

Eltrombopag Dose Adjustment During Reactive Secondary Thrombocytosis in patient with ITP

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Abstract

Eltrombopag is relatively new drug used in Thrombocytopenia. Its dose should be adjusted based on platelets count. It should be stopped when platelets count reach 400,000/mm³. Here, we share our case report of stopping Eltrombopag based on platelets increment in secondary reactive thrombocytosis irrespective of Eltrombopag treatment.

Introduction

Eltrombopag is small-molecule nonpeptide Thrombopoietin Receptor (TPO-R) agonist administered orally. It was approved for treatment of thrombocytopenia to increase platelets count and protect patients from bleeding. It's usually very well tolerated orally and has excellent safety profile with an overall response rate of 60% to 80% [1]. Eltrombopag response is followed by frequent platelets count measurements and subsequently manipulated to achieve adequate platelets count to avoid both thrombocytopenia and thrombocytosis. Eltrombopag can be used as first or second line, alone or in combination with other medications for ITP [2].

In clinical practice, the term 'thrombocytosis' refers to platelet counts above 450,000/mm³ [3]. Thrombocytosis can be primary or secondary to other causes because platelets are acute phase reactant.

The use of Eltrombopag will stimulate the bone marrow to produce platelets and the dose will be adjusted accordingly. In clinical practice, some patient who are already on Eltrombopag may developed rapid platelets count increment due to reactive thrombocytosis. This situation will be challenging to physicians in manipulating the dose of the drug and whether withdrawal of Eltrombopag will be safe and will not expose the patient to risk of bleeding especially patients who are stable on fixed dose for long time.

In this case report, we share our experience in adjusting the dose of Eltrombopag during secondary reactive thrombocytosis.

Case Report/Case Presentation

Our patient is a sixty years old Female who was diagnosed with ITP in October 2018. At that time, an incidental finding of platelets count of 61,000/mm³ was identified. Work up was done and the diagnosis of ITP was made by exclusion followed by starting the patient on steroid. One week later, there was no significant improvement in platelets count as it decreased from 61,000/mm³ to 33,000/mm³.

The decision to start Eltrombopag as second line was discussed with the patient, he agreed and consent was taken. Eltrombopag started on 22/11/2018 with a dose of 25 mg daily. On next check up on 6/12/2018, platelets count improved to 137,000/mm³.

Follow up appointment on 15/1/2019, the platelets count was found to be 40,000/mm³. Eltrombopag was increased to 50 mg daily which showed good response on next follow up appointments by increasing platelets count to 121,00/mm² and 203,000/mm³ consequently in two weeks apart.

The patient maintained adequate platelets count throughout 2019 on Eltrombopag 50 mg daily. In 22/04/2020, the patient developed left foot pain, redness and swelling, he came to hospital and found to have evidence of infection and high inflammatory markers. A diagnosis of cellulitis was made and the patient started on oral antibiotic (amoxicillin with clavulanate) and pain killers. At this time the platelets count jumbled to be 536,000/mm³ as secondary reactive thrombocytosis. Eltrombopag stopped on 30/4/2020 with close observation of platelets count and patient clinical condition.

As patient was receiving treatment for cellulitis, platelets count was maintained over the following two weeks after stopping Eltrombopag between 150,000/mm³ and 200,000/mm³ without significant drop or bleeding symptoms.

Two weeks later, the patient finished antibiotic and his clinical condition improved. His platelets count was checked and found to be 100.000/mm³. Eltrombopag was restarted again on 19/05/2020 and platelets count maintained without dropping. Last platelets count check was found to be 143,000/mm³ on 20/8/2020 while the patient on Eltrombopag 50 mg daily.

Discussion/Conclusion

Eltrombopag is an oral medication, relatively new drug that stimulate the bone marrow to produce platelets. It's taken as once daily tablet on an empty stomach. Eltrombopag used to correct thrombocytopenia that result from various condition such as ITP, Aplastic anemia and chronic Hepatitis C infection associated thrombocytopenia [4,5]. It is also important to note that Eltrombopag is used to note that Eltrombopag may help to control the condition but will not cure it.

Eltrombopag is usually started with low (12.5 mg or 25 mg daily). Then the dose is gradually built up to maintain minimum platelets count > 50,000/mm³ to prevent bleeding. Eltrombopag dose is adjusted as following [6]:

1. Platelets count < 50,000/mm³, the dose should be increased gradually to reach minimum count of 50,000/mm³. maximum dose is 75 mg daily.
2. Platelets count between 50,000/mm² and 200,000/mm³, the dose should be maintained with no change.
3. Platelets count between 200.000/mm³ and 400,000/mm³, the dose should be reduced by 25 mg daily. If taking 25 mg then to be reduced to 12.5 mg daily.
4. Platelets count > 400,000/mm³, withhold dose; assess platelet count twice weekly; when platelet count <150,000/mm³, resume with the daily dose reduced by 25 mg (if taking 25 mg once daily, resume with 12.5 mg once daily).

All of the above-mentioned dose modification is based on platelets count increment that results from Eltrombopag use. With nothing mentioned clearly about secondary reactive thrombocytosis.

In our case, we followed the guidelines by starting the patient on initial dose of 25 mg daily, then and we built up to 50 mg daily to reach stable platelets count above 50,000/mm³. The patient management went smoothly and he was doing very well with stable platelets count and no symptoms of bleeding for more than one year. When he developed cellulitis, platelets count jumped to 536,000/mm³ representing challenging situation to treating team. Literature was reviewed looking for similar situation on how to adjust the dose of Eltrombopag in reactive thrombocytosis but no clear recommendation found.

To avoid exposing the patient to risk of thrombus formation, we decided to take the risk of stopping Eltrombopag taking in consideration that platelets count could drop rapidly and bleeding may occur due to underlying ITP. Fortunately, the challenging situation went safely and the patient maintained platelets count above 50,000/mm³ throughout cellulitis treatment period. No acute drop in platelets count occur, no bleeding occurs and reactive thrombocytosis was enough to prevent bleeding during Eltrombopag free period.

Conclusion;

Eltrombopag can be safely stopped during reactive secondary thrombocytosis due to infection without fear of acute drop in platelets count or bleeding. However, more studies are needed to reproduce the same finding.

Statements

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Statement of Ethics Case approved by HMC medical research center and Subjects have given his written informed consent to publish her case.

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Author Contributions

1. Mohanad Ahmed: Case writing, patient clinical follow up , data collection and analysis , submission to journal.
2. Elabbass Abdelmahmoud: literature review and data collection
3. Elrazi Ali: literature review and data collection
4. Mohamed Yassin: over all observation and guidance.

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