Anti-Cancer Drugs 1996, **7**, pp. 525–526

Clinical report

A prospective cohort study of the effect of vincristine on audition

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We conducted a prospective cohort study of the possible ototoxic effect of vincristine among patients treated for lymphoproliferative malignancies. No deleterious effect of moderate doses of vincristine on pure tone audiometry for air and bone conduction and on speech audiometry could be found. Nevertheless, the isolated finding of sensorineural hearing loss in the only patient who received a high dose of vincristine raises the issue of ototoxicity as a possible dose-related and dose-limiting side effect of vincristine.

Key words: Ototoxicity, vincristine.

Introduction

Vincristine, a tubulin binding vinca alkaloid, is a very effective cytotoxic agent used in most lymphoproliferative diseases. Its best documented side effects include a large variety of neurologic disturbances,[1,2] most strongly associated with the cumulative dose of vincristine. Reports of newly described neurologic side effects[3–5] including cranial nerve damage[6] and our recent report of sensorineural hearing loss due to vincristine[7] persuaded us to conduct a prospective study of the effect of vincristine on hearing.

Patients and methods

Patients treated at the Hematology Institute of the Barzilai Medical Center for Hodgkin's disease or non-Hodgkin's lymphoma were included in the study. They were treated according to the CHOP (cyclophosphamide, adriamycin, vincristine, prednisone) or the MOPP (mustard, vincristine, procarbazine, prednisone) protocols. Vincristine was given as an i.v. bolus of no more than 2 mg per dose. Patients who received a drug known to have a potentially deleterious effect on the eighth cranial nerve, such as cisplatin and gentamicin, were excluded from the study, as were patients with central nervous system involvement, hypercalcemia, hyperviscosity or leukemic stage of their lymphoma. None of the patients received hematopoietic colony-stimulating factor.

Audiometric studies were performed in a noise-free sealed room with a GSI-16 audiometer. All tests were performed by the same audiologist throughout the study. The patients were evaluated shortly before initiation of therapy with the vincristine-containing regimen and again within 3 months after completion of therapy. Each test included a pure tone audiometry (PTA) for air and bone conduction, and a speech audiometry for speech reception threshold (SRT) and discrimination.

Each patient underwent a thorough physical examination by a senior ENT physician in order to exclude chronic otitis or external auditory canal obstruction due to cerumen.

Results

Twenty-three patients were included in the study: 17 patients received the CHOP regimen for non-Hodgkin's lymphoma and six were treated with the MOPP regimen for Hodgkin's disease. Mean age was 56 years (range 19–81). The female:male ratio was 11:12. Total doses of vincristine for individual patients ranged from 6 to 16 mg (mean 12 mg), but one patient, a 56-year-old man with lymphoma, received a total dose of 24 mg. A significant sensorineural hearing loss was found in this patient after treatment, compared with pretreatment testing: PTA and SRT showed a decrease of 10 dB in

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both ears. All other patients, who were treated with lower doses of vincristine, showed no significant changes in PTA or SRT after therapy, compared with baseline testing. There was no high tone sensorineural hearing loss in any treated patient.

Discussion

Vincristine is an antineoplastic drug with a broad spectrum activity against lymphoproliferative malignancies. Neurotoxicity is a dose-limiting side effect of this drug.[1] Neurologic complications may be divided into four groups: peripheral neuropathy, autonomic neuropathy, encephalopathy and cranial neuropathy. Cranial nerve palsies are seen less often than other side effects in patients treated with vincristine.[2]

The lack of data on the possible effect of vincristine on the eighth cranial nerve and recent reports of sensorineural hearing loss associated with vincristine[5,7] led us to conduct a prospective study on the possible effect of vincristine on hearing. Although none of the patients received vincristine alone, the other cytotoxic agents administered (cyclophosphamide, adriamyicine, mustard, procarbazine, prednisone) are not known to be potentially neurotoxic or to exacerbate vincristine neuropathy. We found no effect of the drug on hearing in our cohort of patients, except in the only one who received a high dose of vincristine and showed a significant decrease in both PTA and SRT. Thus, it is possible that high doses of vincristine may have a toxic effect on hearing. Ototoxicity could therefore be a dose-related and a dose-limiting side effect of vincristine.

Since audiometric studies are easily performed and inexpensive, it seems logical to recommend repeated audiogram testing of patients who are candidates for receiving high doses of vincristine. Such a policy could prevent sensorineural hearing loss in this selected population of patients.

References

1. Legha SS. Vincristine neurotoxicity. Pathophysiology and management. *Med Toxicol* 1986; **1**: 421–7.
2. Rosenthal M, Kaufman S. Vincristine neurotoxicity. *Ann Intern Med* 1974; **80**: 733–7.
3. Haim N, Barron SA, Robinson E. Muscle cramps associated with vincristine therapy. *Acta Oncol* 1991; **30**: 707–11.
4. McCarthy GM, Skillings JR. A prospective cohort study of the orofacial effects of vincristine neurotoxicity. *J Oral Pathol Med* 1991; **20**: 345–9.
5. Weintraub M, Adde MA, Venzon DJ, *et al.* Severe atypical neuropathy associated with administration of hematopoietic colony-stimulating factors and vincristine. *J Clin Oncol* 1996; **14**: 935–40.
6. Soysal T, Ferhanoglu, Bilir M, Akman N. Oculomotor nerve palsy associated with vincristine treatment. *Acta Haematol* 1993; **90**: 209–10.
7. Lugassy G, Shapira A. Sensorineural hearing loss associated with vincristine treatment. *Blut* 1990; **61**: 320–1.

(Received 23 April 1996; received in revised form 13 May 1996; accepted 21 May 1996)