Otoprotective Drugs In Noise Induced Hearing Loss

An Essay Submitted For Partial Fulfillment of Master Degree In Otorhinolaryngology

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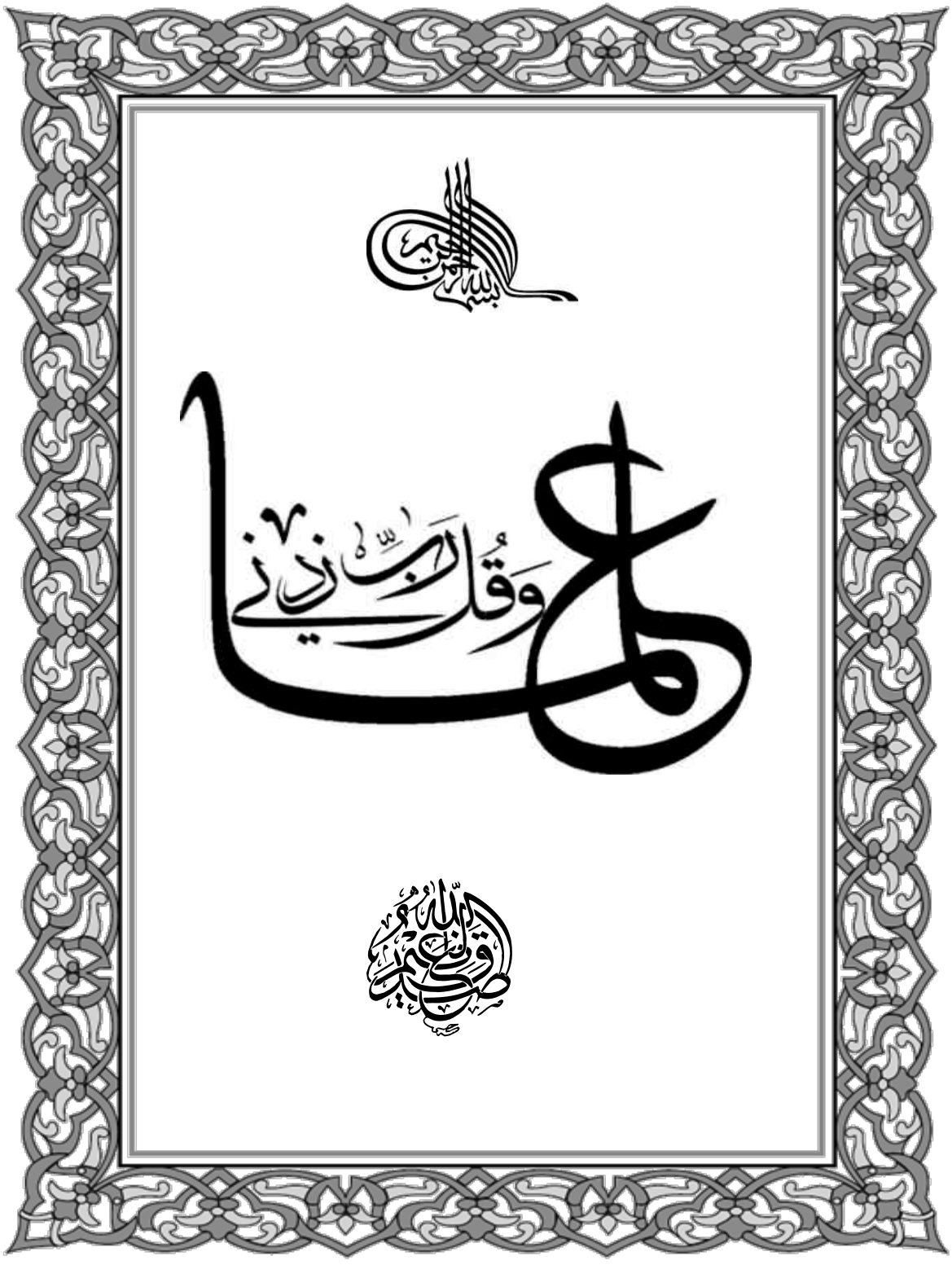

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الأدوية الحافظة للسمع فى
الضوضاء المحرضه على الفقدان السمعى

دراسه مقدمه توطئه للحصول على درجة الماجستير فى جراحة
الأذن و الأنف والحنجرة

مقدمة من

الطبيبة/ داليا حمدى يوسف
بكالوريوس الطب والجراحة

تحت اشراف

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List of Abbreviation

AAT	**:**	Acute Acoustic trauma
ABR	**:**	Auditory brain response
ALCAR	**:**	Acetyl-L-carnitine
ALT	**:**	Alanine transaminase
AMPA	**:**	X-amino-3-hydroxy-5-methyl-4- isoxazolproprionate
ATRA	**:**	All-trans retinoic acid
BDNF	**:**	Brain-derived neurotrophic factor
bFGF	**:**	Basic fibroblast growth factor
BM	**:**	Basilar membrane
CBF	**:**	Cochlear blood flow
CNTF	**:**	Ciliary neurotrophic factor
DOEHRS-HC	:	Defense Occupational Environmental Health Readiness
FA	:	Ferulic acid
FGF	:	Fibroblast growth factor
GDNF	:	Glial cell line-derived neurotrophic factor
GDNF	:	Glial-derived neurotrophic factor
GRs	:	Glucocorticoid receptors
GSH	:	Glutathione
IHCS	:	Inner hair cells
IT	:	Intratympanic
JNK	:	C-Jun NH2-terminal kinases
KM	:	kanamycin
L-NAC	:	N-L acetylcysteine (L-NAC)
LOC	:	Lateral olivocochlear
LSO	:	Lateral superior olive
Mg	:	Magnesium
MOC	:	Medial olivocochlear
MP	:	Methylprednisolone

MSO	:	Medial superior olive
NIHL	:	Noise induced hearing loss
NMDA	:	N-methyl-D-aspartate
NT	:	Neurotrophin
OHCS	:	Outer hair cells
PBN	:	Phenyl N tertbutylnitrone
PBN	:	Phenyl N-tertbutylnitrone
PLZF	:	Promyelocytic leukemia zinc finger protein
PTS	:	Permanent threshold shift
RNS	:	Reactive nitrogen species
ROS	:	Reactive oxygen species
SNP	:	Sodium nitroprusside
SOC	:	Superior olivary complex
SPL	:	Sound pressure level
TNF	:	Tumor necrosis factor
TTS	:	Temporary threshold shifts
4-OHPBN	:	4-hydroxy phenyl N-tert-butylnitrone

Abstract

The study was done to know the different pathways to cell death initiated by noise, and to find out the recent literature targeted to prevent initial ROS formation, maintaining cochlear blood flow, restoring calcium balance in cells and in neurons, preventing calcineurin activation and/or caspase formation, or preventing the late forming ROS and RNS species that appear 7– 10 days post-noise.

Interventions, including antioxidant agents, vasodilators, NTFs, steroids, calcineurin inhibitors, caspase inhibitors, JNK inhibitors, and Src protein tyrosine kinase (Src-PTK) inhibitors
have all been shown at least partially effective in prevention of
auditory deficits, including hearing loss and hair cell death.This is consistent with the global scientific view that damage due to increased ROS generation whether acute or chronic leads to eventual cochlear hair cell damage and death. Given above is a
comprehensive summary of the drug interventions in clinical
trials.However, we believe that some of these drugs may enter the general market in the next few years.

Given the various points of intervention along the cell death
pathways, there are an abundance of potential therapeutic targets. The most effective strategy may include targeting initiating eventsProtective strategies have employed antioxidant compounds, antiinflammatory agents or RNA silencing to achieve positive results.

Key Words:

Noise induced hearing loss\ protection\ drugs.

INTRODUCTION

Psychologists define ‘sound’ as pressure waves travelling through a medium that carry some sort of information, signal or communication. On the other hand ‘noise’ is defined as unwanted sound, sound that doesn’t carry useful information and is generally considered undesirable or unpleasant ***(Coleman et al, 2010).***

Hearing is the perceptual response by the brain to sound waves that are received by the ears. The ear consists of three main divisions. The external ear serves to funnel sound waves into the internal parts of the ear, and also provides a limited amount of assistance to spatial localization of sounds due to its shape. The collected waves travel along the ear canal through to the tympanic membrane (commonly known as the eardrum) causing it to vibrate. The middle ear is composed of structures that transfer the vibration of the eardrum into fluid movement in the adjacent sensory organ in the inner ear called the cochlea. Within the cochlea there is a network of fine sensory hair cells that are moved accordingly and this motion causes the hair cells to create impulses in the auditory or hearing nerve. This translates the incoming pressure changes into neural signals, which are then sent via brainstem auditory centers to the primary auditory centers in the cortex of the brain ***(Zheng et al ,2010).***

Hair cells along the cochlea respond to different frequencies of sound. That is to say they map directly to the frequencies that humans can hear, with certain cells responding to low frequencies (low pitch sounds), others to high frequencies or high pitch sounds ***(Wasim et al ,2010).***

Noise-induced hearing loss (NIHL) is a permanent form of hearing loss that occurs because of exposure to intense sound. After a single exposure there are initial temporary changes in hearing that are reversible, but if the sound is intense enough or repeated, permanent irreversible hearing loss occurs, which is referred to as a permanent threshold shift. In short, noise-induced hearing loss is the deafness that occurs when the ears are exposed to sounds in excess of what they can handle ***(Cascella et al ,2012).***

Physicist's definition of noise that is relevant to noise-induced hearing loss, as any sound can contribute to the disorder regardless of its source or whether it is perceived as desirable or not. In terms of hearing loss, mechanical noise, music, machinery and speech are all potentially as risky as each other. The intensity, duration and cumulative exposure to a sound determine its pathological impact upon the ear ***(Hamaquchi et al ,2012).***

The predominant damage occurs to the hair cells and their associated nerves leading to the hearing loss. When hair cells are

repeatedly exposed to excessive stimulation from intense sound, they become fatigued and fail to respond properly, this manifests as a temporary hearing loss or 'dullness' of hearing after noise exposure (known as temporary threshold shift or TTS), which recovers within 16-24hrs of the exposure. If the excessive stimulation is repeated or sustained for long enough the hair cells will become permanently damaged or die and the threshold shift becomes permanently established ***(Wasim et al ,2010).***

Exposure to high levels of noise is the most common cause of hearing loss in adults. Among the causes of NIHL are: death or damage of the organ of Corti , ischemia of the inner ear, and increased metabolic activity leading to excessive ROS generation and lipid peroxidation. Noise exposure induces reactive oxygen species (ROS) generation in the cochlea as early as 1 hr post exposure, which persist for several days after noise exposure, this leads to hair cell damage and death that continues for days after noise exposure. Control of ROS generation in NIHL may provide an effective therapeutic strategy ***(Peppi et al ,2011).***

Given the various points of intervention along the cell death pathways, there are an abundance of potential therapeutic targets. The most effective strategy may include targeting initiating events and early molecular processes, thus maintaining a cell in a relatively 'normal' physiological state ***(Wasim et al ,2010).***