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Rapid measurement of creatine kinase activity in a coronary care unit using a portable benchtop reflectance photometer

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Abstract

Rapid measurements of plasma creatine kinase activity using an inexpensive benchtop reflectance photometer (Ames Seralyzer) and disposable reagent strips were evaluated in the laboratory and coronary care unit. The system proved simple to use and capable of yielding rapid (four minutes per analysis), precise (coefficient of variation <9%), and accurate results (correlation with routine method 0.995) when used by medical staff. Creatine kinase values were available 6.5-102 hours earlier than routine laboratory data, depending on the time and day of sampling, thereby facilitating appropriate and economic patient management.

This instrument might be used to supplement the routine enzyme service for selected admissions, resulting in greatly improved availability of results and hence contributing to the early discharge of patients from intensive care facilities.

Introduction

With the development of solid phase chemical techniques and small microprocessor controlled instruments^{1,2} we can now perform many biochemical measurements at or near the patient's bedside, and this has created a growing potential for decentralised testing.³⁻⁵ This is particularly relevant in acute care medicine, where the immediate availability of results may be important in diagnosis and treatment. A major concern in such testing,

however, is whether the necessary standards of accuracy and precision can be achieved, particularly by non-laboratory staff.⁶

We report a preliminary evaluation of determinations of creatine kinase activity performed in a coronary care unit using a small benchtop reflectance photometer, the Ames Seralyzer (Ames Division, Miles Laboratories, United Kingdom). Our aims were to investigate the performance of this instrument in the hands of both experienced laboratory personnel and medical staff who had been given basic instruction in its use.

Methods

The principles of operation of the Seralyzer have been described.¹ The analytical procedure entails dilution of plasma and application to the reagent area of a bar coded disposable plastic test strip. Enzyme activity is monitored by the changing reflectance properties of the strip and it is digitally displayed within four minutes. An activity exceeding 1000 U/l is indicated by a flashing display and a further dilution may be analysed if desired, though for clinical interpretation this was considered unnecessary. Instrument malfunction is detected by the internal microprocessor, and coded error messages are displayed when appropriate. Calibration of the instrument was performed as necessary by laboratory personnel using calibrants supplied by the manufacturer.

Analytical performance was assessed in the laboratory over six weeks using lyophilised commercial quality control materials (Gibcotrol, Gibco New Zealand Ltd) and by comparison with creatine kinase results from the routine laboratory automated analysis using an N-acetyl cysteine activated coupled enzyme assay (Boehringer Corporation Ltd, United Kingdom) at 37°C in a Cobas-Bio centrifugal analyser (Roche Diagnostics, United Kingdom).

The clinical evaluation was undertaken over a further six weeks with the Seralyzer situated in the 10 bedded coronary care unit, all measurements being made by the medical staff on samples drawn from most routine admissions. Heparinised plasma samples were analysed according to the manufacturer's instructions. The residual plasma samples were sent to the laboratory for routine cardiac enzyme profile and the results returned to the coronary care unit through the laboratory's normal reporting system. Additional samples were provided daily from the laboratory, including a control sample of known creatine kinase activity and other samples to maintain an independent monitor of performance.

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Results

LABORATORY

Consecutive replicate analyses using the same batch of test strips and fresh pooled plasma samples with mean creatine kinase activities in the range 179-1342 U/l gave coefficients of variation not exceeding 2.8%. The same pooled plasma samples stored at -20°C were analysed over 20 days using several different batches of reagent strips. The maximum overall observed change in activity was -5.4%, which is consistent with losses expected under such storage conditions.

Analyses of fresh control sera over 20 days gave values for mean activities and precision which were not significantly different for the Seralyzer and routine methods of analysis (paired Student's *t* test, Fisher's test; $p < 0.05$) (table I). During the period of laboratory assessment 100 plasma samples with activities up to 1400 U/l were analysed. The overall relation was Y (Seralyzer) = $1.21X$ (routine) - 6.5 ($r = 0.997$), and this relation was used to modify the laboratory reference ranges for creatine kinase for clinical interpretation of Seralyzer values during the rest of the study (men: up to 210 U/l; women: up to 175 U/l). Although recalibration of the Seralyzer is recommended by the manufacturer on a weekly basis, no appreciable deterioration in results was observed over at least 12 days as judged by the performance of control samples.

CORONARY CARE UNIT

Table I shows the day to day performance for quality control samples analysed by medical staff. Mean values with the Seralyzer did not differ significantly from those produced by the routine method. Precision for these samples at levels 1 and 3 was also no different from that of the laboratory. Nevertheless, Fisher testing of the results on level 2 samples, which were used as the control throughout, showed precision which was poorer than for the routine laboratory method but not significantly different from the results obtained with the Seralyzer by laboratory staff.

During the evaluation 71 Seralyzer measurements of creatine kinase activity were made in patients admitted to the coronary care unit. The figure correlates these results with the creatine kinase values from the routine cardiac enzyme profile. The two results marked as open circles were due to incorrectly performed Seralyzer measurements; reanalysis showed the true results to be consistent with the observed overall correlation. Seven samples gave results greater than 1000 U/l but these were not further diluted and are not plotted. For 51 of the measurements the doctor decided before analysis that the result was likely to be of use in management. In 22 of these (43%) immediate patient management was altered (table II). In only one of the 20 analyses thought less likely to be helpful was a change in management made, the patient being transferred to the ward on the basis of a normal creatine kinase activity.

TABLE I—Day to day reproducibility of Seralyzer creatine kinase results obtained in laboratory and coronary care unit compared with routine method

		Quality control sera		
		Level 1	Level 2	Level 3
Seralyzer	Laboratory	Mean (U/l)	78	321
		Coefficient of variation (%)	8.5	6.1
	Coronary care unit	Mean (U/l)	79	325
		Coefficient of variation (%)	8.3	9.4
Routine	Laboratory	Mean (U/l)	74	306
		Coefficient of variation (%)	4.3	3.0
	Coronary care unit	Mean (U/l)	74	306
		Coefficient of variation (%)	4.3	3.0

TABLE II—Changes in management as a result of using Seralyzer in coronary care unit

Action	No	Action	No
Transfer to ward	11	Intra-aortic balloon pumping	1
Discharge home	3	Pulmonary angiography	1
Further treatment	4	Echocardiography	1
{ Antianginal	1		
{ Streptokinase	1		
Total	22

Correlation of Seralyzer creatine kinase results obtained by medical staff with corresponding routine laboratory data. (Two open circles represent measurements performed incorrectly by Seralyzer.)

Twenty nine samples submitted for routine cardiac enzyme profile after Seralyzer analysis were returned to the coronary care unit next day for reanalysis. The mean creatine kinase activity for this group was 254 U/l (range 81-370 U/l) and the coefficient of variation for the replication 7.9%. Table III shows the improved availability of creatine kinase results using the Seralyzer in the coronary care unit for patients admitted during laboratory hours and outside those hours including weekends. The improved availability of results during a bank holiday weekend is shown separately.

TABLE III—Improvements in availability of creatine kinase results using Seralyzer in coronary care unit

Sample collection time	Improvement in availability (hours)	
	Mean	Range
0900-1700	23.2	6.5-53.0
1700-0900	21.8	9.0-46.5
April bank holiday (1200 Saturday till 0900 Tuesday)	70.3	44.5-102.0

Discussion

Among the fundamental criteria for decentralised biochemical testing is the need for acceptable levels of precision and accuracy to be achievable by all users of analytical equipment located peripherally. Doubts have been expressed about the standard of performance of non-laboratory workers using decentralised equipment,^{6,7} but this study showed that essentially comparable precision was attained for Seralyzer creatine kinase determinations by doctors on the coronary care unit and laboratory workers alike. The level of precision achieved in this study by medical staff was also comparable with the findings published by other laboratory workers.^{8,9} Indeed, the reproducibility of the determination when performed by medical staff made the single analysis of samples reliable enough for diagnosis. During the clinical evaluation all eight duty doctors used the Seralyzer so that, while all were proficient in its use, none became sufficiently "expert" to bias the overall assessment of the reliability of the data. Although precision for both groups of users was generally poorer than for laboratory creatine kinase analyses—as would be expected from the relatively higher degree of manual work needed for Seralyzer measurements—only the control sample

data produced by the medical staff differed in statistical significance. We believe that this reflects sample instability¹⁰ rather than simply operator or instrument performance and emphasises the need for careful planning of quality control measures adopted for equipment in use outside the main laboratory. Patients' plasma creatine kinase activities did not show such lability. Using correlation of results with the routine laboratory method as a practical measure of accuracy, both groups found similar positive Seralyzer bias with patients' plasma samples. This has not been observed before,⁸⁻⁹ but difference in calibration materials and the laboratory instruments used for comparisons may account for the finding. The Seralyzer proved reliable throughout, requiring little maintenance other than daily provision of control materials and occasional calibration.

Decentralised testing must make a measurable and economic contribution to patient care, as its use cannot be justified on the ground of technological progress alone. The instrument costs £2900 and creatine kinase test strips cost 44.8p each (both excluding VAT). In view of the time taken to produce controlled results, however, the logical role of the Seralyzer would not be to replace the routine enzyme service from the laboratory but to supplement that service for selected admissions. The ability of medical staff to identify those patients who were less likely to have their management altered by enzyme analysis on admission points to the probable success of such a selective policy and is consistent with the need to exercise discretion in requesting tests.¹¹ The added burden of analysis was thus small and well accepted as the doctors were motivated to produce results of immediate diagnostic utility. The substantial improvement in availability of creatine kinase estimations, particularly at weekends and on a bank holiday when the routine laboratory service was not available, contributed to overall economies, principally in the early discharge of patients from costly intensive care facilities to the general ward or even home.

In conclusion, we have shown that standards of precision and accuracy for Seralyzer creatine kinase analyses similar to those achieved by experienced analysts in the laboratory were attainable by doctors on a coronary care unit. The medical staff were able to produce rapid, reliable results by adhering to a simple analysis protocol after only minimal training in the use of the instrument. Such "real time" cardiac enzyme data aided earlier confirmation of diagnosis and facilitated appropriate patient management. Continuing success in the use of the Seralyzer, however, depends on day to day cooperation with the laboratory to ensure maintenance of performance quality and therefore maximum diagnostic reliability of results.

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Epidemic hypochlorhydria

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Abstract

During a study of gastric secretion four out of six previously healthy subjects developed hypochlorhydria after a transient illness with nausea, vomiting, and abdominal pain. Mean basal and peak acid outputs were 0 and 2.3 mmol (84 mg)/h one month after the onset of illness and 1.5 and 27.0 mmol/h (55 and 984 mg/h) at eight months' follow up. Two of the subjects were followed up at 18 months, when mean basal and peak acid outputs were 3.9 and 33.5 mmol/h (142 and 1221 mg/h).

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No endoscopic abnormality was seen at one and eight months, but biopsies showed active superficial gastritis, which resolved in one subject and became chronic in two. Schilling tests performed in three subjects at eight months showed diminished retention of vitamin B₁₂. During hypochlorhydria a 24 hour intragastric analysis was performed for total and nitrate reducing bacteria, pH, and concentrations of nitrite and total and stable N-nitroso compounds. Of the 48 samples of gastric juice examined, 47 had bacterial growth of more than 10⁶ organisms/ml and 46 had growth of nitrate reducing bacteria of more than 10⁵ organisms/ml. Mean intragastric nitrite concentrations were 10 times higher than in a group of eight healthy controls. Both mean total and mean stable N-nitroso compound concentrations, however, were not appreciably different from those in controls.

Although community transmission was a possibility, serological screening and electron microscopy of gastric biopsy specimens failed to show an infective cause. Transmission of an unidentified enteric pathogen via a contaminated pH electrode was therefore suspected. Thus gastric juice should not be returned to the stomach after contact with a contaminated glass electrode as this is a possible cause of atrophic gastritis.