20-degree head-down position. Tilting the patients from the horizontal position to the 20-degree head-down position led to a large reduction in oVEMP amplitudes to the 500-Hz tone burst (3.02 μV versus 1.17 μV, p = 0.005) and to a smaller one in the 1,000-Hz tone burst (2.28 μV versus 1.78 μV, p = 0.013) in the Meniere's ear. Accordingly, the 500/1,000-Hz frequency-tuning ratio was significantly decreased in the Meniere's ear as a result of this manoeuver (1.36 versus 0.75, p = 0.005). The authors concluded that oVEMP amplitudes and frequency tuning in MD patients showed a similar behavior to that found in healthy control subjects. They stated that oVEMP testing of putative MD patients in the tilted position is therefore unlikely to be diagnostically useful.

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<tr>
<th>CPT Codes / HCPCS Codes / ICD-10 Codes</th>
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<td><strong>Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by &quot;+&quot;:</strong></td>
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<tr>
<td>There are no specific codes for dehydration testing for endolymphatic hydrops, vestibular evoked myogenic potential (VEMP), antibodies against inner ear antigens:</td>
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<td>CPT codes not covered for indications listed in the CPB:</td>
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<td>81406</td>
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Other CPT codes related to the CPB:

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<tr>
<th>Code</th>
<th>Description</th>
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<td>69805</td>
<td>Endolymphatic sac operation</td>
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ICD-9 codes covered if selection criteria are met:

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<tr>
<th>Code</th>
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<td>Abnormalities of gait and mobility</td>
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<tr>
<td>R42</td>
<td>Dizziness and giddiness</td>
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The above policy is based on the following references:


15. Dinces EA. Meniere disease. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed April 2015.


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Amendment to
Aetna Clinical Policy Bulletin Number:
0571 Endolymphatic Hydrops (Meniere’s Disease) Tests

There are no amendments for Medicaid.

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