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Experience with 24-h infusions of ifosfamide/mesna in small cell lung cancer

B. M. J. Cantwell[1], A. L. Harris[1], and J. M. Bozzino[2]

University Departments of [1]Clinical Oncology and [2]Radiotherapy, Newcastle General Hospital, Newcastle upon Tyne, England

Summary: Two studies were carried out (A and B) in order to assess the effectiveness of ifosfamide administered with mesna (IFO/M) in the treatment of small cell lung cancer. The first study (A) was a cross-over study; the second (B) was a randomized trial, and in B IFO/M was evaluated earlier in the course of the disease. IFO/M given be infusion is effective as second-line therapy and can be administered with other cytotoxics at the doses reported here earlier in the course of the disease. The complete remission rates were high.

Aims

The aim of the investigation was to evaluate ifosfamide administered with mesna (IFO/M) in the treatment of small cell lung cancer in two settings.

Methods

The first study (A) was a cross-over study with IFOS/M given after i.v. administration of adriamycin 40 mg/m^2, vincristine 2 mg and VP 16 100 mg/m^2 on day 1 and administration p.o. of VP 16 200 mg/m^2 on days 2 and 3 of each 3-week treatment cycle; two or three cycles of this combination were given as induction therapy. Patients with limited disease and those who had attained partial or complete remission (PR or CR) then received radiotherapy (2400 rad, four fractions over 8 days) to the mediastinum and to the primary lesion. In a second study (B) IFO/M was evaluated earlier in the course of disease in a randomized trial comparing chemotherapy given i.v. in hospital and chemotherapy taken p.o. by out-patients. The medication administered to the "i.v." groups was adriamycin 40 mg/m^2, vincristine 2 mg, and VP 16 100 mg/m^2 all i.v. on day 1, and VP 16 300 mg p.o. on days 2 and 3 for course 1, while for courses 2, 3, and 4 IFO/M was given with reduced doses of VP 16 (200 mg/m^2) and adriamycin (30 mg/m^2). The chemotherapy in the "p.o." group was chlorambucil 6 mg/m^2, procarbazine 150 mg, and prednisolone EC 20 mg daily for 10 days and VP 16 300 mg on days 1–3.

This therapy was also given 3-weekly for a total of four cycles. In both groups, patients who had limited disease and responded well to the therapy also received radiotherapy to mediastinum and brain.

Ifosfamide and mesna were each given in a total dose of 5 g/m^2, mesna being administered i.v. before ifosfamide, simultaneously with ifosfamide in the 24 h infusion, and alone for 8 h after completion of the ifosfamide infusion.

Results

In study A, 70 patients received IFO/M (two or three courses) starting 3–4 weeks after VP 16 with or without radiotherapy. There had been no response to previous therapies in 14 of these patients, 5 of whom (36%) did respond to IFO/M (2 CR, 3 PR). Of the 56 who had responded to previous therapy, 20 had no response to IFO/M, 15 who had previously achieved PR had further tumour shrinkage but did not attain CR, and 21 who had previously achieved CR maintained CR during IFO/M medication. In study B, 26/37 (70%) patients in the i.v. group and 24/36 (67%) in the p.o. group had objective responses, with 14 (37.8%) attaining CR in the i.v. group and 9 (25%), in the p.o. group.

Conclusions

IFO/M given by infusion is active as second-line therapy in SCLC and can be given with other cytotoxics at the doses reported quite early in the course of SCLC, with high CR rates. IFO/M caused relatively little bone marrow damage whether given alone or in combination. Renal failure did not occur in any patient, while there were one episode of haematuria and two mild neuropsychiatric episodes during IFO/M therapy.

Offprint requests to: B. M. J. Cantwell