S U D D E N  H E A R I N G  L O S S  -  
P O S T T R E A T M E N T  R E H A B I L I T A T I O N

S U M M A R Y  O F  T H E  P h D  T H E S I S

P H D  C O O R D I N A T O R ,
P R O F . D R .  M Â R Ț U  V A S I L E  D A N

P H D  S T U D E N T ,
C A V A L E R I U  B O G D A N

I A Ș I
2014
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STATE OF KNOWLEDGE

Sudden deafness is considered a medical emergency requiring immediate clinical and laboratory investigations and appropriate treatment, quickly administered.

Most often, it is defined as a usually unilateral hearing loss, sensorineural, more than 30 decibels, recorded on at least three audiometric frequencies (pure tones) in a row, which was installed within 72 hours.

The challenge brought by this disease is the reduced number of reliable data related to it despite numerous published studies. Until now, not known with certainty any etiology nor fiziopatogenic or curative treatment who will determine with certainty a satisfactory auditory rehabilitation.

Although the disease is classified by the European Commission for Health and Consumer Protection as rare, sudden hearing loss is very disabling for the patient and when became permanent, truly a tragedy. On the other hand, because of this lower prevalence it is very difficult to study SBI in large groups of patients.

SBI incidence was estimated at 5 to 20 cases / 100,000 persons / year with approximately equal distribution by gender or affected side (left or right) (Cobzeanu MD., 2009). Any age group can be affected, but the peak incidence occurs in 5 or 6 decades of life.

Bilateral involvement is rare, and simultaneous bilateral involvement is very rare (Xenellis J.et al., 2007).
The most common form of presentation is unilateral hearing loss observed after awakening (the patient often describes the occurrence of the disease in the night "I woke up this morning deaf") or when he try to use the affected ear.

The etiology of this disease, although it has been widely debated in the research conducted in recent years can be specified only in 10-15% of cases, otherwise idiopathic affection is established.

However, the diagnosis of idiopathic sudden deafness is one of exclusion, which can not be determined until eliminating all possible causal factors such as viral etiology, vascular, trauma, autoimmune and oxidative stress.

Sudden deafness therapy is one of the most controversial topics of debate in the literature of recent years.

Although there is still no effective treatment widely accepted corticosteroids currently are used mostly (Schweinfurth et al., 1996; Fayad, Delacruz, 2003). Methods of administration of the corticosteroid medications have been extensively reviewed in recent years (Parnes et al., 1999; Miller, Schein, 2005).
PERSONAL RESEARCH

STUDY A - CLINICAL AND STATISTICAL STUDY

1. MOTIVATION, AIMS AND OBJECTIVES OF THE STUDY

- achievement a rapid examination protocol applicable to assist in establishing definite diagnosis
- assessment of general and individual parameters of patients included in the study
- interpretation of data obtained from the analysis of the sample of patients diagnosed with sudden deafness
- evaluation of prognostic factors influencing recovery of hearing
- analysis of the treatment methods used in idiopathic sudden hearing loss or in sudden hearing loss caused by different etiologies.
- comparative analysis of recovery of hearing loss obtained after systemic corticoid or local corticoid treatment
- establish opportunities of auditory rehabilitation recommended in patients who could not get a satisfactory aftercare results
- assessment results compared with those published in the literature.
2. MATERIAL AND METHODS

In developing the thesis I analyzed the cases of 88 patients diagnosed with sudden deafness, admitted between 1 January 2009 to 31 July 2014 in the ENT Clinic Rehabilitation Hospital, Iasi.

We conducted a prospective clinical trial of cases of sudden deafness who were hospitalized in the clinic during 5 years.

In data processing were used Microsoft Word (Microsoft Corp.) and MS Excel (Addinsoft SARL, Paris, France).

Information obtained were then statistically analyzed.

In conducting the study sample and considered the following:

- inclusion criteria - are given in the definition of sudden deafness: hearing sudden decrease installed within 72 hours, affecting at least 3 consecutive audiometric frequencies, hearing loss is at least 30 dB.

- exclusion criteria - established outpatient treatment before hospitalization, systemic conditions contraindicate corticoid treatment, infectious ear disease, ear surgery, history of fluctuating hearing loss, Meniere's disease, a history of autoimmune diseases, etc.

The study sought to evaluate patients in the lot after the following parameters:

1. distribution of patients by year of study
2. distribution by sex
3. distribution by age groups
4. distribution by area of origin
5. distribution after unilateral or bilateral location
6. distribution by etiology
7. distribution by duration of time from the onset of the disease until the administration of medication;
8. distribution by the degree of sudden hearing loss;
9. distribution as the frequency of appearance of hearing loss
10. distribution by symptoms associated
11. distribution by the type of treatment administered
12. distribution by hearing rehabilitation after conventional treatment recommended for this condition;
13. distribution by rate of hearing gain after local corticosteroid used associated to systemic or as a first line therapy.

For the diagnosis of sudden deafness, first were required necessarily a clinical examination that included detailed ENT exam, an otomicroscopia for each patient and a liminal tone audiogram performed immediately after the patient's clinical presentation.

After establishing suspicion of sudden deafness all patients were thoroughly examined clinically, laboratory and imaging.

3. RESULTS
We kept the numbering of tables and figures in the thesis.

1. Distribution of patients in the sample by year of study (tab. 8.I.).


Table 8.I. Distribution of patients in the sample by year of study

<table>
<thead>
<tr>
<th>Year</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>11</td>
<td>12</td>
<td>15</td>
<td>14</td>
<td>20</td>
<td>16</td>
<td>88</td>
</tr>
</tbody>
</table>

The number of patients enrolled increased in the last two years. Should also be noted that the sample studied were included patients diagnosed with sudden deafness admitted only until July of 2014, the number of patients could be higher by the end of this year.

2. Patient distribution by age

In terms of age, most patients in the study group were part of the 4th, 5th and 6th decade of life (tab. 8.II.).

Table 8.II. Patient distribution by age
Age groups

<table>
<thead>
<tr>
<th>Year</th>
<th>10-20 years</th>
<th>21-30 years</th>
<th>31-40 years</th>
<th>41-50 years</th>
<th>51-60 years</th>
<th>61-70 years</th>
<th>71-80 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>Absent</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>Absent</td>
</tr>
<tr>
<td>2010</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>Absent</td>
</tr>
<tr>
<td>2011</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>2012</td>
<td>Absent</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>6</td>
<td>2</td>
<td>Absent</td>
</tr>
<tr>
<td>2013</td>
<td>Absent</td>
<td>4</td>
<td>2</td>
<td>5</td>
<td>3</td>
<td>5</td>
<td>Absent</td>
</tr>
<tr>
<td>2014</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>Absent</td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td>15</td>
<td>12</td>
<td>18</td>
<td>18</td>
<td>19</td>
<td>1</td>
</tr>
</tbody>
</table>

Patients aged over 70 years accounted for the lowest percentage, followed by those aged up to 20 years.

In the age groups 21-30 years and 31-40 years were also included a considerable number of patients.

3. Distribution by sex

We have not identified a statistically significant difference in terms of gender division of patients included in the study although the number of men was slightly higher.

4. Distribution of patients according to urban or rural area

In our study we observed a 2-fold higher distribution of patients in urban areas than those in rural areas.

5. Distribution of patients by disease location
Our study group demonstrated unilateral nature of this disease, only four patients setting up a bilateral hearing loss (fig.8.10.).

There was no equal distribution of patients in relation to the location, seeing a more frequent involvement of the left ear.

Fig. 8.10 – Distribution of patients by disease location

6. Distribution of patients by etiology

In the study group, the etiology could be determined with certainty in only 8 patients, two situations in which an etiology viral (herpes simplex) was established, a patient who suffered a cerebral ischemic attack, a patient who was diagnosed with posttraumatic temporal fracture rock with cochlear involvement,
two patients exposed to acute acoustic trauma and two patients diagnosed with acoustic neuroma (fig.8.11).

![Bar chart showing distribution of patients by etiology.](image)

Fig. 8.11 – Distribution of patients by etiology

For the majority of patients included in the study could not clarify the etiology of the condition and they were diagnosed with idiopathic sudden deafness of course after completing thorough diagnosis of all stages of the protocol presented above perform detailed laboratory investigations and imaging possible during hospitalization of patients.

7. Distribution of patients by symptomatology associated

Most often sudden hearing loss was accompanied by tinnitus usually occurs in the same ear, rarely bilateral (tab. 8.IV.). These were reported by 60 patients sampled.

Other symptoms have been reported, but in a much lower percentage. Thus, about 37.5% of patients had associated vertigo and nausea and vomiting 17%. Earache was charged with only 9%
of cases being found here and the two patients diagnosed with Herpes oticus.

Table 8.IV. Distribution of patients by symptomatology associated

<table>
<thead>
<tr>
<th>Associated symptomatology</th>
<th>Tinnitus</th>
<th>Vertigo</th>
<th>Earache</th>
<th>Aural fullness</th>
<th>Nausea/vomiting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>60</td>
<td>33</td>
<td>8</td>
<td>26</td>
<td>15</td>
</tr>
</tbody>
</table>

8. Distribution of patients by the time interval between onset and time of initiation of treatment

Patients from study group were presented in the first seven days in the largest number (tab.8.V), which emphasizes once again that this condition is alarming to patients, may indeed be a real tragedy if the end therapy will not get any hearing rehabilitation.

The category of patients who presented clinical late (after 30 days) after the onset of disease was made up of 11 cases. These patients still receiving the same treatment, but only after being informed of the likelihood of small chances of hearing rehabilitation.
Tab. 8.V. Distribution of patients by the time interval between onset and time of initiation of treatment

<table>
<thead>
<tr>
<th>Time interval</th>
<th>Number of patients/year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2009</td>
</tr>
<tr>
<td>≤ 3 days</td>
<td>2</td>
</tr>
<tr>
<td>4-7 days</td>
<td>5</td>
</tr>
<tr>
<td>8-14 days</td>
<td>absent</td>
</tr>
<tr>
<td>15-30 days</td>
<td>3</td>
</tr>
<tr>
<td>&gt; 30 days</td>
<td>1</td>
</tr>
</tbody>
</table>

9. Distribution of patients according to the degree of sudden hearing loss

According to the degree of hearing loss patients were divided into five categories:

- mild hearing loss (average hearing thresholds <40 dB),
- moderate (average hearing thresholds between 40-69 dB),
- severe (average hearing thresholds between 70-89)
- profound (average hearing thresholds 90-120)
- deafness (no audiometric response to stimulation with 120 dB).

In the study group were predominantly cases of sudden hearing loss of medium and severe degree (61 patients), mild hearing loss was recorded only in eight patients (tab.8.VI). There is also a significant number of patients diagnosed with profound hearing loss and a small number of patients who suffered sudden onset of deafness, but only unilaterally.
Tab. 8.VII. Distribution of patients according to the degree of sudden hearing loss

<table>
<thead>
<tr>
<th>Hearing loss degree</th>
<th>Number of patients /year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2009</td>
</tr>
<tr>
<td>Mild N=8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>absent</td>
</tr>
<tr>
<td>Moderate N=34</td>
<td>4</td>
</tr>
<tr>
<td>Severe N=27</td>
<td>2</td>
</tr>
<tr>
<td>Profound N=16</td>
<td>3</td>
</tr>
<tr>
<td>Deafness N=3</td>
<td>2</td>
</tr>
</tbody>
</table>

10. Distribution of patients according to the degree of hearing recovery

Posttreatment hearing recovery was classified into several degrees (tab.8.IX.):

- no recovery (0-9dB);
- moderate hearing recovery (10-29dB);
- important hearing recovery > 30dB.

Approximately 30% of patients failed to obtain any hearing posttreatment recovery. A significant recovery of hearing thresholds over 30 dB was noted for 29.5% of patients in the study.

Most importantly, 41% of patients were presented partial recovery, moderate between 10 to 30 dB, at the end of treatment.
Table 8.IX. Distribution of patients according to the degree of hearing recovery

<table>
<thead>
<tr>
<th>Year</th>
<th>No recovery &lt;10 dB</th>
<th>Moderate hearing recovery 10-30dB</th>
<th>Important hearing recovery &gt;30dB</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>4</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>2010</td>
<td>3</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>2011</td>
<td>5</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>2012</td>
<td>5</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>2013</td>
<td>5</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>2014</td>
<td>4</td>
<td>8</td>
<td>4</td>
</tr>
</tbody>
</table>

11. Distribution of patients by the administration methods of corticoid treatment

All patients entered the study received corticosteroid medication.

Exception was the clinical case in which the cranio-cerebral MRI examination established the presence of a cochlear fractures occurred as a result of head trauma.

It was considered unnecessary any immediate medical or surgical treatment to recover audition for cochlear lesions. After stabilization, the patient could only benefit from the advantages of the auditory prosthesis implantable devices.
Table 8.IX. The methods of administration of corticosteroid medication used in the study

<table>
<thead>
<tr>
<th>Type of corticoid treatment</th>
<th>Local (intratimpanic)</th>
<th>Combined (systemic+local)</th>
<th>Systemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>7</td>
<td>14</td>
<td>65</td>
</tr>
</tbody>
</table>

We have used three different types of corticosteroid therapy (tab.8.IX):
- systemic therapy
- combined therapy (systemic + local)
- local (intratimpanic) therapy

The most common, systemic corticosteroid therapy was administered alone, 65 of the patients included in the study sample following treatment with Solu-Medrol, 250 mg / day for a period of 7 days.

12. Results of local corticosteroid administered as rescue therapy for refractory sudden deafness systemic treatment (tab.8.X)

Topical corticosteroid medication was used mostly as a salvage therapy in patients with refractory sudden hearing loss (in which there was no recovery audit control tone audiogram performed after systemic corticosteroid treatment).
Although there was a large number of 33 patients in which there was no hearing rehabilitation after treatment of systemic corticoid only some of them have accepted local therapy.

Tab.8.X. Corticosteroid rescue (salvage) therapy

<table>
<thead>
<tr>
<th>Patients with sudden deafness refractory to systemic corticosteroids N=33</th>
<th>Therapeutic response after intratimpanic corticosteroid administration</th>
<th>No therapeutic response after intratimpanic corticosteroid administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients who accepted corticosteroid intratimpanic &quot;rescue&quot; therapy N=14</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>Patients who refused corticosteroid intratimpanic &quot;rescue&quot; therapy N=19</td>
<td>19</td>
<td>0</td>
</tr>
</tbody>
</table>

8.3.14 Results after intratimpanic corticosteroid administered as an initial therapy

In a small number of patients with systemic corticosteroid therapy contraindications or in patients who refused this method of treatment, was administered intratimpanic (local) cortisone
medication. We analyzed recovery recorded auditory tone audiogram performed at the end of corticoid treatment intratampanic administered as initial therapy.

Tab.8.XI. The results of corticosteroid administered as an initial therapy intratampanic in the recovery of auditory

<table>
<thead>
<tr>
<th>Number of patients who received corticosteroid as initial therapy intratampanic</th>
<th>Therapeutic response</th>
<th>No therapeutic response</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>5</td>
<td>2</td>
</tr>
</tbody>
</table>

4. DISCUSSIONS

Yearly distribution analysis of patients entered into the study shows an increase in the incidence of this disease in last years (Fig.8.13.). This can be explained on one hand by the rise in recent years in the outpatient investigation opportunities and sources medical information of patients in clinical increasing the addressability and secondly by enhancing daily exposure to risk factors that may cause the installation of this condition (stress, exposure to intense noise - especially among young people, unhealthy lifestyle, etc. ).

Best represented age groups consist of patients sampled social, decades 4,5 and 6 are in life, so still exposed to risk factors both at work and in leisure. The presence of numerous comorbidities in these age groups may increase the risk of sudden deafness.
Patients in the sample were from urban majority. This distribution put it on account of the existence of a higher exposure to risk factors in urban (sedentary, stress, unhealthy lifestyle, noise from industrial activities or as determined by public transport).

On the other hand, poor health education, lack of financial opportunities and lack of medical offices or facilities of their negative influence of targeting people in rural areas. The etiology of sudden deafness was the subject of numerous research studies in recent years, all concluding that this condition is mostly idiopathic, only 10-15% of cases can be specified a definite cause (Penido N et al., 2005).

In the study conducted by us remains the same incidence of idiopathic sudden deafness percentage of 90.93% was recorded. Idiopathic sudden hearing loss was considered only after careful elimination of all possible causes. For avoiding diagnostic error we rigorously respected well established initial examination protocol. Most patients in our study were presented in the first two weeks of the onset of the disease.

Dramatic nature of the installation of a sudden hearing loss may be responsible for addressing the patient to the doctor early.

When I analysed the time interval from disease onset to treatment for patients in the sample I noticed that the best results were obtained when treatment was administered during the first fourteen days of the occurrence of sudden deafness (fig. 8.30).
Fig. 8.30. Hearing recovery by time interval

In the study group were predominantly cases of medium and severe hearing loss, mild hearing loss was recorded only in 5% of patients. The best results were obtained in hearing rehabilitation in patients who installed a mild to moderate hearing loss (fig.8.33).

If prompt initiation of treatment could make, full recovery of hearing was often recorded on posttreatment audiogram control in these patients.

Thus of the 42 patients who had mild or moderate hipocuzie installed in 13 patients was a total recovery of hearing, 19 patients a satisfactory partial recovery, and 10 of them did not obtain any recovery.
Fig. 8.33. Hearing recovery by hearing loss degree

Were used three types of corticosteroid therapy - systemic administration, combined administration (systemic + local) and topical (transtympanic) (Fig. 8.39).

Systemic administration initiated only after obtaining the informed consent of each patient consisted of administration of solumedrol 250 mg / day, for a short period of 7 days.

Local administration (intratimpanic) of 3–4 μg dexamethasone (dexamethasone phosphate 8 mg / 2 ml) was performed in the study by transtympanic puncture practiced after local anesthesia with lidocaine spray tympanic membrane.

After administration the patient has been placed in the lateral decubitus position the contralateral eye for 20 minutes and to avoid ingestion.
Systemic corticosteroid often failed to provide significant auditory rehabilitation among patients in our study, even if they were present positive prognostic factors for achieving favorable results posttreatment.

In our study we used local therapy intratimpanică mostly as salvage therapy for rehabilitation listening in patients with sudden deafness installs refractory to systemic corticosteroid treatment. It was only 7 patients administered as first line therapy, the reduced due to the recommendation of the patient reticenții part to the use of an invasive method and, on the other hand due to the existence of controversial results reported in some studies previous clinical.

Initially the 41,77% of the patients obtained no hearing recovery after systemic corticosteroid treatment. But of them a percentage of 42.42% (14 patients) accepted transtympanic method topical corticosteroid medication as rescue therapy, recorded at the end of treatment transtympanic hearing recovery in 71% of them (10 patients), thereby reducing to 31% recovery rate of patients without hearing.
We believe that are needed further study to analyze the effects of corticosteroid therapy administered varied from a much larger sample of patients. Also, a large sample can ensure the improvement of the statistical value of the final results. Sudden deafness is still a rare condition will be necessary to extend research along several years in order to obtain a sample of study with a large number of cases.
STUDY B - ANALYSIS THE CORTICOSTEROID TREATMENT EFFECTS ON OXIDATIVE STRESS

1. MOTIVATION, AIMS AND OBJECTIVES OF THE STUDY

The second trial was conducted in the research as objective evidence of the beneficial role that had corticoid treatment both by boosting the body's antioxidant capacity and by reducing oxidative stress levels, the possible mechanisms involved in determining the therapeutic effects of corticosteroid therapy.

AIM OF THE STUDY

• assess the role of oxidative stress represented by the occurrence of idiopathic sudden deafness;

• analysis of a small sample of patients diagnosed with idiopathic sudden deafness, to assess the activity of antioxidant enzymes superoxide dismutase and glutathione peroxidase, and the end product of lipid peroxidation, malondialdehyde - induced by oxidative stress;

• supporting the beneficial role of corticosteroid therapy in reducing lipid peroxidation

• supporting the beneficial role of corticosteroid therapy in stimulating the body's antioxidant capacity

• appreciation of the mechanisms by which corticoid treatment
determine the best results in the recovery of sudden hearing loss. Increased levels of oxygen free radicals may be involved in triggering sudden deafness (Halliwell B., 1994).

The imbalance between oxygen free radical concentration and total antioxidant capacity (TAC) is considered potential pathogenetic mechanism that causes vascular endothelial dysfunction and cochlear level.

2. MATERIAL AND METHODS

This study included 10 patients diagnosed with idiopathic sudden deafness ENT hospitalized in Iasi Rehabilitation Hospital in September 2013 in July 2014.

They made two pair samples that included the same ten patients who investigated both pre and post activity of antioxidant enzymes superoxide dismutase (SOD) and glutathione peroxidase (GPx) and the concentration of malondialdehyde (MDA), the end product of lipid peroxidation.

All enrolled patients following systemic corticoid treatment consisted of intravenous methylprednisolone sodium succinate (Solu-Medrol (r), Pharmacia Enterprises SA Belgium).

Audiometry post-treatment control was performed on the last day of the corticosteroid and at one month.

3. RESULTS

Analysis of SOD activity (superoxide dismutase) performed before and after treatment corticoid by performing Student t test found obtaining posttreatment values increased significantly (p =
0.0024, p <0.05) of the antioxidant enzymes in all ten patients entered in the study (tab. 9.II.).

Table 9.II. The activity of superoxide dismutase (SOD) before and after treatment corticoid

<table>
<thead>
<tr>
<th>SOD baseline level</th>
<th>SOD posttreatment level</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 4,334338</td>
<td>5,462202</td>
</tr>
<tr>
<td>2 4,210633</td>
<td>5,846208</td>
</tr>
<tr>
<td>3 4,488294</td>
<td>6,137325</td>
</tr>
<tr>
<td>4 4,493869</td>
<td>8,149991</td>
</tr>
<tr>
<td>5 4,395247</td>
<td>6,301433</td>
</tr>
<tr>
<td>6 4,383488</td>
<td>6,485131</td>
</tr>
<tr>
<td>7 4,236701</td>
<td>5,638926</td>
</tr>
<tr>
<td>8 4,448156</td>
<td>6,128311</td>
</tr>
<tr>
<td>9 4,261183</td>
<td>5,922278</td>
</tr>
<tr>
<td>10 4,330056</td>
<td>6,355901</td>
</tr>
</tbody>
</table>

The analysis of GPX (glutathione peroxidase) activities performed before and after corticoid treatment by Student t test was also found posttreatment values increased significantly (p <0.0001, p <0.005) of the antioxidant enzymes compared with baseline levels (fig.9.III).
Tabel 9.III. The activity of GPx (glutathione peroxidase) before and after treatment corticoid

<table>
<thead>
<tr>
<th>GPX baseline level</th>
<th>GPX posttreatment level</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
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For patients entered in the study were also analyzed values MDA (malondialdehyde), the end product of lipid peroxidation of polyunsaturated fatty acids, due to increased free radical concentration of oxygen at the cellular level.

After administration of corticoid treatment yielded much lower values statistically significant (p = 0.0003, p <0.05), Student's t test (Tab.9.IV).
4. DISCUSSION

Most studies conducted in recent years in the treatment of sudden deafness concluded that the best hearing recovery was obtained after corticosteroid administration.

However, although corticosteroid treatment is the most common medication administered by clinicians to patients diagnosed with idiopathic sudden deafness, the intimate mechanisms by which corticosteroids exert their therapeutic effect

<table>
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<th>Patient</th>
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are still not fully understood until now (Nagashima, Kiyokazu 2006).

To this end, during the second trial were analyzed changes caused by corticoid treatment on oxidative stress by investigating the level of lipid peroxidation (MDA determination) and the antioxidant enzymes SOD and GPx activity before and after treatment.

Analysing data obtained in our study and those reported by other studies conducted in recent years we can conclude that systemic corticosteroid treatment administered for a short period of time, seven days as was done in our study actually decreases the lipid peroxidation caused by oxidative stress, thus proving its usefulness in combating the harmful effects induced by it.

In our study, by analyzing the enzymes SOD and MDA levels we have demonstrated the effect of stimulating the body's antioxidant system activity induced by systemic corticoid treatment. It should be emphasized that these results were obtained after short-term systemic corticosteroid treatment.
GENERAL CONCLUSIONS

Sudden deafness occurred in full health of patients represented a true drama for which of him, and sometimes ended with permanent hearing loss, hearing only remaining recoverable in these cases just hearing aids.

In most cases could not be identified etiology of sudden sensorineural hearing loss but sometimes this was due to lack of funds to carry out detailed laboratory investigations and imaging.

Patients with suspected idiopathic sudden sensorineural deafness should be followed up, as the certainty of the diagnosis (new elements that may provide the opportunity to identify the cause may occur during this follow-up).

Our study results proved the need of quickly recommended corticoid treatment ± medication associated, because satisfactory auditory rehabilitation was recorded when it was made in the first 7-10 days after the onset of hearing loss.

Drug treatment administered to our patients resulted in an audiometric win rate of over 50% only 40% of patients in the group, in other cases recorded either no improvement or a partial recovery of hearing.

Emphasize the need for discovery of new therapeutic methods effectiveness.
The best rate of hearing gain was recorded in patients receiving corticosteroid therapy within the first two weeks of the onset of the disease.

Treatment of sudden deafness is an area where even the last decade were conducted intensive studies, ongoing research is so far unsuccessful, to establish a therapeutic methods to bring fully satisfactory results.

The absence of satisfactory therapeutic results and side effects that could occur after systemic administration of corticosteroid medication were drawbacks which required the use of survey techniques topical corticosteroid medication. Topical corticosteroid medication techniques used in the study were the transtympanic and tympanocentesis puncture with placement of transtympanic aerator.

Transtympanic administration of corticosteroid medication also presented drawbacks such as difficulties in middle ear anatomy and post-procedural complications and the variability of the therapeutic results obtained.

We emphasize the need to establish standardized techniques for applying topical medications through the round window membrane, as yet remains unclear at present which of the various methods used is most effective.

In our study we used local therapy (intratimpanic) mostly as salvage therapy for rehabilitation listening in patients with sudden deafness refractory to systemic corticosteroid treatment.

Local corticoid therapy was recommended as first-line therapy in a small number of patients and this is determined on the one hand by the reluctance of patients to an invasive technique, on the other hand by the variability of outcomes management efficiency intratimpanic communicated studies in recent years.
We believe there is need further study to analyze the effects of local corticosteroid administered to a sample of patients much larger.

Also, a large sample can ensure the improvement of the statistical value of the final results. Sudden deafness is still a rare disease and it will be necessary to extend research along several years to obtain a study sample containing a large number of cases.

Increased levels of oxygen free radicals observed in patients in the sample may be involved in triggering sudden deafness.

Malondialdehyde (MDA) an end product of lipid peroxidation, a major mechanism of occurrence of cellular damage involves oxidation of polyunsaturated fatty acids with the formation of reactive species and toxic products showed reduced activity in all patients in the study after corticosteroid administration.

We considered potential pathogenetic mechanism that causes vascular endothelial dysfunction cochlear level, imbalance between oxygen free radical concentration and total antioxidant capacity (TAC).

This hypothesis was supported by the results obtained in the second trial conducted, which were analyzed changes caused by corticoid treatment on oxidative stress by investigating the level of lipid peroxidation (MDA determination) and the activity of antioxidant enzymes SOD and GPx before after treatment.

MDA decreased levels in all patients placed in the sample after treatment supports the hypothesis of the beneficial effect of corticosteroid therapy on reducing oxidative stress and its harmful effects.
I realized that dosing posttreatment activity of these antioxidant enzymes, SOD and GPX in our study are particularly important because in investigating oxidative stress, diminished their activity or excess ROS causing many harmful oxidative effects.

SOD and GPX activity, antioxidant enzymes evaluated in our study was significantly improved in all patients, after the systemic corticosteroid administered for a period of 7 days.

In our study by analyzing the enzymes SOD and MDA levels have proved the effect of stimulating the body's antioxidant system activity induced by systemic corticoid treatment, the only research of its kind conducted in our country.

Analysing data obtained in our study and those reported we conclude that systemic corticosteroid treatment administered for a short period of time, seven days as was done in our study actually decreases the lipid peroxidation caused by oxidative stress, thus proving usefulness in combating the harmful effects induced by it.

In conclusion, the data obtained by analyzing the results of studies allow us to support the need recommendation of local corticosteroid first choice for a short period of time to avoid on the one hand the side effects of systemic therapy, on the other hand to avoid induced by prolonged duration of treatment effects that follow actually neutralize them, such as enhancing lipid peroxidation, decreased antioxidant capacity.

Auditory prosthetic rehabilitation was recommended for all patients included in the study after administration of treatment was not granted a hearing or the recovery was insignificant. The doctor had to counter any fears the patient that hearing aids may prevent subsequent recovery of hearing; possibility of spontaneous recovery or aftercare will remain for a prosthetic ear.
Continued future pathogenesis studies and clinical trials are needed for good management of this condition.

ORIGINALITY AND THE TIMELINESS OF THESIS
THEORETICAL AND PRACTICAL CONTRIBUTIONS TO THE DEVELOPMENT RESEARCH AREA

I. This paper falls in basic and applied scientific research trends present in Europe and around the world, addressing a wide range discussed in many research activities in recent years.

II. The thesis represents the first doctoral dissertation in Romania, which analyzes compared results given by two methods corticoid treatment, systemic and local patients diagnosed with sudden deafness.

III. The novelty of this work are:

1. The first study conducted in Romania on a sample of patients diagnosed with idiopathic sudden deafness, which analyzes the effects of corticosteroid-induced antioxidant enzymes superoxide dismutase on and glutathione peroxidase and malondialdehyde concentration, the end product of lipid peroxidation induced by stress oxidative.

2. The study results suggest for the first time mentioned the involvement of changes made on antioxidant enzymes and malondialdehyde in triggering mechanisms that induce corticosteroid medication therapeutic outcomes for hearing recovery in patients diagnosed with sudden deafness.
SELECTIVE REFERENCES


5. Avissar N, Finkelstein JN, Horowitz S, Willey JC, Coy E, Frampton MW. Extracellular glutathione peroxidase in


12. Benjamin E Schreiber, Charlotte Agrup, Dorian O Haskard, Linda M Luxon Sudden sensorineural hearing loss. The


32. Hanyu Liang, Si-Eun Yoo, Ren Na, Christi Walter, Arlan Richardson and Qitao Ran. The distinct in vivo roles of the long-form and short-form of glutathione peroxidase 4: the short-form is essential for somatic cell functions and the long-form is important for male fertility. In The FASEB Journal, 2009


