A Systematic Review

Of Systemic Therapy For Idiopathic Sudden Sensorineural Hearing Loss

SUBMITED FOR PARTIAL FULFILMENT OF MASTER DEGREE IN OTOLARYNGOLOGY

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Abbreviations

ATA	**Atmosphere absolute**
ATP	**Adenosine tri-phosphate**
CT	**Computed Tomography**
dB	**Decibel**
DNA	**Deoxyribonucleic acid**
DNFB1	**Dinitrofluorobenzene 1**
EGb	**Ginkgo biloba extract**
gm	**Gram**
GJB2	**Human gene encoding for Gap junction protein, beta 2**
H.E.L.P	**Heparin-Induced-Extracorporal-LDL-Precipitation**
HBO	**Hyperbaric oxygen**
HBOT	**Hyperbaric oxygen therapy**
HES	**Hydroxyethyl starch solution**
HIV	**Human immunodeficiency virus**
HL	**Hearing level**
HSV	**herpes simplex virus**

IL1	**interleukins 1**
ISSHL	**Idiopathic sudden sensorineural hearing loss**
IU	**international unit**
IV	**Intravenous**
Kg	**Killogram**
kHz	**Kilo-Hertz**
LDL	**Low-density lipoprotein**
Mg	**Milligram**
Mg2+	**Magnesium ion**
MgSO4	**Magnesium sulfate**
Mm	**Millimeter**
MRI	**Magnetic resonance imaging**
NF-kB	**Nuclear factor Kappa B**
NIDCD	**National Institute on Deafness and Other Communication Disorders**
O2	**Oxygen**
PGE1	**Prostaglandin E1**
PTA	**Pure tone audiometry**

RCT	**Randomized controlled trial**
RNA	**Ribonucleic acid**
rt-PA	**Recombinant tissue plasminogen activator**
SD	**Sudden deafness**
SDS	**Speech Discrimination Score**
SHL	**Sudden hearing loss**
SNHL	**Sensorineural hearing loss**
SSNHL	**Sudden sensorineural hearing loss**
TNF	**Tumor necrosis factor**
μm	**Micrometer**

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Introduction

Sudden sensorineural hearing loss (SSNHL) is characterized by a rapid progression of hearing impairment over seconds to days. No universally accepted definition exists, although The National Institute on Deafness and Other Communication Disorders (NIDCD) defines sudden sensorineural hearing loss as a rapid loss of hearing, occurring over a period of up to 3 days. The hearing loss must be of at least 30 dB in three connected frequencies. Further, the NIDCD indicates that sudden sensorineural hearing loss should be considered a medical emergency. Other definitions include hearing loss over a period of less than 12 or 24 hours to stress the concept of sudden hearing loss **(Chau et al, 2010).**

Although not all investigators adhere rigorously to the definition proposed by the NIDCD, most studies include patients who have suffered at least a loss of 20 dB at more than one frequency over less than a 72-hour period **(O'Malley and Haynes, 2008)**.

The incidence of SSNHL has been estimated to range from 5 to 20 per 100,000 persons per year. Any age group may be affected, but the peak incidence occurs in the 5^{th} or 6^{th} decade of

life. Bilateral involvement is rare, and simultaneous bilateral involvement is very infrequent. The most common presentation is a unilateral hearing loss upon awakening or when attempting to use the affected ear. Some patients note a sudden, stable hearing loss, whereas others experience a rapidly progressive loss **(Chau et al.2010).**

Sudden sensorineural hearing loss has been described as a medical emergency. The abrupt development of an unexpected sudden sensory deficit warrants consideration of this situation as an emergency by medical professionals and lay personnel. Despite the dramatic presentation, in most cases, sudden sensorineural hearing loss is the presenting symptom of a pathophysiology that has yet to be identified. In as many as 88% of patients, a battery of diagnostic testing fails to yield an identifiable cause **(O'Malley and Haynes, 2008)**.

Aim of the Work

The aim of this study is to conduct a systematic review on the efficacy of different types of systemic therapy in treatment of ISSNHL.

A meta-analysis, if feasible, to answer this question: Does patients with ISSNHL get hearing benefits from different types of systemic therapy?

Etiology

The precise cause of sudden sensorineural hearing loss has not been identified, but several pathophysiological mechanisms have been proposed.

1. Infectious causes

Evidence from case series suggests that mumps virus can be a cause, accounting for about 7% of adult cases. Varicella-zoster virus can also cause such hearing loss in patients presenting with Ramsay-Hunt syndrome (herpes zoster oticus). Many other viruses (rubella, cytomegalovirus, influenza, Epstein-Barr virus, herpes simplex type I and II virus) have been postulated as possible causes of sudden sensorineural hearing loss, but serological, epidemiological, and histopathological data are not conclusive **(Wilson et al, 1983).**

Bacterial meningitis is a well recognized cause of sensorineural hearing loss, Lyme disease should be considered in endemic areas and lassa fever has been reported as a common cause in west Africa. Sudden sensorineural hearing loss has also been described as a presenting feature of fungal meningitis, otosyphilis and HIV **(Schreiber et al, 2010).**

There are four types of direct and indirect evidence for the viral theory of SSNHL:

(1) Temporal association of SSNHL with active viral upper respiratory illness.

(2) Serologic evidence of active virus infection.

(3) Histopathologic examination of postmortem human temporal bones.

(4) Animal experiments demonstrating virus penetration of the inner ear **(Rauch, 2004).**

2. Vascular causes

Studies have investigated several possible mechanisms including atherosclerosis, hypotension, thrombophilia, vasospasm, hyperviscosity and embolism. However, there is no hard histological evidence for vascular occlusion being a common cause of this disorder **(Schreiber et al, 2010).**

However, there are 3 types of circumstantial evidence to support the vascular theory of SSNHL:

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).**

3. Miscellaneous causes

A. Endolymphatic hydrops, an excess of endolymph in the scala media of the labyrinth, is a pathological finding that is commonly associated with Ménière's disease—a clinical diagnosis, which classically presents with sudden unilateral hearing loss, tinnitus, and vertigo. The underlying pathophysiological mechanism of endolymphatic hydrops remains obscure, although several pathways have been proposed. Endolymphatic hydrops has also been reported with other otological disorders, including so-called immune-mediated inner-ear disorder and pathological changes giving rise to sensorineural hearing loss such as syphilitic labyrinthitis **(Garcia Berrocal et al, 2002).**

B. Sudden sensorineural hearing loss is sometimes associated with systemic immune-mediated diseases. Moreover, patients with this disorder can have evidence of T-cell and antibody recognition of inner-ear antigens. However, the role of tissue-specific immune-responses is poorly defined **(Berrocal et al, 2006)**.

C. Several genetic diseases have been linked with sudden sensorineural hearing loss, including mutations of GJB2 (DNFB1; encoding connexin 26), the presence of a widened vestibular aqueduct in Pendred syndrome, branchio-oto-renal

syndrome, renal tubular acidosis, Fabry's disease and mutations in the mitochondrial 12S ribosomal RNA gene.

D. The most common neoplastic disease associated with sudden sensorineural hearing loss is vestibular schwannoma, which usually presents with unilateral tinnitus and progressive sensorineural hearing loss, although it can present with sudden loss in a few cases. Sudden sensorineural hearing loss has also been reported with various cerebello-pontine angle lesions; including meningioma .Sudden sensorineural hearing loss can rarely be seen as a paraneoplastic occurrence, sometimes in association with paraneoplastic sensory neuronopathy, or as a complication of meningeal carcinomatosis. It has also been reported as a presenting symptom of chronic myeloid leukaemia. **(Schreiber et al, 2010).**

Pathology and Pathophysiology of SSNHL

Merchant et al. (2005) in their study describe the temporal bone histopathology in 17 ears with idiopathic sudden sensorineural hearing loss reported that the most common abnormality in cases without recovery of hearing is atrophy of hair cells and supporting cells of the organ of Corti, with variable involvement of other structures and without fibrous or osseous proliferation in the inner ear. A minority of cases show non–hair cell lesions such as isolated cochlear neuronal loss. The histopathologic data do not support the concept of membrane breaks or perilymphatic fistulae of the oval or round window membranes as a cause of ISSHL. In addition, the data also indicate that vascular occlusion as an etiologic event for sudden deafness is a rare event. The hallmark of a vascular insult to the cochlea consists of deposition of connective tissue and new bone, which was observed in only one of their 17 cases and has been reported in only 2 of 27 ears with ISSHL in the literature. (**Schuknecht**, **1993**).