increased CK-BB in serum in the absence of brain damage, we have not used it for prognostication after cardiac arrest. Instead, we use the cerebrospinal fluid creatine kinase (CSF CK) and recently have confirmed the findings of our retrospective study (3) in a prospective study (3). CSF CK, not serum CK, seems to be a valid index of brain damage after cardiac arrest.

References

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Detection of Myocardial Infarction

To the Editor:
Recent literature (1–4) shows (a) a high failure rate in premortem diagnosis of acute myocardial infarction (AMI) in patients in whom it was subsequently confirmed at autopsy, (b) poor sensitivity when diagnosis of AMI requires inversion of the ratio of isoenzyme fractions 1 and 2 of lactate dehydrogenase ("flipped" LDH-1/LDH-2) and electrocardiographic (ECG) evidence of evolving Q-waves, (c) elevated MB fraction of creatine kinase (CK-MB) to be the most reliable indicator of AMI, and (d) poor prognosis for patients in whom AMI is difficult to confirm based on traditionally used criteria of elevation of cardiac enzymes, flipped LDH-1/LDH-2, and ECG evidence of evolving Q waves.

One would expect that such studies would lend to increasing reliance on accurately measured CK-MB and minimize the importance of ECG and flipped LDH-1/LDH-2 in confirming AMI. Yet some investigators (e.g., 5) judge diagnostic accuracy of methods used to measure CK-MB on how well they agree with the diagnosis based on ECG results and "flipped" LDH-1/LDH-2. Such comparison would make accurate CK-MB methods appear to have poor specificity, even though they correctly indicate the diagnosis of AMI in patients who do not have specific ECG evidence due to nontransmural infarction or previous history of infarction and/or who do not have flipped LDH-1/LDH-2. Such conclusions perpetuate the use of methods that are not capable of diagnosing AMI in certain groups of patients.

The occurrence of flipped LDH-1/LDH-2 in conjunction with AMI depends on many factors, possibly including age and sex. In a study in which five methods for measuring CK-MB (electrophoresis, column, immunochromatographic, immunoradiometric, and B-unit radioimmunoassay) and two methods of measuring LDH-1 (electrophoresis, immunochromatographic) were compared on serial samples of 80 patients suspected of AMI, we observed that all methods agreed with the diagnosis in 90% of patients who were younger than 50 years. The agreement among methods, and with the diagnosis, decreased as the age of the patient increased and was only 45% for patients whose age was 70 years or greater.

There were 27 men and 16 women in this study who were diagnosed to have AMI and whose CK-MB values were indicative of AMI by all five methods. The incidence of "flipped" LDH-1/LDH-2 ratio was 82.7% in men, 62.5% in women. The incidence of flipped LDH-1/LDH-2 was only 33.3% in women 70 years old or older.

Both the patient and the hospital working under the DRG system suffer when diagnosis of AMI is missed due to inaccuracy on ECG and LDH results. As indicated before, patients whose diagnosis of AMI is difficult are high-risk patients who could benefit from modern medical procedures if their AMI is correctly diagnosed. The hospital would spend considerable resources in attending to such patients and yet receive lower reimbursement for a non-AMI DRG, which is significantly lower than an AMI DRG, by incorrectly diagnosing the patient as "MI rule out."

References

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Positive Diphenhydramine Interference in the emt-d.a.u.™ Assay

To the Editor:
The emt-d.a.u.™ assay (Syva Co., Palo Alto, CA) is a popular and rapid method for detecting drugs of abuse in urine. With the assay we recently encountered a "false positive" result for methadone in a urine sample that contained diphenhydramine (Benadryl™, Parke-Davis). This compound is not listed in the manufacturer's guide as a potential interference (1).

Diphenhydramine added to urine to give a concentration of 10 mg/L gave a reading equivalent to or exceeding that of the low calibrator (methadone, 0.5 mg/L) with emt-d.a.u. lots M-O-1A and N-O-1A. Urine from three patients receiving from 100 to 200 mg of diphenhydramine per day were positive for methadone by the emt assay. The presence of diphenhydramine and the absence of methadone in each urine was confirmed by clinical history and by conventional thin-layer chromatography (2).

Laboratories using this methodology for detecting drugs of abuse in urine should be aware that low concentrations of diphenhydramine, a commonly prescribed drug, can give false positives for methadone. The above examples also emphasize the need to confirm all positive results in a drug-screening program with a second analytical technique.

References

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Effect of Hemochromatosis on Hepatic Cytochrome P450 and Antipyrine Metabolism in Humans

To the Editor:
The biochemical basis for the hepatotoxicity and carcinogenicity of severe iron overload remains uncertain. We (1,2) and others (3,4) recently reported that iron-loading of rats, by a variety of experimental protocols, significantly decreased concentrations of hepatic cytochrome P450, a key hemoprotein in