CLINICAL VIGNETTE

Substitution of GLP-1 Medications in Ambulatory Care

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Case Presentation

A 64-year-old male with stage 4 chronic kidney disease and well controlled type 2 diabetes mellitus (T2DM) for over 10 years (last HbA1c 7.1%) contacted his primary care provider (PCP) for a refill of liraglutide 1.8mg daily. Due to formulary changes and supply issues, his PCP instead prescribed Ozempic (semaglutide) 1.0mg weekly. He continued on repaglinide three times per day with meals and sliding scale insulin aspart.

One day after starting semaglutide, the patient reported nausea and hypoglycemic with low of 63 mg/dL which was noted during a diabetes follow-up visit. Due to the hypoglycemia, he was instructed to stop the insulin aspart, while continuing weekly semaglutide and repaglinide with meals. At phone follow-up two days later, the patient denied further hypoglycemic episodes but reported ongoing nausea, poor appetite, and diarrhea. Because his symptoms were not improving, he was seen in the emergency department later that day. Labs were notable for Na 128 mmol/L (range 136-146), Hco2 13.5 mmol/L (range 21-31.0), Cr 3.59 mg/dL (range 0.66-1.28), and glucose 222 mg/dL (range 70-110). Table 1 includes labs prior to and upon admission. He was admitted to the MICU for acute on chronic kidney failure. He was started on IV fluids and completed infectious and gastrointestinal evaluation which were unremarkable. All of his diabetes medications were discontinued, and symptoms and labs improved and he was discharged four days later on basal bolus insulin. His admitting symptoms were attributed to initiation of full dose semaglutide, which resulted in dehydration and precipitated acute on chronic renal failure.

Table 1: Lab Trends Before and After Admission

Lab Test	17 days prior to admission	On admission	Reference Range
SODIUM	131 (L)	128 (L)	136-146 mmol/L
POTASSIUM	5.3	6.4 (H)	3.5-5.3 mmol/L
CHLORIDE	102	102	95-110 mmol/L
CARBON DIOXIDE	21	13.5 (L)	21-31.0 mmol/L
UREA NITROGEN	33 (H)	48 (H)	5-25 mg/dL
CREATININE	2.75 (H)	3.59 (H)	.66-1.28 mg/dL
EGFR	23	17	> 90 mL/min/m^2
GLUCOSE	185 (H)	222 (H)	70-110 mg/dL

Discussion

This patient developed severe GI symptoms resulting in ICU care after a switch between glucagon-like peptide-1 receptor (GLP-1) receptor agonists.

GLP-1 receptor agonists with efficacy in diabetes management and weight loss are being utilized more widely by a myriad of medical specialists, including primary care, endocrinology, cardiology, hepatology, and bariatric medicine. Commonly used GLP-1 receptor agonists and their features are listed in Table 2.

The exponential increase in GLP-1s use has led to intermittent national shortages and formulary changes that require patients to switch between agents.[1] Some patients switch due to preference and adherence, as medications that are taken less frequently are often preferred. Others switch due to differences in cost and insurance coverage.[2,3] Within the first year of treatment with GLP-1 receptor agonists, up to one-fourth of patients switch to another medication to lower blood glucose levels, include other GLP-1 receptor agonists.[2] Lack of clear guidance on how to safely switch between GLP-1 agents can lead to adverse outcomes noted in our case.

When switching patients between GLP-1 receptor agonists, providers can consider several actions to reduce adverse effects. When switching between GLP-1 receptor agonists, providers should first consider starting at the lowest dose or at an equivalent dose to reduce the risk of GI adverse events. Dose

can be slowly titrated, especially if there is prior history of side effects.[2,3] Table 2 provides dose equivalency between GLP-1 agents as proposed by Almandoz et al.[2] Our patient was switched from liraglutide 1.8mg to semaglutide 1.0mg. Both were full doses of their medicines, Table 2 presents dose equivalency between liraglutide 1.8mg and semaglutide 0.5m. Hospitals have used dose equivalency information to prevent adverse effects in other patients switching between GLP-1 agents.

Table 2: Names, Features, and Equivalent Doses of Common GLP-1 Receptor Agonists

Generic Name	Indications	Frequency and Route of Administration	Low Dose	Medium Dose	High Dose	Very High Dose
Lixisenatide (Adlyxin)[4]	Glycemic control for T2DM	Once daily; Subcutaneous	10 μg	20 μg		
Exenatide (Byetta)[5]	Glycemic control for T2DM	Twice daily; Subcutaneous	5 μg	10 μg		
Exenatide extended release (Bydureon)[6]	Glycemic control for TD2M	Once weekly; Subcutaneous			2mg	
Liraglutide (Victoza)[7]	Glycemic control for T2DM; Reduce cardiovascular risk for patients with T2DM and established cardiovascular disease; Weight loss	Once daily; Subcutaneous	0.6 mg	1.2 mg	1.8 mg	
Dulaglutide (Trulicity)[8]	Glycemic control for T2DM; Reduce cardiovascular risk for patients with T2DM and established cardiovascular disease	Once weekly; Subcutaneous		0.75 mg	1.5 mg	
Semaglutide (Ozempic)[9]	Glycemic control for T2DM; Reduce cardiovascular risk for patients with T2DM and established cardiovascular disease; Weight loss	Once weekly; Subcutaneous		0.25 mg	0.5 mg	1 mg
Oral Semaglutide (Rybelus)[10]	Glycemic control for T2DM	Once daily; Oral	3 mg	7 mg	14 mg	

The type of GI adverse events may affect the titration timeline.[3] Pancreatitis and cholecystitis are also possible side effects. If they occur, it is important to avoid future GLP-1 receptor agonist therapy. Physicians should be mindful of the half-lives and timing of the medication switch. If switching from a once-daily to a once-weekly GLP-1 receptor agonist, patients can receive the new dose the day after their last dose of the daily medication. However, if switching from a once-weekly to a once-daily GLP-1 receptor agonist, they should wait until the day they would have received the next dose of their once-weekly medication.[2,3] In general, it is important to be aware of adverse GI effects and consider waiting for symptoms to resolve before switching.

Finally, dietary recommendations may help prevent GI adverse effects. Consuming smaller portions and avoiding high-fat foods may decrease symptoms.[11,12] Other mitigating measures, include natural antinausea supplements like ginger, or increasing liquid intake may be helpful.[11] Physicians should maintain open communication to ensure patients are following recommendations and to provide guidance on specific side effects.[2] Follow-up in 2-3 months is recommended to reassess dose titration or additional diabetes medications.[2]

Conclusion

GLP-1 receptor agonists are increasingly used and patients may require switching between agents. This patient illustrates why providers should be aware of side effects, dose equivalency, and recommended approaches to enhance safety when prescribing GLP-1 receptor agonists.

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