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Letter to the Editor

False-positive Ketonuria during Ifosfamide and Mesna Therapy

BRIAN M. J. CANTWELL*, JANE POOLEY and ADRIAN L. HARRIS
University Department of Clinical Oncology, Regional Radiotherapy Centre, Newcastle General Hospital, Newcastle-upon-Tyne NE4 6BE, U.K.

MESNA (sodium 2-mercaptoethane sulphonate), a thiol compound, in appropriate doses and scheduling greatly reduces urotoxicity associated with the antineoplastic oxazaphosphorine cytotoxics ifosfamide and cyclophosphamide [1–3]. The major toxic metabolite producing haemorrhagic cystitis associated with these drugs is acrolein [4], which can be inactivated by mesna. False-positive ketonuria has been found in six patients receiving mesna during high-dose cyclophosphamide treatment but not in five patients receiving cyclophosphamide without mesna [5]. The false-positive result obtained with mesna using Ames multistix reagent is due to the sulphide component of mesna which reacts with the sodium nitroprusside of the test reagent [5].

We have treated more than 120 cancer patients with more than 320 courses of ifosfamide and mesna. Ifosfamide was given as a 24-hr intravenous (i.v.) infusion of 5-g/m^2 in 3 l of dextrose saline preceded by a l-g/m^2 i.v. bolus of mesna. Four grammes of mesna per square metre was given by infusion over a 32-hr period starting at the same time as ifosfamide, and in general treatment courses were repeated 3-weekly to a maximum of three courses per patient. Frusemide 40 mg i.v. was given at the start of therapy and as necessary to maintain a urine output of 100 ml/hr. Urine testing using Ames multistix during ifosfamide and mesna usually revealed false-positive ketonuria in moderate-to-large amounts. A more detailed examination of this phenomenon was made in 43 patients, 39 with small cell lung cancer and four with pleural mesotheliomas. There were 31 males and 12 females, with mean age of 57.5 ± 6.1 (± S.D.). Nine patients received other cytotoxic drugs with ifosfamide and mesna and 34 patients did not. Each patient had a minimum of two urine tests for ketones during therapy. A total of 354 urine tests were made during 87 ifosfamide and mesna courses, and all tests revealed false-positive ketonuria. Approximately 10% of urine tests showed small, 40% showed moderate and 50% showed large amounts of false-positive ketonuria.

At the start of ifosfamide and mesna patients had routine urine cultures. Two patients had asymptomatic urinary infection and one developed severe haemorrhagic cystitis within 24 hr after ifosfamide and mesna, at which time ketonuria was also noted. This rapidly resolved with co-trimoxazole, to which the *Escherichia coli* urinary infection was sensitive. Bacterial urinary tract infections may predispose to delayed haemorrhagic cystitis following high-dose cyclophosphamide, despite mesna prophylaxis [6]. Two other patients developed microhaematuria during ifosfamide and mesna. No abnormalities of serial serum urea and creatinine occurred, but more detailed tests of renal function were not made. Individual patients were given a maximum of three ifosfamide and mesna courses.

False-positive ketonuria is common if not invariable during i.v. mesna therapy and could cause confusion in diabetic patients. Its presence is a useful check that patients received mesna. Despite mesna and false-positive ketonuria, haemorrhagic cystitis can be precipitated by co-existing asymptomatic urinary infection.

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*To whom requests for reprints should be addressed.

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