

A Study to Assess Ototoxicity in Patients Receiving Anti-Tubercular Therapy

Dr Jagannath. B¹, Dr Shazia²

¹Head of Dept of ENT, Kempegowda Institute Of Medical Sciences, K.R. Road V.V Puram, Bangalore- 560004, Karnataka India
Email: [jashmidr12\[at\]gmail.com](mailto:jashmidr12[at]gmail.com)

²Senior Resident, Scott's ENT Hospital, Lucknow- 226022, UP India
Email: [shazia.darkangel\[at\]gmail.com](mailto:shazia.darkangel[at]gmail.com)

Abstract: *Objectives:* To assess the incidence of ototoxicity in patients receiving ATT. To assess the onset of clinical symptoms of ototoxicity with pure tone audiometry findings. To assess whether the ototoxicity is reversible or irreversible. *Materials and Methods:* A prospective observational study was conducted in 100 patients who were diagnosed with tuberculosis. Follow-up was carried out at intervals of 2 months from the initiation of treatment until it's completion. After the completion of the treatment, patients identified with ototoxicity were followed up for a year to note PTA. *Results:* Most common age group affected was 40-49 years of life (66.6%), p value – 0.740 Male: Female ratio is 1.6:1. Giddiness, Headache, Nystagmus and Tinnitus are present in 20, 25, 7 and 15 patients respectively by the end of 2 months during the course of treatment. Decreased hearing is commonly seen by the end of 2nd month, 20%, which gradually increased to 21% by end of the course of treatment. On PTA findings 15 Male and 5 female patients had HFL by the end of 2nd month (p value -0.274). On 1-year follow-up 21 patients had irreversible hearing and HFL in the PTA report.

1. Introduction

Tuberculosis (TB) is a bacterial infection caused by mycobacterium tuberculosis complex¹. WHO declared TB as a global emergency in 1993¹. Incidence of active pulmonary tuberculosis in India is estimated to be as high as 3 million new cases per year worldwide^{1,2,3}. Isoniazid(H) (300mg), Rifampicin(R) (450mg), Pyrazinamide(Z) (1500mg), Ethambutol(E)(1200mg), and Streptomycin(S)(750mg) are the primary anti-tubercular drugs used¹. Toxicity to the auditory and vestibular system is a well-known complication in Anti – Tubercular Therapy (ATT)³. Ototoxic complaints seen in this therapy are dizziness, tinnitus and hearing loss^{3,4}. Alteration in drug regimen following early detection of hearing loss by Pure Tone Audiometry (PTA), prior to its clinical presentation helps curtail further loss of hearing before it can adversely affect the ability to communicate.

2. Materials And Methods

A prospective observational study was conducted in the department of ENT, Kempegowda Institute Of Medical Sciences, Bangalore from June 2015 till January 2017. 100 patients who were diagnosed with tuberculosis and met the inclusion criteria, were selected for the study. Inclusion Criteria was:

- 1) Adults of both sexes aged 18-60 years
- 2) Patients having Tuberculosis (New extra pulmonary, Relapse , Failure, Defaulter)
- 3) Newly enrolled at the study centre for the DOTS therapy
- 4) No evidence of hearing loss prior to the commencement of treatment
- 5) Informed written consent

Prior to initiation of therapy at our center, all patients had undergo detailed vestibular and cochlear function evaluation. Follow up was carried out at intervals of 2 months from the initiation of treatment until it's completion.

After the completion of the treatment, patients identified with ototoxicity are followed up for a year to note PTA.

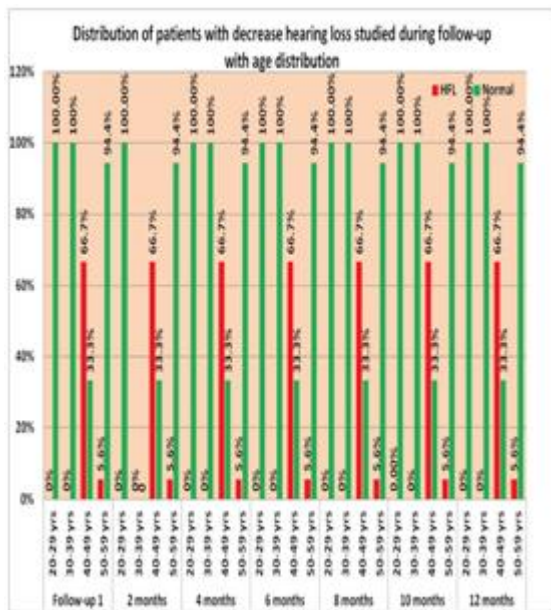
3. Method of Statistical Analysis

The results were presented in number and percentage for dichotomous data in Table and Figure. Univariate analyses of the dichotomous variables encoded were performed by means of the Chi square test with Yates correction if required. In all the above tests the “p” value of less than 0.05 was accepted as indicating statistical significance.

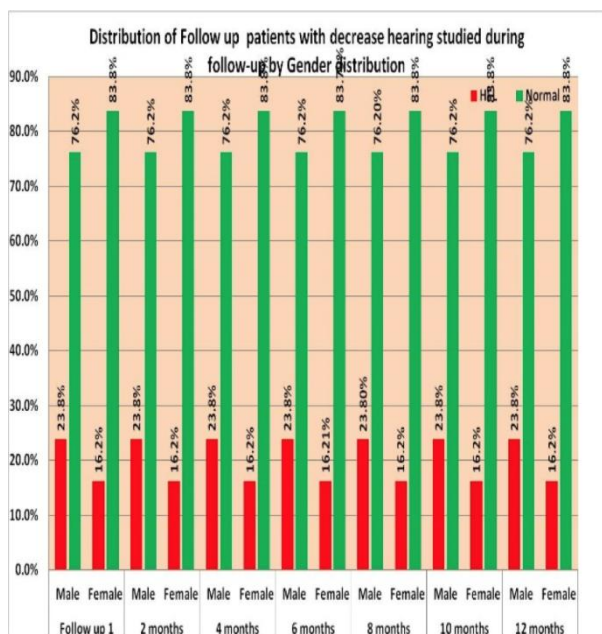
4. Result

Most of the patients enrolled in the study were in 40-49 years, 32 patients. Next common age group affected was 50-59 years. Male predominance is found in our study. Male: Female ratio is 1.6:1. Giddiness was commonly seen by the end of the 2nd month, 23%, which gradually decreased to 20% by the end of the course of treatment. Headache was commonly seen by the end of 2nd month, 9%, which gradually increased to 25% by the end of course of treatment. Tinnitus was commonly seen by the end of the 4th month, 15%, which gradually decreased to 15% by the end of course of treatment. Decreased hearing was commonly seen by the end of 2nd month, 20%, which gradually increased to 21% by end of the course of treatment. Nystagmus was commonly seen by the end of 4th month, 10%, which gradually decreased to 7% by end of 6th month and to 0% by the end of course of treatment. HFL is present in 20 patients by the end of 2nd month and it gradually increased to 21 by end of 8th month. The most common age group affected was 40- 49 years (66.6%), p value – 0.740. Next group affected was 50-59 years (5.5%) this result was persistent throughout the course of treatment. 15 (23.8%) Male patients had HFL by the end of 2nd month and this result was persistent throughout the course of treatment (p value - 0.274). 5 female patients had hearing loss by the end of 2nd month, which increased to 6 (16.21%) by end of 4th

month. This result was persistent throughout the course of treatment. 15 (23.8%) male patients had hearing loss in PTA during follow up. 6 (16.21%) female patients had hearing loss during follow up This PTA result was persistent for 1 year follow up. P value – 0.441. The most common age group affected was 40-49 years (66.6%) had decreased hearing loss during follow up. The next group effect was 50-59 years, 5.5%. This result was persistent till 1 year follow up. 15 (23.8%) male patients had hearing loss during follow up. 6 (16.21%) female patients had hearing loss during follow up This result was persistent for 1 year follow up. P value – 0.441.



Graph 1



Graph 2

5. Discussion

MDR-TB is a growing problem throughout the world. Streptomycin plays a major role in the management of multidrug resistant mycobacteria³. Toxicity to the auditory

and vestibular system is a well-known common complication of the treatment with aminoglycoside antibiotics³. In the present study, the incidence of ototoxicity was 21%. Similar results were seen in a study conducted by Katijah et al which had hearing loss in 33% of patients⁵. Duggal et. al, studied ototoxicity caused by streptomycin and also showed similar results, 18.7% of patients had hearing loss⁶. In contrast, a study conducted by De Jager et al. showed 3 Of 5 patients (60%) treated with streptomycin eventually developed ototoxicity⁷. Similar high incidence of ototoxicity was reported in a prospective study of 53 patients by Fausti et al., 47%⁷. Similarly, in a study conducted by De Lima et al., where hearing sensitivity of 36 cured TB patients who had been treated with streptomycin was assessed, findings indicated that 75% of the participants presented with auditory disorders⁸. De Lima et al. Reported that of those patients who presented with auditory disorders (75%), 85% presented with bilateral HFL⁹. In our current study all 21 patients had bilateral HFL. However, the precise incidence of ototoxicity remains controversial. Study conducted by Sharma et al showed that most of the patients developed hearing loss during 4-5th week of therapy. Study conducted by B.E. Gulbay et al in their study showed Ototoxicity appeared on 25±8.1 day of treatment (14–46 days)⁸. Study conducted by Gulbay et al had Tinnitus (in 9 patients), dizziness/vertigo (in 5 patients), loss of balance (in 3 patients) and hearing disturbance (in 2 patients) were recorded in the ototoxicity group⁸. Khatijah et al. reported that symptoms such as tinnitus, vertigo, nausea and hearing loss will wear-off and no further investigations or follow-up were recommended. In the present study there was no recovery of hearing loss, all 21 % of patients had irreversible hearing loss, till 1 year follow-up. Similarly, Duggal et al in his study noticed that hearing loss once developed has been found irreversible and none of the patients showed improvement till 1 year follow up^{9,10}

6. Conclusion

Streptomycin plays a major role in the management of multidrug resistant mycobacteria. Toxicity to the auditory and vestibular system is a well-known common complication of the treatment with aminoglycoside antibiotics. Audiologic changes have been reported in patients of MDR-TB using streptomycin which can potentially affect the communication ability of the patients. But careful early audiologic monitoring may help in limiting this damage which once developed is permanent

References

- [1] Webster M. definitions-Tuberculosis report a problem.
- [2] Konstantinos A. Testing for tuberculosis. Australian prescriber. 2010 Feb;33(1).
- [3] World Health Organization, Global Tuberculosis Programme. Global Tuberculosis Control: WHO Report. Who; 2008.
- [4] Shrivastava JP, Woike P, LokeshTripathi DR, Mangal KS. Profile of Nodal Tuberculosis at a Tertiary Care Centre, Gwalior, India.
- [5] Katijah KS, Anniah M, Precious MN. Ototoxic effects of tuberculosis treatments: How aware are patients?.

- African Journal of Pharmacy and Pharmacology. 2009 Aug 31;3(8):391-9.
- [6] Duggal P, Sarkar M. Audiologic monitoring of multi-drug resistant tuberculosis patients on aminoglycoside treatment with long term follow-up. BMC Ear, Nose and Throat Disorders. 2007 Nov 12;7(1):1.
- [7] De Jager P, Van Altena R. Hearing loss and nephrotoxicity in long-term aminoglycoside treatment in patients with tuberculosis. The International Journal of Tuberculosis and Lung Disease. 2002 Jul 1;6(7):622-7.
- [8] Fausti SA, Frey RH, Henry JA, Olson DJ, Schaffer HI. Early detection of ototoxicity using high-frequency, tone-burst-evoked auditory brainstem responses. J Am Acad Audiol. 1992 Nov;3(6):397-404.
- [9] Lima ML, Lessa F, Aguiar-Santos AM, Medeiros Z. Hearing impairment in patients with tuberculosis from Northeast Brazil. Revista do Instituto de Medicina Tropical de São Paulo. 2006 Apr;48(2):99-102.
- [10] Huang MY, Schacht J. Drug-induced ototoxicity. Medical toxicology and adverse drug experience. 1989 Dec 1;4(6):452-67.