Cancer Chemother Pharmacol (1981) 5: 207

Cancer Chemotherapy and Pharmacology

Cyclophosphamide and Diabetes

R. G. Henderson and R. D. Rubens

Imperial Cancer Research Fund Breast Cancer Unit Guy's Hospital, London SE1 9RT, Great Britain

Little information is available about the effect of cytotoxic drugs on diabetes mellitus. Cyclophosphamide has been reported to be a possible cause of mild diabetes [2], but Kruger [1] described two diabetics whose blood sugar levels fell during treatment with cyclophosphamide. In one case the insulin requirement was reduced to one quarter, and in the other, treatment with carbutamide was discontinued. Indeed, the cyclophosphamide data sheets (WB Pharmaceuticals and Montedison) warn that the hypoglycaemic effect of sulphonyl ureas may be enhanced. We report here a patient whose insulin requirement increased during cytotoxic treatment.

A 67-year-old female diabetic had been treated with insulin for 50 years, and she had learnt to adjust the dosage according to need. She had taken thyroxine 0.2 mg daily for 25 years for myxoedema. In May 1979, she underwent mastectomy for breast carcinoma and received adjuvant therapy with tamoxifen. In August 1980, cutaneous and lymphatic recurrence required cytotoxic treatment. Treatment with a combination of cyclophosphamide, methotrexate, and 5-fluorouracil (CMF) was selected. On day 1, cyclophosphamide 150 mg PO daily was started and she was given methotrexate 45 mg and 5-fluorouracil 900 mg IV. On day 8, because of leucopenia (3,000 per μl) and elevated urea and creatinine (10 mmol/l and 129 μmol/l, respectively) the doses were reduced to methotrexate 25 mg and 5-fluorouracil 500 mg, and cyclophosphamide was continued at a dose of 70 mg daily until day 14, when it was stopped. Before treatment with CMF the patient's daily insulin requirement was Rapitard 10 unids bd and Actrapid 18 units mane. This had been stable for the previous 6 months. Within 24 h of the commencement of CMF the insulin requirement increased, and after 3 days it restabilised at approximately Rapitard 14 units bd and Actrapid 22 units mane. High random blood sugars (range 10.8 mmol/l to 31.2 mmol/l) and a 1%–2% glycosuria confirmed poor control during this time. Within a day of completing the course of cyclophosphamide the insulin requirement reverted to pretreatment levels. In subsequent courses of CMF, cyclophosphamide was given as single IV injections on days 1 and 8 only and covered by a small arbitrary increase of 2 units in both insulin types for those days only. The diabetes has remained under satisfactory control and after four courses of CMF an objective regression of the breast cancer has been achieved.

In this case the increased insulin requirement appeared to be linked to cyclophosphamide administration. The cause of this effect is obscure but possibilities may include the general malaise and nausea produced by this drug, a direct anti-insulin action or elevation of blood cortisol in response to stress. The effect of cyclophosphamide on diabetic control is variable and should be remembered when diabetics are being given cytotoxic treatment.

References

1. Kruger H (1977) Cited in Martindale: The extra pharmacopoeia, 27th ed. Pharmaceutical Press, London, p 136
2. Pengelly CR (1965) Br Med J 1: 1312

Received November 21/Accepted November 21, 1980

0344-5704/81/0005/0207/$ 01.00