Clinica Chimica Acta 451 (2015) 257–262

Contents lists available at ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/clinchim

A roadmap to defining the clinical reportable ranges of chemistry analytes: Increasing automation efficiency and decreasing manual dilutions

Sheng-Ying Lo, Geoffrey S. Baird, Dina N. Greene *

Department of Laboratory Medicine, Chemistry Division, University of Washington, Seattle, WA, United States

ARTICLE INFO

Article history:
Received 26 June 2015
Received in revised form 11 September 2015
Accepted 5 October 2015
Available online 8 October 2015

Keywords:
Laboratory management
Beckman AU
Onboard dilution
Manual dilution
Automation

ABSTRACT

Background: Proper utilization of resources is an important operational objective for clinical laboratories. To reduce unnecessary manual interventions on automated instruments, we conducted a workflow analysis that optimized dilution parameters and reporting of abnormally high chemistry results for the Beckman AU series of chemistry analyzers while maintaining clinically acceptable reportable ranges.
Methods: Workflow analysis for the Beckman AU680/5812 and DxC800 chemistry analyzers was performed using historical data. Clinical reportable ranges for 53 chemistry analytes were evaluated. Optimized dilution parameters and upper limit of reportable ranges for the AU680/5812 instruments were derived and validated to meet these reportable ranges. The number of specimens that required manual dilutions before and after optimization was determined for both the AU680/5812 and DxC800, with the DxC800 serving as the reference instrument.
Results: Retrospective data analysis revealed that 7700 specimens required manual dilutions on the DxC over a 2-y period. Using our optimized AU-specific dilution and reporting parameters, the data-driven simulation analysis showed a 61% reduction in manual dilutions. For the specimens that required manual dilutions on the AU680/5812, we developed standardized dilution procedures to further streamline workflow.
Conclusions: We provide a data-driven, practical outline for clinical laboratories to efficiently optimize their use of automated chemistry analyzers. The outcomes can be used to assist laboratories wishing to improve their existing procedures or to facilitate transitioning into a new line of instrumentation, regardless of the instrument model or manufacturer.

1. Introduction

National health expenditure (NHE) in the United States has experienced unprecedented growth. In particular, the Centers for Medicare and Medicaid Services reported a NHE of $2.9 trillion for 2013 and projected an annual growth rate of 5.7% between 2013 and 2023 [1]. To offset this escalating healthcare expenditure, clinical laboratories are faced with the challenge of advancing productivity and quality whilst simultaneously reducing cost. The introduction of automation and high-throughput chemistry analyzers has provided a solution to these challenges by allowing clinical laboratories to perform high-volume testing with increased reproducibility and reduced error. In addition, the use of automated instruments has decreased the number of full-time equivalents required by clinical laboratories, which can translate into significant savings [2].

While automation has revolutionized laboratory testing, successful implementation requires efficient alignment of automated instruments and manual workflows. Specifically, the automated capabilities of instruments need to be evaluated and adjusted in the context of minimizing manual involvement, thereby, redirecting technologist time toward performing highly complex manual tasks. Our large, academic institution recently replaced our Beckman UniCel DxC 800 Synchron Clinical Systems (DxC) with Beckman AU 680 and 5812 (AU) for testing 53 serum/plasma/urine analytes that are commonly measured as part of routine chemistry testing. One of the major distinctions between the two Beckman instruments is the number of analytes with extended onboard measurement range (OB range). The DxC utilizes an over-the-range of detection and correction (ORDAC) function capable of extending the analytical measurement range (AMR) by 1.5- to 6.5-fold using reduced specimen volume per reaction when results exceed the upper end of the AMR. The AU instrument, in contrast, employs two onboard dilution mechanisms to generate extended onboard measurement range for any analytes that are unperturbed by dilution. In particular, the AU can create an onboard pre-dilution specimen that extends the AMR by 3-, 5-, or 10-fold, and it can also use a reduced specimen volume

Abbreviations: AU, Beckman AU 680 and 5812; DxC, Beckman UniCel DxC 800 Synchron Clinical Systems.

* Corresponding author.
E-mail address: dngreene@uw.edu (D.N. Greene).

http://dx.doi.org/10.1016/j.cca.2015.10.006
0009-8981/

per reaction to extend the AMR by 2-fold. This feature provides individual laboratories with the flexibility to either validate the analyte-specific onboard dilution factors recommended by the manufacturer (less than 5-fold) or alternative onboard dilution factors to match the population-specific clinical reportable range.

2. Materials and methods

2.1. Laboratory data

This clinical laboratory quality improvement project was performed at the University of Washington Medical Center (Seattle, WA) and granted an exemption of review from the UWMC institutional review board. Results for 53 analytes generated from the DxC between January 2013 and December 2014 were queried from the laboratory information system (Sunquest, ver 7.1). Results were specifically retrieved if their numerical value exceeded the analyte's validated AMR of the DxC or AU (N = 23,856). Laboratory results were de-identified and grouped by analyte for analysis.

2.2. Chemistry analyzers and specimen criteria

Specimens were measured using the chemistry analyzer connected to the Beckman Power Processor Sample-Handling System. With this total laboratory automation system, specimens required technologist intervention only in special circumstances. For example, manual intervention was required when a particular middleware rule was violated, such as when lipemic index indicated that ultracentrifugation was required to prevent lipemic interference, or if manual dilutions were required. All ORDAC, onboard dilutions, and manual dilutions were validated to meet the compliance requirements for College of American Pathologists accreditation [3]. In order to accommodate a complex patient population, including transplant and trauma patients, our laboratory policies for the majority of the DxC assays did not include a maximum dilution factor. Manual dilutions up to 10-fold were validated for DxC in duplicates by confirming that the results from diluted specimens, after correcting for dilution factor, were within 5% of the neat specimens. With the validation of a 10-fold dilution, all higher dilutions were subsequently assumed validated using the rationale that differences in the final reaction mixture composition was negligible when compared to the 10-fold dilution. In particular, minimal changes were expected when the final volume of specimen is less than 10% serum or plasma and when the reagent composition includes all of the co-factors necessary for the chemical reaction. A different dilution validation approach was utilized for the AU. Specifically, for the optimized AU-dilution parameters, dilution corrected results agreed within 10% of the neat results in duplicates. This strategy was employed to prevent reporting of erroneous results due to excess dilution.

Our acceptable specimen types for each analyte were determined using manufacturer recommendations, and a separate policy for serum and plasma was not implemented when both were deemed acceptable specimen types. Hence, analyte specific dilution effects due to serum versus plasma were not evaluated as the optimized dilution parameters were only performed on serum or plasma.

2.3. Data analysis

To calculate the number of laboratory results measured on the DxC that required manual dilution, all results above the AMR or, when applicable, ORDAC range, were counted. Per our laboratory DxC policy, specimens with measured analyte results above the AMR or ORDAC range were manually diluted until a numerical result was obtained unless otherwise indicated (validated as described above). To simulate the number of Beckman AU-specific manual dilutions, the same data set was analyzed according to the AMR or onboard measurement range, which accounts for any automated onboard dilutions, and "greater than" reporting system. All data analyses were performed using Microsoft Excel or GraphPad Prism 6.0.

3. Results

The upper analytical measurement range, extended onboard range, and manual dilution range for the Beckman DxC and AU instruments are summarized in Table 1 (40 serum/plasma and 13 urine analytes). The DxC had ORDAC function available for 15 of 40 serum/plasma and 3 of 13 urine analytes. Per our DxC laboratory policy, all analytes, except serum/plasma total carbon dioxide and HDL cholesterol, with concentrations greater than the AMR or ORDAC range, were manually diluted until a numerical value was obtained before reporting. The calculated maximal dilution factors used for each analyte were all within 100-fold dilution as shown in Table 2. For the AU, 33 of 40 serum/plasma and 10 of 13 urine analytes had an onboard dilution that extended the AMR by 2-, 3-, 5-, or 10-fold. Per manufacturer's recommendation, the 10-fold onboard dilution was rarely implemented except for analytes where the 10-fold extension in AMR was deemed necessary for our patient population, such as creatine kinase. Manual dilutions on the AU were standardized from our previous workflow on the DxC. Specially, one pre-defined manual dilution of either 2-, 3-, 11-, or 51-fold was instituted for 13 analytes after reviewing DxC historical results that were greater than the onboard measurement range of the AU (Table 2). These pre-defined manual dilutions can be coupled to specific pipetting protocols and allow for extension of clinical reportable ranges. Using these pre-defined parameters, a small percentage of abnormally high chemistry results on the AU would need to be reported as "greater than" the upper limit of the clinical reportable range.

To maximize reporting of an exact numerical result for our patient population, the optimized AU-specific onboard and manual dilution factors were defined using historical results above the validated AMR of the AU (Table 2). For example, lipase had 129 historical results above the AU AMR (3–600 U/l) with 2549 U/l and 11,406 U/l representing the 80th percentile and the maximum, respectively. With this lipase distribution, a 5-fold onboard dilution factor was selected from the available AU-defined onboard parameters (2-, 3-, 5-, or 10-fold) to extend the onboard measurement range (3–3000 U/l) and a 51-fold dilution was chosen from the pre-defined manual dilution options (2-, 3-, 11-, and 51-fold) to extend the clinical reportable range (3–30,000 U/l). By using this data-driven approach, we were able to designate dilution parameters for lipase that would accommodate most, if not all, of the patient population without unnecessary manual interventions. In addition, to ensure that these high lipase results would not be over diluted such that they would drop below the lower end of the AMR after either a 5-fold onboard or a 51-fold manual dilution, we calculated the maximum allowable onboard and manual dilution factor. For lipase, the maximum allowable onboard and manual dilution factor was <200 (upper AMR/lower AMR) and <1000 (upper onboard range/lower AMR), respectively, suggesting that these optimized dilution parameters would be compatible with the validated AMR of the assay. Prior to finalizing and implementing the lipase onboard and manual dilution factors, we validated these parameters per accreditation guidelines and ensured that the clinical reportable range would fulfill the clinical needs of the ordering provider. Similar reasoning was applied for defining the onboard dilution factor and pre-defined manual dilution for other analytes. Note that some of the analytes we assessed did not require an onboard or manual dilution to be defined due to lack of clinical indication and historical results above the validated AMR or the onboard range.

Our retrospective analysis showed that 5447 serum/plasma specimens and 2253 urine specimens measured by the DxC during a 2-y period required manual dilution (Fig. 1). When applying this data to the AU using the parameters outlined in Table 1, our simulation revealed only 2741 serum/plasma specimens and 251 urine specimens required manual dilutions, reductions of 50% and 89%, respectively. This translates to a decreased manual dilution requirement for 26 of 40 serum/plasma