Clinical Impact of Sample Interference on Intensive Insulin Therapy in Severely Burned Patients: A Pilot Study

Nam K. Tran, PhD, MS, FACC; Zachary R. Godwin, BS; Jennifer C. Bookhold; Anthony G. Passerini, PhD; Julian Cheng, BS; and Morgan Ingemason, BS

1Department of Pathology and Laboratory Medicine, University of California, Davis, School of Medicine; and
2Department of Biomedical Engineering, University of California, Davis

Background

IIT for TGC significantly reduces mortality and morbidity in critically ill patients. Inaccurate glycemic measurements during IIT precipitate dangerous glycemic excursions and poor outcomes. Abnormal hematocrit and oxidizing substances may contribute to erroneous glucose meter system (GMS) results. Hemocencentration is commonly seen during the acute burn shock phase. Anemia is also common due to iatrogenic losses. High dose ascorbic acid therapy given intravenously is believed to reduce fluid requirements by mitigating oxidative stress during the burn shock phase. Ascorbic acid falsely depresses measurements by interfacing with the glucose biosensor electrochemistry.

Hypothesis and Specific Aims

Hypothesis: We hypothesize that automatic hematocrit and high dose ascorbic acid interference correction in GMS improves TGC in burn patients.

Specific Aims:
1. Quantify the effect of hematocrit and high dose ascorbic acid therapy on GMS measurements.
2. Determine the clinical effect of auto-corrected GMS measurements during IIT.

Materials and Methods

Prospective observational study:
- Pilot randomized controlled trial: Auto-correcting modified glucose oxidase-based GMS (GMS1, StatStrip Glucometer, Nova Biomedicals, Waltham, MA) versus auto-correcting glucose dehydrogenase-based GMS (GMS2, AccuCheck Advantage, Roche Diagnostics, Indianapolis, IN).
- 60 unique severely burned blood samples were tested on GMS1 and GMS2, and the hospital laboratory chemistry analyzers.
- Hematocrit was determined in parallel using the hospital laboratory hematocrit analyzers.
- Samples from two burn patients receiving high dose ascorbic acid therapy as part of routine care were tested on all 3 devices.
- Twelve severely burned (25%, TBSA burned) burn patients (avg 36.8 years) were enrolled. Patients were randomized to have IIT guided by either GMS1 or GMS2.
- IIT protocol targeted a TGC interval of 111 to 151 mg/dL.
- GMS testing was performed every hour, drawn from arterial blood.
- Paired laboratory plasma glucose testing performed every 12 hours.
- Clinicians were blinded to results.

Results

Prospective Results: GMS1 results were similar to paired laboratory analyzer results (mean [SD]: bias -0.75 [4.0] mg/dL, n = 60, P = 0.214). GMS2 results were significantly higher than paired laboratory measurements (mean [SD]: bias 5.56 [8.7] mg/dL, n = 60, P = 0.048). Mean GMS2 bias for anemic samples was 9.6 [8.7] mg/dL. For normohematocytic and polychromatophilic samples, mean GMS2 bias was -3.9 [9.2] and -21.8 [18.9] mg/dL respectively. GMS2 results were significantly lower than laboratory results in patients that received high dose ascorbic acid (500 mg/kg in 1 L Lactated Ringer’s therapy) (mean bias: 29.2 [27.2], n = 15 paired measurements, P < 0.001). Results were similar between the laboratory analyzer and GMS1 (mean bias: 0.58 [4.3], n = 15 paired measurements, P = 0.564).

Interventional Results: Age, burn size, mean hematocrit, and admission MODS were similar between the two study groups. Patients in GMS2 group had significantly higher mean GMS bias (P < 0.001), mean insulin rates (P < 0.001), and hypoglycemic excursions (P < 0.001), including 4 severe hypoglycemic excursions. Glycemic variability analysis revealed MAGE (P = 0.049), MODD (P = 0.069), and CONGA (P = 0.035) to be significantly lower (i.e., low glycemic variability) in the GMS1 group than the GMS2 group.

Conclusions

• The study reports that the implementation of an auto-correcting POC GMS robust to confounding factors enables proper IIT and improves glycemic control.
• Automatic GMS hematocrit correction reduced glycemic variability, insulin rates, and hypoglycemic events. Moreover, in patients receiving high dose ascorbic acid, the auto-correcting GMS reported results comparable to the gold-standard clinical laboratory analyzer.
• The non-correcting GMS generated erroneous results that could lead to excessive insulin dosing and increased risk for hypoglycemic events.
• We recommend caution when using non-correcting POC GMS in burn patients with anemia and/or receiving high dose ascorbic acid.
• Larger clinical studies are warranted to verify the utility of various measures of glycemic variability and determine outcomes associated with highly accurate GMS testing in the burn patient population.

References


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Contact Information

Zachary Godwin
Department of Pathology and Laboratory Medicine
3435 Tupper Hall
University of California Davis
Davis, CA 95616
530-752-8471
zachary.godwin@ucdavis.edu