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Pathologic Erythrocyte Deformability in Patients With Sudden Sensorineural Hearing Loss

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Abstract

Objective: To evaluate if viscoelastic properties of blood influence suffering sudden sensorineural hearing loss and the capacity to respond after a specific therapy.

Patients and methods: A longitudinal prospective study included 85 ears bearing sudden deafness. In them, the mean hearing loss compared to the healthy ear and the recovery ratio were measured at the onset and 6 months after a treatment with corticoids and piracetam. In addition, tinnitus or vestibular symptoms, whole blood filterability (WBF) and erythrocyte deformability—by means of the erythrocyte rigidity index (ERI)—were determined and noted at the beginning and the end of the study.

Results: Mean hearing loss was 30.3±19.7% at the onset, and 25.8±39% at the end. Forty-one ears showed a recovery of more than 75%. In these (48% of the entire study group), an increase in WBF and a decrease in ERI were observed (P<.001). Ears without tinnitus or vestibular crisis recovered more hearing at 6 months and showed a significant improvement in WBF and ERI, not detected among patients with these clinical findings. There were good correlations between mean hearing loss at onset and WBF, and between recovery and ERI at 6 months, but without statistical significance. Arterial hypertension, cardiopathy and hypercholesterolemia were the most frequently detected diseases in patients, while hypertension and hyperuricemia showed a better hearing recovery ratio.

Conclusions: The blood viscosity parameters WBF and ERI offer useful information about the risk of suffering sudden deafness and the capacity to recover hearing with reactive therapies.

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Deformabilidad eritrocitaria patológica en pacientes con sordera súbita

Resumen

Objetivos: Evaluar si las propiedades viscoelásticas de la sangre influyen en la posibilidad de padecer sordera súbita o en la capacidad de responder a un tratamiento específico.

Pacientes y métodos: Fueron estudiados 85 oídos de pacientes con sordera súbita, midiendo el porcentaje de hipoacusia al inicio y el grado de recuperación a los 6 meses tras un tratamiento con corticoides e piracetam. También se anotó la presencia de acúfenos o síntomas vestibulares y se determinó en sangre periférica la filtrabilidad en sangre total (FST) y el índice de rigidez eritrocitaria (IRE).

Resultados: La pérdida media al inicio clínico fue del 30,3 ± 19,7% y a los 6 meses del 25,8 ± 39%. En 41 oídos se observó una recuperación auditiva superior al 75% pasado este tiempo. En este grupo -el 48% del total– la FST se elevó y el IRE descendió (p < 0,001 en ambos). Los oídos sin acúfeno ni vómito recuperaron más audición a los 6 meses y mostraron mejoría significativa en su FST y en el IRE. El grado de hipoacusia al inicio se correlacionó con la FST y el de recuperación con el IRE, pero de forma estadísticamente no significativa. Los antecedentes de hipertensión arterial, cardiopatías e hipercolesterolemia fueron los más comúnmente detectados. Hipertensión e hipercitrinemia mostraron mayor capacidad de recuperación.

Conclusiones: Los parámetros de viscosidad sanguínea FST e IRE se correlacionan bien con el riesgo de padecer sordera súbita y la capacidad de una adecuada recuperación de la misma con terapias reactivas.

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Introduction

There has been a recent work on sudden deafness in the national scientific literature which is highly useful due to the simplicity of its concepts and definitions. It enables an appropriate standardisation of the degree of hearing loss, establishes prognostic clinical patterns and offers the possibility of generating a database on this entity. In short, it opens the door to a systematisation of this pathology.

Nevertheless, no clear risk factors for suffering an episode of sudden hearing loss have yet been established. The predisposition of patients with diabetes or myocardial or cerebral ischemia is well known, so it is reasonable to suggest similar aetiopathogenic reasons. Similarly, treatments designed for these conditions could represent an effective alternative in sudden hearing loss.

Vascular changes have been postulated as the main factor for the hearing symptoms, given their chronobiological features. Although viral and immune-mediated hypotheses have offered histopathological validations, currently neither offer a clear explanation for the rapid onset of hearing loss. Although the prodromes of a viral infection can be clearly silent, a clinical onset of hearing loss due to isolated involvement of the organ of Corti or cochlear duct is unlikely. Furthermore, although the identification of anti-HSP-70 bands appears to be the norm in corticosteroid-sensitive patients on suspicion of autoimmune disease, the transit of these autoantibodies requires a period of cochlear damage which exceeds the concept of sudden hearing loss.

It would be more easily understandable that a microcirculatory block could generate neurological damage with such velocity. Something which is so commonly studied in cardiovascular disease becomes an enigma in the labyrinth. The association of a viral or immune etiology with a cascade of events leading to hyperviscosity processes is becoming increasingly accepted due to verifications through capillary viscometry.

Our group aims to study some of the viscoelastic properties of blood from patients with sudden deafness and whether these properties are correlated with the subsequent evolution of the symptoms. These results could help to understand the onset of symptoms and to establish a prognostic risk factor for the disease, and even for responding to previously designed therapies.

Materials and Methods

Study Design and Assessment of Hearing Loss

We conducted an observational, descriptive, longitudinal and prospective study of all patients attended due to sudden hearing loss at our department between January 1, 2001 and 2011. The diagnosis was established by liminal tone audiometry according to the diagnosis established by Plaza et al. in 2011. In this sense, the degree of hearing loss was obtained by considering the sum of the airway thresholds at frequencies of 500, 1000, 2000, and 3000Hz, with the application of their equivalence in percentage according to current legislation. The audiometric graph also reported another parameter to be assessed: the mean value of the airway thresholds for all 7 frequencies studied, between 500 and 8000Hz.

However, these values were considered absolute when not compared with the contralateral ear, which had not suffered damage, as mentioned by the updated Spanish Consensus. Therefore, we addressed the 3 variables mentioned above referring to the hearing threshold of the “healthy” ear simply by obtaining the difference between the absolute value thereof in the damaged ear and in the non-damaged.
Pathologic Erythrocyte Deformability in Patients With Sudden Sensorineural Hearing Loss

Epidemiological Characteristics

These were related to aspects obtained from the clinical history and included age and gender, personal medical history and any immediately preceding circumstances that might be related to the auditory event. The presence or absence of these characteristics, as well as the shape of the audiometric graph, was correlated with respect to the variable hearing recovery above 75% or absence of recovery.

Monitoring and Treatment

The 3 variables resulting from the audiometric graph were studied at the time of onset of hearing loss and 6 months later. Attended patients were admitted for intravenous treatment during 4–5 days and then switched to an oral treatment. This treatment generally consisted of methylprednisolone at doses of 1 mg/kg/day for 10 days, progressively reduced for 30 days, with gastroprotection. Piracetam was associated at a dose of 9 g/day for 8–10 days, and maintained for at least 3 months. In cases with associated vestibular crises, we included parenteral sulpiride on demand, up to 200 mg/8 h. We also noted the coincidence of tinnitus.

We conducted an MRI imaging study of the auditory pathway in all patients, as well as an assessment of autoimmunity in peripheral blood, including determination of leukocytosis, absolute lymphocytosis, acute phase reactants, T4/T8 ratio, immunoglobulin levels, complement factors, rheumatoid factor, ANA, ANCA and anti-HSP70 antibodies by Westernblot against bovine cochlear antigen extract.

Haemorheological Parameters

WBF was assessed using the Reid–Dormandy method, measuring the time taken to filter 1 ml of blood anticoagulated with EDTA through 13 mm polycarbonate filters with 5 μm diameter pores under a negative pressure of 20 cm of water. WBF was calculated adjusted to the haematocrit of each patient according to the following equation:

\[ WBF = \frac{\text{blood volume}}{\text{filtration time}} \times Ht \]

The previously established reference range was between 17 and 22.8 μl/s.

Erythrocyte deformability was expressed as the ERI according to the Expert Panel on Haemorheology of the International Committee for Standardisation in Haematology. This was calculated by measuring the filtration time of a red cell suspension from a patient adjusted to a haematocrit of 8% (TF₈₄) and matched to the filtration time of an acellular, buffered PBS solution (TFPBS), according to the following equation:

\[ ERI = \frac{(TF₈₄ - TF PBS)}{(TF PBS \times 8)} \times 100 \]

The previously established reference range was between 7.39 and 8.81.

Exclusion Criteria

Among patients diagnosed with sudden hearing loss, those subjects in whom the following requirements did not concur were not admitted to the study:

1. Failure to present an audiometric study at the beginning of the symptoms and prior to the start of treatment, as well as at 6 months.
2. Failure to undergo imaging tests (MRI of auditory pathway) and/or determination of peripheral blood parameters related to their state of immunomodulation.
3. Failure to obtain data on the viscoelastic properties of blood, in particular the determination at the beginning had to be performed before the start of treatment.

Inadequate completion of treatment did not represent a reason for exclusion of an individual from the study.

Data Processing

We reviewed the audiometric graph at baseline and at 6 months, as well as that obtained in the healthy, contralateral ear. In addition, we made comparisons between hearing loss and degree of recovery—measured as the mean of the 7 frequencies, the sum of the 4 conversational frequencies and the percentage of hearing loss—and the haemorheological parameters presented. Furthermore, we attempted to correlate the presence or absence of tinnitus and/or vertigo symptoms with the capacity for hearing recovery and changes in viscosity markers.

When we made comparisons of a quantitative variable with a normal distribution between 2 different populations or at 2 different times within the same group, we also calculated the Student’s t-test in order to compare their means and standard deviations. The correlation of 2 different quantitative variables within the same population group was studied by calculating the equations of the regression lines and obtaining their corresponding correlation coefficient. This was done using the statistical package SPSS 20.0.0 provided by IBM and Microsoft Office Excel 2003 for Windows XP. We considered as statistically significant differences those with a value of P<.05.

Results

In the 10 years of follow-up we collected data from 85 patients (47 males and 38 females) diagnosed with sudden hearing loss, aged between 17 and 72 years (39.5±13.1 years). Involvement was unilateral in all cases. The percentage of hearing loss at the onset was 41.9%±21.6% and after 6 months it was 37.4%±39.2%, without any adjustments to the unaffected ear. Thus, there was no statistically significant improvement. Fig. 1 shows the audiometric records of airway thresholds in the damaged ear at the onset and at 6 months. At baseline, the mean threshold of the 7 frequencies studied was 56.1±17.5 dB HL compared to 50.6±21.9 dB HL at 6 months.

However, when we adjusted hearing loss to the threshold of the unaffected, contralateral ear, the degree of hearing loss at the onset was 30.3%±19.7% (ranging between 3.7%
Tinnitus affected 45 individuals, of which only 12 recovered more than 75% of their hearing. Vestibular crises were recorded in 20 subjects, of which 5 showed this recovery. Since 9 individuals presented both symptoms, we noted 29 patients without them. These data are shown in Table 1, which also reflects low WBF and ERI values at the onset among individuals with both symptoms. While the WBF value decreased even more at 6 months among individuals with tinnitus, it underwent a non-significant improvement among patients with vertigo. The ERI values fell in both groups after treatment, without reaching statistical significance. WBF improved and ERI decreased among patients without tinnitus or vertigo, in a statistically significant manner for both parameters. These patients also presented better filterability and erythrocyte deformability values than patients with tinnitus and/or vertigo, both at baseline and at 6 months of treatment.

We also performed a comparison of quantitative audiometric variables (hearing loss at onset, mean threshold of the 7 frequencies at 6 months and hearing recovery at 6 months) with rheological variables (WBF and ERI at baseline and at 6 months) through regression curves. We only obtained clinically relevant, although not statistically significant, correlation coefficients between WBF and the percentage of hearing loss at the onset ($r = -0.0313x + 18.406$; $R = 0.6204$), and between the mean thresholds and the percentage of recovery and ERI at 6 months of treatment ($y = 0.3351x + 7.9053$; $R = 0.6656$).

Among the purely clinical characteristics of affected patients, we should point out that in 72 there was some personal history of interest (84.7%), with the most frequent being arterial hypertension in 39 subjects, cardiomyopathy in 37, arrhythmia in 28, hypercholesterolemia in 25 and diabetes in 21. Among these symptoms, arterial hypertension and hyperuricemia were the groups with the highest percentage of subjects who recovered hearing above 75%. The circumstances considered as a possible trigger mechanism included infection, trauma and dysbarism, with the main cause reported being a clearly stressful or anxiety-generating social environment (Table 2).

Alterations in peripheral blood were not significant in any case. Hypocomplementemia was detected in 6 patients, half of which recovered hearing above 75%. In 4 of these cases and in the 1 patient diagnosed with systemic lupus, ANA titers were positive at the time of diagnosis. In one patient the previously diagnosed autoimmunity was noteworthy, as he was in prior maintenance treatment with prednisone 15 mg/day. The ERI value was high, and therefore his erythrocyte deformability was decreased at first, but this became normalised after the treatment protocol, coinciding with hearing recovery. The 1 patient diagnosed with ulcerative colitis and 3 others presented anti-HSP70 antibodies. In 2 cases there was no auditory gain or improvement in the determination of erythrocyte deformability.

**Discussion**

The viscoelastic properties of blood vary with changes in microcirculatory flow. This is due to modifications in
Table 1  Audiometric and Rheological Characteristics of Subjects With Sudden Hearing Loss According to Their Concomitant Symptoms.

<table>
<thead>
<tr>
<th></th>
<th>Tinnitus (n=45)</th>
<th>Vertigo (n=20)</th>
<th>No Tinnitus or Vertigo (n=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% hearing loss at baseline</td>
<td>30.17±16.52%</td>
<td>33.72±15.02%</td>
<td>25.41±13.61%</td>
</tr>
<tr>
<td>Patients who recovered hearing&gt;75%</td>
<td>12 (26.6%)</td>
<td>5 (25%)</td>
<td>24 (82.7%)</td>
</tr>
<tr>
<td>WBF at baseline, µl/s</td>
<td>18.02±0.97</td>
<td>17.61±1.02</td>
<td>18.22±0.99</td>
</tr>
<tr>
<td>WBF at 6 months, µl/s</td>
<td>17.42±0.91*</td>
<td>17.93±0.88</td>
<td>20.02±1.13**</td>
</tr>
<tr>
<td>ERI at baseline</td>
<td>7.52±0.42</td>
<td>7.74±0.31</td>
<td>7.59±0.44</td>
</tr>
<tr>
<td>ERI at 6 months</td>
<td>7.39±0.25</td>
<td>7.69±0.28</td>
<td>7.15±0.33**</td>
</tr>
</tbody>
</table>

ERI, erythrocyte rigidity index; WBF, whole blood filterability.
* P<.01.
** P<.001.

Table 2  Personal History and Circumstances Related in Time With the Case of Sudden Hearing Loss Collected in the Anamnesis, as Well as Description of the Audiometric Graph Detected Upon Admission.

<table>
<thead>
<tr>
<th>Clinical history</th>
<th>n</th>
<th>Hearing Recovery&gt;75%</th>
<th>No Recovery or Greater Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHT</td>
<td>39</td>
<td>29 (74.3%)</td>
<td>7 (17.9%)</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertrophic</td>
<td>21</td>
<td>12 (57.1%)</td>
<td>2 (9.5%)</td>
</tr>
<tr>
<td>Ischemic</td>
<td>15</td>
<td>4 (26.6%)</td>
<td>8 (53.3%)</td>
</tr>
<tr>
<td>Dilated</td>
<td>6</td>
<td>4 (66.6%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>28</td>
<td>11 (39.3%)</td>
<td>12 (42.8%)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>25</td>
<td>9 (36%)</td>
<td>13 (52%)</td>
</tr>
<tr>
<td>DM</td>
<td>21</td>
<td>9 (42.8%)</td>
<td>10 (47.6%)</td>
</tr>
<tr>
<td>Hyperuricemia</td>
<td>17</td>
<td>13 (76.4%)</td>
<td>1 (5.9%)</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>15</td>
<td>7 (46.6%)</td>
<td>5 (33.3%)</td>
</tr>
<tr>
<td>CVE</td>
<td>12</td>
<td>2 (16.6%)</td>
<td>7 (58.3%)</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>9</td>
<td>4 (44.4%)</td>
<td>3 (33.3%)</td>
</tr>
<tr>
<td>Active hepatopathy</td>
<td>6</td>
<td>3 (50%)</td>
<td>1 (16.6%)</td>
</tr>
<tr>
<td>Prior neoplasm (disease-free)</td>
<td>6</td>
<td>2 (33.3%)</td>
<td>2 (33.3%)</td>
</tr>
<tr>
<td>Active neoplasm</td>
<td>1</td>
<td>0 (0%)</td>
<td>1 (100%)</td>
</tr>
<tr>
<td>Autoimmune disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLE</td>
<td>1</td>
<td>1 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Sjögren syndrome</td>
<td>1</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>1</td>
<td>1 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Smoking&gt;10 cg/day</td>
<td>59</td>
<td>35 (59.3%)</td>
<td>21 (35.6%)</td>
</tr>
<tr>
<td>Overweight (BMI&gt;25)</td>
<td>56</td>
<td>30 (53.3%)</td>
<td>21 (37.5%)</td>
</tr>
<tr>
<td>Drinking&gt;50 g/day (slight)</td>
<td>14</td>
<td>7 (50%)</td>
<td>3 (21.4%)</td>
</tr>
<tr>
<td>Prior circumstances</td>
<td>22</td>
<td>15 (68.2%)</td>
<td>5 (22.7%)</td>
</tr>
<tr>
<td>Significant social-working stress</td>
<td>11</td>
<td>6 (54.4%)</td>
<td>3 (27.2%)</td>
</tr>
<tr>
<td>Upper airway pathology</td>
<td>7</td>
<td>5 (71.4%)</td>
<td>2 (28.5%)</td>
</tr>
<tr>
<td>Air decrease/increase</td>
<td>2</td>
<td>1 (50%)</td>
<td>1 (50%)</td>
</tr>
<tr>
<td>Hospital admission</td>
<td>2</td>
<td>0 (0%)</td>
<td>1 (50%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1</td>
<td>1 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Surgery under general anaesthesia</td>
<td>1</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Humerus fracture</td>
<td>1</td>
<td>1 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Intake of cocaine in the previous 24 h</td>
<td>1</td>
<td>0 (0%)</td>
<td>1 (100%)</td>
</tr>
<tr>
<td>Audiometric curve</td>
<td>85</td>
<td>41 (48.2%)</td>
<td>37 (43.5%)</td>
</tr>
<tr>
<td>Predominance of loss in acute frequencies</td>
<td>32</td>
<td>22 (68.75)</td>
<td>10 (31.2%)</td>
</tr>
<tr>
<td>Predominance of loss in low frequencies</td>
<td>25</td>
<td>4 (16%)</td>
<td>19 (76%)</td>
</tr>
<tr>
<td>Pantonal loss</td>
<td>15</td>
<td>10 (66.6%)</td>
<td>2 (13.3%)</td>
</tr>
<tr>
<td>Bowl-type loss</td>
<td>6</td>
<td>2 (33.3%)</td>
<td>3 (50%)</td>
</tr>
<tr>
<td>Plateau-type loss</td>
<td>5</td>
<td>3 (60%)</td>
<td>1 (20%)</td>
</tr>
<tr>
<td>Deep-severe loss/cophosis</td>
<td>2</td>
<td>0 (0%)</td>
<td>2 (100%)</td>
</tr>
</tbody>
</table>

AHT, arterial hypertension; BMI, body mass index; CVE, cerebrovascular event; DM, diabetes mellitus; SLE, systemic lupus erythematosus. Each group defined is shown with the percentage of subjects with a hearing recovery above 75% or without recovery or even greater loss.
erythrocyte deformability observed at different shear conditions. The shear rate results from the difference observed between 2 adjacent layers of moving blood fluid per unit distance between them. Under physiological flow conditions the shear velocity of blood is of several hundreds of s⁻¹ in most of the vascular tree. However, in post-capillary venules there is a high risk that this rate decreases or is cancelled, especially in sub-centimetre organs with non-vicariant vascularisation, that is, without anastomotic networks that can compensate endoluminal obstructions.¹²

The labyrinth presents this microcirculatory peculiarity, since its oxygen is supplied exclusively through the cochlear branch of the posterior inferior cerebellar artery or internal auditory artery.¹³ This is divided into the common cochlear and anterior vestibular arteries. In turn, the first is divided into the main cochlear, for the upper three-quarters of the cochlea, and the cochleovestibular, which provides a cochlear branch for the most inferior quarter and another vestibular branch.¹⁴

Since this is a terminal irrigation, the deterioration in filterability of erythrocytes through it generates episodes of ischemia with variable duration, intensity and symptoms but with a rapid onset. The duration of symptoms depends largely on the capacity of the organism to correct this decrease in blood filterability, acting exogenously on the factors involved in this process: improving erythrocyte deformability, removing plasma substrates (fibrinogen, LDL cholesterol, triglycerides, globulins...) or lowering haematocrit and platelet aggregability.¹² These are urgent actions which warrant intravenous therapies with rheoactive agents, antiplatelet agents, vasodilators, normovolemic haemodilution or rheopheresis techniques which clear proaggregatory molecules from the blood. It is understandable that, when the limitation on erythrocyte filterability is notable, the possibility of involvement of major labyrinthine vessels becomes greater and the accompanying clinical symptoms of hearing loss, dizziness, tinnitus and vestibular crises also become more marked.

WBF is a process which accurately reproduces the conditions of microcirculatory flow. The shear force in human terminal arterioles—such as the main cochlear artery—is approximately 150 dyn/cm² or 15 Pa, but a maximum value of 200 Pa is admissible. The filtering conditions of the system employed in vitro can work at pressures of 15–30 Pa, so it is accepted as a reliable reproduction of human cochlear pathophysiology. WBF has been explained as the result of the combination of several factors: erythrocyte deformability and aggregability, plasma and blood viscosity, circulating macromolecules, leukocytosis and number, volume and aggregability of platelets.

Of these, erythrocyte deformability determined quantitatively as ERI seems the most influential parameter for the access of blood flow to the labyrinth. While the stria vascularis acts as the main nutrient organ in the cochlea, its oxygenation and cleaning of free radicals take place at the expense of modiolar venules and arterioles with calibres ranging between 15 and 20 µm.¹³,¹⁴ If the diameter and minor volume of red blood cells are 8 µm and 70 femtolitres, respectively, their aggregability represents a risk factor for vascular occlusion.¹⁵

Erythrocyte deformability is basically defined as the capacity of red blood cells to rapidly change their shape when subjected to tensile conditions.¹⁶ It depends on 3 factors: (1) shape, which is conditioned by erythrocyte morphology and is quantified by the surface-volume ratio; (2) internal viscosity of the erythrocyte, which depends on the mean corpuscular haemoglobin concentration and its physical–chemical state; and (3) the viscoelastic properties of the membrane, which are mainly determined by the behaviour of the spectrin–actin network.

Disorders in any of these 3 aspects may reduce this parameter. The end result causes selective microangiopathy, which must be prevented immediately, since subsequent lymphoplasmacytic infiltration and fibro-osseous obliteration of the scala tympani ensue rapidly due the presence of reactive oxygen species.¹⁷ It has been proven that a decrease in aggregability improves deformability and various agents with an optimiser effect of the membrane lipid bilayer have shown their effectiveness in other organs.

Several publications have reported a state of blood hyperviscosity in subjects with sudden hearing loss,¹⁸,¹⁹ as well as the relationship between this condition and impaired erythrocyte deformability.²⁰,²¹ In addition, rapid modifications have succeeded in reversing the degree of hearing loss. The ears of subjects with decreased erythrocyte deformability and blood filterability are more prone to a more pronounced, perceptual, sudden hearing loss and are also less prone to recovery, coinciding with previous communications.²²,²³ However, it should be noted that the root causes of blood hyperviscosity at a specific moment in the chronobiology of an individual are numerous (Table 3) and, where possible, should be identified or ruled out when a haemoreological parameter is detected at levels outside the normal range.

The ultimate mechanism which generates alterations in erythrocyte deformability is still unclear. It is known that conditions which impair deformability–diabetes, dyslipidemia, hypertension–pose a risk factor for sudden hearing loss and significant limitations on their reversal,²³,²⁴,²⁵ so the epidemiological features observed in our patients do not represent a new finding. Dysfibrinogenemia, macroglobulinaemia and haemoglobinopathy act in a similar manner by reorganising erythrocyte membranes.²⁶ However, aphaeresis often does not generate the expected benefit. With no haemostatic hyperactivity, antiaggregation and anticoagulation do not offer significant efficacy within the arsenal of therapeutic possibilities. Findings of elevated blood viscosity in infectious episodes and obstruction in microcirculation have supported the idea of a rheological alteration as the generator of cochlear damage and ultimate cause of hearing loss.²⁸,²⁹

Alterations in erythrocyte deformability as the ultimate generator mechanism of hearing loss are founded when this dysfunction is equated to those of other organs with terminal circulation and similar findings in the viscoelastic properties of blood.¹² This mechanism would unify all the causes involved in the occurrence of sudden-onset sensorineural hearing loss, so it seems reasonable to suggest that the erythrocyte alterations detected could be responsible for the sudden loss of speech hearing, taking into account that it appears in most causes attributed to this entity–vascular, viral and autoimmune. The present article does not
Table 3 Possible Causes Generating a Pathological Environment of Blood Hyperviscosity.

<table>
<thead>
<tr>
<th>Alterations in extracellular content</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Exogenous vasoooclusion with slowing of microcirculation</em></td>
</tr>
<tr>
<td>Brainstem or cerebellopontine angle tumours</td>
</tr>
<tr>
<td>Arteriovenous malformations</td>
</tr>
<tr>
<td>Angulations of posterior inferior cerebellar artery</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Presence of high-molecular weight substrates in blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waldenstrom macroglobulinemia (IgG, A, D or E or kappa or lambda light chains)</td>
</tr>
<tr>
<td>Multiple myeloma M protein (IgM and/or kappa or lambda chains)</td>
</tr>
<tr>
<td>Type III hypersensitivity circulating immunocomplexes</td>
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<table>
<thead>
<tr>
<th>Modifications in the concentration of red blood cell proaggregating molecules</th>
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<tbody>
<tr>
<td>Monoclonal hypergammaglobulinemia due to lymphoproliferative processes</td>
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<tr>
<td>Polyclonal hypergammaglobulinemia versus infectious exogenous agents (paramyxovirus, herpesvirus, influenza virus, measles, HIV, syphilis, states of septicaemia)</td>
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<tr>
<td>Essential cryoglobulinemia or associated to vasculitis or paraneoplastic syndromes</td>
</tr>
<tr>
<td>Autoantibodies in autoimmune diseases (SLE, rheumatoid arthritis, scleroderma, polyarteritis nodosa, mixed connective tissue disease, thyroiditis, antiphospholipid syndrome)</td>
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<tr>
<td>Elevated LDL cholesterol fraction</td>
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<tr>
<td>Hyperfibrinogenemia–dysfibrinogenemia</td>
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<tr>
<td>Other fibrinolysis disorders (plasminogen deficits)</td>
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<tr>
<td>Uraemia</td>
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<td>Hyperuricaemia</td>
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<th>Disorders of blood cellular families</th>
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<td>Red blood cells</td>
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<tr>
<td>Membranopathies</td>
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<tr>
<td>Schizocytosis, elliptocytosis</td>
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<tr>
<td>Metabolic structural alterations or paraneoplastic syndromes</td>
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<td>Glycosylation of the membrane by diabetes mellitus</td>
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<tr>
<td>Excess of fatty acids and/or LDL cholesterol in lipid bilayer</td>
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<tr>
<td>Rigidity of membrane due to antiphospholipid antibodies</td>
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<tr>
<td>Repetitive trauma due to elevated shear status in arterial hypertension</td>
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<tr>
<td>Alteration in intracellular contents</td>
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<tr>
<td>Elevation of mean corpuscular haemoglobin or mean corpuscular volume</td>
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<tr>
<td>Haemoglobinopathies (thalassemias, presence of foetal haemoglobin, spherocytosis, drepanocytosis)</td>
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<tr>
<td>Alteration in number (polyglobulia)</td>
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<td>Decrease in plasmatic volume (diarrhoeas, laxatives, diuretic agents)</td>
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<tr>
<td>Primary polyglobulia with normal EPO</td>
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<tr>
<td>Excessive EPO due to chronic hypoxia (carbon monoxide intoxication, smoking), renal ischemia or renal tumour</td>
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<tr>
<td>Essential polyglobulia</td>
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<tr>
<td>Exogenous elevations of haematocrit</td>
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<tr>
<td>Myelodysplastic syndromes (polycytemia vera)</td>
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<tr>
<th>Leukocytes</th>
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<tr>
<td>Significant excess in number and volume</td>
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<tr>
<td>Leukaemic reactions (response after bone marrow transplant, systemic infections)</td>
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<td>Lymphomas and leukaemia</td>
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<td>Myelodysplastic syndromes (chronic myeloid leukaemia)</td>
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<th>Platelets</th>
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<tr>
<td>Focal activation of aggregability by collagenosis (mixed connective tissue disease).</td>
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<tr>
<td>Elevation of volume</td>
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<td>Myeloproliferative syndromes with megakaryocytosis</td>
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<td>Elevation of mean platelet volume</td>
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<td>Paraneoplastic syndromes</td>
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<td>Increase in number</td>
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<tr>
<td>Myelodysplastic syndromes (essential thrombocytosis)</td>
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<tr>
<td>Response as acute phase reactant to systemic infections and septicaemias</td>
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EPO, erythropoietin; HIV, human immunodeficiency virus; LDL cholesterol, low-density lipoprotein cholesterol; SLE, systemic lupus erythematosus.
attempt to distinguish between patients with markers for thrombophilia, metabolopathy or immune-mediation. The use of an agent with a marked rheoactive effect during the acute phase of the crisis appears to limit this damage, regardless of the comorbidities displayed by the patient.

This work aims to open the way for intervention with rheoactive agents in a prospective manner, in a cohort study in which isolated agents would be administered within a double-blind trial, so as to compare their effectiveness against empirical corticosteroid therapy. The induction of altered states of erythrocyte deformability in animal models should be the first step in an attempt to verify possible functional damage to the cochlea and its response to therapies which specifically target this endovascular dysfunction. Until then, further discussion on processes which produce cochlear damage by modifying blood viscoelasticity variables and which are candidates for treatment would not be feasible.

Therefore, we propose the introduction of rheoactive measures, perhaps the most accessible being drug treatment with high doses of piracetam, in all patients with clinical onset of what is perfectly definable as sudden hearing loss syndrome (similar clinical manifestations due to different causal factors). This treatment should be not only complementary to other alternatives, but also systematic upon objective observation of altered erythrocyte deformability.

Conflict of Interests

The authors have no conflict of interests to declare.

References