the risk of carcinoma in situ. A recent retrospective report indicates that the risk of carcinoma in situ may be most pronounced in men with seriously affected spermatogenesis and therefore low sperm counts.[18] In another study of infertile men two cases of carcinoma in situ were found in men with sperm counts below 2.5 million/ml and severe testicular atrophy (≤ 10 cm^3).[19] In retrospectively reviewed material from our department we found carcinoma in situ in two of 31 infertile men who had had bilateral biopsy performed because of low sperm counts, testicular atrophy, and irregular ultrasonic echo pattern (unpublished data). Men with such low sperm counts and atrophic testis size comprised less than 20% of our population in the prospective study. There is, therefore, a need for prospective studies to evaluate whether the risk of carcinoma in situ is significantly increased in a subpopulation of infertile men with very severe oligozoospermia and pronounced testicular atrophy accompanied by very irregular echo pattern.

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Comparison of two assays for measuring plasma concentrations of paracetamol

C V Egleston, C Browning, I Hamdi, G Campbell-Hewson, S M Robinson

An overdose of paracetamol can cause fatal hepatic necrosis, but acetylcysteine is an effective antidote if given early.[1] An estimation of plasma concentrations of paracetamol is required if a patient is suspected of having taken a toxic dose. We compared the AcetaSite test card and Stat-Site reflectance meter (GDS Diagnostics, Elkhart, IN), a bedside method of determining paracetamol concentrations that takes 2 minutes, with the Quantase assay (Porton Products, Maidenhead), an established laboratory method.

Patients, methods, and results

Altogether 192 patients were recruited into the study; of these, 92 had taken paracetamol. Patients who had not ingested paracetamol but required venepuncture for other reasons made up the control group. A blood sample was obtained 4 hours after suspected overdose or on arrival if 4 hours had already passed. A drop of this blood was used to measure paracetamol concentration with the AcetaSite card and Stat-Site meter, and the remainder was sent to the laboratory. Medical and nursing staff were trained to use the equipment before the study started.

A statistical method first described by Bland and Altman[2] was used to assess agreement between the laboratory standard and the AcetaSite test. This method plots the difference between results obtained by a standard and a new test against the mean of these measurements. Logarithmic transformation of the data was performed because the data were not normally distributed.

The figure uses untransformed data to show the relationship between paracetamol concentrations obtained with the laboratory test and those obtained with the AcetaSite test. The limits of agreement are 0.16 and 5.04—that is, in 95% of cases the AcetaSite result was between 0.16 and 5.04 times the laboratory result. The results for five patients fell outside these limits. There were six false negative results but no false positive results. The median time for a result to be available from the laboratory was 28.5 minutes (range 3-166 minutes).

Comment

The wide limits of agreement in this study suggest that there are considerable discrepancies between the two methods in assessing plasma concentrations of

Department of Accident and Emergency Medicine, Norfolk and Norwich Hospital, Norwich NR1 3SR
C V Egleston, *senior registrar*
Department of Accident and Emergency Medicine, Addenbrooke's NHS Trust, Cambridge CB2 2QQ
C Browning, *senior house officer*
G Campbell-Hewson, *registrar*
S M Robinson, *consultant*

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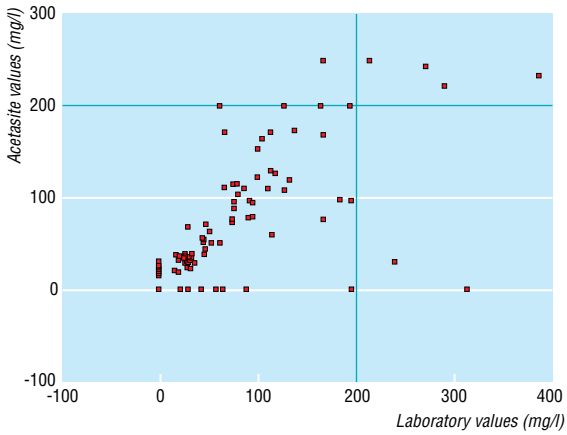
Department of Clinical Biochemistry, Addenbrooke's NHS Trust
I Hamdi, *senior registrar*
Correspondence to: Dr Robinson

paracetamol. Differences between the AcetaSite and laboratory results were spread randomly between high and low concentrations of paracetamol. Treatment with acetylcysteine would have been withheld from three out of the five patients whose results were outside the limits of agreement, had the decision to treat been based only on the result from the AcetaSite test. This might have resulted in a poor outcome.

Impressive performance characteristics are reported in the datasheet for the AcetaSite test and Stat-Site reflectance meter when compared with the GDS enzymatic liquid reagent ($r=0.970$) and the TDX (Abbott) liquid reagent ($r=0.983$). For the data sheet, accuracy was assessed using whole blood, plasma, and serum samples with known concentrations of paracetamol and a small number of clinical samples (n=42). The methodology may partially explain the discrepancy between the results found in our study and those found in preclinical testing; correlation does not assess the degree of agreement but rather the relationship between the two tests.[2] Also, the use of samples with known concentrations in a laboratory environment may not accurately replicate analysis of samples obtained in a clinical setting.



Scattergram of untransformed data comparing results obtained by AcetaSite test with values obtained in the laboratory (mg/l). Dotted lines show concentrations at which treatment with acetylcysteine would be indicated in groups not considered to be at high risk (4 hours after ingestion)

Operator error may explain why some of the results from the AcetaSite test bear little relation to the results found with the laboratory tests. Although the majority of department staff attended two training sessions, difficulties in using the Stat-Site meter were reported by some inexperienced operators. The production of a simple algorithm for using the card and meter reduced the number of difficulties reported.

The rapidity with which the AcetaSite results were available could have been advantageous if the results had been in agreement with the laboratory results. This study found that the AcetaSite test should not replace the standard Quantase assay.

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Comparison of case fatality in smokers and non-smokers after acute cardiac event

Gabe S Sonke, Alistair W Stewart, Robert Beaglehole, Rod Jackson, Harvey D White

Department of Community Health, Faculty of Medicine and Health Science, University of Auckland, Private Bag 92019, Auckland, New Zealand
Gabe S Sonke, *postgraduate student*
Alistair W Stewart, *biostatistician*
Robert Beaglehole, *professor*
Rod Jackson, *associate professor*

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Although smoking is a major modifiable risk factor for acute myocardial infarction, it has also been associated with an up to twofold lower risk of dying in hospital after an acute myocardial infarction.[1 2] We analysed data from a community based register of coronary heart disease to determine whether differences in case fatality (the proportion of those dying) between smokers and non-smokers are restricted to patients who have been admitted to hospital and to evaluate possible explanations for this smoker's paradox.

Subjects, methods, and results

All deaths related to coronary causes and all admitted patients aged 25-64 who met predefined criteria for myocardial infarction or coronary death were identified in Auckland, New Zealand, between 1986 and 1992 as part of the World Health Organisation MONICA (monitoring trends and determinants in cardiovascular disease) project. Study criteria, and methods of case finding and data collection procedures have been published.[3 4] Postmortem examinations were performed on 63% of those who died from cardiac causes. Deaths before admission to hospital, deaths within 28 days after admission, and the total number of deaths were measured. Smoking was determined by direct questioning of surviving patients and of relatives of those who died. Patients were classed as current smokers (those who smoked at least one cigarette a week at the onset of symptoms or gave up smoking less than one month before the index event), ex-smokers (those who had abstained from smoking for at least one month before the onset of symptoms), or non-smokers (those who had never smoked). Logistic regression models were used to assess the effects of smoking on case fatality after adjusting for age, sex, history of myocardial infarction, and history of angina. For those admitted to hospital, adjustments were based