A Case of Refractory Hypoglycemia with DPP-IV Inhibitors in a Patient with CKD and Paraproteinemia

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Introduction

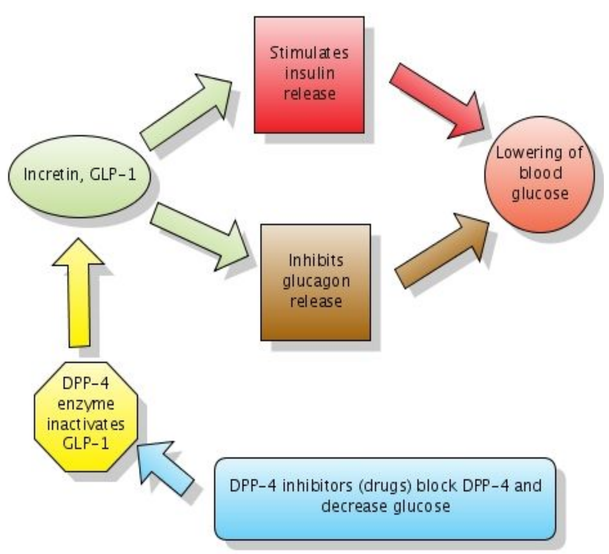
- Severe and prolonged hypoglycemia can be life threatening and may be associated with increased mortality in patients with diabetes.
- We highlight a case of refractory hypoglycemia in an elderly, diabetic patient with chronic kidney disease (CKD) despite treatment.

Case Report

- 76-year-old male with history of hypertension, paroxysmal atrial fibrillation, type 2 diabetes mellitus (T2DM), CKD Stage III, and paraproteinemia (MGUS) presented with dyspnea and generalized weakness. He was admitted for worsening renal failure, uremia, and anasarca.
- His renal function worsened from a baseline creatinine of 2.2 mg/dL to 4.12 mg/dL and subsequently developed recurrent episodes of hypoglycemia as low as 48 mg/dL despite discontinuation of home medications (insulin glargine, glimepiride, and sitagliptin). HbA1C was 7%.
- He was given ampules of D50. On day 2, patient had persistent hypoglycemia, so a D10 infusion was initiated.

Case Report Continued

- Day 3 – Hemodialysis was initiated for progressive renal failure/ anasarca, but he continued to have hypoglycemic episodes. On day 5, following his third dialysis session, his glucose levels began to normalize.
- Over a 5-day period he required a total of 29 ampules of D50 and 72 hours of a D10 drip.
- At discharge, his renal function returned to baseline and his T2DM regimen was adjusted to insulin glargine and lispro.



Pharmacokinetics of Sitagliptin

Parameter	Value
Bioavailability	> 85%
Half-life	Approximately 12 hours
Absorption	1 - 4 hours
Distribution	38% protein-bound
Metabolism	Not appreciably metabolized
Elimination	Renal (80% unchanged)

Discussion

- Eighty-seven percent of sitagliptin (80% unchanged) is excreted through urine in patients with CKD.
- Both plasma concentrations of sitagliptin and its terminal half-life are increased by four-fold, thus potentiating the risk for hypoglycemia.
- Sitagliptin is well tolerated as monotherapy for patients with T2DM and CKD. However, when used in combination therapy in the setting of CKD the risk for refractory hypoglycemia increases.

Discussion Continued

- DPP-IV inhibitors are not dialyzable, so emergent hemodialysis is limited as a treatment option.
- We believe our patient's acute renal failure, superimposed on CKD and paraproteinemia, led to an unexpected increase in the concentration of sitagliptin in plasma. This increased level, in addition to impaired renal clearance, inadvertently resulted in refractory hypoglycemia.
- Dialysis likely aided in the clearance of protein deposition in the kidneys which improved renal function, thus allowing sitagliptin to be cleared and his hypoglycemia to subsequently resolve.

Conclusion

- Among U.S. adults 18 years of age and older with diabetes, 37.0% had CKD, and over half of those had moderate to severe CKD.
- Hospitalists should be aware of the potential for refractory hypoglycemia when sitagliptin is used in combination with other diabetic medications in the setting of AKI superimposed on CKD as it can threaten patient safety in the hospital environment.

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