Opinion

i-STAT – Combining Chemistry and Haematology in PoCT

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Abstract
Point-of-care testing (PoCT) is traditionally considered a branch or offshoot of clinical chemistry. The appearance on the market of small, light, inexpensive, multi-purpose, point-of-care analysers, which combine a number of widely differing analytes, has to some degree upset this paradigm. Such analysers, however, are invaluable in some clinical settings.

Specialties other than clinical chemistry may have differing views on traditional test management, particularly with regard to quality control (QC), quality assurance (QA), and training. These views must be considered when designing an overall PoCT management plan. Test management issues should be resolved by taking the view that it is a 'point-of-care' test, and by looking at the specific test technology and method involved, rather than by just assuming it is a 'haematology' or a 'chemistry' test.

Clinical users of a combined PoCT system are principally interested in the generation of good quality results. To avoid confusion, any advice given to clinical staff regarding their analysers should be clear, concise, and above all else, consistent.

Introduction
PoCT is often regarded as a part or branch of clinical chemistry by many laboratory and clinical professionals. This paradigm has probably arisen because historically a majority of point-of-care tests such as blood gas analysis and blood glucose testing have indeed been derived directly from clinical chemistry. In some institutions, this continues to be the case.

Whilst this attachment has continued to serve PoCT well into the 21st century, an increasing number of testing devices are being marketed which perform tests such as the white cell count (WCC), haematocrit (Hct) and haemoglobin (Hb), prothrombin time/international normalised ratio (PT/INR), activated clotting time (ACT), and the activated partial thromboplastin time (APTT). These tests are usually regarded as 'haematology' tests and are commonly used in the management of infection, haemorrhage, and oral and intravenous anticoagulants.[1,2]

Point-of-care haematology testing can be performed with dedicated PoCT analysers. However, the Abbott i-STAT (Abbott Laboratories, Abbott Park, IL, USA) analyser is capable of performing a wide variety of point-of-care tests on the same instrument. These tests include arterial and venous blood gas and electrolytes, common metabolites, cardiac troponin I (TnI), Hct and Hb, and coagulation tests such as the INR and ACT.

Here I describe the selection, management and use of the i-STAT analyser as a combined chemistry/haematology analyser in an integrated testing network consisting of 195 analysers, covering approximately 140 sites across the state of Queensland. This network is considered the largest in the world and provides basic testing capabilities over a considerable geographical area. Only 33 of the analyser locations have on-site laboratories; the remainder are non-laboratory sites such as small rural hospitals and primary health care clinics. All tests at these sites are performed by registered nurses or medical officers.[3]

Running a Combined Chemistry/Haematology Point-of-Care Service – Why We Use the i-STAT
The Pathology Queensland Point of Care Testing network originated in 2001 with the aim of providing on-site access to basic pathology tests for the many small rural and remote hospitals in Queensland. Long specimen transport

distances, intermittent transport availability and high summer temperatures continually challenged the ability of established laboratories to provide reliable results in an acceptable time frame for management of the acutely ill patient. Often a simpler solution was to fly the patient to a larger facility for testing and treatment.

The on-site testing requirements for these small district hospitals are not extensive. They do not have intensive care or complex surgical units to support. Most of their immediate needs can be supplied by a few 'basic' chemistry and haematology tests.[4]

The i-STAT analyser with its mix of tests covering basic chemistry and haematology covers most of these needs. The only important test missing is the WCC differential which can be supplied by other point-of-care instruments.[5]

The immediate availability of these tests can literally mean the difference between keeping and treating an emergency patient on the one hand and an emergency medivac flight on the other. It can also mean a safer and better managed stay for less acute inpatients.[4]

Many of these remote facilities conduct oral anticoagulant outpatient clinics or hospital in the home programs, where the availability of PoCT can reduce or eliminate the need to recall a patient for treatment changes.[6]

i-STAT - Instrument Description and Testing Technologies

The i-STAT is a cartridge-based analyser with all the analytical requirements for the performance of a test contained within an individual cartridge. The test sample and reagents never enter the 'analyser' which transforms electrical signals from the test cartridge into human-readable results.

The individual tests are arranged in traditional blood gas or chemistry groupings on a single use cartridge. To switch from one test group to another, one simply changes to a different cartridge type.

Blood gases, electrolytes, creatinine and urea are performed using a miniaturised version of traditional electrode technology contained within the test cartridge.

TnI and brain natriuretic peptide (BNP) tests use a sandwich-type immunoassay with electrochemical rather than optical detection.

PT/INR uses a recombinant human thromboplastin with electrochemical detection of the 'clotting' endpoint. This is achieved through thrombin cleaving an electrochemical substrate rather than fibrinogen. INR is 'calibrated' using the same 'International Sensitivity Index' system as is used for laboratory thromboplastin reagents.

Measurement of Hct is based on plasma conductivity; the electrical resistance of a whole blood sample is proportional to its Hct. There are some limitations to this method as significant deviations from an assumed plasma protein concentration may affect results. Haemoglobin concentration is calculated from the Hct using a standard equation.

Communications Technology

The i-STAT analyser is capable of transmission control protocol/internet protocol (TCP/IP) communication through its downloader module and any standard network to a middleware program known as the computer data system (CDS). The CDS is used to store patient results, remotely program the analysers, track QC and QA, and communicate results to a laboratory information system (LIS). Although the analyser can be used in a stand alone mode, the true power of the system only becomes available when all the analysers are linked through the CDS to a LIS.

QC and QA Requirements

QC of the 'Analyser'

QC of the 'analyser' itself is achieved by use of an electronic check cartridge which simulates the signal from a real test cartridge at low and high signal points. The response is compared with reference values programmed into the analyser firmware, taking the place of a conventional bi-level control check. This process while checking the *analyser,* does not check the cartridges.

QC of the Test Cartridges

Due to the wide range of tests performed by the analyser, a variety of QC materials are required although the processes are simplified as far as possible.

QC of the blood gas/chemistry cartridges is performed using routine liquid bi- or tri-level aqueous control material familiar to operators of conventional blood gas analysers.

A frozen plasma-based material is used for TnI and BNP QC.

Coagulation tests utilise a lyophilised citrated whole plasma material which is re-calcified immediately prior to use. This type of material may be unfamiliar to clinical chemistry staff or even coagulation staff used to more conventional controls.

Control of the Hb/Hct requires a specific fixed whole blood control material, similar to controls used by haematology analysers. This type of material is also seldom used in clinical chemistry.

The manufacturer's recommendation for cartridge QC is to test multiple levels on each lot number at delivery. Further QC should be in line with local practice and regulation.

QA

The manufacturer's recommendations for QA are restricted to observance of local recommendations and regulations.[7]

Tailoring a Management Program for the i-STAT – Combining Chemistry and Haematology PoCT

The best approach is to look at the PoCT system as a new way to provide a pathology testing service, and to construct a dedicated management framework accordingly. Elements of good laboratory practice such as QC, QA and training programs are naturally retained but they require modification to suit the purposes of remote PoCT and non-laboratory users.

The process begins with careful study of the i-STAT instrument and its testing methodologies, combined with input from multiple pathology disciplines. Drawing from our data outlined above, we note:

- Use of disposable test cartridges which the user does not need to 'calibrate' in the field.
- As the sample makes contact only with the cartridge, the analyser does not get 'dirty' or require regular maintenance beyond a simple electronic QC check each day of use and a wipe clean as required. The user cannot run a cartridge without having performed the electronic QC check.
- Test cartridges require QC on delivery and at monthly intervals, and have a variety of storage options including extended storage at 2–8 °C, or 14-day storage at standard room temperature.
- Most testing technologies draw from their corresponding laboratory equivalent and yield generally comparable test results.

Pathology Queensland has a dedicated multidisciplinary PoCT working party which has oversight of point-of-care testing including the i-STAT network. The group has a varied membership comprising representatives from clinical chemistry, haematology, microbiology and quality management as well as scientific and clinical end users from all levels of the chain. The chair and deputy chair are a multi-skilled pathologist and scientist respectively. The organisation is modelled after specialist PoCT consulting groups as used and peer recommended in the USA and UK/Europe. The difference here is that the group administers an entire state rather than a single hospital.[8-10]

This management system ensures that the testing policy and procedure are sourced from recognised discipline experts but implemented with the aim of an integrated multidisciplinary PoCT service.

The working party oversees a hub and spoke arrangement where the central laboratory in Brisbane coordinates large regional laboratories, which in turn coordinate district laboratories that service their own group of district hospitals and health centres. The regional laboratories manage the local purchase, QC and distribution of test cartridges as well as the installation of new analysers and training of operators as required.

All regional laboratories use exactly the same QC, QA and training models as developed and implemented by the central working party. A complete on-line training module ensures that consistent training and advice is available to more than 3500 clinical users across the state.[11]

Linking all i-STAT analysers through a CDS in Brisbane with results sent to the state-wide LIS used by Pathology Queensland means that up-to-date patient results can be viewed anywhere in the state, an important consideration when acutely ill patients are transported between facilities.

Pathology Queensland follows the Australasian Association of Clinical Biochemists (AACB) PoCT working party recommendations for cartridge based analysers[12] and uses RCPA QAP materials for all its laboratory site analysers. All laboratories involved are National Association of Testing Authorities (NATA) accredited.

QC and QA are monitored centrally through both the CDS and external QA reports. Monthly quality reports and a regular newsletter are e-mailed to i-STAT resource staff in the supervising and district laboratories, and to interested clinical unit managers in more remote areas.

Problems and Issues

The majority of clinical users believe that the benefits to patient care of this network outweigh any disadvantages; however, over a number of years of operation we have documented some recurrent issues.

The transient nature of rural clinical staff necessitates a continual need for operator training, a potential burden to small district laboratories. This consideration was one major driver to develop the online training module.

Testing errors appear to be largely confined to the pre-analytical phase, with incorrect specimen collection and handling, and failure to enter the required patient identifiers being standout issues. These issues are specifically targeted

in our online training, monthly quality reports and advanced training workshops.

Equipment reliability has been largely good, with most failures attributable to rough handling, contamination with blood or attempted use outside the instrument design parameters.

Conclusion

For the clinician in a rural hospital, we have provided:

- a multipurpose analyser which requires a single daily quality check that is easy to perform and virtually no routine maintenance;
- quality checked cartridges traceable to a registered laboratory;
- flexible cartridge storage options;
- test results comparable to routine laboratory results and immediately available both locally and across the state;
- an online training system;
- ready access to consistent expert advice at a local, district and state-wide level;
- regular quality updates and reports;
- the backing of a state-wide NATA-accredited pathology service.

Mr Cameron Martin is a member of AACB PoCT Working Party Committee.

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