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Chronic Use of Long-Acting Somatostatin Analogues and Pancreatic Insufficiency in Patients with Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs): An Under-Recognized Adverse Effect

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BACKGROUND: Somatostatin analogs (SA) are used in GEP-NETs and acromegaly. Adverse events with SAs include biliary disorders, gastrointestinal disorders, injection-site pain, hyperglycemia, and conduction abnormalities. Pancreatic insufficiency (PI) is often misdiagnosed or diagnosed after a delay in patients receiving SAs. We present our experience with PI developing in patients following SA.

METHODS: Retrospective chart and pharmacy review of patients with GEP-NETs (6/2009 - 6/2017) was completed. Data collected included demographics, dose/duration of long and short-acting SA, antidiarrheal use, pancreatic enzyme replacement (PER), proton pump inhibitors (PPI), and laboratory data (chromogranin A (CgA), urine 5-HIAA, quantitative fecal fat).

RESULTS: 110 patients (age 29-87) with GEP-NETs were identified. 104 patients received LA octreotide and 6 lanreotide. Of these, 23 received SA octreotide for worsening diarrhea, 96 had intensification of antidiarrheal and 1 received xermalo. 79 patients were evaluated by either nutrition or gastroenterology. Quantitative measurement of fecal fat was performed in 47 patients with worsening diarrhea despite stable or improved CgA/urine 5-HIAA. 19 had evidence of steatorrhea and received PER: who received PER @ 500 units/kg/meal to a maximum of 10,000 units/kg per day. 13 received PPI concomitantly

while 6 started when symptoms did not improve with PER. Nutrition recommended low fat diet. 14 of 19 had improvement in diarrhea within 4-8 weeks. Two were non-compliant and 3 were found to have motility disorders. Deficiency of vitamins and trace elements was found in 11 of 19 patients, which led to supplementation.

CONCLUSION: Our experience constitutes the first study addressing PI as a rare but serious complication of chronic use of SAs. Although SA are used to treat diarrhea, paradoxically, they can worsen diarrhea secondary to PI through inhibition of pancreatic enzymes, secretin and CCK. Early referral to gastroenterologist/nutritionist may aid in earlier, prompt diagnosis and treatment of this under-diagnosed, under-published side effect of SA and decrease the cost.