Rapid Onset Antipsychotic-Induced Diabetes and the Role of Semaglutide:
Case Report, Literature Review, and Protocol Development

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The case:

- A 27-year-old Black woman with schizophrenia was almost continuously hospitalized in several hospital systems from May 2022 until discharge from our institution in May 2023
- Started clozapine in Dec 2022 for refractory psychosis
- Hemoglobin A1C increased from 5.4 to 12.6% in 4 months
- Body weight increased by 19.4 kg
- Received medications for glucose management according to inpatient diabetes standard-of-care, including metformin and basal-bolus insulin therapy, which she continued to take upon discharge

Our patients at risk:

- Individuals with serious mental illness (SMI), including schizophrenia, experience increased rates of metabolic syndrome and associated poor outcomes compared to the general population, in part due to antipsychotic-induced weight gain (AIWG)[1]
- Individuals with psychiatric disorders and type 2 diabetes (T2D) often perform limited diabetes self-care management
  - This is compounded by fear of AIWG and weight gain from current standard-of-care insulin secretagogues and insulin therapy, as well as lack of necessary skills needed to dose and administer insulin injections[2]

Why semaglutide?

- Daily and once weekly glucagon-like peptide (GLP-1) receptor agonists have been observed to be effective in the management of AIWG and hyperglycemia in individuals with T2D and SMI[3]
- More recently, case reports suggest that semaglutide is effective in the management of AIWG[4] and T2D[5] in individuals with SMI
- Randomized-controlled trials (RCTs) investigating the use of semaglutide in individuals with schizophrenia with and without diabetes are now underway[6]

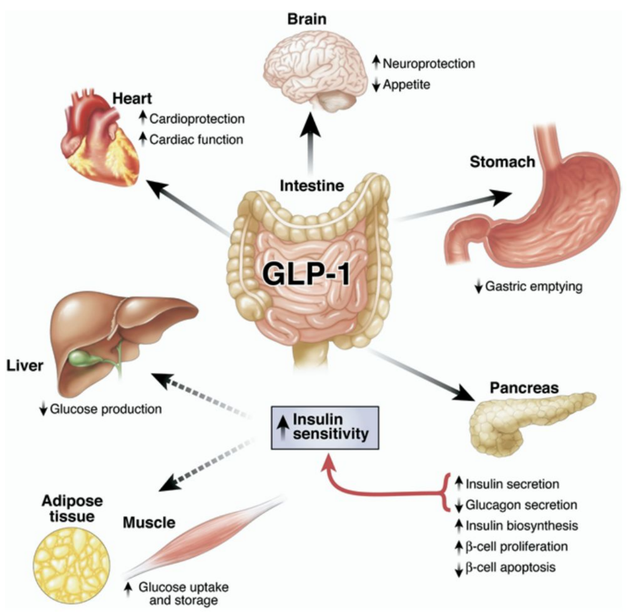

Fig. 1. Mechanism of action of GLP-1[7]

NYP Semaglutide Initiation Protocol

- Our institution developed a protocol for inpatient initiation of weekly subcutaneous semaglutide for individuals with T2D on atypical antipsychotic medications for SMI management

Objectives:

- To evaluate semaglutide use and prescribing practices in adult inpatient behavioral health units and to assess staff adherence to hospital protocol:
  - Inpatient behavioral health units with anticipated minimum stay of ≥ two weeks,
  - T2D,
  - atypical antipsychotic use, and
  - confirmed outpatient insurance coverage/patient affordability to maintain use of a GLP-1 receptor agonist
- To address any unmet diabetes management need with the use of semaglutide

Contraindications:

- Absolute: a personal or family history of medullary thyroid cancer (MTC) or multiple endocrine neoplasia syndrome type 2 (MEN2)
- Relative: pregnancy, history of/suspected pancreatitis

Patient selection and medication administration:

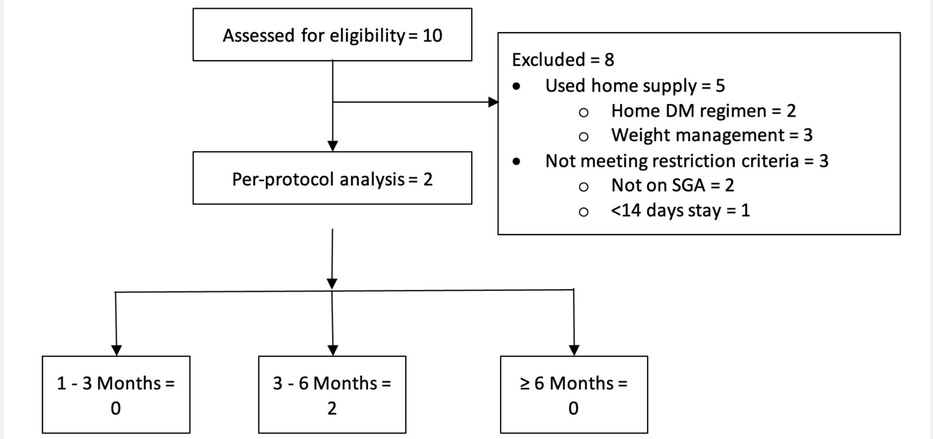

Fig. 2. Flow diagram for patient data analysis September 2023 to present[8]

Fig. 3. Ozempic® titration schedule[9]

Table 1. Financial impact[8]

	Unit Price ($)	Quantity	Total Cost ($)
Semaglutide injection 0.25 mg or 0.5 mg per dose (2 mg/1.5 mL)	872.04	1	872.04
Semaglutide injection 0.25 mg or 0.5 mg per dose (2 mg/3 mL)	897.41	15	13,461.22
Semaglutide injection 1 mg per dose (4 mg/3 mL)	908.68	10	9086.82
Total from September 2023 to April 2024		26	**23,402.08**

Table 2. Per-protocol analysis, Δ at study endpoint from baseline in several biomarkers[8]

	Patient 1	Patient 2
HbA1c, % Δ	-0.9	-0.8
BMI, kg/m^2 Δ	-0.4	-0.3
7-day average FBG, mg/dL Δ	-176	-52
SBP, mmHg Δ	-3	-7
DBP, mmHg Δ	-2	-2
Total cholesterol, mg/dL Δ	-6	-11
LDL, mg/dL Δ	-3	-28
24-hour prandial insulin, units Δ	-13	-4
24-hour basal insulin, units Δ	-10	-4

Discussion:

- To ensure standardized tracking and to reduce confounding factors, patients who did not meet the restriction criteria or who used home supply were excluded from the protocol analysis
- Of the 10 patients who started semaglutide injection in the inpatient setting, **two patients** met the criteria to be included in the analysis
- **In these two individuals, inpatient semaglutide injection demonstrated positive effects in reduction of HgA1c, weight, fasting blood glucose, total cholesterol, LDL, and overall insulin needs**

Limitations:

- As with most retrospective post-prescription reviews, some intrinsic shortcomings in capturing biomarkers and relevant data are evident
- Impact on overall insulin usage may not necessarily reflect the intended therapy plan due to site-specific prescriber preferences and resources
- Because of the small sample size, data lacks statistical significance

Summary:

- GLP-1 receptor agonists are a promising tool for the management of AIWG and antipsychotic-induced diabetes in individuals with SMI
- Semaglutide administration appears to integrate well into current models of psychiatric care, giving psychiatrists an opportunity to pursue a solution to the side effects of our medications while working collaboratively with our internal medicine colleagues

Next steps:

- We look forward to the results from ongoing RCTs
- We believe that semaglutide has the potential to revolutionize metabolic syndrome management in SMI

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