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ORIGINAL ARTICLE

Sandostatin desensitization–a strategy useful for patients with carcinoid tumors, intolerant to sandostatin

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Abstract Sandostatin immediate release (IR) is frequently used to treat patients with carcinoid tumors. However, some patients are unable to tolerate the immediate side effects of sandostatin IR leading to discontinuation of the drug. There is no literature available to guide the management of patients' sensitivity/intolerance to sandostatin IR. We report a 49-year-old male with carcinoid tumor who was intolerant to sandostatin IR initially but was able to tolerate the drug after we employed a desensitization strategy.

Keywords Carcinoid · Sandostatin · Long-acting sandostatin · Depot preparation

Introduction

Since the original publication by Rubin et al. [1], sandostatin LAR has been effectively used for the control of carcinoid syndrome in thousands of patients. Before a patient can be started on LAR formulation, he should be able to tolerate the IR formulation. There are no guidelines in the literature to help manage patients' sensitivity/intolerance to sandostatin IR. In this paper, we report a case of sandostatin IR intolerance, which was successfully overcome by desensitization strategy.

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Case report

Forty-nine-year-old white male was evaluated for a 1-week history of painless jaundice. He reported facial flushing but otherwise was asymptomatic with no other significant history. The physical examination was unremarkable except for notable facial flushing. Diagnostic work-up revealed distension of the gall bladder, dilatation of the common bile duct (1.9 cm), hepatic ducts and a 3.5 cm hypodense lesion in the head of the pancreas. Patient underwent endoscopic retrograde cholangiopancreatography (ERCP) with stent placement; common bile duct biopsies and brushings did not reveal malignancy. Subsequent CT scan of the abdomen showed multiple 10–15 mm ill-defined hepatic lesions and increased fullness in the pancreatic head. A CT-guided biopsy of the pancreas revealed a low-grade neuroendocrine tumor of the pancreas head and neck. Indium-111 octreotide uptake was noted in the head and neck of the pancreas and in the two hepatic lesions. Patient had an elevated chromogranin-A level of 6. While the patient was waiting for surgery (whipple procedure), he was started on sandostatin 150 μg sq twice daily, to be continued for 2 weeks, followed by long-acting sandostatin (LAR) once every month.

However, patient reported severe nausea, vomiting, diarrhea, abdominal cramps after each 150 μg dose and did not wish to continue taking the drug. Since there is no literature to guide the management of these patients, we attempted a trial of gradually increasing the dose of sandostatin, starting at a very low dose of 25 μg sq twice a day. As the patient tolerated the dose, it was doubled every 3 days to eventually reach a target dose of 150 μg, which was within the recommended range for achieving a steady state concentration. In about 10 days, patient was taking the target dose of 150 μg sq twice daily. The patient tolerated the drug at the

target dose without severe gastrointestinal side effects initially seen. Subsequently, the patient was started on the sandostatin LAR injection, 20 mg intramuscularly. He tolerated the sandostatin LAR well and attained relief from his flushing.

Discussion

There are no guidelines to manage the drug intolerance/sensitivity that some patients with carcinoid tumor develop to sandostatin IR. We described a successful desensitizing strategy that can be useful in such patients.

Since native somatostatin has only limited clinical usefulness due to the need for intravenous administration, the short duration of action (half-life <3 min), and the post-infusion rebound hypersecretion of hormones [2, 3], synthetic somatostatin analogs were developed. Octreotide was the first such analog. Its elimination half-life after subcutaneous administration is 2 h, and rebound hypersecretion of hormones does not occur [4]. Somatostatin and its analogs exert their effects through interaction with somatostatin receptor (sst) subtypes 1–5 (sst1 to sst5). Somatostatin binds with high affinity to all somatostatin subtypes, whereas octreotide binds with a high affinity to sst2 and with a somewhat lower affinity to the sst3 and sst5 receptors [5].

Common adverse effects of treatment with somatostatin analogs include nausea, abdominal cramps, mild steatorrhea, flatulence and loose stools. These symptoms start within hours of the first sq injection, are dose-dependent, and usually subside spontaneously within the first few weeks, despite continued treatment. The occurrence of these adverse effects can be readily understood from the physiologic actions of somatostatin on the gastrointestinal tract and exocrine pancreas (stimulates water and electrolyte absorption, inhibits pancreatic exocrine secretion, reduces splanchnic blood flow, inhibits gastric acid and pepsin secretion). The resolution of these symptoms with continued treatment supports the concept of a rapid adaptation to the effects of somatostatin on the function of the gastrointestinal tract and pancreas [4]. However, the gastrointestinal tract and pancreas do not adapt rapidly in some patients, and they are unable to tolerate the drug.

Due to the adverse events associated with the use of sandostatin IR, the optimum approach for using this drug is to initiate therapy in the form of sq injections of the IR formulation for 3–7 days to test for tolerability before giving the LAR formulation i.m. A reasonable starting dose for the IR formulation is 150 μg sq three times daily [6].

However, in patients as we describe here who do not tolerate starting doses of 150 μg sq thrice daily, it is important to desensitize them or give time for the gastrointestinal tract and pancreas to adapt to the effects of sandostatin by utilizing a much lower starting dose and graded increase, rather than discontinuing the drug. Drug discontinuation keeps a useful and effective drug from being utilized in carcinoid tumor.

In conclusion, sandostatin IR can be successfully utilized in patients who are unable to tolerate the recommended standard dose of 150 μg by starting at a much lower dose of 25 μg and gradually increasing it to the target dose of 150 μg. Subsequently, the sandostatin LAR can be given to these patients and is well tolerated. Further studies need to be done to confirm our findings.

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