Extensive Evaluation of Sample Interferences on Point-of-Care Glucose Meters against an IDMS Reference Method
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**Background:** Tight glycemic control (TGC) helps reduce hyperglycemia and subsequent mortality in intensive care unit (ICU) patients. Handheld blood glucose monitoring systems (GMS) are ideal for guiding intensive insulin therapy and maintaining TGC. However, while many of these GMSs are used in hospitals, they have not been fully validated in the ICUs. Poor performance results in inappropriate insulin dosing and increases risk for dangerous hypo- or hyperglycemic events. In recent years, sample interferences have emerged as a significant challenge for GMSs. The objective of this study was to determine the effects interferences on GMSs and the impact of autocorrecting biosensors on glucose measurement accuracy when compared to an isotope dilution mass spectrometry (IDMS) reference method.

**Methods:** We investigate the effects of ascorbic acid (AA), beta-hydroxybutyrate (BHB), galactose (GAL), lactose (LAC), L-glutathione (L-GLU), and N-acetylcysteine (NAC) on GMSs from manufacturers A, B, and C. Whole blood samples were collected from 12 healthy adult (age≥18 years). Interferences were tested at 3 levels for 5 glucose levels (range: 2.8 to 27.6 mmol/L). Each sample was tested 5 times. Results were compared to an IDMS method (Agilent HP 5975, Wilmington, DE) calibrated using a 4-level traceable standard (NIST, SRM 917a). Two-way ANOVA and pairwise analyses were performed to identify significant differences between GMS versus the reference for each interference level.

**Results:** AA significantly affected GMS from manufacturers B (mean [SD] bias: 44.1 [11.6] mg/dL, P<0.001) and C (12.5 [44.3] mg/dL, P=0.013). BHB significantly affected the GMS from manufacturer C (-33.1 [50.1] mg/dL, P<0.001). LAC significantly affected GMS from manufacturers B (62.6 [15.8] and C (-46.6 [40.2] mg/dL, P<0.001). L-GLU significantly affected GMSs from manufacturer B (32.6 [19.7] mg/dL, p<0.001). NAC significantly affected GMSs from manufacturer B (20.8 [17.9] mg/dL, p<0.001). GAL significantly affected GMSs from manufacturers B (93.8 [22.1] mg/dL, P<0.001) and C (-56.5 [38.7] mg/dL, P<0.001).

**Conclusions:** Accurate glucose monitoring improves TGC and outcomes in ICU patients. Critically ill patient samples may contain numerous interferences from endogenous and exogenous sources. GMSs from manufacturers B and C were significantly affected by several interferences despite their autocorrecting features. Clinicians must be aware of drug interferences in critically ill patients.