Clinical examination of labyrinthine-defective patients out of the vertigo attack: sensitivity and specificity of three low-cost methods

La valutazione clinica del paziente labirintopatico dopo la fase acuta: sensibilità e specificità di tre metodiche a basso costo

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Summary

Many reports have appeared in the medical literature concerning the clinical examination at the bedside of patients with vertigo and, even if few controversial opinions exist, the observation of one or more kinds of nystagmus is generally regarded as suggesting an organic aetiology. So far, the presence of nystagmus has been generally considered to be crucially important for clinicians who are daily asked to differentiate between an “organic” cause of vertigo (for example, a labyrinthine dysfunction) and a “non-organic” cause of vertigo, such as a panic disorder. Albeit, it should not be forgotten that the central nervous system is able to resolve the asymmetry of vestibulo-ocular reflexes, due to a peripheral vestibular failure, by means of compensatory mechanisms so that nystagmus is rapidly abolished after the acute attack of vertigo. In addition, visual fixation elicits sub-cortical inhibitory pathways to the vestibular nuclei so that spontaneous nystagmus is remarkably reduced by light. In order to more easily detect nystagmus, attempts have been made to minimize the interference of visual fixation by means of positive lenses (Frenzel’s glasses) and light occluding masks with infrared cameras (videonystagmoscopy) which have in part replaced direct observation of the patient’s eyes, albeit no systematic validation of the advantages has been reported yet. To investigate the usefulness of these 3 low-cost methods to detect nystagmus, 528 outpatients presenting peripheral vestibular hypofunction, diagnosed by a complete audiological and vestibular examination, including caloric tests, were enrolled in the present study, while 133 subjects with normal vestibular function acted as a control group. All patients and control subjects underwent a standardized clinical examination based on search for spontaneous, positioning and head-shaking nystagmus detected by direct observation of patient’s eyes, Frenzel’s glasses and videonystagmoscopy. Specificity of the three techniques were 35.6, 43.7 and 91.6, whilst sensitivity was 88.7, 88.7 and 84.2, respectively. Finally, discriminant analysis based

Key words
Vertigo • Labyrinthine dysfunction • Nystagmus • Frenzel’s glasses • Videonystagmoscopy

Parole chiave
Vertigine • Disfunzione labirintica • Nistagmo • Occhiali di Frenzel • Videonistagmoscopia

Riassunto

Nella letteratura medica si rilevano molti dati riguardanti l’eseame clinico, non strumentale, del paziente affetto da vertigine e, con pochi pareri discordanti, è opinione diffusa che la presenza di uno o più tipi di nistagmo sia indice di un’ezioologia organica. Pertanto, la presenza di un nistagmo rilevabile è considerata di importanza cruciale per i clinici che giornalmente si debbono occupare di distinguere tra cause “organiche” di vertigine (come, ad esempio, una disfunzione labirintica) e cause “non organiche” come i disturbi da attacco di panico. Tuttavia si deve ricordare che i meccanismi di compenso, messi in atto dal sistema nervoso centrale per diminuire gli effetti di un’asimmetria dei riflessi vestibolo-oculo-motori dovuta ad un deficit labirintico, sono in grado di abolire rapidamente il relativo nistagmo dopo la fase acuta della vertigine. Inoltre, la fissazione visiva, attraverso l’attivazione delle vie cerebello-vestibolari inhibitrici, è in grado di ridurre e/o abolire tali nistagmi spontanei. Allo scopo di minimizzare quest’interruzione della luce ambientale sul rilevamento del nistagmo di origine labirintica, i ricercatori hanno tentato di ridurre l’effetto della fissazione visiva grazie all’impiego di lenti fortemente positive (occhiali di Frenzel) e di maschere occludenti dotate di diodi e videocamere all’infrarosso (videonistagmoscopia) che hanno parzialmente sostituito l’osservazione diretta degli occhi del paziente anche se gli eventuali vantaggi di tali tecniche non sono ancora stati sottoposti ad una verifica sistematica. Pertanto, lo scopo di questo studio è stato quello di verificare la capacità dei 3 sovracitati metodi nel rilevamento clinico del nistagmo in un campione di 528 pazienti ambulatoriali affetti da ipofunzione labirintica di diversa origine, ben documentata da esami audiometrici e vestibolari completi di prove caloriche. Un gruppo di 133 soggetti con funzione vestibolare normale è stato selezionato come gruppo di controllo. Sia i pazienti che i soggetti normali sono stati sottoposti ad un esame clinico standardizzato e basato sul rilevamento del nistagmo spontaneo, di posizione ed a manovra di scuotimento del capo mediante l’osservazione diretta degli occhi del paziente in ambiente illuminato, l’uso degli occhiali di Frenzel e
on the presence/absence of at least one kind of nystagmus was computed for each technique and showed that videonystagmoscopy allowed the examiner to correctly classify both pathological and normal subjects more frequently (> 77% of cases) than the other two methods (about 50%). It is concluded that only videonystagmoscopy is an acceptable technique for screening a labyrinth defect in a population of outpatients with vertigo.

**Introduction**

Vertigo has been included as one of the first ten causes of referral to the Emergency Unit but it is a very common symptom also in general practice. Systematic reviews, both in primary care and in combined otolaryngology and neurology multidisciplinary clinic, clearly indicate that vertigo is caused by a peripheral vestibular disorder, in most cases, even if clinicians must be aware of a possible psychogenic origin and that neurological diseases, such as acute stroke syndrome, multiple sclerosis and cerebral tumours are relatively uncommon causes. Therefore, an important aspect of the management of patients with vertigo is differentiation between peripheral and central involvement of the vestibular system. To this end, a meticulous clinical history and evaluation of the associated symptoms are useful diagnostic tools. Vertigo of central origin is, to a large extent, associated with neurological symptoms (diplopia, ataxia, headache, dysarthria) whilst vertigo, due to peripheral causes, is often associated with otologic symptoms, such as tinnitus and hearing loss. Bearing in mind that it is sometimes difficult to distinguish between otologic causes of vertigo (i.e., vestibular neuritis, Ménière’s disease, viral labyrinthitis, perilymphatic fistula and acoustic neuroma) and that a definitive diagnosis requires specific and expensive equipment for neuro-otologic and audiometric investigations, a first orientating examination should be performed in order to identify the presence of a labyrinth defect in order to proceed with a correct diagnostic workup. For this purpose, various techniques in the screening of vestibular function, at the bedside, have been proposed, all of which based on the identification of a spontaneous, positional or provoked nystagmus that could suggest asymmetry of the vestibulo-ocular reflexes, due to canal paresis, in most cases.

During the acute attack of peripheral vestibular vertigo, patients usually present a spontaneous nystagmus with the fast phase beating to the intact labyrinth, ataxia and or/a tendency to fall towards the affected side and intense neurovegetative symptoms (nausea, vomiting); these symptoms represent the basis of an easy differential diagnosis. With time, clinicians should be aware that nystagmus of labyrinthine origin, with the exception of the paroxysmal positional type, is rapidly abolished by central compensation and adaptive mechanisms so that it could be difficult to discover after the acute attack. In addition, nystagmus, due to a peripheral vestibular disorder, with the exception of the benign paroxysmal type, is remarkably reduced by visual fixation that activates the cerebellar inhibitory projections to the vestibular nuclei thus this observation may be conditioned by the lighting. In addition, it should be remembered that the use of vestibular sedatives rapidly reduces symptoms and clinical signs. Taken together, these factors often make clinical identification of nystagmus difficult following the acute attack of vertigo. The most common, non-invasive and low-cost procedures used to detect nystagmus are based on the direct observation of the patient’s eye, the use of Frenzel’s glasses which have + lenses that partially prevent fixation and of a light-occluding mask with infrared light-emitting diodes and one or two infrared CCD cameras connected to a portable video-monitor (videonystagmoscopy). Even if there is little experimental evidence that videonystagmoscopy is more reliable than both direct observation and Frenzel’s lenses, since these latter do not completely eliminate gazing and, therefore, patients tend to suppress nystagmus and of a light-occluding mask with infrared light-emitting diodes and one or two infrared CCD cameras connected to a portable video-monitor (videonystagmoscopy). The purpose, therefore, of the present study was to determine the sensitivity and specificity of these physical and basic instrumental examinations with respect to the presence of a peripheral vestibular hypofunction, as diagnosed by a complete audiological and vestibular examination including caloric tests, in a large population of patients with vertigo, as a consequence of a peripheral vestibular disorder, during compensation.

**CLINICAL EXAMINATION OF LABYRINTHINE-DEFECTIVE PATIENTS**

Con videonistagmoscopio dotato di doppia camera all’infra-roso, la specificità dei tre metodi di osservazione è risultata di 35,6, 43,7 e 91,6, mentre la sensibilità è stata rispettivamente di 88,7, 88,7 e 84,2. In fine l’analisi discriminante, basata sul binomio assenza/presenza di almeno un tipo di nistagmo, ha evidenziato che la videonistagmoscopia consente di classificare correttamente entrambi i soggetti patologici e il controllo in una percentuale superiore al 77% mentre le altre due tecniche si sono attestate a ridosso del 50%. La conclusione principale è stata che soltanto la videonistagmoscopia può essere considerata una tecnica soddisfacente nello screening clinico dei pazienti ambulatoriali affetti da vertigine.
Materials and methods

Enrolled in the study were 528 patients, selected in the University Hospital Centre for Vestibular Diagnosis and Rehabilitation, University of Modena, Italy, on the basis of a well-diagnosed peripheral vestibular hypofunction and 133 subjects with normal vestibular function, well-matched for sex and age in the period 2001-2003. The study group thus comprised 231 males and 430 females, mean age 54.6 years (range 14-80, SD = 15.9). None of these patients were examined during the acute attack of vertigo. All patients and controls were submitted to a complete audiological and vestibular examination by the staff personnel. The computerized electro-oculographic battery included tests for exploring oculomotor (saccades and smooth-pursuit) and optokinetic functions, spontaneous and gaze nystagmus, 3 cycles of sinusoidal rotation testing with a maximum speed of 60°/sec for vestibulo-ocular reflex and bithermal irrigation (30 °C and 44 °C) of both ear canals for labyrinthine activity. The vestibular paresis formula of Jongkees et al. was used 24: \[
\frac{\left( R \ 30 \ ^\circ \ C + R \ 44 \ ^\circ \ C - L \ 30 \ ^\circ \ C - L \ 44 \ ^\circ \ C \right)}{\left( R \ 30 \ ^\circ \ C + R \ 44 \ ^\circ \ C + L \ 30 \ ^\circ \ C + L \ 44 \ ^\circ \ C \right)} \times 100
\]
where, for example, R 30 °C is the maximum slow phase velocity of nystagmus induced by the caloric irrigation of the right ear canal with 30 °C warm water. Vestibular paresis was defined as > 25% asymmetry between the right- and left-side responses. This formula is widely considered highly reliable in detecting unilateral peripheral vestibular loss 25-26. The vestibular examination was completed by cerebral computed tomography (CT) or Magnetic Resonance Imaging (MRI), in most cases, and patients with central involvement of the vestibular system were excluded.

The pathological group was represented by miscellaneous otological causes of vertigo including Ménière’s disease (252 cases), vestibular neuritis (180 cases), sudden deafness with labyrinthine dysfunction (68 cases), traumatic involvement of the inner ear (10 cases). It also included 7 cases of surgical labyrinth deafferentation (vestibular neurectomy) for acoustic neuroma and 11 cases of patients with central vestibular hypofunction 27. The test was considered positive if nystagmus appeared within 20 s after the head shaking and if at least 5 beats of nystagmus were clearly recognizable, regardless of their direction 29-31.

Materials and methods

Spontaneous nystagmus was observed with the patient sitting on the bed, motionless and relaxed. The test was considered positive if a spontaneous nystagmus was detected, regardless of its degree and direction.

Positional nystagmus was investigated by inviting patients to lie supine with the head resting on the bed, to lie supine with the head hanging downward (Rose’s position) and to lie first on the right side and then on the left, with the head on a pillow in order to maintain the head, neck and trunk on the same horizontal plane. The test was considered positive if positional nystagmus was detected in one or more positions and if present while patients were gazing forward (primary position).

Finally, patients underwent a vigorous shaking of the head, in a horizontal sinusoidal fashion, for 20 s, at a frequency of about 2 Hz with 30°-45° excursions to both sides, with eyes closed. The patients were instructed to open their eyes at the end of the head shaking and to stare straight ahead. The test was considered positive if nystagmus appeared within 20 s after the head-shaking and if at least 5 beats of nystagmus were clearly recognizable, regardless of their direction 29-31.

Subjects were, therefore, classified as labyrinthine-defective patients if one or more tests for each technique (direct observation, Frenzel’s glasses and videonystagmoscopy) allowed the examiner to detect nystagmus.

Statistical analysis

Sensitivity of each technique was calculated according to the following formula:

\[
\text{Sensitivity} = \frac{\text{number of subjects identified as pathological/total number of labyrinthine-defective patients}^(*)}{100}
\]

Specificity of each technique was calculated according to the following formula:

\[
\text{Specificity} = \frac{\text{number of normal subjects diagnosed not pathological/total number of normal subjects}^(*)}{100}
\]

(*): taking the caloric test and Jongkees’s formula as the “gold standard” according to the American Academy of Neurology 25.

Finally, discriminant analysis 32 that indicates the percentage of subjects classified correctly in the two groups (normal subjects vs. labyrinthine-defective
patients) was analysed. The concept underlying discriminant analysis is represented by a linear combination of predictor variables (i.e., the presence/absence of nystagmus) that are formed and served as the basis for classifying cases into one of the groups. This function was obtained using the statistical package SPSS/PC+.

**Results**

Direct observation of the patient’s eye, in the light, allowed the examiner to observe spontaneous nystagmus in 101 (19%) labyrinthine-defective patients and in 5 (4%) normal subjects. Head-shaking nystagmus was evoked and observed in 106 labyrinthine-defective patients (20%) and in 13 (11%) normal subjects. Positional nystagmus was not detected in any of the normal subjects and in only 34 patients (6%) (Table I). A total of 15 normal subjects showed one or more types of nystagmus. On the other hand, only 188 labyrinthine-defective patients showed nystagmus. Consequently, sensitivity and specificity of direct observation of patient’s eyes were 35.6 and 88.7, respectively.

Comparable percentages of spontaneous, positional and provoked nystagmus were revealed in normal subjects by the mean of Frenzel’s glasses. This technique allowed the examiner to observe spontaneous nystagmus in 106 patients, provoked nystagmus and positional type in 140 (26%) and 160 (60%) cases, respectively. A total of 15 normal subjects and 231 patients exhibited at least one type of nystagmus. Sensitivity and specificity of the clinical examination by means of Frenzel’s glasses were 43.7 and 88.7, respectively.

Furthermore, videonystagmoscopy did not significantly increase the percentages of spontaneous, provoked and positional nystagmus in normal subjects. Spontaneous nystagmus was present in 10 (7%) cases, positional and head-shaking nystagmus was observed in 2 (1.5%) and 13 (10%) cases, respectively. A greater increase in the observation of nystagmus was obtained by means of videonystagmoscopy in the pathological sample; spontaneous nystagmus was detected in 254 cases (48%), head-shaking-nystagmus in 366 cases (69%) and positional nystagmus in 222 cases (34%) (Table I). No nystagmus, of any type, was detected in 44 patients and consequently specificity increased to 91.6. Since 19 normal subjects (14%) showed at least one type of nystagmus, sensitivity of videonystagmoscopy decreased to 84.2 (Table II).

Finally, discriminant analysis revealed that the direct observation of a combination of spontaneous, head shaking- and positional nystagmus, in the light, is statistically able to predict a correct classification both of normal and pathological subjects in 46.3% of cases. The majority of misclassified cases belong to the labyrinthine-defective patients (Table III).

The use of Frenzel’s glasses increased this percentage to 52.8% due to the moderate increase in correct classification of labyrinthine-defective patients. Finally, discriminant power of videonystagmoscopy was 77.6% due to the increase in correct classification of pathological subjects.

**Discussion**

This study revealed that bedside examination of labyrinthine-defective patients following an acute attack of vertigo, unsatisfactory sensitivity (< 50%) if performed both by means of direct observation of patient’s eyes and Frenzel’s glasses.

It is, therefore, confirmed that visual fixation re-

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**Table I.** Numbers and percentages of cases with visible spontaneous, positional and head-shaking nystagmus according to the three different examination techniques.

<table>
<thead>
<tr>
<th></th>
<th>Spontaneous nystagmus</th>
<th>Head-shaking nystagmus</th>
<th>Positional nystagmus</th>
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<tr>
<td></td>
<td>Patients (%)</td>
<td>Controls (%)</td>
<td>Patients (%)</td>
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<tr>
<td>Direct observation</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>427 (81)</td>
<td>128 (96)</td>
<td>422 (81)</td>
</tr>
<tr>
<td>Present</td>
<td>101 (19)</td>
<td>5 (4)</td>
<td>106 (20)</td>
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<tr>
<td>Frenzel’s glasses</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>422 (80)</td>
<td>128 (96)</td>
<td>388 (74)</td>
</tr>
<tr>
<td>Present</td>
<td>106 (20)</td>
<td>5 (4)</td>
<td>140 (26)</td>
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<tr>
<td>Videonystagmoscopy</td>
<td></td>
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<tr>
<td>Absent</td>
<td>274 (52)</td>
<td>123 (92)</td>
<td>162 (31)</td>
</tr>
<tr>
<td>Present</td>
<td>254 (48)</td>
<td>10 (8)</td>
<td>366 (70)</td>
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markably reduced or abolished nystagmus due to a peripheral vestibular disorder.

On the other hand, only observation of the patient’s eye, in total darkness, as in infrared videonystagmoscopy, significantly increases sensitivity of the vestibular bedside examination. On the other hand, it should be pointed out that the specificity of the 3 methods is almost the same (about 85%). In fact, the presence of a visible nystagmus, also in those conditions in which visual suppression is not sufficiently abolished, is a reliable clinical sign of peripheral vestibular dysfunction.

It should be noted that in our series about 14% of the normal subjects exhibited one or more types of nystagmus and that this percentage is considerably smaller than those of other studies33-35. A factor possibly accounting for this discrepancy is that, in the aforementioned trials, normal subjects were all enrolled on the basis of a negative history for balance disorders and vertigo but were not submitted to a complete otoneurological investigation, including caloric tests, thus probably missing underlying peripheral vestibular dysfunction.

The results of this study are supported by the greater power of discriminant analysis (77.6%) provided by videonystagmoscopy with respect to direct observation (46.3%) and Frenzel’s glasses (52.8%). In this experiment, we did not include patients with paroxysmal positional vertigo, which is one of the most common causes of labyrinthine dysfunction, since the diagnosis of this otorhinologic disorder requires observation of the pathognomonic paroxysmal nystagmus only during the acute attack. In the intercritic period, the absence of nystagmus, in the tests we used, would have apparently increased the number of false negative subjects, but it should be remembered that these patients rarely present also labyrinthine hypofunction to the calorick test which we considered the “gold standard” in accordance with the American Academy of Neurology 25.

Our data confirm previous results22 23 that indicated the advantage of videonystagmoscopy in detecting vestibular system abnormalities and clearly showed that this kind of vestibular bedside examination provides clinicians with a satisfactory sensitivity and specificity in relation to the presence of a peripheral vestibular disorder, also after the acute attack of vertigo.

These results reveal some important clinical implications. Family doctors and ENT specialists could play an important role in the diagnosis of peripheral vestibular disorders also after the acute vertigo attack. The study of spontaneous, positional or head shaking nystagmus, also by the simple direct observation of patient’s eyes, could, indeed, identify a labyrinthine defect also out of crises and during vestibular compensation in more than 35% of cases, so that patients could be correctly referred for a complete audiological and vestibular examination. This procedure might reduce multidisciplinary counselling (often used for dizzy patients) and lead to a good balance between diagnostic effectiveness and cost containment.

It is worthwhile pointing out that the increased specificity of the vestibular bedside examination provided by videonystagmoscopy requires a greater initial cost, for the basic instrument, but is strongly recommended to avoid false negatives.

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<th>Table II. Specificity and sensitivity of different techniques for observation of nystagmus of labyrinthine origin.</th>
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<tr>
<td><strong>Direct observation</strong></td>
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<td>Specificity</td>
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<td>Sensitivity</td>
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<th>Table III. Discriminant analysis of the three different bedside vestibular examinations: correct and misclassified cases in the entire population.</th>
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<td><strong>Correct classification (%)</strong></td>
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<td><strong>Direct observation</strong></td>
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<td>Normal subjects</td>
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<td>Patients</td>
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<td>Discriminant analysis</td>
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