Further Studies on the Control of Vestibular Toxic Effects of Streptomycin by Dramamine*

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In our previous article we stated that dramamine (dinenhydri-nate) afforded symptomatic relief of the dizziness which is encountered during streptomycin therapy and we voiced the belief that dramamine might prevent the toxic effects of streptomycin on the vestibular apparatus. At this time we wish to report our further work on this subject.

Evidence continues to appear in the literature indicating the success of dramamine in controlling motion sickness.5 The usefulness of this drug in other conditions in which the vestibular apparatus seems to be affected, such as the nausea of pregnancy,3 radiation sickness,1 migraine,2,7 and the nausea of aureomycin therapy,8 among others, is borne out by many authors.

Reports on the toxic effects of streptomycin are less numerous and this evidently is due to smaller doses of the drug being used. Glorig6 believes that irreversible changes in both divisions of the eighth nerve are produced by amounts of more than one gram per day, and Carr, et al.4 state that neurotoxic reactions to streptomycin might be avoided or minimized by keeping the maximal concentration in the blood stream at less than 50 micrograms per cubic centimeter.

It still is debatable whether the lesion in the vestibular apparatus is peripheral or central. Winston and his co-workers,10 in continuing their experimental work on cats, again conclude that the lesion is central, while Glorig6 believes that it is in the end organ. The central site seems to be the most logical from the work of Schiff, et al.9 The effects produced in their experimental animals by d1-isopropyl fluorophosphate are similar to those occurring in streptomycin toxicity, and the fact that local application of the drug did not produce forced circling movements, while injections into the blood did, favors this theory. These workers believed that

*Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.
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dramamine exerted its effect, because of its atropine-like properties, by its antagonistic action against an excess amount of acetylcholine produced by the di-isopropyl fluorophosphate in the brainstem. Winston and his collaborators confirmed this in their experiments on normal human subjects, showing that dramamine counteracts the emetic action of morphine, perhaps by virtue of the fact that it may be an antiacetylcholine agent.

Our present study concerns 54 patients admitted to the tuberculosis service of this hospital, twenty-six of whom were given streptomycin in a dosage of 1 gram a day for periods of 21 to 120 days, with an average of 70.3 days, along with 150 mgm. of dramamine daily for the duration of therapy. None of these patients complained of dizziness during the course of treatment, and the audiometric and caloric stimulation tests made after the cessation of therapy, and 90 days later, did not show any essential change over those made before streptomycin was begun. The eosinophiles in the blood averaged 2.8 at the beginning of therapy, 7.1 during the middle of their course, and 4.1 at the close.

Twenty-eight patients were given 1 gram of streptomycin daily for 30 to 120 days, with an average of 65.1 days. Of these, four (14.2 per cent) who received the drug for an average of 97 days, complained of dizziness from seven to 44 days after therapy was begun, with an average of 21.5 days. Dramamine was given in a dosage of 150 mgm. a day and symptoms disappeared in from three to 20 days, with an average of 10 days. None of these patients showed any deviation from the pre-treatment audiometric or caloric findings. The eosinophiles in this group averaged one at the onset of therapy, 3.5 at the time dizziness began, and 2.2 at the end. The remaining 24 patients exhibited no symptoms during treatment, and the cochlear and vestibular findings showed no changes. The eosinophiles averaged 3.5, 5.1, and 4.2 respectively.

Discussion

While it is impossible to state how many patients who were receiving dramamine would have complained of dizziness if the drug had not been given, we believe that the same percentage would have been found as was observed in the other group. We feel that this symptom was prevented by the use of dramamine. The absence of toxicity, as far as the cochlea and vestibule are concerned, in the group who did not receive dramamine at any time, is due, we believe, to the smaller amount of the drug being used at the present time. Our previous statement that there was not an allergic reaction to streptomycin is borne out by the eosinophilic determinations.
SUMMARY

In view of the work which has shown that dramamine is an antagonist of acetylcholine and since it is likely that streptomycin is a cholinergic agent, we believe that when streptomycin is administered dramamine should be given also, to eliminate any toxic effects on the vestibular apparatus.

RESUMEN

En vista del trabajo que ha demostrado que la dramamina es un antagonista de la acetilcolina y puesto que posiblemente la estreptomicina es un agente colinérgico, creemos que la dramamina debe administrarse también para eliminar los efectos tóxicos sobre el aparato vestibular.

RESUME

Etant donné qu'il a été démontré que la dramamine est un antagoniste de l'acétylecholine, et étant donné ce qu'on sait de l'action physiologique de la streptomycine, les auteurs pensent qu'il faut associer la dramamine à l'administration de streptomycine pour éviter les actions toxiques sur l'appareil vestibulaire.

REFERENCES