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Drug's Cause Ototoxicity

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Abstract: *Now a days, we are using thousands of medicines, but few of us know the toxic effects of the medicines. One of these toxic effects is ototoxicity, which is a pharmacological toxic effect that occurs in different categories of medicine. Ototoxicity is the property of being toxic to the ear, specifically the cochlea or auditory nerve and sometimes the vestibular system. On the study of toxic effects, it shows they are either irreversible or reversible. Hence the diagnosis and effective treatment of ototoxicity is challenging, even today, but a lot of clinical study is being done with new medicine to minimise this Ototoxicity effect.*

Keywords: Drug, Symptoms, Mechanism, Prevention, etc

I. INTRODUCTION

Hearing loss is the most common sensory disorder worldwide. Sensorineural hearing loss may be genetic or acquired worldwide. Sensorineural hearing loss may be genetic or acquired. Hearing loss can be inherited, caused by medication (Streptomycine), or caused by other factors, but it can also be caused by a combination of factors (Otomycosis is a fungal ear infection).The World Health Organization [WHO] estimates that around 466 million people worldwide suffer from disabling hearing loss, and that by 2050, more than 900 million people will have this condition. Ototoxicity came to the forefront of clinical attention with the discovery of streptomycin in 1944. Streptomycin is used to treat tuberculosis.

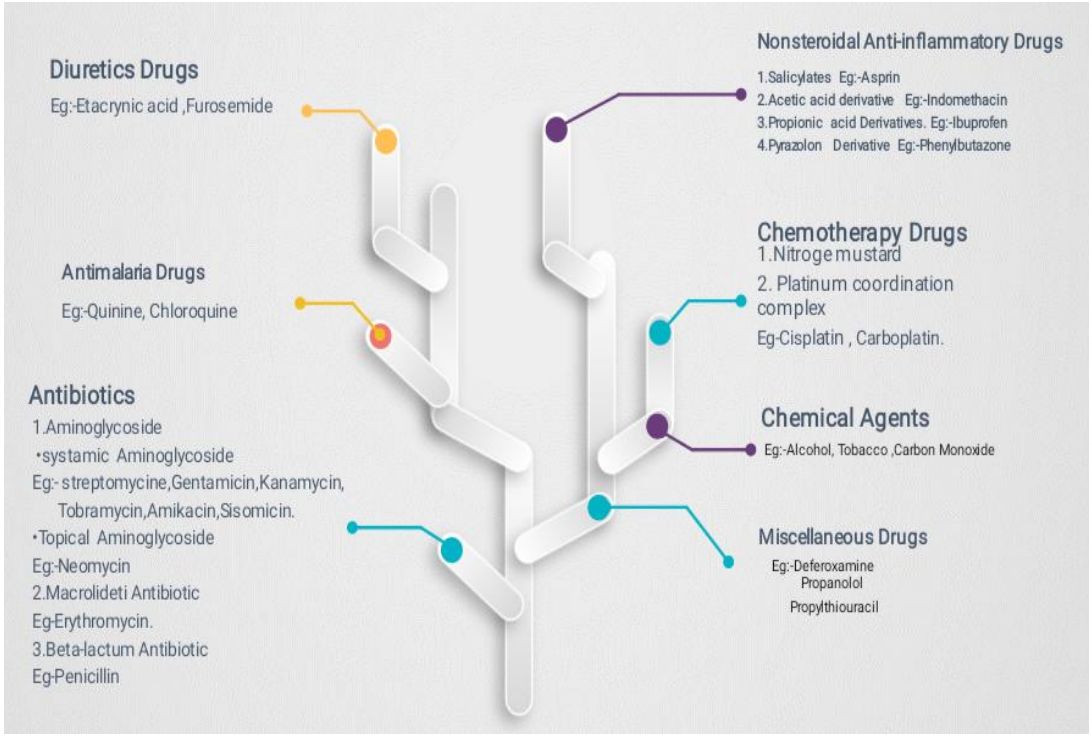

Figure 1

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Ototoxicity is the property of being toxic to the ear, specifically the cochlea or auditory nerve. The majority of ototoxicity is seen in elders. The affirmation was found to cause ototoxicity. As mentioned at Folsom, the medication prescribed for a long period of time will cause permanent hearing loss, which may be irreversible or reversible; both possibilities exist. Ototoxicity is caused by nearly 100 different drug classes. There are different categories of medicine responsible for it, as classified in [Figure II.2]. It may cause permanent loss of hearing, and the risk of developing hearing disorders is a very serious health condition. Among the medications that cause ototoxicity are most antibiotics, anti-cancer drugs, and non-steroid anti-inflammatory medications.

II. MEACHNIZUM OF OTOTOXICITY

2.1 Meachnizum of Action [Aminoglycoside]

Ototoxicity is more likely to be encountered when therapy is continued for more than one week , at higher doses.otoxicity is greate when plasma concentration of the drug is persistently high and above the threshold value.High concentrations are found in the renal cortex and in the endolymph and the perilymph of the inner ear. This perhaps contributes to their nephrotoxicity and ototoxicity [eighth cranial nerve damage]. The comparative toxicity of an Aminoglycoside Antibiotics mentioned in chart **(Figure 2).** The kanamycin and Amikacin produce greater cochlear damage then other aminoglycoside, but the vestibular damage is caused more by Streptomycin and Gentamicin.

Clinically, aminoglycoside drugs mainly enter the inner ear through systemic and topical pathways. In the systemic pathway, the drug passes through the blood-labyrinth barrier [BLB] and enters the inner ear through the striavascularis. In topical administration, the drug can bypass the BLB into the middle ear and then through the round window into the inner ear. The drug is absorbed either by endocytosis on the apical surface or by transduction channels Early genetic analysis showed that the susceptibility of aminoglycosides was related to mitochondrial DNA mutations, which inhibited the synthesis of mitochondrial proteins. However, evidence is accumulating to suggest that the overactivation of N-methyl-D-aspartate (NMDA) receptors and the production of free radicals are also important factors in the ototoxicity of aminoglycosides . The mechanism of aminoglycosides-induced ototoxicity is very suitable. How does aminoglycoside cause hearing loss has been a hot research topic. Associations Between Susceptibility to Aminoglycosides and Mitochondrial DNA Mutation Mitochondria are energy providers and mediators of cell apoptosis. [Death of cells which occurs as a normal] , which play an important role in cell survival . Aminoglycoside susceptibility has been reported to be related to genetic background in many individuals.

Systemic used Aminoglycoside	Ototoxicity Vastibular	Ototoxicity cochlear
1. Streptomycine	++	±
2. Gentamicin	++	+
3. Kanamycin	+	++
4. Tobramycin	+±	+
5. Amikacin	+	+±
6. Sisomicin	+±	+
7. Netilmicin	+±	+

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2.2 Meachnizum of Action [Diuretics]

Certain types of diuretics are associated with varying levels of risk for ototoxicity. Loop and thiazide diuretics carry this side effect. The loop diuretic furosemide is associated with ototoxicity, particularly when doses exceed 200 mg per hour. The risk increases when these drugs are used in the presence of renal insufficiency. The related compound ethacrynic acid has a higher association with ototoxicity, and diuretics are thought to alter the ionic gradient within the striavascularis. Causing factors appear to be increased endolymph salt content and a direct toxic action on hair cells in the internal ear.

2.3 Meachnizum of Action [Chemotherapy Agent]

Platinum-containing chemotherapeutic agents, including cisplatin and carboplatin, are associated with cochleotoxicity, characterised by progressive, high-frequency hearing loss with or without tinnitus [ringing in the ears]. The severity of cisplatin-induced ototoxicity is dependent upon the cumulative dose administered and the age of the patient, with young children being most susceptible.The exact mechanism of cisplatin ototoxicity is not known. The drug is understood to damage multiple regions of the cochlea, causing the death of outer hair cells as well as damage to the spiral ganglion neurons and cells of the striavascularis. Long-term retention of cisplatin in the cochlea may contribute to the drug's cochleotoxic potential. Once inside the cochlea, cisplatin has been proposed to cause cellular toxicity through a number of different mechanisms, including the production of reactive oxygen species (ROS). The decreased incidence of oxaliplatin ototoxicity has been attributed to decreased uptake of the drug by cells of the cochlea.
Reversiblototoxicity is also caused by vinca alkaloids, including vincristine.

III .SOME SERIOUS SYMPTOMS

3.1 Hearing Loss

Loss of hearing

3.2 Vertigo

Where a person has the sensation of moving or of surrounding objects

3.3. Tinnitus

Tinnitus is the perception of sound when no corresponding external sound is present; it may also sound like a clicking, buzzing, hissing, or roaring. The sound may be soft or loud, low or high-pitched, and appear to be coming from one or both ears. Most of the time, it comes on gradually. The sound may interfere with concentration or cause anxiety or depression in some people.

3.4 Nystagmus

It is generally an involuntary, rapid, and rhythmic eye movement. Sideways, on both sides, up and down, or rotational movements are all possible. It may be present continuously or occur when looking in certain directions.

3.5 Damage Semicircular Canals

The semicircular canals or semicircular ducts are three semicircular, interconnected tubes located in the innermost part of each ear. The three canals are the horizontal, superior, and posterior semicircular canals.

3.6 Damage of Cranial Nerve VIII

The vestibulocochlear nerve known as the eighth cranial nerve, transmits sound and equilibrium information from the inner ear to the brain

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3.7 Genetic

Hearing loss can be inherited. More than 40 genes have been implicated in the cause of deafness. There are more than 300 syndromes with related hearing loss, and each syndrome may have causative genes

3.8 Nephrotoxicity

The toxicity is related to the total amount of drug received by the patient.

3.9 Cochlear Damage

Hearing loss affects the high frequency sound first , then progressively encom passes the lower frequencies . No regeneration of the sensory cells occurs ; auditory nerve fibres degenerate in a retrograde manner - deafness is permanent . Older patients and those with preexisting hearing defect are more susceptible .Initially , the cochlear toxicity is asymptomatic and can be detected only by audiometry . Tinnitus then appears , followed by progressive hearing loss.

3.10 Neuromuscular Blockade

All aminoglycosides reduce ACh release from the motor nerve endings . They interfere with mobilization of centrally located synaptic vesicles to fuse with the terminal membrane as well as decrease the sensitivity of the muscule end plates to ACh. The neuromuscular block produced by aminoglycosides can be partially antagonized by i.v. injection of a calcium salt .

3.11 Cardiotoxicity

Several experimental and clinical studies support the fact that increased oxidative stress and apoptosis have been involved in cisplatin-mediated cardiotoxicity.

3.12 Hepatotoxicity

Clinical studies have proven that cisplatin-induced liver damage can occur either alone or in combination with other drugs. Cisplatin-induced hepatotoxicity was exacerbated by oxidative stress.

V. PREVENTION

No specific treatment may be available, but withdrawal of the ototoxic drug may be warranted when the consequences of doing so are less severe than those of the ototoxicity. Co-administration of anti-oxidants may limit the ototoxic effects. some of the recent drugs available to treat ototoxicity**.**

5.1 Otoxicity Induced by Aminoglycoside Precautions

1. Avoid aminoglycoside specially [Streptomycin and Gentamicin] due to produce high susceptability .
2. Caution use in elder patients they are high susceptability towards kidney damage.
3. Avoid aminoglycoside use with cause synergistic effect to cause Nephrotoxicity damage
4. Neuromuscular block cause aminoglycoside can be antagonized by IV injection of a calacium salt.
5. Avoid aminoglycoside in pregnancy due to risk of foetal ototoxicity

5.2 Ototoxicity Caused by Chemotherapy Agent

1. Administration of amifostine has been used in attempts to prevent cisplatin-induced byototoxicty.

5.3 Ototoxicity caused by Antiseftic and Chemical Agent Precaution

1. Topical alcohol based prepration used in ear treatment should be avoided

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