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False-positive ketone tests: a bedside measure of urinary mesna*

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Summary. The sulfhydryl mesna is increasingly used to protect the bladder and kidney from effects of chemotherapy with ifosfamide and cyclophosphamide. Mesna reacts with reagents on urinary test strips designed to detect ketones. Test-strip results were correlated to sulfhydryl concentrations in 931 urine specimens obtained after infusions of mesna. These data may be used to estimate urinary mesna concentrations at the bedside or to test compliance in outpatients given oral mesna therapy.

Introduction

Clinical trials have shown that the sulfhydryl mesna (2-mercaptoethanesulfonate sodium) reduces the incidence of hemorrhagic cystitis associated with ifosfamide and its isomer, cyclophosphamide, by neutralizing toxic urinary metabolites [1, 7, 9, 10]. Thus, coadministration of mesna in patients receiving these cytotoxic drugs is likely to become standard clinical practice. Interestingly, when urinary concentrations are sufficiently high, mesna reacts with reagents on urinary test strips designed to detect ketones [2–5]. Such false-positive results have misled clinicians to attribute toxic effects of ifosfamide to an alleged ketone and can also lead to inappropriate therapeutic interventions. We wish to reemphasize the occurrence and clinical implications of these false-positive ketone results with an illustrative case study and suggest that these findings may, when recognized and interpreted correctly, prove useful as a means of bedside estimation of urinary mesna concentrations.

Patients and methods

During a phase II study of ifosfamide at St. Jude Children's Research Hospital [8], urine specimens were monitored to establish a quantitative relationship between the ketone test-strip results and urinary free sulfhydryl concentrations. Children and adolescents in this study received 15-min infusions of mesna (400 mg/m^2) at 0, 4, and 6 h after the infusion of 1.6 g/m^2 ifosfamide. A total of 931 urine specimens were obtained at times up to 4 h after 480 doses of mesna in 21 patients. After estimation by laboratory technologists of the apparent "ketone" concentration indicated by urinary test strips (Chemstrip, Boehringer Mannheim), urinary mesna concentrations were determined with Ellman's reagent [6].

Results

Urinary test-strip reaction

A proportional relationship was detected between the mesna concentration and the urinary test-strip reaction (Fig. 1). Shortly after infusions of mesna, the millimolar urinary concentrations of this agent were associated with 3+ ketonuria. The intensity of reaction of mesna with the test strip decreased to undetectable levels during the subsequent 4 h after patients had voided their bladders.

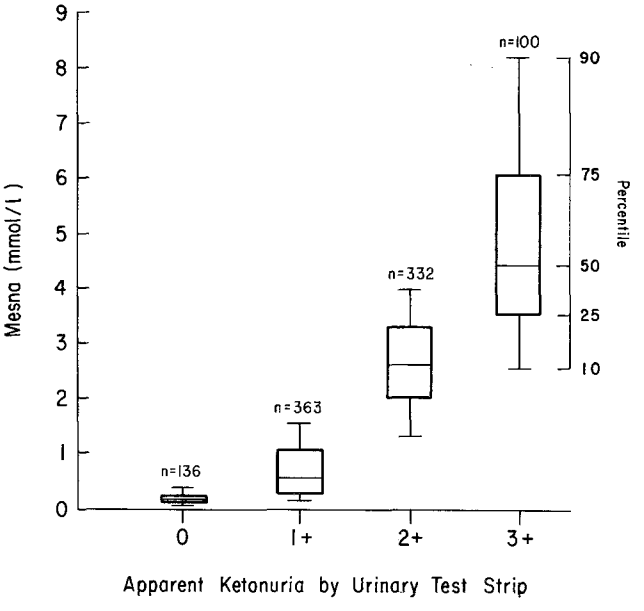

Fig. 1. Urinary free sulfhydryl concentrations predicted by the intensity of reaction of urinary test strips for ketones

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Illustrative case study

A patient participating in this phase II study exemplifies the problems associated with misinterpretation of urinary test-strip results. During treatment of a 16-year-old girl for a disseminated endodermal sinus tumor, moderate to strongly positive ketonuria was observed at the bedside on a urinary test strip. Her most recent dose of mesna (400 mg/m^2) had been infused 1 h earlier. She was febrile, neutropenic, and cachectic and had shown somnolence and inappropriate behavior – compatible with ifosfamide neurotoxicity [8, 10] – during the previous 24 h. The creatinine clearance rate was 69 ml/min per 1.7 m^2. Serum obtained through the central venous access device for hyperalimentation disclosed a glucose concentration of 207 mg/dl. Although glucosuria was not detected, insulin was given, resulting in symptomatic hypoglycemia (50 mg/dl), which was promptly corrected.

Discussion

The data presented in Fig. 1 can be used to estimate urinary mesna concentrations at the bedside (e.g., to ensure that urinary mesna is present in children who void frequently) or to test for compliance by outpatients given oral mesna therapy. If there is clinical suspicion of ketonuria in a patient receiving mesna, a drop of glacial acetic acid on the test strip will disperse color due to mesna without affecting that due to ketones [4, 5]. Ketonuria can also be distinguished from this drug interference by reexamination of the urine after mesna has been expelled from the bladder during micturition.

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