

**Does Intratympanic steroid injection**  
**improves hearing in idiopathic sudden**  
**sensorineural hearing loss**

**Meta-Analysis study**

For partial fulfillment of master degree in otorhinolaryngology

Presented by

**Shereen Hamdy Gaafar**

M.B.B.cH.

2006

Under the supervision of

**Prof. DR. Hesham Y. ElSherbiny**

Professor of otorhinolaryngology

Faculty of medicine

Ain shams university

**DR. Tamer A. Abou El Ezz**

Lecturer of otorhinolaryngology

Faculty of medicine

Ain shams university

**2009**

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ رَبِّ اشْرَحْ لِي صَدْرِي {25} وَيَسِّرْ لِي  
أَمْرِي {26} وَاحْلُلْ عُقْدَةً مِّن لِّسَانِي {27}  
يَفْقَهُوا قَوْلِي {28}

صدق الله العظيم

سورة طه

## **ACKNOWLEDGMENT**

I would like to express my deep gratitude to **Professor Dr. Hesham Elsherbiny** professor of otorhinolaryngology Ain-Shams University, for his helpful and constructive suggestions, and for the continuous encouragement that he generously offered during this work.

I am also very grateful to **Dr. Tamer Abou El Ezz**, Lecturer of otorhinolaryngology Ain-Shams University for his great and smart guidance and supervision of this work; also he devoted much of his precious time and effort in order to achieve this work in a successful form.

I am also very thankful to **Prof. Dr. Foad Abass**, head of department of otorhinolaryngology in MUST University for his continuous support.

## **Table of contents**

Abbreviations	II
List of figures	IV
List of tables	V
Introduction	1
Etiology, pathology and Pathophysiology of ISSNHL	4
Evaluation, treatment and prognosis of ISSNHL	12
Intratympanic steroid therapy	25
Aim of work	45
Materials and methods	47
Characteristics of studies	54
Discussion	80
Conclusions	87
Recommendations	90
Summary	93
References	98
Arabic summary	109

## Abbreviations

<b>ABR</b>	Auditory Brain Stem Evoked Response
<b>ATP</b>	Adenosine Tri-Phosphate
<b>CBC</b>	Complete Blood Picture
<b>CO2</b>	Carbon Dioxide
<b>CT</b>	Computed Tomography
<b>CSF</b>	Cerebro-Spinal Fluid
<b>CMV</b>	Cytomegalovirus
<b>DNA</b>	Deoxyribonucleic Acid
<b>G</b>	Gauge
<b>HIV</b>	Human Immunodeficiency Virus
<b>HL</b>	Hearing Loss
<b>ISSNHL</b>	Idiopathic Sudden Sensorineural Hearing Loss
<b>IL1</b>	Interleukin 1
<b>IT</b>	Intratympanic
<b>IV</b>	Intravenous
<b>K</b>	Potassium
<b>kHz</b>	Kilo-Hertz
<b>meq</b>	Milliequivalent
<b>mg</b>	Milligram
<b>mm</b>	Millimeter
<b>ml</b>	Milliliter

<b>mV</b>	Millivolt
<b>MRI</b>	Magnetic Resonance Imaging
<b>Na</b>	Sodium
<b>NFκB</b>	Nuclear Factor Kappa B
<b>l</b>	Liter
<b>LAM</b>	LASER Assisted Myringotomy
<b>LFSL</b>	Low Frequency Sensorineural Hearing Loss
<b>PTA</b>	Pure Tone Average
<b>RWM</b>	Round Window Membrane
<b>RW</b>	Round Window
<b>SHL</b>	Sudden Hearing Loss
<b>SDS</b>	Speech Discrimination Score
<b>TNF</b>	Tumor Necrosis Factor
<b>ug</b>	Microgram
<b>um</b>	Micrometer
<b>ul</b>	Microlitre

## List of figures

<b>Fig No.</b>	<b>Subject</b>	<b>Page</b>
<b>Figure(1)</b>	Showing histo-pathological findings in the inner ear where there is atrophy in hair cells of organ of corti.	10
<b>Figure(2)</b>	An audiogram showing a case with severe ISSNHL	15
<b>Figure(3)</b>	(A)Micro-Wick (B) Placement of a micro-wick through tympanic membrane (C)Insertion of ventilation tube (D) RW shown through a ventilation tube	31 31 32 32
<b>Figure(4)</b>	(A)Showing placement of RW micro-catheter. (B)Catheter tip. (C)Intra-operative view of an implanted catheter.	34
<b>Figure(5)</b>	Fine needle injection in the middle ear through the tympanic membrane.	35
<b>Figure(6)</b>	Showing 2 methods of steroids administration (LAM) and tympanostomy.	36
<b>Figure(7)</b>	(A) A diagram showing the different concentrations of steroids in perilymph. (B) ) A diagram showing the different concentrations of steroids in endolymph	41 41

## List of tables

<b>Table No.</b>	<b>Subject</b>	<b>Page</b>
<b>Table (1)</b>	Illustrates the number of articles found on the pub-med	49
<b>Table (2)</b>	It shows the results of meta-analysis study	52
<b>Table (3)</b>	A comparison between many articles done on Intratympanic steroid perfusion in ISSNHL	86



# ***Introduction***

## **Introduction**

Idiopathic Sudden sensorineural hearing loss (ISSNHL) is considered an otologic emergency requiring immediate and careful clinical intervention, followed by appropriate and specific treatment **(Ahn et al., 2007)**.

ISSNHL is defined as the rapid decline in hearing in less than 3 days >20 db in >3 contiguous audiometric frequencies without any identifiable cause **(Byle, 1984)**.

ISSNHL occurs over a short period of time and may vary from a mild to profound hearing impairment in otherwise normal hearing individuals. The disorder has an estimated incidence of 5-20 cases per 100,000 populations **(Mattox et al., 1977)**.

In some cases the patient feels a pop or senses the sudden onset of tinnitus and the hearing drops precipitously, in other cases the hearing drops over a few minutes or few hours, other patients awakens in the morning with hearing loss. This condition, however constitute a medical emergency because the window of opportunity for treatment is narrow and early administration of steroids is more efficacious than watchful waiting **(Rauch, 2004)**.

No single treatment exists leading to complete recovery to pre-hearing loss levels. Proposed treatments have included vasodilators, steroids (Intratympanic or systemic), antiviral agents, hyperbaric oxygen and plasmapheresis (**Slattery et al., 2005**).

**Meta-analysis** will be the statistical method used in this study to determine the efficacy of Intratympanic steroid therapy in the treatment of ISSNHL.

**Meta-analysis** is a quantitative statistical procedure that synthesizes findings across many studies, overcoming the problems of small samples and diverse outcomes and programs. According to **Tobler, 1986**, the computation of the effect size is dependent on statistically significant results. Instead of discounting the studies whose results do not reach statistical significance, as would be the case in a literature review, the quantitative results of each study are converted into a common metric (effect size). There by allowing comparison of results across studies.

***Etiology, pathology  
and  
Pathophysiology of  
ISSNHL***

## **Possible Causes of ISSNHL**

In the vast majority of patients with ISSNHL, no specific cause can be identified, therefore, the disease is called “Idiopathic” an exclusion diagnosis. A review of 837 patients with sudden hearing loss between 1989 and 1993 found that 88% were ultimately deemed idiopathic (**Fetterman et al., 1996**).

The most popular theories as to cause ISSNHL include viral infection, vascular insufficiency, immune mediated reaction, and intra-labyrinthine membrane rupture. 60% of patients with ISSNHL have an elevation in serum viral titers compared with 40% of control (**Wilson et al., 1983**). Cytomegalovirus (CMV), mumps, and rubella have been identified in the inner ear of patients with ISSNHL (**Cole, 1988**).

There are 4 types of direct and indirect evidence for the viral theory of ISSNHL: 1-Temporal association of ISSNHL with active viral upper respiratory illness. 2-Serologic evidence of active virus infection. 3-Histopathologic examination of post mortem human temporal bones. 4-Animal experiments demonstrating virus penetration of inner ear (**Mattox et al., 1977**).

There are 3 types of circumstantial evidence to support the vascular theory of ISSNHL: 1-Sudden onset. 2-Case reports of

sudden deafness with known systemic vascular disease. 3- Histopathologic demonstration of cochlear changes caused by vascular occlusion (**Rauch, 2004**). Certain prothrombotic risk factors and genes have been associated with ISSNHL (**O'Malley and Haynes, 2008**).

Studies have shown that there are alteration in the blood and red cell filterability. And an association between ISSNHL and slow blood flow in the vertebrobasilar system, it has been reported that reduction in cochlear blood flow results in cochlear hypoxia due to edema of the capillary cells. Spontaneous perilymphatic fistulae have also been implicated in ISSNHL (**Banerjee and Parnes 2005**).

ISSNHL is classified with some of these inner ear disorders as immune mediated. **McCabe, 1979** first introduced the concept of autoimmune inner ear disease. There may be other immune mediated but not autoimmune causes of ISSNHL (**Freedman et al, 1996**). Also it was found that there is association of ISSNHL with known inner ear diseases as Wegner's disease, Cogan's syndrome (main target organs cornea and inner ear) and temporal arteritis (**O'Malley and Haynes, 2008**).

Cochlear membrane rupture is a cause of sudden hearing loss (SHL), either spontaneous in cases of ISSNHL or occur in a patient

with a history of temporal bone trauma and stapedectomy that damage the internal membranes of the cochlea and results in hearing loss. The concept of spontaneous cochlear membrane rupture is different, so there seems to be little objective evidence to support the idea that a substantial percentage of ISSNHL is caused by spontaneous cochlear membrane rupture **(O'Malley and Haynes, 2008)**.

Other diseases that can result in SHL must be excluded to diagnose ISSNHL as: Acoustic neuroma, Meniere's disease, syphilis, diabetes mellitus, multiple sclerosis, Lyme disease, mumps, polyarthritis nodosa, Cogan's syndrome and migraines **(Fetterman et al., 1996)**.

## **Pathology and Pathophysiology of ISSNHL**

Some studies have described the postmortem pathologic findings in the temporal bone of patients with sudden deafness. The temporal bones were prepared in the standard manner for light microscopic study including fixation in 10% formalin, decalcification with ethylene diamine tetra-acetate, embedment in celloidin, serial sectioning at a thickness of 20 um and staining of every tenth section with haematoxylin and eosin **(Schuknecht, 1993)**.