Auditory assessment for neonates received Gentamicin in neonatal intensive care in Port Said Governate

Thesis

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٢٠١٢

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Adel Ahmed Ali Ibrahim

List of Abbreviations

AABR : Automated Auditory brain stem response
ABR : Auditory brain stem response
AD : Autosomal dominant
ANSD : Auditory neuropathy spectrum disorder
AR : Autosomal recessive
BERA : Brainstem Electric Response Audiometry
BPD : Bronchopulmonary dysplasia
CDC : Centers for Disease Control
CHL : Conductive hearing loss
CL : Clearance
C_{max} : Peak serum concentration
C_{min} : Trough serum concentration
CMV : Cytomegalovirus
dB : Decibel
DPOAEs : Distortion Product Otoacoustic Emissions
EAC : External auditory canal
ECMO : extracorporeal membrane oxygenation
EOAES : Evoked otoacoustic emissions
GA : Gestational age
GJB٢ : Gap Junction Beta ٢
IHC : Inner hair cell
JCIH : Joint Committee on Infant Hearing
LBW : Low birth weight
MIC : Minimum inhibitory concentration
NF٢ : Neurofibromatosis ٢
OAE : Otacoustic emissions
OHC :Outer hair cell

List of Abbreviations. (cont)

OM	: Otitis media
OME	: Otitis media with effusion
PPHN	: Persistent pulmonary hypertension
PKs	: Pharmacokinetics
SNHL	: Sensorineural hearing loss
SOAEs	: Spontaneous otoacoustic emissions
XL	: X-linked
SOAEs	: Stimulus-Frequency Otoacoustic Emissions
STORCH	: Syphilis, Toxoplasmosis, Rubella, Cytomegalovirus, Herpes virus
TEOAEs	: Transient Evoked Otoacoustic Emissions
TM	: Tympanic membrane
UNHS	: Universal neonatal hearing screening
VLBW	: Very low birth weight
Vd	: Volume of distribution
WHO	: World health organization

List of Tables

List of Tables (cont.)

List of Figures

List of Figures (cont.)

List of Figures (cont.)

CONTENTS

Page

INTRODUCTION

Hearing loss is an etiologically heterogeneous trait with many known genetic and environmental causes ***(Nance,*** ***).*** The most common non genetic causes are infections, Rh incompatibility, ototoxic drugs, prematurity, and noise-induced hearing loss ***(American Academy of Pediatrics, ٢٠٠٧).***

Sixty% of neonates receive at least one antibiotic and ٤٣٪ of the antibiotics administered to these neonates are aminoglycosides ***(Pacifici,*** ***).*** The most common aminoglycoside used in the neonatal intensive care unit is gentamicin ***(Clark and Spitzer,*** ***٢٠٠٦).***

Aminoglycosides retain activity against the majority of Gram-negative clinical bacterial isolates in many parts of the world ***(Falagas et al.,*** ***).*** So it is part of the ١st line antibiotics in most neonatal units across the world ***(Contopoulos-Ioannidis,*** ***).***

Also, extremely high antibiotic resistance rates of neonatal Gram-negative pathogens have been reported in developing world ***(Litzow et al.,*** ***).*** But the prevalence of gentamicin resistance has remained relatively low in most of centers ***(Jones et al.,*** ***).***

Gentamicin is inexpensive, widely available and a highly effective antibiotic for treating serious infection in young infants in developing countries ***(Bang et al.,*** ***).*** However, the negative aspect of gentamicin therapy after long-term use refers to its adverse effects, which are mostly nephrotoxicity and ototoxicity ***(Yang et al.,*** ***).***

In spite of the risk for toxicity, as well as the costs associated with monitoring serum concentrations, gentamicin is preferred over cefotaxime and ceftriaxone for coverage of suspected gram-negative infections in neonates ***(Murki et al.,*** ***).***

Gentamicin toxicity is balanced against its therapeutic value. It should probably be reserved for the treatment of severe infections in life saving situations and in these cases the ototoxicity is of secondary importance and an important factor against its use and control of treatment is paramount ***(Bulger et al., ١٩٩٣)***.

The recent emergence of resistant Gram-negative bacteria, in conjunction with an improved safety profile of the aminoglycosides through once daily dosing, has revived the interest in the clinical utility of these antibiotics ***(Leibovici et al.,*** ***).***

'Once a day' dosing, by providing more time for clearance, may avoid the toxic effects of gentamicin due to slower clearance ***(Begg et al.,*** ***).*** This regimen has been associated with diminished accumulation in renal tubules and inner ear ***(Contopulos-Ioannidis,*** ***).***

Gentamicin in controlled therapeutic doses has a less ototoxic and vestibulotoxic effect in newborns than it does in older children or in adults ***(Aust and Schneider,*** ***).*** The incidence of gentamicin nephrotoxicity and ototoxicity in neonates is not well established and, seems to be considerably less than that in adults ***(de Hoog et al.,*** ***).***

Most studies in infants and children from different parts of the world however, show that hearing loss is a rare complication of aminoglycoside therapy ***(Rao et al.,*** ***;*** ***Nestaas et al.,*** ***; Darmstadt,*** ***).***

Limited available data show that gentamicin induced hearing loss contributes to only a small proportion of deafness in community and do not show any significant hearing loss in gentamicin treated neonates. Individuals with certain identifiable mutations have higher susceptibility to aminoglycoside induced hearing loss ***(Brunton et al.,*** ***).***

Some individuals have genetic predisposition for developing hearing loss and they can develop permanent hearing loss with therapeutic concentrations and even single doses of aminoglycosides. About ٢٥٪ of individuals with aminoglycoside induced hearing loss have maternal relatives with drug related hearing loss ***(Bitner-Glindzicz and Rahman,*** ***)***.

The combination of otoacoustic emissions and auditory brainstem responses can be used to determine the status of the peripheral and central auditory system ***(Korres,*** ***;*** ***Suzuki and Suzumura,*** ***)***.

Both technologies are non-invasive recording of physiologic activities that are easily recorded in newborn. Two steps processes using otoacoustic emissions followed by auditory brainstem responses in those who failed the first test is often used to improve test performance ***(Nelson et al.,*** ***).***

AIM OF THE WORK

١- To estimate the incidence of hearing impairment in gentamicin treated neonates without other risk factors compared to neonates without risk factors for hearing loss among neonatal intensive care unit patients in Port Said governorate.

٢- Assessment the correlation of hearing loss with duration of gentamicin therapy.

ANATOMY & PHYSIOLOGY OF EAR

I. Anatomy of the Ear:

The auditory pathway can be divided into two parts; the peripheral auditory system (the ear and primary neurons, i.e., the auditory and cochlear nerves), the central auditory system from cochlear nucleus to cortex ***(Erol-Başar,*** ***).***

The peripheral auditory pathway is divided audiologically into a conductive and a sensorineural path ***(Bireny et al.,*** ***).*** The conductive part consists of the pinna, external auditory canal (EAC) and the middle ear. Sensorineural pathway includes the cochlea and part of the ٨th cranial nerve (Figure ١) ***(Isaacson and Vora,*** ***).***

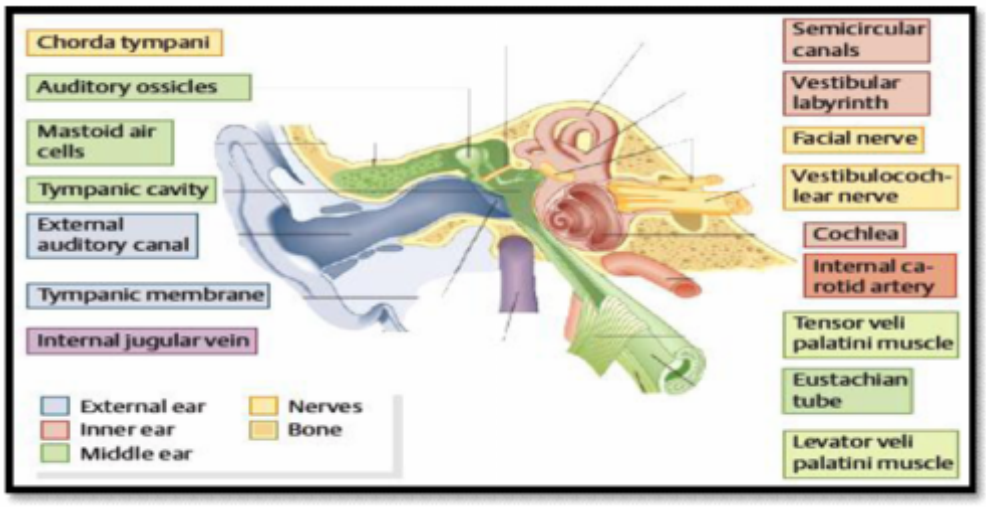

Figure ( ): *Anatomy of the ear* ***(Kenneth,*** ***).***

١. The External ear:

Two structures make up the external ear: a flexible, oval shaped structure "pinna" attached to the head, and the auditory canal that leads to the middle ear ***(Lalwani,*** ***).***

a) The pinna (Auricle):

The pinna projects from the side of the head at an angle of ٢٥° to ٣٥° (mean value ٣٠°) to the occipital scalp and serves as a sound collector ***(Sclafani and Ranaudo,*** ***).*** The auricle is a semicircular plate of elastic cartilage characterized by a number of ridges or grooves (Figure ٢). The major ridges of auricle are the helix and antihelix, the tragus and antitragus which surround the concha, which is the scaphoid depression posterior to the external auditory meatus ***(Gacek,*** ***).***