A COMPARISON OF THE OTOTOXICITY OF STREPTOMYCIN AND DIHYDROSTREPTOMYCIN

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The ototoxicity of streptomycin in the treatment of tuberculosis was first described by Hinshaw and Felpman (1945) (1). They observed in their original series of 34 patients one case of transient deafness and three cases of disturbed vestibular function. Molitor and his collaborators (1946) (2), who first noticed similar changes in dogs, suggested that they might represent the labyrinthine disturbance. Grizzle and Gutting (1953) (3) studied the vestibular ototoxicity of streptomycin and dihydrostreptomycin experimentally in cats. They showed that the rate of onset of vestibular disturbances during streptomycin administration varied directly with the dosage administered.

In the present paper authors report on comparative study of the ototoxicity of streptomycin and dihydrostreptomycin.

MATERIALS AND METHODS

Seventy-six patients with pulmonary tuberculosis, in some instances with additional tuberculous lesions, at the Sanyoso Sanatorium were used.

Thirty-nine of these 76 patients were treated with streptomycin sulfate (Groud A) and thirty-seven of these 76 patients were treated with dihydrostreptomycin sulfate (Group B). Each patients received 0.5 gram daily of either streptomycin or dihydrostreptomycin for total of 60 days with rare exceptions.

Of these group A, 14 had far advanced tuberculosis, 22 moderately advanced and 3 minimal disease.

Of these group B, 12 had far advanced disease, 23 moderately advanced, and 2 minimal.

Detailed medical records were maintained for each patient. Special note was made of sputum bacteriology, X ray changes, bronchoscopic changes, temperature trends, body weight and ototoxic manifestations. The ototoxic manifestations were studied both by subjective report of the patients and by some objective tests.

Objective vestibular and auditory tests were routinely done, with few exceptions, 1, prior to therapy, 2, at the conclusion of the 60 days of therapy, 3, one months post-therapy, and 4, two months post-therapy. A few patients have been followed even longer. More frequent tests were done when a change of stutus was suggested clinically.

Hearing was checked by pure tone audiometry, using 51A audiometer.

Vestibular responses were observed by the post-rotatory nystagmus by the Barany method and Honjo method.

The first patient was started on therapy in January 1952. The last of the series started in April 1952, and finished the 60 day course January 1954.

RESULTS

Of the 39 patients who received streptomycin (Group A), five cases evidenced any manifestation of vestibular disturbance, three of mild degree, two moderately severe. Three cases of mild degree were subjective only, transient vertigo of minimal degree. No auditory disturbance, however, occurred in the group.

Of the 37 patients on dihydrostreptomycin, four cases had auditory disturbances, three of mild degree, one moderately severe. Vestibular disturbances were evident in only one (Table I).

TABLE I
Ototoxity

Drug	Auditory disturbances		Vestibular disturbances	
	Mild	Moderate	Mild	Moderate
Group A. Streptomycin 39 cases	0	0	3	2
Group B. Dihydrostreptomycin 37 cases	3	1	1	0

Auditory disturbances:

Four of the patients receiving dihydrostreptomicin showed auditory disturbances. Three had disturbances of mild degree only, that was drop of 20 decibles or more at 500–4000 cycles per second, compared to pretreatment thresholds. In each case the impairment became manifest after completion of the course of treatment, the earliest one week post-treatment, the latest two months post-treatment. Once manifest, the drop became greater in two of the patients over a two month interval. The maximum change was 30 decibels.

The patient (K. T.) on dihydrostreptnmycin who had a moderate hearing loss was a 27 year old man with far advanced pulmonary tuberculosis. There was no history of an ear disease. At the end of treatment a hearing loss and noises were clinically apparent in his both ears and demonstrable by audiogram. Three weeks post-treatment it had progressed so that at 500 c.p.s. there war approximately a 20 decibel drop, at 1.000 c.p.s. a drop of 35 decibels, and at 2,000, 4,000, 8,000 and 10,000 c.p.s. a drop of 40–50 decibels, compared to the pre-treatment thresholds (Fig. I.).

Vestibular disturbances:

As mentioned above, only one patient of these on dihydrostreptomycin had some manifestation of vestibulur distnrbance, and it was only of a minimal, transient, subjective nature.

Of the five patients on streptomycin who showed vestibular disturbances,

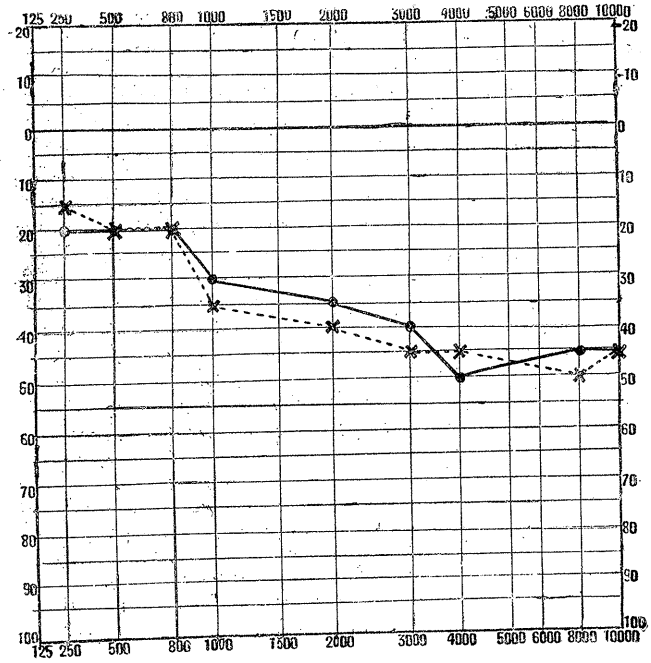

Fig. 1. – Audiogram of patient K. T. showing progressive post-therapy hearing loss.
•–A. C. right ear
x–A. C. left ear

three had only slight difficulty. This was characterized by subjective vertigo, i, e, a false sense of motion. more or less throughout the course of therapy. It ceased on discontinuance of the drug.

Two of the patients on streptomycin had vestibular disturbances of moderate degree.

One was an eighteen year old girl (M. A.) with far advanced pulmonary tuberculosis.

Two days after completion of therapy, she had the complaint of severe dizziness along with nausea, vomiting and unsteadness. A horizontal-rotatory nystagmus second degree to her left was present. One week later the post-rotatory test evidenced vestibular dysfunction of the both ears (Table II).

The second patient (M.H.) was a 21 year old man with far advanced pulmono-laryngeal tuberculosis. During the treatment he complained dizziness with nausea and headache. There was a first degree nystagmus to the left and past pointing was to his right. The fuuctional test showed the vestibular reaction to be abnormal (Table II).

TABLE II

Post-rotatory nystagmus of vestibular disturbed cases (M. A and M. H)

Case		Ba/ra/ny method Second	Honjo method Second
M. A.	↘	6	5
	↙	8	6
M. H.	↘	10	5
	↙	9	7

COMMENT

It is evident from this study that the ototoxicic effects by streptomcin are definitely and predominantly upon the vestibular apparatus.

Equally definite is the predominant neurotoxicity of dihydrostreptomycin on auditory apparatus. It may be postulated that the vestibular dysfunction is reversible because the apparatus is an order, more primitive mechanism.

The newer exceedingly delicate auditory apparatus, on the contrary, has little recuperative ability.

SUMMARY

A comprision of the ototoxicity of streptomycin and dihydrostreptomycin in patients with tuberculosis, was performed.

The predilection for vestibular toxicity by streptomyciu, and auditory toxicity by dihydrostreptomycin, was established.

REFERENCES

1) HINSHAW, C. AND FELDMAN, H. : Streptomycin in the Treatment of Clinical Tuberculosis : A Preliminary Report, *Proc. Staff Meeting, Mayo Clinic* **20** : 313–318, 1945.

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