Reviewer's report

Title: Warfarin and boceprevir interaction causing subtherapeutic INR: a case report

Version: 1 Date: 6 September 2014

Reviewer: Danielle C Gatti

Which of the following best describes what type of case report this is?: Unreported or unusual side effects or adverse interactions involving medications

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: No

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: No

Will the case report make a difference to clinical practice?: Yes

Is the anonymity of the patient protected?: Yes

Comments to authors:

This is a very well written case report which further looks at the potential for possible induction of warfarin metabolism by protease inhibitors. However, there are some concerns that I would like the authors to further address.

First, throughout the patient’s course of therapy, the patient was admitted to the hospital due to thrombocytopenia and was also treated for two suprapubic abscesses. However, there is no mention of any other medications that the patient may have received while in care for these two separate incidences. As we know, many medications, especially antibiotics can affect the patient’s INR.

Also, because the patient was admitted for thrombocytopenia and suffered from
anemia, was the dose of ribavirin decreased at any point during his course of therapy?

The author states that there is no known drug interaction with warfarin and ribavirin or peginterferon. However, there are articles, which suggest possible interactions with these medications, which should be mentioned and ruled out.

In an article by Schulman, after the initiation of interferon and ribavirin, the dosage requirement of warfarin progressively increased over the course of a month. After the discontinuation of these agents, the patient’s warfarin requirement fell to a level similar to the baseline. Schulman S. Inhibition of warfarin activity by ribavirin. Ann Pharmacother. 2002; 36:72-4. If the dose of these agents were ever decrease, this could also potentially cause variations in the INR.

What is also interesting is that when the boceprevir was discontinued, the patient’s weekly warfarin requirements did not return to baseline. In fact, it remained about 50% higher (23.75mg) than the patient’s initial weekly dose of 15mg. Additionally, the INR did not increase when the boceprevir was discontinued, which was thought to be causing the induction of the warfarin metabolism. Was there a Drug Interaction Probability Scale score calculated for this case report? Could this interaction be concluded as probable?

Lastly, it is also worth mentioning if the patient’s INR was being checked via a lab drawn venous puncture or through a point of care (POC) INR device. POC INR devices list anemia as a potential limiting factor in INR accuracy.

I agree that the protease inhibitors may cause some induction of warfarin metabolism and this needs to be further investigated. We also need to keep this potential interaction in mind while adjusting warfarin therapy in our patients that are undergoing Hep C treatment. However, this patient does have many variables during his course of therapy, which may have contributed somewhat to his variances in his INR, and the author should address.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Declaration of competing interests: none of the above