Acute Hyperglycemia After Influenza Vaccination in a Patient With Type 2 Diabetes
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There are 29.1 million people in the United States living with diabetes (1). Except in cases with contraindications, annual influenza vaccination is recommended for all people with diabetes to reduce morbidity, mortality, and health care costs associated with influenza illness (2,3). There were 12 influenza vaccines available for the 2016–2017 influenza season. These vaccines were categorized into inactivated or live, quadrivalent or trivalent, and high-dose or standard-dose formulations (2).

Common adverse reactions of pain, soreness, fever, muscle aches, fatigue, redness, or swelling may occur after intramuscular vaccine administration (4). Hyperglycemia is not noted as an adverse reaction in vaccine package inserts; however, reports of its occurrence have been documented in the Vaccine Adverse Event Reporting System (VAERS) (5). Since 1991, there have been 946 reports of hyperglycemia with all available vaccines and 361 reports of hyperglycemia with all types of influenza vaccines. When looking specifically at the trivalent influenza vaccine, there have been 235 reported cases, with 70.6% reported during the first 4 days after vaccine administration (5).

In light of these reports, a literature search was performed to obtain more information about acute hyperglycemia after vaccine administration. The search failed to yield any literature reports specifically related to blood glucose elevations. Much of the literature focused on confirming the overall safety and benefits of vaccines in patients with diabetes. A Google search using the same terms did not yield any published data but did lead to multiple discussion boards on which patients had expressed concerns about blood glucose elevations observed after receiving a vaccine. The following case study describes an instance of acute hyperglycemia after influenza vaccination in a patient with type 2 diabetes.

Case Presentation
A 41-year-old Caucasian man (height 170.2 cm, weight 101.6 kg) with a history of type 2 diabetes without microvascular complications contacted a pharmacist-led outpatient referral clinic to report elevated blood glucose after receiving a trivalent inactivated influenza vaccine (Seqirus Pty Ltd., Parkville, Victoria, Australia), 0.5 mL intramuscularly. He reported feeling fatigued and groggy 2 hours after vaccination and having a blood glucose level of 264 mg/dL 6 hours after vaccination. The patient’s self-monitoring of blood glucose (SMBG) log entries are depicted in Table 1.

In light of these reports, a literature search was performed to obtain more information about acute hyperglycemia after vaccine administration. The search was performed with the advanced search option in PubMed using the terms “hyperglycemia,” “blood sugar,” “blood glucose,” “vaccines,” “influenza vaccine,” “diabetes,” and “immunizations.” The search failed to yield any literature reports specifically related to blood glucose elevations. Much of the literature focused on confirming the overall safety and benefits of vaccines in patients with diabetes. A Google search using the same terms did not yield any published data but did lead to multiple discussion boards on which patients had expressed concerns about blood glucose elevations observed after receiving a vaccine. The following case study describes an instance of acute hyperglycemia after influenza vaccination in a patient with type 2 diabetes.
blueberry breakfast biscuits (36 g carbohydrates) with a non–sugar-sweetened drink for breakfast, lamb with rice and salad for lunch, and chicken with green beans for dinner. These were typical meals for him.

The patient’s medical history included type 2 diabetes (diagnosed in 2001), gastroesophageal reflux disease, allergic rhinitis, and osteoarthritis. One month earlier, at his regular appointment, his SMBG results averaged 109 mg/dL fasting, 122 mg/dL before lunch, and 124 mg/dL postprandial, all within American Diabetes Association–recommended target ranges (6) (Table 2). Three weeks before his vaccination, the patient had an A1C of 7.2%, blood glucose of 120 mg/dL, serum creatinine of 0.81 mg/dL, and calculated creatinine clearance of 136 mL/min (using the Cockcroft-Gault equation with adjusted body weight of 80.3 kg) (7,8). He reported adherence to his medication regimen, which included glipizide 5 mg twice daily with meals and omeprazole 20 mg every morning. He was not taking any over-the-counter or herbal products. His family history included a father with type 2 diabetes but otherwise nothing contributory.

The patient lives at home with his wife and daughter. He reported social alcohol use only and denied tobacco or illicit substance use.

Discussion

Hyperglycemia has been reported in post-marketing surveillance of influenza vaccinations. However, several limitations to the VAERS, especially its voluntary nature, result in under-reporting and inconsistencies in reporting. In addition, details related to events vary significantly among reports, with much of the data unconfirmed (9). Because of the nature of these reports, we cannot assume that they all occurred in people with diabetes. However, diabetes is characterized by a loss of homeostatic glucose control secondary to insulin secretory defects and increased resistance; given both the documented loss of homeostatic glucose control secondary to insulin secretory defects and increased resistance; given both the documented loss of homeostatic glucose control and the high frequency of glucose monitoring in people with diabetes, it is likely that most of the reported instances of post-vaccination hyperglycemia would have been in people with diabetes.

Transient fluctuations in blood glucose are multifactorial. In this case presented here, one probable mechanism for the hyperglycemia is stimulation of the immune system resulting in some degree of stress response. Physiologic stress, whether from surgery, infection, injury, or acute illness, has the potential to increase counterregulatory hormone levels. Most notable among these are epinephrine and cortisol, which increase in response to stress and result in elevated blood glucose. People with diabetes are unable to rapidly counteract such elevations in blood glucose. Thus, mild physiologic stressors could potentially lead to observable hyperglycemia.

Our patient’s diabetes was well controlled with sulfonylurea monotherapy, indicating relatively preserved insulin secretion and sensitivity. As observed from the patient’s SMBG results, the influenza vaccine had a substantial hyperglycemic effect that normalized within 72 hours and did not require intervention.

With our analysis of the report revealing no other contributory factors, it seems likely that the observed hyperglycemia was associated with the vaccination. Potential limitations to this conclusion include the

| TABLE 1. Patient’s SMBG Results Around the Time of Vaccination |
|---------------------------------------------------------------|
| **Morning (Fasting) Blood Glucose (mg/dL)** | **Blood Glucose Before Lunch (mg/dL)** | **Blood Glucose 1–2 Hours After Dinner (mg/dL)** |
| Day –1 | 112 | NR | NR |
| Day 0* | 117 | NR | 264 |
| Day 1 | NR | NR | 188 |
| Day 4 | NR | NR | 117 |
| Day 5 | 89 | NR | |

*Day of vaccination. NR, not reported.

| TABLE 2. Patient’s SMBG Results 1 Month Before Vaccination* |
|-------------------------------------------------------------|
| **Morning (Fasting) Blood Glucose (mg/dL)** | **Blood Glucose Before Lunch (mg/dL)** | **Blood Glucose 1–2 Hours After Dinner (mg/dL)** |
| 109 | 96 | 125 |
| 80 | 114 | 87 |
| 125 | 155 | 131 |
| 122 | NR | 153 |

*Values were from the previous clinic visit, which occurred ~35 days before vaccination. NR, not reported.
absence of blood glucose readings from post-vaccination days 2 to 3 and our reliance on the patient’s SMBG results and verbal recall of diet and medication adherence. However, our patient historically exhibited consistent blood glucose control and was actively involved in his disease management. Based on previous interactions, we have no reason to doubt the information reported to us or the ability of our patient to accurately report this event.

The purpose of this case report is to alert health care professionals about this potential effect, which is not described in vaccine package inserts or commonly used drug databases. We agree with the vaccination recommendations for people with diabetes and believe that the benefit outweighs the risk of transient, acute hyperglycemia. Patient knowledge and involvement remain the cornerstones of diabetes management. Therefore, it is important to educate patients and alleviate concerns that may arise during their routine SMBG, while emphasizing the importance of vaccines. We do not recommend changes in pharmacotherapy or SMBG frequency after vaccination because such changes would place an unnecessary burden on patients. Our hope is that future research may shed more light on this phenomenon and enhance understanding vaccination in people with diabetes for both patients and health care professionals.

Duality of Interest
No potential conflicts of interest relevant to this article were reported.

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