Author's response to reviews

Title: Use of Activated Factor VII in Mitral Balloon Valvuloplasty Complicated by Hemopericardium.

Authors:

Jeremy Steele (jeremy.steele27@gmail.com)
Igor Mamkin (igor_mamkin@yahoo.com)
Berhane Worku (bmworku@hotmail.com)
Iosif Gulkarov (iog9001@nyp.org)

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Author's response to reviews: see over
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Prof. Michael Kidd, Editor-in-Chief

Please find attached our revised manuscript entitled “Use of Activated Factor VII in Mitral Balloon Valvuloplasty Complicated by Hemopericardium.” by Steele and collaborators, which we would like to submit for publication in Journal of Medical Case Reports. We have examined the reviewer’s comments to the manuscript and have tried to address each point raised by each Reviewer.

The first reviewer felt that our article failed to mention an algorithm for peri-procedural bleeding in terms of quantity of bleeding considered acceptable. A general algorithm for management of these patients was summarized in our introduction, but it fails to indicate specific thresholds for different interventions. We added a summary of the algorithm in discussion section (page 5, first paragraph). As clinicians we believe that the care in these types of patients should be individualized, and thresholds for interventions are highly dependent on the judgement and level of comfort of the practitioners taking care of a patient with mediastinal bleeding. The most important aspect in the care of these types of patients is timely resuscitation, and hemodynamic stability. If the patient was unstable at any point after the procedure it would have significantly lowered our threshold for more definitive surgical intervention. The patient was hemodynamically stable throughout his care. This stability gave us time to correct coagulopathy and attempt treatment with Factor VII. Use of Factor VII was not a random decision. We use Factor VII occasionally in cardiac surgery for postprocedural refractory bleeding. Our experience with this agent was very positive, and therefore we felt that extrapolating this experience to management of the case presented in our manuscript was reasonable.

The first reviewer rightly pointed out that one should not draw a conclusion based on this case report that the management of periprocedural mediastinal bleeding entails mainly observation and treatment with Factor VII. The main message of our article is to let the clinical community know that Factor VII can be used successfully in the treatment of persistent mediastinal bleeding following mitral valvuloplasty, and therefore may be considered if patient is hemodynamically stable prior to surgical intervention. To our knowledge this is the first report of this kind in the literature. It provides practitioners treating patients with valvuloplasty related hemorrhage another tool that potentially may save the patient the morbidity of an open operation to control bleeding.

The second reviewer’s comment regarding the dramatic differences in mediastinal drainage before and after Factor VII administration is very valid. The patient had at least hourly surveillance of the pericardial sac by a cardiologist at the bedside using transthoracic echocardiography (page 4, line 10-11), thereby ensuring complete emptying of the sac prior to administration of Factor VII. The drainage didn’t taper off gradually over “several hours”, but ceased almost immediately after Factor VII was administered.
Even though there is no scientific way of proving that resolution of bleeding was related to Factor VII administration, based on the presence of persistent bleeding for 3 hours, despite corrected coagulopathy, we believe the timing between treatment with Factor VII and cessation of drainage is not coincidental. As per request of the reviewer we also provided quantities of blood product administered to the patient to correct coagulopathy (page 4, line 12).

Upon the second reviewer’s request we provided the details regarding the informed consent for the publication of this case report (page 6, line 11).

In addition to the list of approved indications for the use of factor VII, we listed some other off label uses of factor VII in clinical practice and its relative cost. (page 5 page 13-15).

The reviewer also inquired on why we think Factor VII is more efficacious than conventional treatment. It appears that Factor VII is more effective than conventional treatment in the management of refractory bleeding in patients with no coagulation abnormalities due to “thrombin burst” and platelet activation that leads to a more effective platelet plug and sealing of bleeding vessels. The mechanism is outlined in greater detail in the last paragraph of the Discussion.

Finally, in response to the reviewer’s appropriate suggestion we changed our conclusion from “activated Factor VII…” should be considered prior to..” to “may be considered”.

We reformatted the title of our manuscript to follow the suggested structure.

We also added ethnicity of the patient in the case presentation.

We also replaced “activated Factor VII” with abbreviation “aFVII” in the body of the text.

We hope that these changes will make our manuscript suitable for publication in your journal.

Sincerely,

Iosif Gulkarov, MD