BACKGROUND

• SSAs are the most commonly used agents in the treatment of GEP-
  NETs for both symptom control and to improve disease-free survival
  (DFS).
• Due to the long course of disease and the urgency presented by the
  symptoms secondary to the hormonal secretion, management of the
  syndrome often becomes the primary treatment focus.
• Furthermore, other treatment options for GEP-NETs, such as
  chemotherapy and targeted agents may not necessarily translate to
  improvements in syndrome control.
• There are many over-the-counter medications available to
  individuals experiencing chronic diarrhea. However, the mechanism by
  which these agents act does not address the mechanisms underlying
  the diarrhea induced in carcinoid syndrome.
• Though SSAs are effective in reducing the frequency of bowel
  movements and episodes of flushing, but we’re often forced to
  increase SSA dose and frequency well above label or use
  supplemental short-acting doses to help maintain control.
• Further, many patients develop lethapathy.
• Despite all these efforts, many patients do not experience improved
  syndrome control.
• The most commonly reported adverse events include injection-site
  discomfort and erythema, gastrointestinal (GI) disturbances such as
  diarrhea, abdominal pain, nausea and vomiting, biliary sludge or
  gallstones, and abnormal glucose metabolism.
• As these agents mimic Somatostatin, they can inhabit pancreatic
  hormones, leading to pancreatic insufficiency.
• EPI is misdiagnosed leading to increasing SSAs dosage, use of
  short-acting or additional medications that not only burden the quality
  of life of these patients or cause additional adverse events but also add to
  cost of treatment.
• This common but under-acknowledged condition is easy to diagnose and
  treat.

OBJECTIVES

Primary Objectives
• To identify incidence of EPI in pts. receiving SSAs for GEP-NETs
  • To evaluate the benefit of pancreatic enzyme replacement (PER) in
    these pts
Secondary Objectives
• To determine the clinical and laboratory manifestations in patients
  receiving SSAs for GEP-NETs
• To compare the financial impact of using PER versus
  intensified of the syndrome treatment.

PATIENTS & METHODS

• Retrospective chart and pharmacy review of patients with histologically
  confirmed GEP-NETs (6/2005 - 6/2017) was performed.
• Data collected included demographics, symptoms including diarrhea, weight
  loss, flatulence, etc., dose-duration of long and short-acting
  SSAs, use of antidiarrheal medications including OTC, use of
  PER, use of proton pump inhibitors (PPI) or H2-blockers, and
  laboratory data, particularly tumor related markers
  chromogranin-A (CgA), urine 5-HIAA, along with radiological
  imaging (CT scan, MRI, Outrootide scan).
• Diarrhea was defined as > 2 stools in addition to chronic
  baseline diarrhea while on SSAs and weight loss > 10% of
  baseline despite adequate caloric intake.
• Steatorrhea was suspected when the patient has large, “greasy”, and foul-
  smelling stools.
• Currently the gold standard test to diagnose steatorrhea remains the 72
  hour fat balance method (normal output is <7 g of fat per
  24-hour period).
• Regarding EPI, records were searched for any consults made
  with the nutritionist or a gastroenterologist before or after, and
  laboratory results if available on quantitative fecal fat, blood
  levels of fat soluble vitamins, such as Vitamine A, D, E, K and
  elements including Magnesium, Potassium, Zinc, Chromium, Selenium, Iron, and
  iodine.
• EPI was graded according to the Pancreas exocrine enzyme
  Table 1: Grades of Pancreatic exocrine enzyme deficiency per (CTCAE).

RESULTS

• 110 pts. (age 29-87) with GEP-NETs were identified. Study schema and
  demographic features are shown listed in Figure 2 and Table 1.
• Based on the previous data including perfusion studies, PER was
  dosed to administer 3000 to 5000 USP units of lipase per
  meal to achieve normal fat digestion and absorption.

Efficacy

• Diagnosis of PEI is confirmed by two types of tests:
  • Direct test based on aspiration of the pancreatic contents during secretin
    or secretin/cholecystokinin/cerulein administration (only available in a few
    centers; invasive)
  • Indirect tests: CCA, Acid steatoct, Fecal elastase 1, 13-C-mixed
    tricyclic breath test, Fecal chymotrypsin, secretin-enhanced MRCP,
    Nutritional status: Mg, Albumin, pre-albumin, retinol binding protein,
    ferritin, hemoglobin
• CONCLUSIONS
  • Our experience constitutes first study addressing PEI as a rare but
    serious complication of chronic use of SSAs.
  • Although SSAs are used to treat diarrhea, paradoxically they can
    worsen diarrhea secondary to PEI.
  • Early recognition and diagnosis of this under-diagnosed and under-
    reported side effect of SSAs can improve not only diarrhea and weight
    in these pts but also can reduce cost of using short-acting SA and
    antidiarrheal.
  • We believe this is an extremely topic to interest internists,
    gastroenterologists, oncologists and surgeons, who need to be fully
    aware of this under-diagnosed toxicity associated with chronic use
    of SSAs.

BIBLIOGRAPHY