Development and validation of accessible laboratory tests to inform the clinical management of propanil and paracetamol self-poisonings

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Abstract

Background: This research is based around the need for the development of low cost diagnostic tests for propanil and paracetamol poisoning. Both sit at either end of the spectrum of clinical toxicology. Propanil poisoning is relatively rare but it has high rates of mortality, despite being cheap to treat; however, it is generally under treated, which contributes to the high death rate. Paracetamol poisoning is very common and has a low overall mortality rate, but it is relatively expensive to treat and is generally over treated, which contributes to the very high costs to health systems. **Objective:** The overall aims of the study were to develop and validate tests to aid treatment of propanil and paracetamol poisoning and to successfully introduce them into clinical practice in a resource-limited setting. **Method:** A simple bedside test was developed by preparing standard methaemoglobin blood samples and spotted on a white absorbent material for the determination of methaemoglobin. The red, blue and green colour values of standard methaemoglobin were used to prepare the colour chart. The chart was validated using standard methaemoglobin blood samples and then used in the clinical measurement of methaemoglobin in patients with propanil poisoning. The Glynn and Kendal colorimetric method was modified for the paracetamol assay. This assay was validated by measuring the paracetamol concentration in stored clinical samples and the results were compared with those of a current gold-standard high-performance liquid chromatography method. A prospective survey, assessing the clinical use of the paracetamol assay, was performed on all patients with paracetamol poisoning. **Results:** The red colour value was linearly

related to the percentage of methaemoglobin (R^2=0.9938), with no effect of absolute haemoglobin concentration. The mean inter-observer (N=21) agreement and weighted *k* values for the scanned methaemoglobin spots using the colour chart were 94% and 0.83%, respectively. The mean inter-observer (N=9) agreement and weighted *k* values for the freshly prepared methaemoglobin sample with the chart were 88% and 0.71%, respectively. Clinical use of the colour chart also showed good agreement with spectrometric measurements. The recovery study in the paracetamol assay showed an excellent correlation ($R^2 > 0.998$) for paracetamol concentrations from 25 to 400 mg/l. There was also excellent correlation with the high-performance liquid chromatography method ($R^2 = 0.9758$). In the clinical cohort study, use of the antidote N-acetylcysteine was avoided in over a third of patients who had their plasma paracetamol concentration measured. The cost of consumables used per assay was $0.50 (US). **Conclusion:** Both developed methods are simple and reliable and could be used in both rural hospitals where laboratory facilities are not available, and in urban hospitals. Introducing these methods into resource-poor clinical settings has the potential for significant clinical and economic impacts on the management of poisoning.