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Ototoxicity Induced by Anti Tubercular Drugs: A Brief Case Report

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ABSTRACT

Reversible and irreversible ototoxicity in the potential adverse effect of aminoglycosides therapy. Long term used Aminoglycosides they can cause Neuromuscular blockage and nephrotoxicity. In this case study 40 years old female, weighing 50 kg was brought to the hospital with chief complains of tinnitus, hearing loss, and vertigo for past 1 week. She had a known relapsed case of smear positive pulmonary tuberculosis and was taking regular second line anti-tubercular drugs therapy (Isoniazid, Rifampicin, Pyrazinamide, Ethambutol, and Streptomycin) from last 3 month. Pulmonologist had stopped inj. Streptomycin 1gm BD but other IInd line ATT medication was continued. Although there are many case reports already done previously, Aminoglycosides (AGs), induced ototoxicity particularly in tuberculosis patients, we come over the first case of AGs induced ototoxicity in TB patients. In this case patient condition was resolved only after discontinuation of streptomycin.

INTRODUCTION

AGs can potentially cause ototoxicity due to mitochondrial gene mutation [1,2]. Streptomycin (a AGs) is part of the drug regimen in relapsed tuberculosis [3]. Patients on tuberculosis re-treatment are recruited longitudinally from Direct Observation Therapy-Short (DOTS) course centres. Early detection of ototoxicity was determined using the American Speech and AGs Hearing Association criteria and genetic analysis to determine relevant mitochondria gene AGs mutations. [4] Streptomycin is also used in many diseases like, Meniere's disease and other advanced bacterial infections usually in the combination with the other antimicrobials [5]. Streptomycin on long duration medication, causes the damage to cochlear and vestibular portion of the inner ear [6,7]. Loss of the vestibular sensitivity causes difficulty walking and oscillopsia. Loss of hearing generally occur after a short latent period (7-10 days) at 1 gm/day or higher doses and slowly worsens [8].

CASE STUDY

A case of 40 years old female, weighing 50 kg was brought to hospital with chief complains of tinnitus, hearing losses, vertigo for past 1 week with no past & family history of hypertension (HTN), diabetes mellitus (DM), thyroid disease & PTB. Patient was smoker and non- alcoholic. At the time of general vital study PR- 114 bpm, BP-145/100 mmHg, oxygen saturation 101% at the atmospheric air and cardiac sounds S1, S2 positive were noted. She had a past history of pulmonary tuberculosis (2 year back), but at that time patient was completed six months course of first line anti-tubercular DOTS therapy (CAT Ist). She had a known case of relapse smear positive pulmonary tuberculosis and taking regular second line anti-tubercular drugs therapy (Isoniazid, Rifampicin, Pyrazinamide, Ethambutol and Streptomycin) for last 2 month. After 6th week of IInd line anti-tubercular drug treatment, patient was developed with the problems like tinnitus & hearing losses related problem. Pulmonologist had stopped the Inj. Streptomycin as this drug was responsible for ototoxicity in the long-term use of the therapy. But other IInd line ATT medication (HRZE) was continued. Pulmonologist had advised the patient for routine lab test like CBCs, LFTs, KFTs, Chest X-RAY. On the same day, pulmonologist prescribed the following drugs to the patient after examination:

1. Injection Pantoprazole - 40mg TDS
2. Hold Inj. Streptomycin 1 gm with continuation of CAT II ATT drugs.
3. Tab. Pyridoxine 20 mg OD
4. Inj. Piperacillin + Tazobactam 4.5 mg TDS, IV
5. Tab Montelukast+ levocetirizine HS
6. Nebulization with Formoterol 6 mcg& budesonide 200 mcg BD

On the 2nd day, Blood pressure was recorded as 145/110 mmHg and pulse rate was 112 beats per minute. According to the laboratory reports, Patient liver function test (LFT), CBCs all count was normal limits. Fresh complain of Patient was constipation, vertigo, tinnitus (hearing losses); pulmonologist referred the patient to ENT department for the ototoxicity related problem. ENT References (Table 1).

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Table 1: ENT Reference.

S. No.	Drugs Prescribed (Brand Name)	Generic Name	Dose	Indication
1.	Cap. Neurobion forte	Vitamin B_{12}	100mg	BD
2.	Tab. Vertimin- 16	Bitahistine	16mg 1/2	BD
3.	Syp. Sucral-O	Sucralfate, Oxetacaine	3 TSF	TDS
Stop Inj. Streptomycin Rx. Continue same treatment				

Table 2. Discharge Medication.

S. No	Drugs prescribed (Brand name)	Generic Name	Dose	Indication
1.	Tab. AKURIT-4	Tab. Isoniazid, Tab. Rifampicin Tab. Ethambutol Tab. Pyrazinamide	300 mg 450 mg 800 mg 1200 mg	OD- BBF
2.	Tab. Benadon	Tab. Pyridoxine	20 mg	OD-HS
3.	Tab. Pentop	Tab. Pantoprazole	40 mg	OD- BBF
4.	Tab. Dolo-650	Tab. Paracetamol	650 mg	SOS
5.	Syp. R-Qual	Multivitamin	200ml	TDS-3 TSF
Ensure protein powder, 2TSP- BD with water/milk After meals				

Table 3: Causality Assessment of Suspected ADRs.

ADRs	CAUSALITY		
	Naranjo's Scale	WHO-UMC	Karch and Lasagna Scale
Streptomycin Induced Ototoxicity	Probable	Probable	Probable

On the 3rd day, Blood pressure was normal i.e. 120/70 mmHg and pulse rate were 86 beats/min with SPO2 concentration 97%. Patient fresh complaints of whole-body ache. On 4th day, patient complains loss of appetite, on brief discussion of pulmonologist with a clinical pharmacologist, counselling along with diet assessment was done of patient. Patient was advised to take proper fluid, high protein and diet rich in fibers. Pomegranate juice was advised to be avoided. On 5, 6, 7, 8, 9 10th days, no fresh complaints were seen, all vitals were normal. On the basis of subjective & objective observation, Pulmonologist had made a final diagnosis of anti-tubercular drug (Streptomycin) induced Ototoxicity. After staying 10^{th} days in hospital, patient condition was improved & then cap. Neurobion-forte was stopped. Patient discharged with appropriate medication & patient counselling after advising review once in a month with LFTs reports (Table 2).

DISCUSSION

Hearing loss is irreversible most of the time, and audiometric monitoring is preponderant before, during and after therapy [1,2]. Many are the publications present on mechanisms of drugs induced ototoxicity, their monitoring, prevention and control. Ototoxicity is an irreversible side effect of AGs. This adverse effect is dose-dependent and compounded by the narrow therapeutic range of a AGs and the wide inter-individual variability in the pharmacokinetics of the drug (According to De Jager and Van Altena et al 2002), and could manifest as either cochlea damage with permanent hearing loss or vestibular damage with dizziness, ataxia and/or nystagmus (According to Duggal and Sarkar et al 2007). AGs cause damage by mitochondrial protein production disruption, cellular membrane potentials changes, interaction with the transition metals, free radicals' formation, c-Jun N-terminal kinase (JNK) activation, caspases and nucleases [9]. Therefore, in the early stages of AGs ototoxicity conversational hearing might not be affected. While AGs preferentially target bacterial ribosome, the inner ear and kidney are known to receive collateral damage. Hearing loss can be conductive or sensorineural. Before hearing can be tested, the status of the auditory channel and tympanic membrane must be determined. This is performed with a combination of otoscopy and tympanometry [10,11].

CLINICAL INTERVENTIONS

- ✓ Upon discussion, clinicians along with health care professionals can design a prophylactic regime to treat the non-intentional effects in DOTS therapy. Multivitamins medication along with pyridoxine (vitamin B6) and cyanocobalamine (vitamin B12), can be given alongside the therapy with in definite intervals of 45-60 days for 7-8 days.
- ✓ Peripheral neuropathy, psychosis, hepatotoxicity & hypovitaminosis are the most important problems in TB patients. Multivitamins + pyridoxine along with ATT therapy can be prescribed to combat the unwanted side effects of these drugs.
- ✓ As a clinical pharmacist, prescription review should also be done as, drugs containing B6 and B12 both belong to vitamin B complex category, a combined drug should be given, additionally pantoprazole, a PPI drug should be indicated BD before meals rather than TDS so that to maintain the patient quality of life and bypassing drug related side effects, eventually PPIs (pantoprazole) shouldn't be given with INH as it reduces the effect of INH showing Drug- Drug Interaction.

ADR ANALYSIS

On assessing past and present medical and medication from the patient, the developed ADRs are suspected with anti-tubercular drugs. After analyzing the ADR profiles of anti-tubercular drugs, it was found that the probable drug i.e. Streptomycin induced ototoxicity. As a clinical pharmacist we made further assessment to build a relationship between the probable drug and the developed adverse effect, that causality assessment with the help of Naranjo's scale, WHO-UMC ADR assessing scale as well as Karch and Lasagna scale which are represented below (Table 3).

ADR MANAGEMENT

Usually, the management of ADRs includes withdrawal/ suspension, dose reduction of suspected/ probable drug and administration of supportive therapy. In this issue, to treat ATT (streptomycin) induced psychosis the drug was withdrawn and a started modified ATT therapy was given.

CONCLUSION

Drug induced ototoxicity is the adverse effects seen in most of the TB patients; On concluding, the ototoxicity induced by AGs is managed by providing supportive care and discontinuation of the particular drugs. Clinicians & Pulmonologist must take a prophylactic drive once every two months on patients indicated streptomycin. Medication review is the key process for a clinical pharmacist so as to avoid medication error, prescription error, dosing error etc. Patients with tuberculosis are very susceptible to other infections and other morbid condition so proper review, counselling and treatment should be given to the patients. It improves the diseased conditions as well as the patient's quality of life.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

ETHICAL CONSIDERATION

None

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