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COCHLEAR TOXICITY OF STREPTOMYCIN IN MAN

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Thirty five patients of either sex suffering from tuberculosis were administered streptomycin 0.75 g (im daily, upto 14 yr and above 45 yr of age) and 1 g (im daily for age 15-45 yr) with other antitubercular drugs and followed for audiological status. Five patients were dropped as they developed vestibular dysfunction.

Varying degree of hearing loss was detected in 4 of 10 patients in group I (below 15 yr), in 2 of 9 patients in group II (15-45 yr) and in 6 of 11 patients in group III (above 45 yr). Cochlear toxicity of streptomycin was not found to be related to does or duration of therapy. Supportive therapy restored hearing in 2 patients of group I and 1 of group II. None of the patients in group III showed recovery.

It is recommended that patients on long-term streptomycin therapy should be periodically subjected to audiometric examination to detect any hearing loss.

Key words : streptomycin ototoxicity adverse reaction deafness

INTRODUCTION

Aminoglycoside antibiotics can cause damage to both the vestibular and cochlear parts of the inner ear, but they do tend to cause preferential damage to one or the other (1); although streptomycin mainly causes dysfunction of vestibular mechanism, deafness is not uncommon. The latency, however, varies with individual and at times it is unrelated to the dose of antibiotic (2). Friedman (3) has suggested this latency to regenerative power of the hair cells which, for a while, may be able to counter-balance or even overcome the toxic effects of the antibiotic.

The present study was designed to detect hearing loss by periodic audiometry in patients with tuberculosis treated with streptomycin and also to assess the efficacy of supportive therapy in restoring the cochlear function.

MATERIALS AND METHODS

35 patients of either sex identified as suffering from pulmonary tuberculosis, tuberculous cervical lymphadenitis, tuberculous meningitis and tuberculous laryngitis were selected from tuberculosis and chest diseases and E.N T. Out-patients department at J.N. Medical College, Aligarh. Exclusion criteria were associated hepatic or renal disorder, pregnancy and any middle ear disease. The patients were grouped according to age into group I upto 14 yr (12 patients), group II between 15-45 yr (10 patients) and group III above 45 yr (14 patients). Besides other anti-tubercular drugs which included rifampicin and isoniazid, streptomycin was administered im daily in dose of 0.75 g (group-I & group-III) and 1 g (group-II). Before the start of antitubercular regimen patients were subjected to detailed audiological and vestibular examination. Audiological status was

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recorded with the help of pure-tone Audiometer (Make-Arphi) and repeated at weekly interval upto 6 weeks or whenever patient complained of any adverse reaction attributable to the drug.

The patient when complained or identified as having hearing loss on audiometry was subjected to supportive therapy which included calcium pentothenate (275 mg im daily × 5 days) cyclandelate (200 mg × TDS orally × 10 days) and Vit. B1, B6 and B12 in higher doses.

Five patients two each from group I and III and one from group II were excluded from the study as streptomycin had to be withdrawn following the development of vestibular dysfunction.

RESULTS

Perceptive deafness mainly related to high frequency sound was detected on audiometric examination in all age groups following intramuscular administration of streptomycin. The onset was early in group III (above 45 yr) as compared to younger age groups. The proportion of patient affected was also higher in Group III Table-I.

Six of the 11 patients in group III developed hearing loss. First case to be recorded was of tubercular meningitis developing sudden, severe and irreversible loss after 10 injections of streptomycin others developed diminition in hearing acuity after 15 to 28 days of streptomycin administration. None of these patients recovered following supportive therapy.

Four patients of group I (below 14 yr) developed mild to moderate hearing loss (50 to 65 dB). The onset was later (4–5 weeks) as compared to group II & III (Table-1). Supportive therapy resulted in partial recovery in two patients.

Two patients in group II (15-45 yr) developed hearing loss after 25th & 26th injections of streptomycin. Final audiogram showed partial recovery only in one patient after supportive therapy. The hearing loss was moderate & varied from 55 to 80 dB.

DISCUSSION

Several antibiotics are capable of causing ototoxic damage to inner ear. However, it is the aminoglyco-

TABLE I : Pre and post-streptomycin audiogram of patients showing impaired hearing.

Group	*Frequency CPS*	*Hearing threshold level Average in dB*				*Day of appearance of hearing loss*
		Before streptomycin		*After streptomycin*		
		AC	BC	AC	BC	
I	500	20	25	50	45	
Up-to 14 yr	1000	20	20	50	50	20-32
n=4	2000	15	20	50	50	
	4000	20	20	65	No response	
II	500	20	25	55	55	
15-45 yr	1000	20	20	65	No response	
n=2	2000	25	25	No response		25-36
	4000	25	30	No response		
III	500	35	40	No response		
Above 45 yr	1000	35	35	No response		
n=6	2000	40	45	No response		10-28
	4000	40	40	No response		

side group of antibiotics which are the main offenders. Streptomycin toxicity although manifests mainly as vestibular dysfunction but deafness may also occur (2, 4). This could result even following oral administration or topical application (5). The mechanism of ototoxicity is unclear but electron microscopic studies of the inner ear of cats showed that it could result from inhibition of protein synthesis (6), causing initial damage to organ of Corti hair cells followed by involvement of nerve fibers and ganglion cells (7, 8). The process is dose related and has been confirmed in human studies (1).

Audiometric evaluation could detect hearing loss before it was noticed by patients. The type of deafness observed in the present study was perceptive and was localized to endorgan (cochlear). The characteristic initial effect was detected as high frequency hearing loss. Mild to moderate sensori-neural deafness was observed in 12 of 35 patients treated with injectable streptomycin. The development of deafness in a proportion of cases following 10 in some and 36 injections in other patients indicate that this adverse effect is probably unrelated to dose. However, most of the patients developed hearing loss during 4-5th week of therapy.

Streptomycin administration was discontinued in 5 patients who developed vestibular toxicity. The cochlear effects were therefore monitored in remaining 30 from whom 12 developed varying degree of sensori-neural deafness. In group I & II representing age upto 45 yr, deafness appeared after a minimum of 20 injections of streptomycin while in group III the appearance of cochlear damage occured earlier (Table I). Hearing loss was more at higher frequencies and severity was more marked in older age group. Greater ototoxic susceptibility to streptomycin at higher age group has been attributed at atherosclerotic changes in stria vascularis leading to reduced vascularity. Streptomycin induced ototoxicity is usually irreversible (2, 9). Supportive therapy attempted in the present study could partially restore hearing (10-20 dB) in three patients of group I and II and none in group III.

Although familial predisposition to streptomycin ototoxicity suggesting autosomal dominant inheritance is established (10, 11). None of the patients included in the present study gave any familial history of aminoglycoside induced toxicity. Other factors including dose and duration of therapy, age of patients and renal function have been attrib ted to contribute the ototoxic effects of streptomycin (9, 12). It is only a proportion of the population which is susceptible to the ototoxic effects of streptomycin. The preferential susceptibility of a proportion of population indicate the involvement of associated hypersensitivity in the causation of ototoxic effects of streptomycin (1, 3).

Since-prediction of ototoxic susceptibility cannot be made it is necessary that patients on long term streptomycin therapy should be subjected to periodically monitored audiometry for detection of any impairement of hearing to prevent any permanent irreversible damage to inner ear.

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