Eltrombopag : How secure in triple therapy of HCV ?

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Abstract

Triple therapy of hepatitis C usually leads to some hematological and dermatological side effects. Thrombocytopenia is one of the most common side effects that are encountered during triple therapy. Eltrombopag was approved for the treatment of patients with chronic hepatitis C and thrombocytopenia to allow the initiation and maintenance of interferon based therapies. During eltrombopag therapy, some side effects like headache, abdominal pain, and some complications such as portal vein thrombosis, deep vein thrombosis and arterial thrombosis were observed more frequently than placebo. We described here a patient who developing thrombosis secondary to eltrombopag in receiving triple therapy. (Acta gastroenterol. belg., **2015**, 78, **445-446**).

Key words : Trombosis, hepatitis C, safety, triple therapy.

Dear Editor,

A 64-year-old female patient was diagnosed with hepatitis C virus (Genotype 1b)-induced compensated cirrhosis and administered interferon alfa-2a plus ribavirin therapy for three months initially and then for four months ; the therapies were discontinued due to primary nonresponse and thrombocytopenia (more than 2-log reduction was observed in the HCV RNA level at third month of treatment), respectively. The patient does not have any other chronic illnesses. There are no features in the family history. The patient is a non-smoker and does not consume alcohol. Except for the treatment of hepatitis C, the patient had no history of drug use. The patient was started on triple therapy of pegylated interferon alfa-2a, ribavirin, and telaprevir. The pretreatment number of platelet was 62.000/μL. At the third week of treatment, the platelet number went down to 33.000/μL and eltrombopag 50 mg/day was added to the treatment. Platelet counts following eltrombopag increased from 56.000/μL on the first day to 127.000/μL on the fifth day. On the fifth day, left side paresis, bilateral blurred vision, numbness on the right side of the body, and dysarthria developed. The carotid Doppler was normal. Intracranial Magnetic Resonance Angiography revealed right sided cerebral infarction. Hereditary and acquired causes, all of which can lead to thrombosis, were excluded. Eltrombopag plus triple therapy was discontinued. Acetylsalicylic acid was initiated. The follow-up control of the patient one month after discontinuation of therapy revealed a 105.000/μL thrombocyte count and the patient was neurologically asymptomatic. Although negative HCV RNA was observed at the end of the first month of treatment, the patient relapsed six months after the discontinuation of therapy.

As is known, triple therapy of hepatitis C usually leads to some hematological and dermatological side effects. Thrombocytopenia is one of the most common side effects (1).

Eltrombopag is an agonist of the TPO receptor, which is the physiological target of the hormone thrombopoietin. Even though it was only used to increase the number of platelets to lower the risk of bleeding in immune thrombocytopenic purpura initially (2), later, eltrombopag was approved by the Food Drug Administration (FDA) for the treatment of patients with chronic hepatitis C and thrombocytopenia to allow for the initiation and maintenance of interferon-based therapies (3).

During eltrombopag therapy, portal vein thrombosis and arterial thrombosis at normal or even subnormal platelet levels were observed more frequently than placebo (4). Therefore, eltrombopag should only be used when the benefits of doing so clearly outweigh the risks in high-risk patient groups (5). Although the mechanism of thrombosis during eltrombopag therapy is not clear, increases in both platelet count and platelet activity may play a role (4). Afdhal *et al*. reported that thrombosis risk is higher when the platelet count is over 200.000/μL (4). If the platelet count rises to > 150.000/μL, consideration should be given to reducing the eltrombopag dose. In high-risk patients, eltrombopag should be used in a dose that is sufficient to achieve and maintain the target platelet count of ≥ 50.000/μL. Ideally, platelet count should not be allowed to rise above 100.000/μL in high-risk patients (4,5).

Consequently, eltrombopag is a useful drug not only for initiating and maintaining hepatitis C therapy, but also for sustaining the virological response. It should be noted that severe complications such as ischemic stroke due to thrombosis can be seen and that high platelet counts should be avoided. Also, the need for eltrombopag to treat chronic hepatitis C will disappear in the future when interferon free regimens become available.

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Submission date : 12/06/2015
Acceptance date : 24/06/2015

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