Intratympanic Dexamethasone as First-Line Treatment for Selected Patients With Hearing Loss

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There is no consensus among ENT (ear, nose and throat) physicians on the causes, diagnosis and especially therapeutic approach in sensorineural hearing loss (SSHL). The present paper describes our experience with intratympanic dexamethasone injection as initial treatment for selected patients with the sudden sensorineural hearing loss. The results obtained were fully encouraging. The sustained and coherent approaches of the national ENT society through his section of otoneurology, can lead to a diagnostic and therapeutic consensus in the sensorineural hearing loss. Further, the National Health Insurance House must introduce in the methodological norms the therapeutic variants and the concrete conditions for their realisation, in order to have a common medical practice

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The sudden sensorineural hearing loss (SSHL) is considered as *sensorineural or perceptual hearing loss cases with a sudden onset, within 72 hours, with a loss of over 30 dB, in at least three consecutive frequencies of tonal audiometry, without other prior otological history,* in accordance with National Institute of Deafness and Other Communications Disorders (NIDCD-(2015). If previous audiometry is available, this should be used as a baseline reference; if no previous audiometry is available, in unilateral cases the healthy contralateral ear should be used as a reference. Many authors also consider as *probable sudden sensorineural hearing loss (SSHL) cases of sensorineural or perceptual hearing loss that affect only 2 or 3 frequencies, with losses of 10-20 dB, appearing in less than 12 h, including deafness appreciated upon waking in the morning, which recover rapidly*. The disease appears in the *clear sky*, without prodromes. Mostly is a consequence of a single episode and the anamnesis does not record fluctuating hearing loss [1-9].

The mentioned nasoslogical entity occurs in healthy patients - without a personal otological/general history and can be recovered totally or partially. Is almost pathognomonic the description of patients reporting that they slept healthily and in the morning they found the hearing loss. Diabetic patients with retinopathy should have more hearing loss, given the similarity of the microvascular blood supply of the ear to that of the eye.

The sudden sensorineural hearing loss (SSHL) represents about 1% of sensorineural hearing loss cases, with an incidence of 5-20 cases per 100 000 inhabitants per year. Is it at the same time the reason for presenting to the ENT emergency units of 1.4 % patients. It was classically considered as an ENT emergency for which each clinic had to have a standard medical protocol. Today, taking into account that almost 40% of patients experience a spontaneous remission, the sudden deafness can be considered as a *delayed urgency.* Otherwise, there is no consensus among ENT physicians on the causes, diagnosis and especially therapeutic approach in the sensorineural hearing loss.

The present paper describes our experience with intratympanic dexamethasone injection as initial treatment for selected patients with the sudden sensorineural hearing loss.

Experimental part

A prospective study was conducted involving 43 patients, coming from two hospitals (the National Institute of Aeronautical and Spatial Medicine and the Institute of Phonoaudiology and Functional ENT surgery), in the strict order of ENT emergency room presentation, between February 2015 and March 2016.

A common diagnostic and treatment protocol in sudden sensorineural hearing loss (SSHL) / sudden deafness (SD) was previously established, and all selected patients signed informed consent. This protocol was approved by the Ethics Committee at our institutions.

Thus, concerning the diagnostic part of the protocol, it has been established that for a patient presenting at the ENT emergency room, both detailed anamneses with complete audiological study and complementary laboratory / imaging exams will be performed. The common denominator of the laboratory examinations was the following set of analyses: full blood count, blood coagulation, erythrocyte sedimentation rate (ESR), reactive protein (CRP), syphilis specific serology and serum concentration of thyroid stimulating hormone (TSH). Imaging exploration was represented by nuclear magnetic resonance imaging (MRI) or computer tomography (CT) for the situation where MRI was contraindicated.

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Through this diagnostic algorithm, we tried to introduce into the study only patients with the idiopathic sudden sensorineural hearing loss (SSHL).

After establishing the diagnosis of sudden sensorineural hearing loss, all patients were explained the therapeutic options available in the clinic (1. abstention and surveillance 2. local, oral or systemic corticotherapy and 3. hyperbaric therapy), theirs concrete application modalities (individually or in a double / triple association, as initial treatment or salvage treatment, doses, schedules) and theirs specific indications / contraindications.

Thus, after ensuring that all 174 patients affected in the mentioned period (between February 2015 and March 2016) by idiopathic Sudden Sensorineural Hearing Loss (SSHL) understood the existing therapeutic options, we selected the patient group for intratympanic dexamethasone injection as initial treatment.

With the purpose of selecting patients who opt for intratympanic dexamethasone injection as primary and exclusively treatment, we used the following inclusion criteria:

- the early onset of treatment (≤ 10days),
- the occurrence of disease in young/active patients (≥ 18 years and ≤ 65 years).
- Mild hearing loss impaired on an ascending curve.

Patients who presented local or general affections that can explain the genesis of sudden deafness by themselves or those who benefited from previous medical treatment were excluded.

Regarding the injection concreting technique we must mention that it has been achieved into the operating room – in the regime of day surgery, with patients in the supine position. After local disinfection, we administered anaesthesia with lidocaine spray at 10%, in a cotton swab for 10 min. Under to-microscopy vision, with a fine needle (21-27)µm and using one mL tuberculin syringe, we have the technique of intratympanic application of the drug. We constantly used the posteroinferior quadrants of the tympanic membrane as the application area. We found that 0.4 - 0.5 mL of dexamethasone fill the tympanic cavity. At each injection, the ENT surgeon's team assured that there is enough substance in the middle ear. Dexamethasone (4 mg/ 1mL), was administered weekly in doses of 1 mL (two injections of 0.5 mL per week), for three consecutive weeks. The total dose was 12 mg/ 3mL.

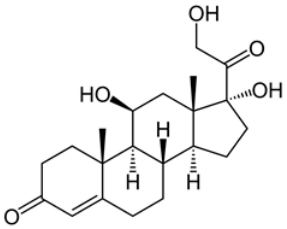

Fig1. Dexamethasone - molecular formula ($C_{22}H_{29}FO_5$) and structure

The technique was performed by the same team of two ENT surgeons both at The National Institute of Aeronautical and Spatial Medicine and at The Institute of Phonoaudiology and Functional ENT surgery. The conditions (equipment and materials) in the operating block were similar (fig. 2 and 3).

The presence of anesthesiology team in the *Operating Room Block* was included in the informed consent and was a very solid argument for the patient choice. Otherwise, ten patients required mild sedation at the first injection sessions. Without sedation it would have been impossible to achieve intratympanic injection in these ten patients.

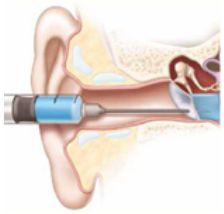

Fig.2 Intratympanic Dexamethasone injection

Fig.3 Tuberculin syringe and solution of Dexamethasone (4 mg/ 1mL)

To optimise the access of the drug to the round window, we instructed all patients to maintain the head tilted 45° towards the healthy side for 25-30 min.

We also instructed all patients to refrain from swallowing with the purpose to avoid the rapid elimination of dexamethasone through the Eustachian tube. There are many arguments in recent studies according to which the dexamethasone levels in the perilymph were highly dependent on the period when the drug remained in the middle ear.

Both at diagnosis and after intratympanic dexamethasone injection all patients were evaluated by audiometry, using standardized methods for pure-tone threshold audiometry and speech intelligibility. All audiometric studies were performed by the same certified audiologist under standard conditions. Pure-tone average (PTA) was calculated as an average of the threshold measured at 0.25, 0.5, 1, 2, 4, and 8 kHz.

Regarding statistical analysis, the majority of data are presented in numeric and percent form. Between statistical tests, chi two techniques, rank sum test or the Fisher exact test was chosen for categorical data analysis. All statistical analysis used the Statistical Package for the Social Sciences (SPSS) software 16.0. For Windows. Was accepted as statistically significant an alpha value <0.05.

Results and discussions

Among 174 patients affected in the mentioned period (between February 2015 and March 2016) by idiopathic Sudden Sensorineural Hearing Loss (SSHL), we evaluated 43 patients (27 male and 16 women) that completed the protocol and had met the exclusion / inclusion criteria.

All patients were treated with transtympanic therapy - as primary and exclusively treatment.

Of the data analysis resulted that the mean age was 47 years. In general, after the onset of symptoms, patients presented themselves quite quickly at ENT emergency room. The mean time of presentation was 5.3 days. Two additional signs have occurred more frequently – tinnitus and vertigo. Tinnitus was present in 33 (76.74%) patients. Dizziness was always associated with tinnitus and was present in 12 (27.90%) of cases. Because among the inclusion criteria in the study for was included the mild hearing loss, the mean of initial pure tone audiometry (PTA) was quantified at 58 dB for the whole group.

For most authors, successful treatment of SSHL has defined arbitrarily. In the present study, we decided to consider as improvement of hearing, an improvement of the PTA of >10 dB. In these conditions, we have achieved success in 42 (97.67%) patients (an increase better than 10 dB). The most important finding is, however, an improvement better than 30 dB which was obtained in 32 (74.40%) patients. The mean of hearing improvement post-treatment was 44.7%. Unfortunately, during the study, a patient's hearing worsened. There was no complication specific to this type of treatment.

Table 1

CRITERIA FOR HEARING IMPROVEMENT IN SSHL ACCORDING TO SIEGEL

Response	Average auditory recovery
Full recovery	Until obtaining a final PTA <25 dB, or independently of dB gained
Partial improvement	Improvement >15 dB, but final PTA between 25-45 dB
Slight improvement	Improvement >15 dB, but final PTA >45 dB
No improvement	Improvement <15 dB

Table 2

CRITERIA FOR HEARING AN IMPROVEMENT IN SSHL, ACCORDING TO SUDDEN DEAFNESS RESEARCH COMMITTEE, JAPAN

Response	Average auditory recovery
Full recovery	Until obtaining a PTA <20 dB, or until the threshold of the contralateral healthy ear.
Good improvement	Improvement >30 dB.
Slight improvement	Improvement 10-30 dB.
No improvement	Improvement <10 dB

The impact of the initial magnitude of hyperacusis it was not a goal of this paper because we have selected through inclusion criteria only patients with the mild hearing loss.

Patients follow-up was conducted at 30, 90 and 180 days of diagnosis. The periodic review included tonal and verbal audiometry.

The auditory thresholds for all frequencies (0.25, 0.5, 1, 2, 4, and 8 kHz) were determined and expressed in dB.

The successful treatment criteria of SSHL is arbitrarily defined by most authors. All authors analysed the average of auditory thresholds on all frequencies (0.25, 0.5, 1, 2, 4, and 8 kHz). For example, we present the therapeutical success criteria formulated by Siegel (table 1) as well as by the Japanese Committee on Sudden Deafness (table 2).

First of all, must be highlighted the higher incidence of disease in men in the evaluated group. A possible explanation would be the particularities of the personality of the male patients: active and involved people who did not want hospitalization and for which an outpatient therapeutic solution was ideal. A very interesting observation consisted in the fact that auditory recovery at 30 days was virtually equal with final hearing gain.

The discussion of the solution chosen therapy should be started from the analysis of patho-physiogenic mechanisms involved in the occurrence of Sudden Sensorineural Hearing Loss (SSHL). As we have mentioned, there is no consensus on the exact mechanisms. In concrete terms, the theories most commonly advanced are vascular, autoimmune, and viral.

In the vascular theory, it is stated that the cochlea has a terminal vascularization, without collaterals (like retina or heart). Consequently, is very sensitive to ischemia. The thesis is supported by the fact that it suddenly occurs, similar to cerebral infarction or transient ischemic attacks. The identification of antibodies against inner ear antigens and the formation of immunocomplexes in the vascular stria and the endolymphatic sac are the landmarks in the autoimmune theory. The third theory (viral) emphasizes that viruses can cause sudden deafness both by acute infection and by reactivation of a latent infection, this being the mechanism that is suspected with the virus of varicella-zoster and herpes simplex virus type. The pathogenic effects of diabetes on the ear requires a special note, because can be a combination of neuropathic and angiopathic status. Otherwise, the diabetic patients with microangiopathic modifications in the endolymphatic sac were noted to have the greatest degree of hearing loss [10,11].

There is a definite correlation between the patho-physiogenic mechanism and the therapeutic approach. A first option is an abstention and surveillance. Secondly, the classic corticotherapy must be mentioned, given in local, oral or systemic procedure. Finally, the hyperbaric therapy seems to be increasingly used and are correlated with the vascular theory. In turn, the specifically use of intratympanic dexamethasone (Dex-IT) for Sudden Sensorineural Hearing Loss, can be done in several ways - as primary and exclusively treatment, as adjunctive therapy to the standard procedure adopted (i.e., systemic steroids) and as salvage therapy after failure of intravenous steroids.

We chose the mentioned protocol based on the study of the recent literature review. We aimed at obtaining a rapid minimum effective concentration, keeping it an optimal time - three weeks and a minimal activity limitation of patients.

We selected only the patients with hearing the loss in low frequency and ascending curve for the present study, due to the very good prognosis in general. To better understand the role of audiometry curves, were investigated for each patient, the presence of one of the five types of audiometry curves in sudden deafness: A. low frequency (better prognosis). B: pantonal C: high frequencies. D: medium frequencies. E: residual hearing (cophosis). Being a first time proposed method as primary

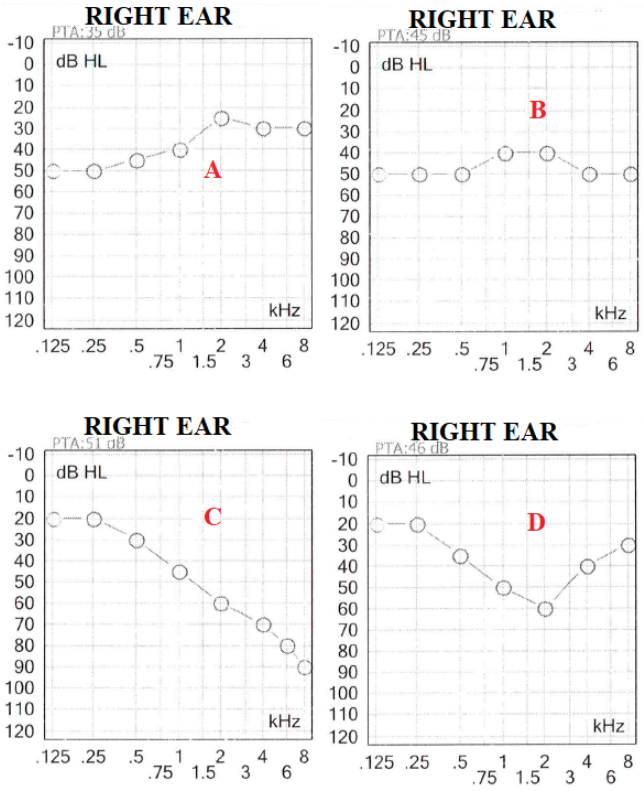

Fig.4 Audiometry curves in sudden deafness. A: low-frequency B: pantonal. C: high frequencies. D: medium frequencies.

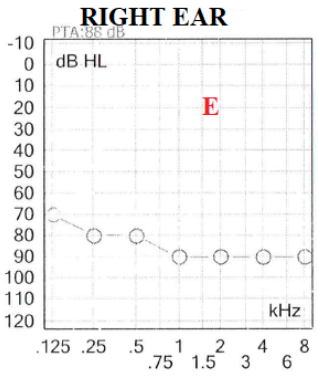

Fig.4 Audiometry curves in sudden deafness. E: residual hearing (cophosis).

and exclusively treatment, we sought to maximize our chances of success (fig.4).

The intratympanic treatment presents at the same time some indisputable advantages. First of all, the procedure can be administered in outpatients. However, it was preferred the variant in the operating room to avoid septic complications and to give the patient greater confidence. In the hands of an experienced ENT surgeon is a straightforward procedure and can be applied soon after diagnosis. Patients describe it as a little painful procedure and can be used in situations where systemic corticotherapy is contraindicated (*e.g.*, immune suppression, HIV, tuberculosis, diabetes).

The disadvantages of the method are few and meaningful. The minimally invasive nature may be mentioned and also the possibility of occurrence of tympanic membrane perforation or otitis media. Temporary dizziness has been reported in some cases [12,16].

Conclusions

The notable effectiveness of Dex-IT in the treatment of Idiopathic Sudden Sensorineural Hearing Loss obtained in our study (74%) was statistically demonstrated and represents a viable option for patients who, for whatever reason, cannot be treated with systemic steroids (diabetic patients) or refuse this therapeutic way. Some study does demonstrate the relationships between diabetes and hearing loss and suggests that screening all patients with diabetes for hearing the loss in a prospective manner may be useful for a clearer understanding of this disease process [10,11]. The presence of anesthesiology team in the *Operating Room Block* was a very solid argument for the treatment patient choice (Dex-IT) and has been shown to be useful for anxiolytic therapy of ten patients. The results obtained on the selected patient's group were entirely encouraging. The sustained and coherent approaches of the national ENT society, through his section of otoneurology, can lead to a diagnostic and therapeutic consensus in the sensorineural hearing loss. Further, the National Health Insurance House must introduce in the methodological norms the therapeutic variants and the concrete conditions for their realization, in order to have a common medical practice for each specific patients group.

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