Comparison of assays for measuring plasma paracetamol. Possibility of calibration error needs evaluation

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Abstract
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Comparison of assays for measuring plasma paracetamol

Possibility of calibration error needs evaluation

Eggleston et al report a significant difference in plasma paracetamol concentrations assayed with the AcetaSite bench assay and a standard laboratory assay.1 Rapid and accurate determinations of plasma paracetamol concentrations are crucial in the expeditious and appropriate administration of antidotal treatment, which prevents severe liver damage if given sufficiently early in the course of poisoning.2 We compared two methods for estimating plasma paracetamol (Cobas paracetamol assay kit (Cambridge Life Sciences, Ely) and AcetaSite blood acetyaminophen (paracetamol) test (Cambridge Life Sciences) with a standard high performance liquid chromatographic method.1 We used the methods on 35 samples from 23 patients presenting between 5 and 50 hours after a paracetamol overdose who claimed to have taken a mean of 220 g (range 5-50 (SD 15.1) g) of paracetamol alone. Samples were taken and stored at −40°C, and all assays were performed in our laboratory. The figure shows the results obtained with the three methods. Compared with high performance liquid chromatography, the AcetaSite assay overestimated plasma paracetamol concentration in a considerable number of cases; the difference was significant (P = 0.002, paired t test). There was no significant difference between the results obtained with the Cobas assay and high performance liquid chromatography (P = 0.81, paired t test). The Pearson correlation coefficients of the AcetaSite and Cobas assays with standard high performance liquid chromatographic estimation of paracetamol metabolits were 0.97 and 0.97 respectively. We believe that the most likely source of the discrepancy between the AcetaSite assay and the other methods in our study was a calibration error within the AcetaSite method. All assays were carried out in our laboratory by an experienced clinical chemist (by contrast, some of the assays in Eggleston et al’s study were done by emergency doctors). We therefore believe that operator error is an unlikely explanation for the results of our study or those of the study reported by Eggleston et al. The possibility of a calibration error in the AcetaSite system requires further evaluation; external calibration is not possible with this assay. Eggleston et al do not make clear what results they obtained in the 100 patients who had apparently not taken paracetamol but from whom blood was taken for assay. These results should have been negative by both methods; this is an important point for exclusion of false positive results. In patients who admit to having taken paracetamol, interference in the assay by other drugs taken concurrently is a potential source of error.

Trained and education in use of assay are important

Education—Eggleston et al compared the accuracy of a standard laboratory paracetamol assay with that of a rapid bedside test (AcetaSite).1 Eggleston et al used a statistical method developed by Bland and Altman2 to assess agreement between the two methods of clinical measurements. The limits of agreement were calculated to be 0.16 and 5.04. This translates into poor agreement between the two assays, with 95% of values obtained with AcetaSite being between 0.16 and 5.04 times the values obtained with the laboratory assay. The authors concluded that the AcetaSite test should not replace the established laboratory method. We have also evaluated the AcetaSite test, recruiting 58 patients to our study. Four sets of results were excluded from the analysis because the Stat-Site meter recorded a maximum of > 250 mg/l (by contrast, the laboratory gave a specific reading). At the lower end of the range (< 20 mg/l) 15 sets were excluded for similar reasons. On the remaining 39 samples, using Bland and Altman’s test, we found our limits of agreement to be 0.79 and 1.1. Our results therefore suggest good agreement between the two assays. The performance of the AcetaSite (r = 0.97) matches closely that shown in the dataset for AcetaSite compared with standard reagents (r = 0.97 and r = 0.983). When evaluating a new technology, such a contrast between studies merits careful analysis. Eggleston et al make some suggestions for the reason for the poor agreement between the two assays in their study. Although there may be other reasons, the most likely is training and education. Our study was carried out by the six middle grade doctors in the accident and emergency department and a small number of senior house officers after a one to one training programme. An algorithm card was used from the outset (modified after piloting). Particular attention should be paid to this much overlooked aspect of study design if accurate results are to be attained and valid conclusions drawn.

We believe that the AcetaSite test does provide a rapid and accurate bedside assay of paracetamol concentrations. Further analysis in our study, however, indicates that