Journal of Diabetes Science and Technology
2021, Vol. 15(2) 517–518

DOI: 10.1177/1932296820948544
journals.sagepub.com/home/dst
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Effect of Repeated Doses of Acetaminophen on a Continuous Glucose Monitoring System with Permselective Membrane

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Keywords
Dexcom G6, acetaminophen, permselective membrane, interference

Continuous glucose monitoring systems use an electrochemical methodology for measuring glucose in interstitial fluid (ISF). Dexcom G6 uses a measurement voltage where other common compounds may get oxidized. The diffusion membrane can block some of the interfering compounds; however, not all compounds can be blocked due to their molecular mass. Dexcom G4 and G5 systems showed significant interference from acetaminophen.[1-3] Dexcom introduced a permselective membrane in G6 that blocks the diffusion of acetaminophen to the electrode surface thereby minimizing its effect.[4]

In the clinical study performed by Dexcom, the study participants were asked not to take any acetaminophen from the day before sensor insertion until the in-clinic session, where study subjects were asked to take 1 g of acetaminophen and were followed for 8 hours. The study's objective was met in that the observed mean interference effect was 3.1 ± 4.8 mg/dL, which was statistically significantly lower than the performance goal of 10 mg/dL. The authors concluded that this interference effect would have a negligible effect on bolus insulin administered. The authors argued that because the temporal profile of interference with G4 sensors follows that of ISF and plasma acetaminophen concentrations,[2] studies of higher or repeated doses were unnecessary.

Since the interference from acetaminophen is reduced by using a permselective membrane, its effectiveness should be demonstrated by challenging the membrane with repeat doses of acetaminophen. We evaluated the effect of repeated doses of acetaminophen on G6 sensor performance in a clinical study. Fifteen adult subjects with diabetes wore one sensor in the abdomen. Data from 14 adult subjects (1 lost the sensor before in-clinic session) were collected over one 13-hour period during 3-7 days of the sensor wear. Each subject had a 1-hour baseline phase where venous blood was collected every 10 minutes. After this first hour, a dose of 1000 mg acetaminophen was given with a meal and venous samples were collected every 20 minutes for the next 4 hours. This step of acetaminophen ingestion and venous sample collection was repeated two more times in 4-hour intervals. Plasma venous samples were measured on a YSI2300 system. The maximum average bias from YSI and baseline after each administration of acetaminophen are presented in Table 1. A maximum average sensor bias of 7.2 mg/dL (normalized to the baseline offset) was observed around 4 hours after the first dose (the magnitude of the interference is consistent with the +5.2 mg/dL reported by Dexcom in the Instructions for Use).[5] After the second dose, the maximum average sensor bias was approximately 8.6 mg/dL, which increased to 14.0 mg/dL after the third dose, suggesting that the permselective membrane may fail to effectively block acetaminophen after repeated doses.

Table 1. The Maximum Average Bias from YSI and Baseline at Each Ingestion of 1000 mg of Acetaminophen Administered 4 Hours Apart on Dexcom G6.

Dosing period	Bias from YSI, mg/dL	Bias from baseline, mg/dL
Pre-dose (baseline)	15.1	0
Post first dose	22.3	7.2
Post second dose	23.7	8.6
Post third dose	29.1	14.0

The magnitude of interference from acetaminophen on G6 will have minimal impact on insulin dosing. However, the biases are large enough for the sensors to potentially miss hypoglycemic conditions, specifically clinically significant hypoglycemia. This study did not follow the subjects over

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multiple days and, therefore, the effect of higher doses or continued use of acetaminophen over multiple days on sensor performance is not known.

Acknowledgments

We are deeply indebted to the research participants. Our sincere thanks to all the staff of Clinical Trials of Texas.

Declaration of Conflicting Interests

The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Study was funded by Abbott Diabetes Care.

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