

### Introduction

Semaglutide is a glucagon-like peptide-1 receptor agonist prescribed for diabetes, with recent indication and significant off-label use in metabolic disease and weight loss. Refractory hypoglycemia is not expected after semaglutide use but has been reported in patients using compounded semaglutide<sup>1,2</sup>. Patient with refractory hypoglycemia often require ICU-level care for frequent blood glucose monitoring and dextrose infusions.

### Case Presentation

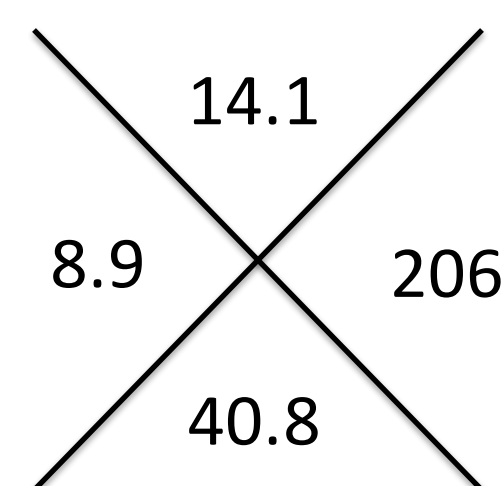
60M with a history of hypertension and hyperlipidemia presented via EMS for a seizure. He had been using Ozempic® (semaglutide) for 3 weeks and increasing the dose independently (0.25mg on week one, 0.35mg on week two, and 0.65mg on week three). Shortly after injecting himself, the patient had tonic-clonic shaking, and his friend called EMS. On EMS arrival, the patient was no longer shaking but was found to be hypoglycemic to 33 mg/dL (72 to 108 mg/dL). EMS gave him 1 ampule of 50% dextrose en route to the ED.

On arrival to the ED, the patient's repeat blood glucose was 34 mg/dL

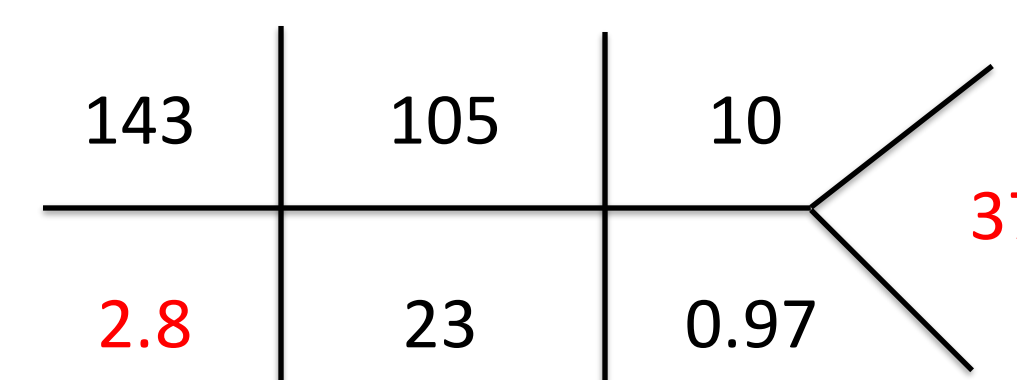
VS: T: 36.3C, HR: 85, BP: 107/57, RR: 20 SpO2: 99% on room air

Physical examination: Regular HR, lungs clear to auscultation, abdomen soft, nontender. Intermittently alert & oriented x3, no facial asymmetry or droop, 5/5 strength in upper and lower extremities, no sensory deficits.

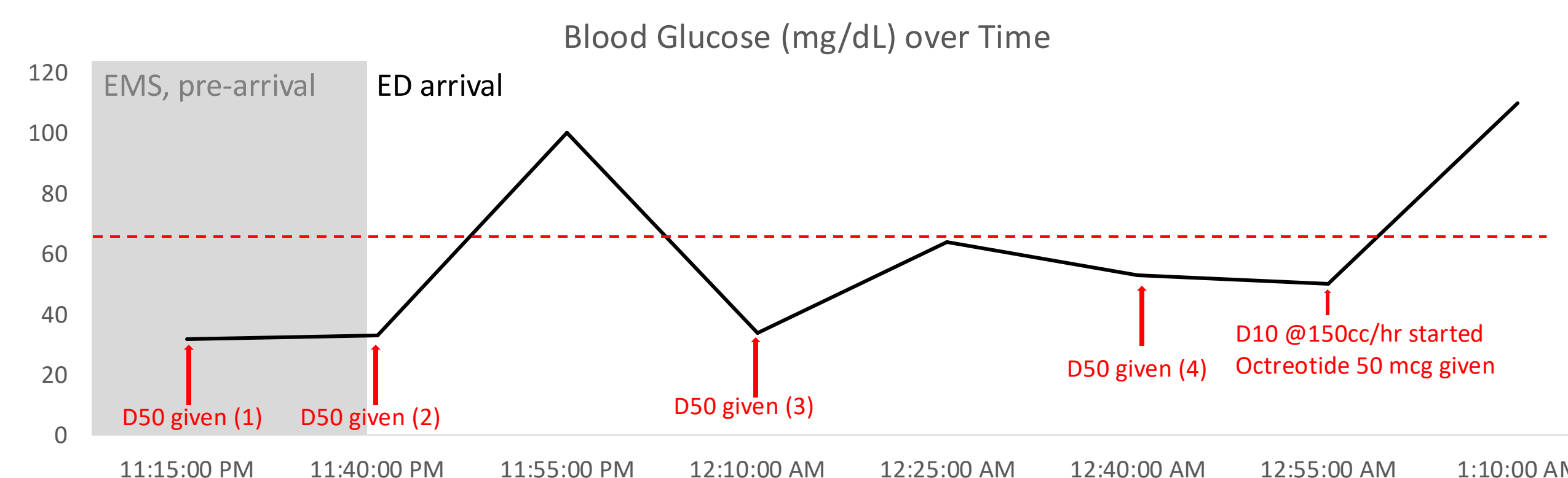
### Initial Workup



Troponin: 5 pg/mL  
Alcohol: 203 mg/dL  
Lactate: 3.7 mmol/L



CTb: No change compared to last CT  
CXR: No acute cardiopulmonary process



Despite 4 ampules of 50% dextrose, the patient remained hypoglycemic and was started on a continuous dextrose infusion (D10 at 150cc/hour) and octreotide 50mcq q6hours. The patient was admitted to the medical intensive care unit (MICU) for frequent blood glucose monitoring. He endorsed he received the Ozempic® pen from a friend.

While hospitalized, additional labs returned:

- Insulin level: 24.6uIU/mL (1.9-23.0uIU/mL)
- Pro-insulin level: <4.0pmol/L (<18.8pmol/L)
- C-peptide level: 0.41ng/mL (1.1-4.4ng/mL)
- Sulfonylurea analysis: negative

The patient was weaned off dextrose-containing fluids within 24 hours and discharged home in good conditions in 48 hours.

### Discussion

We suspect this patient used insulin being sold as semaglutide<sup>3</sup>. Insulin and sulfonylureas have narrow therapeutic windows and can lead to refractory hypoglycemia with variable lengths of hypoglycemia depending on the agent used<sup>4,5,6</sup>. With rising rates of obesity, an increasing number of clinicians are prescribing semaglutide for metabolic syndrome and weight loss. Many patients are turning to websites that do not require a physician's prescription to obtain the drug.<sup>7</sup>



Original Ozempic® pen (above) and counterfeit version of Ozempic® (below), both of which were found at wholesalers across Europe during drug shortage in 2023<sup>8</sup>

### Case Conclusions

This case covers the management of refractory hypoglycemia attributed to the emerging threat of counterfeit Ozempic® use. Both counterfeit and compounded products have been linked to refractory hypoglycemia. Emergency physicians must maintain a high index of suspicion for unintentional insulin or sulfonylurea overdose or side effects of compounded semaglutide in patients with refractory hypoglycemia after semaglutide use.

### References

<sup>1</sup>Haynes, K. (2024, Apr 19). *Unveiling the Dangers of Compounded Ozempic*. Kherkher Garcia. <https://www.kherkhergarcia.com/unveiling-dangers-compounded-ozempic/>  
<sup>2</sup>Suran M. As Ozempic's Popularity Soars, Here's What to Know About Semaglutide and Weight Loss. *JAMA*. 2023;329(19):1627-1629. doi:10.1001/jama.2023.2438  
<sup>3</sup>Wingrove P. Exclusive: Suspected fake Ozempic linked to three US cases of hypoglycemia. Reuters. Published Winter 1, 2024. Accessed January 25, 2024. <https://www.reuters.com/business/healthcare-pharmaceuticals/suspected-fake-ozempic-linked-three-us-cases-hypoglycemia-2024-01-24/>  
<sup>4</sup>Arem R, Zoghbi W. Insulin Overdose in Eight Patients. *Medicine*. 1985; 64 (5): 323-332.  
<sup>5</sup>Baumgartner K, Devgun J. Toxicology of Medications for Diabetes Mellitus. *Crit Care Clin*. 2021 Jul;37(3):577-589. doi: 10.1016/j.ccc.2021.03.007. PMID: 34053707.  
<sup>6</sup>Stapczynski JS, Haskell RJ. Duration of hypoglycemia and need for intravenous glucose following intentional overdoses of insulin. *Ann Emerg Med*. 1984;13(7):505-511. doi:10.1016/s0196-0644(84)80513-2  
<sup>7</sup>Winkler R, O'Brien SA. How dozens of websites sell knock-off drugs, no prescription required; online sellers are advertising semaglutide and tirzepatide, the active ingredients in ozempic, wegovy and mounjaro, at deep discounts with research-use disclaimers the FDA has called 'bogus'. *Wall Street Journal* (Online). Aug 16 2023. Available from: <http://turing.library.northwestern.edu/login?url=https://www.proquest.com/newspapers/how-dozens-websites-sell-knock-off-drugs-no/docview/2851135220/se-2>  
<sup>8</sup>Tirrell, M. European regulators warn of fake Ozempic pens found at wholesalers in EU, UK amid shortage. *CNN*. October 8, 2023. Accessed September 10, 2024.