Interferent Effect of Hydroxyurea on Continuous Glucose Monitoring

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While currently available continuous glucose monitoring (CGM) systems have continually improving accuracy that has revolutionized modern diabetes care, potential medication interferences are recognized for all available CGM systems (1). For Dexcom CGM systems, hydroxyurea was recently recognized as an interfering substance that can falsely elevate sensor glucose (SG) readings (2), but the data demonstrating this interference have not been previously published.

We report a patient with type 1 diabetes taking hydroxyurea who experienced falsely elevated SG values using the Dexcom G5 and G6 CGM systems, which led to the recognition of the interferent effect of hydroxyurea.

A 69-year-old woman with type 1 diabetes using an insulin pump (Medtronic Paradigm Revel 723) and real-time CGM (initially Dexcom G5, then G6) took hydroxyurea (1,000 mg daily) for treatment of essential thrombocytosis. She noted that, for approximately 6 h after taking hydroxyurea, SG measurements predictably and markedly increased, even while fasting and when the time of hydroxyurea ingestion varied. In addition, the glucose management indicator (7.6%) based on 14-day average SG (170 mg/dL) was significantly higher than concomitant glycated hemoglobin (6.3%, 45 mmol/mol), suggestive of artifactual discordance.

Subsequently, the patient simultaneously wore the Dexcom G6 (San Diego, California) and FreeStyle Libre 2 (Abbott, Abbott Park, Illinois) CGM systems for 14 days to assess differential effects of hydroxyurea on the two systems. On three test days, the patient fasted for 4 h before and at least 8 h after hydroxyurea ingestion. Approval was obtained from the Northwestern University Institutional Review Board.

SG values on both CGM systems were comparable to plasma glucose measurement at the clinical laboratory (<15% difference).

The Dexcom and Libre systems showed parallel postprandial glucose rises (Fig. 1, blue arrows). In contrast, following hydroxyurea administration in the fasting state, the two sensors showed divergent results: SG increased for approximately 6–10 h after hydroxyurea administration on the Dexcom, but not Libre, system (Fig. 1, red arrows). On the three test days, peak SG values on the Dexcom system following hydroxyurea ingestion (with corresponding SG values on the Libre system) were: 8 November, 10 P.M.: Dexcom 254 mg/dL (Libre 128 mg/dL); 10 November, 11:50 P.M.: Dexcom 216 mg/dL (Libre 90 mg/dL); 11 November, 10 P.M.: Dexcom 194 mg/dL (Libre 89 mg/dL). These findings were consistent with the previously noted artifactual SG elevation on the Dexcom system resulting from hydroxyurea administration. The interferent effect had been reported to Dexcom and a label change had ensued shortly thereafter, following U.S. Food and Drug Administration recommendations.

Analytical interference as a result of various medications is a known potential source of measurement error for all CGM systems (1). Hydroxyurea has not previously been reported to impact capillary or interstitial glucose measurements. Interestingly, hydroxyurea derivatives were previously reported to have hypoglycemic effects (3). One study reported increased serum glucose levels associated with hydroxyurea use among children with sickle cell anemia (4).

While hydroxyurea is not a commonly used medication, this case serves as a reminder of several salient general principles. First, it serves as a reminder to listen to our patients. The absence of corroboration in the existing medical literature may not equate to the absence of veracity. Our patients possess the most intimate knowledge of their own daily glycemic patterns; we owe it to them to pay heed to their personal observations, even when the existing literature is not supportive. Second, in this era of web-based diabetes management software and remote CGM interpretation, this case reminds us of the therapeutic modifications borne out of the "old-fashioned" interpersonal exchange of ideas that would be lost by solely "online" data review. Third, in embracing the revolutionary and ever-growing benefits of CGM use, we must also pause to consider the infrequent instances of limitation, no matter how

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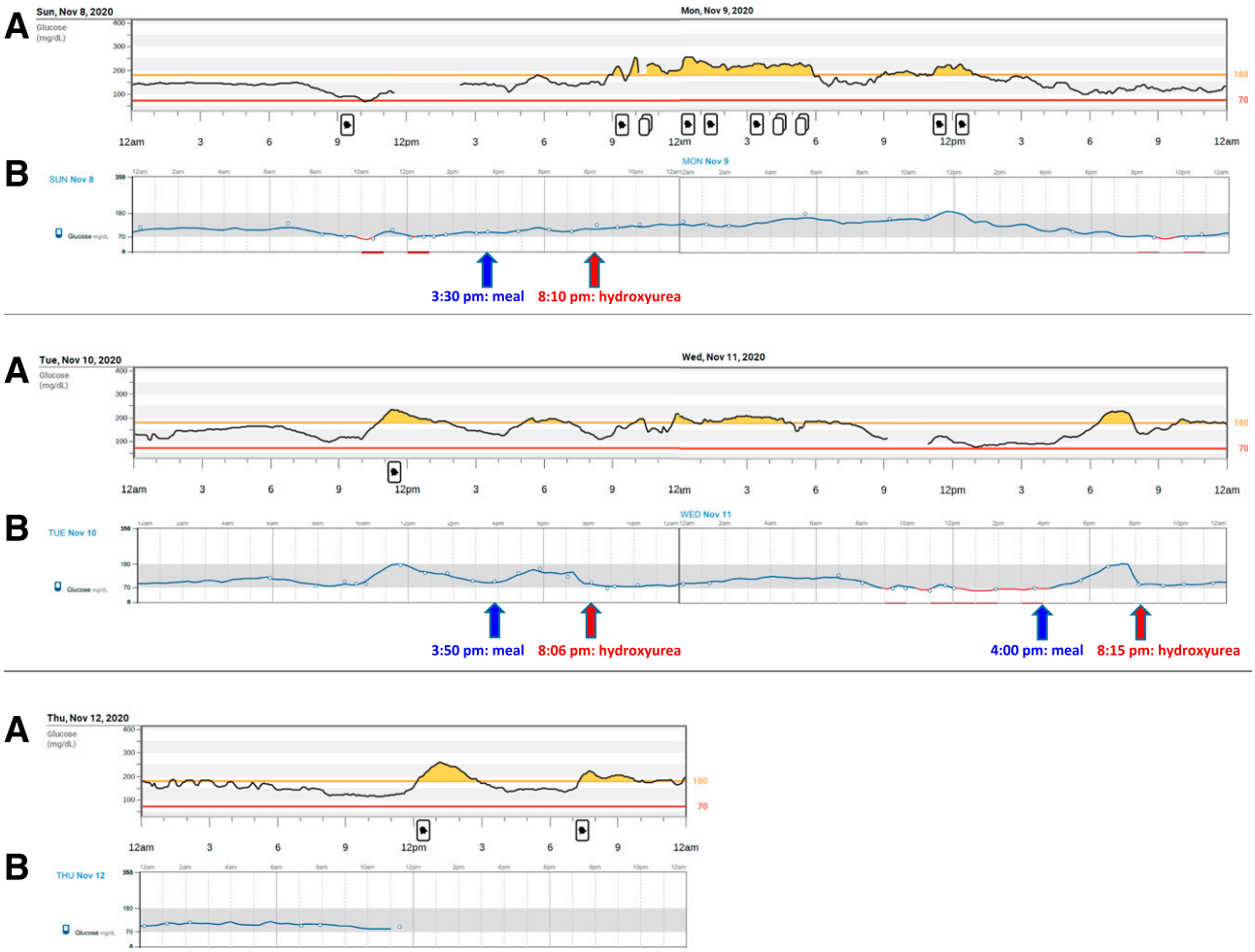

Figure 1—Simultaneous CGM tracings obtained on the Dexcom G6 system (*A*) and the Abbott FreeStyle Libre system (*B*). Blue arrows indicate the meal 4 h prior to hydroxyurea administration on the test days, and red arrows indicate hydroxyurea administration in the fasting state on the test days.

rare. If the patient presented here were transitioned to a hybrid closed-loop algorithm that modified insulin dosing based on artifactually elevated SG readings, she would likely experience hypoglycemia and undue risk. These accuracy limitations are not unique to any particular manufacturer or technological platform. The onus is upon clinicians to carefully evaluate individual scenarios in which any apparent incongruence exists.

In summary, our case demonstrated for the first time that hydroxyurea is an interferent in a commonly used CGM system, and providers must be aware that these CGM data must be disregarded for several hours after each hydroxyurea administration. This medication-induced interference with CGM and by extension hybrid closed-loop insulin delivery is fortunately rare, and these minor limitations pale in comparison with the wide-ranging, unprecedented, and revolutionary benefits that these technologies have afforded to people living with diabetes.

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