that in excessive concentrations may cause acute liver damage and acute renal failure (1). Although the normal elimination of ACET seems to involve conjugation of a toxic alkylation metabolite with liver glutathione to yield a detoxified conjugation product, excessive doses of ACET deplete liver glutathione stores, causing accumulation of the toxic metabolite N-acetyl-imidoquinone (1–3).

Acetylcysteine (NAC, N-acetyl-3-mercaptoalanine) is the drug of choice for the treatment of an ACET overdose. Although the mechanism responsible for the ability of NAC to serve as an effective antidote in vivo has not been fully elucidated, a major route of detoxification seems to depend on the ability of NAC to serve as a potent sulfhydryl donor that restores depleted hepatic reduced glutathione (3).

A 28-year-old woman was recently admitted to the emergency room of our hospital after a confirmed (suicidal) ACET overdose. One hour after treatment with NAC was initiated (150 mg/kg of body weight, infused i.v. for 15 min), a blood sample was withdrawn for ACET assay in our laboratory. We routinely assay ACET by an enzymatic assay (GDS enzymatic acetaminophen, GDS Diagnostics) based on the hydrolysis of ACET by acylamidase to yield p-aminophenol and acetate. The p-aminophenol is measured colorimetrically by its conversion to indophenol in the presence of o-cresol, using peridate as a catalyst. Unexpectedly, no ACET was found in the serum despite the patient’s ingestion of a toxic dose of the drug. A similar enzymatic assay (acetaminophen assay, cat. no. 503–10, Diagnostic Chemical) that uses acyl amidohydrolase to cleave the amide bond in ACET but in which the formed p-aminophenol reacts with 8-hydroxyquinoline in the presence of manganese ions to form the colored compound 5-(4-iminophenol)-8-quinolone, also failed to detect ACET in the sample.

In contrast to the two enzyme-based assays that failed to demonstrate ACET intoxication, the TDx assay (Abbott Laboratories) confirmed high, toxic concentrations of the drug in the same blood sample. The TDx assay is based on the competition between ACET in the sample and tracer-labeled ACET for a specific antibody and measures the change in the polarization of fluorescent radiation emitted by the fluorescence-labeled tracer.

These conflicting results and a recent report on false negative results for urinary ACET screening in the presence of NAC (4) raised the possibility that NAC interferes with the
Toxic Levels of Acetaminophen
Produce a Major Positive Interference on Glucometer Elite and Accu-chek Advantage Glucose Meters

To the Editor:

Bedside capillary glucose monitoring has become widespread in most hospitals. Glucose meters have been shown to provide a reasonably acceptable degree of accuracy compared with laboratory instruments when proper quality control is in place (1). However, a recent clinical case shows that such systems have limitations in hospital settings.

A 55-year-old woman was admitted to the emergency room with suspected acetaminophen overdose. She had been found lying on the floor of her apartment in an altered level of consciousness, and a bottle of acetaminophen was discovered beside her. The patient had recently been hospitalized for a period of three months for depression. She had no history of diabetes. Capillary blood glucose as measured with the Glucometer Elite (Bayer) at the emergency room showed values of 8.4, 12.8, and 9.4 mmol/L (samples taken within 2.5 h of arrival). Serum analysis in the laboratory (Vitros 700 XR) gave glucose values <1.1 mmol/L for two different samples taken during that same time interval. Because of the discrepancy between the capillary glucose meter values and the serum glucose values measured by Vitros, the patient’s serum was analyzed for glucose at another laboratory by Synchron CX-3 (0.11 mmol/L), Synchron CX-5 (0.2 mmol/L), and Radiometer EML 105 (0.0 mmol/L). Her serum acetaminophen (Vitros 700 XR) was at the highly toxic concentration of 2904 μmol/L. Despite appropriate treatment, the patient died the next night.

After ruling out a glucose meter defect as the source of the erroneously high glucose readings, acetaminophen interference was suspected. We therefore measured glucose on heparinized venous blood supplemented with different amounts of acetaminophen (50 μL of aqueous solution per mL of blood). The blood samples were drawn from healthy volunteers who were not taking any medication. Some of these blood samples were made hypoglycemic by incubation at 37°C for 4 h. Confirmation of acetaminophen concentrations was done by measurement on a Vitros 700 XR. Simultaneous measurements of venous blood glucose was done on five different glucose meters according to the manufacturers’ instructions. Glucose measurements were also done on whole venous blood (EML 105) and plasma (Vitros 700 XR, Synchron CX-3, and CX-5). Results of the glucose measurements on the Glucometer Elite (meter #1) and the Accu-chek Advantage (meter #2) showed a positive interference that increased with the amount of acetaminophen added (Table 1). Maximal deviations of 4.4 and 4.5 mmol/L were seen at the highest acetaminophen concentration. The Precision QID (meter #3) showed a negative interference (1.0 mmol/L at the highest acetaminophen concentration). No interferences were seen from the One Touch Profile (meter #4), the SureStep (meter #5), and from the laboratory glucose measuring instruments, including the EML 105. The Glucometer Elite and the Accu-chek Advantage were used to measure a low blood glucose value in the presence of the highest acetaminophen concentration tested above. A positive interference of the same amplitude was again observed (4.4 and 4.1 mmol/L, respectively), showing that the extent of the interference varied directly and in an absolute fashion with acetaminophen concentration, regardless of actual glucose concentration.

References


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