Reassessment of Anion Gap Reference Range Following Implementation of New Chemistry Analyzers: The Fairview Experience

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Recently, our institution transitioned from a chemistry analyzer that was based on dry slide technology (OCD Vitros) to a system employing wet chemistry-based assays (Siemens Vista 1500). For all measured analytes, reference ranges were verified for assays on the new instruments with at least 40 healthy individuals before going live as recommended by Clinical and Laboratory Standards Institute (CLSI) guidelines (C28-A3). However, following the implementation of the Vista instruments, clinicians began reporting an increase in low anion gaps without clinical explanation. Thus, our objective was to investigate whether the increase in low anion gaps was secondary to the instrument change. Review of validation data for the components of the anion gap calculation – sodium, chloride and bicarbonate – revealed that all three analytes passed reference range verification. However, we hypothesized that a combination of subtle shifts in these measurements could result in a larger change in anion gap. To test this hypothesis, a retrospective analysis of patient data distributions over two months before (n = 33,815) and after (n = 35,677) implementation of the Siemens Vista analyzer was performed using JMP software. With implementation of the new analyzer, the median anion gap dropped from 11 mmol/L (2.5th to 97.5th percentile range = 5.3-17 mmol/L) to 7 mmol/L (2.5th to 97.5th percentile range = 3.0-12 mmol/L). Additionally, we identified subtle shifts in two components of the anion gap – the median sodium decreased from 140 (2.5th to 97.5th percentile range = 131-146 mmol/L) to 137 (2.5th to 97.5th percentile range = 129-142 mmol/L) while the median chloride increased from 103 (2.5th to 97.5th percentile range = 93-110 mmol/L) to 105 (2.5th to 97.5th percentile range = 95-111 mmol/L). The combination of these subtle shifts in electrolytes largely explains the decrease in anion gap median after implementation of new instrumentation. Based on this data, the anion gap reference range was lowered to 3-14 mmol/L (from 6-17 mmol/L). In conclusion, our experience demonstrates that, while the analytes in calculations such as anion gap may pass reference range verification during instrument validation, propagation of subtle shifts may lead to a significant reference range shift for calculated values. Such calculated determinants (including plasma osmolality, fractional excretion of sodium, etc.) should also be subject to reference range verification, much like their constituent variables in the equation that are analytically measured. Additionally, large-scale retrospective data analysis post go-live can provide greater power for detecting reference range shifts.

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