LETTERS

Be careful before prescribing warfarin and octreotide together: a new drug-drug interaction report

Dear Editor,

Octreotide is a cell cycle phase-specific (G1-phase) synthetic somatostatin analog that is used to control hormone-mediated symptoms in gastro-entero-pancreatic (GEP) endocrine tumors such as insulinoma, gastrinoma, VIPoma, glucagonoma, acromegaly, and carcinoid tumors[1].

Warfarin is frequently used by patients with thromboembolic disorders who require anticoagulant therapy. Warfarin is associated with many drug and food interactions[2] but potential interactions between warfarin and octreotide have not yet been reported in literature.

A 42-year-old male patient who was investigated for deep vein thrombosis was diagnosed with a pancreatic mass. A subtotal pancreatectomy, splenectomy, and lymph node dissection were performed. The pathology result was grade II, well-differentiated neuroendocrine carcinoma with three metastatic lymph nodes. Octreotide sintigraphy and chromogranin was normal and staged as T2N1M0.

After 6 months, the cancer relapsed at the mediastinal and intraabdominal lymph nodes. Octreotide LAR started owing to his asymptomatic status and relapsing low-grade disease. The patient was also using warfarin for previous deep vein thrombosis.

Two months later, the patient was admitted with an INR level of 8.5. During this time, octreotide was administered two times. The patient was not taking any medication or food that would cause an interaction with coumadin. The patient was recognized to have drug-drug interaction between coumadin and octreotide. The patient was discharged with octreotide and low molecular weight heparin. No major bleeding occurred.

Warfarin is well known to frequently interact with many drugs and foods. It consists of two optically active isomers: R-enantiomer and S-enantiomer[3]. The more potent S-isomer is metabolized by cytochrome P-450 (CYP) 2C9, and the R-isomer is metabolized by CYP 1A2 and CYP 3A4[3]. Many of the drugs identified to potentiate warfarin's effect are known inhibitors of CYP 2C9, CYP 1A2, and CYP 3A4[3].

In an in vitro study, Liddle et al. showed that in cultured human hepatocytes, exposure to GH increased *CYP3A4* gene expression[4]. Octreotide inhibits endogenous GH that may reduce CYP3A4 activity and increase the warfarin effect which may be the cause of high INR in this case.

In conclusion, warfarin and octreotide are widely used in different clinical indications. We wish to alert the clinicians who prescribe these two medications concomitantly for drug-drug interaction.

References

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Conflict of interest

None.

Keywords: Octreotide LAR, warfarin, drug interaction, cytochrome P450

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