The use of fondaparinux with mechanical mitral valve replacement in a HIT like situation: A case report

Randa Tabbah[1] and Rachoin Rachoin[1]

[1]CHUNDS

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Abstract

While there is currently no literature for the use of fondaparinux in patients with mechanical heart valves, this drug may offer an option for bridging of such patients who cannot use heparin due to severe thrombocytopenia induced by chemotherapy and high thrombosis risk concomitantly.

Introduction:

Fondaparinux is a factor Xa inhibitor used for venous thromboembolism prevention and treatment [1]. It has a low affinity for platelet factor 4, making it an alternative agent to unfractionated heparin (UFH) and low-molecular weight heparin (LMWH) and a plausible consideration for patients with a history of HIT with decreased platelets and hypercoagulable state [2,3]. The use of fondaparinux as a bridging therapy in patients with mitral mechanical heart valve replacement and severe thrombocytopenia due to chemotherapy has never been discussed before in the literature.

We report a case of a patient with a mechanical mitral valve replacement and thrombocytopenia chemotherapy induced with a successful bridging with fondaparinux. While there is currently no literature for the use of fondaparinux in patients with mechanical heart valves.

Clinical presentation:

A 68-year-old woman with a past medical history of mechanical mitral valve replacement, hypertension, diabetes, obese and chronic atrial fibrillation on chronic warfarin anticoagulation with an INR in range between 2,5 and 3,5 compliant to medical therapy presented to the emergency room complaining of fatigue, alteration of general condition and epistaxis.

Additionally, her past medical history included breast cancer diagnosed 1 year ago and the patient was treated with Doxorubicin. She had her last chemotherapy session 1 week before her symptoms. No fever, nausea, vomiting nor night sweats. Her laboratory results in the emergency room revealed a hemoglobin of 9.2 g/dl, platelet count of 10,000/mm3 and an INR of 2,3. Her serum creatinine and blood urea nitrogen were normal. Subsequently, warfarin was held, and the patient received platelets transfusion. The second day blood labs revealed a hemoglobin level of 8g/dl and a platelet count of 20000/mm3 with an INR of 1,9. Blood transfusion was also given. Patient was not in range anymore and to balance the risk of bleeding and valve thrombosis was the main issue because as known mechanical mitral valve are at high risk of thrombosis. Fondaparinux was recommended after both hematology and cardiology discussion. Drug was suggested as a bridging therapy until the patient had regain normal platelet levels. Fondaparinux was initiated on the 1st day at 7.5 mg subcutaneously once daily based on a weight of 80 kg, and a calculated creatinine clearance of 65 ml/min. Warfarin was initiated 5 days after the patient recovered from her thrombocytopenia with a normal level of 150000/mm3 for an INR goal of 2,5–3,5. Therapeutic INR was reached 4 days after

where patient was receiving concomitant warfarin and fondaparinux. No signs or symptoms of bleeding or thrombosis had been exhibited. By the time fondaparinux was interpreted, patient had a therapeutic INR of 3 and remained on warfarin alone. Cardiac ultrasound was done revealing a good functional metallic mitral valve and a good LV function. No complications were seen.

Discussion:

Despite serval studies on Direct anticoagulant (DOAC), warfarin remained the gold standard therapy for patient with mechanical valve. The use of DOAC in patients with mechanical heart valves was associated with increased rates of thromboembolic and bleeding complications compared to warfarin and showed no benefit but an excess risk [4]. The river trial showed a non-inferiority to warfarin with bioprosthetic mitral valve in case of atrial fibrillation [5]. The use of DOAC with mild thrombocytopenia is an option but as shown in this case patient has both severe thrombocytopenia and a mechanical valve [6]. Per ESC guidelines 2017 bridging is recommended in case of a metallic mitral valve with UFH or LMWH when VKA is interrupted. Targeted INR in case of medium to high thrombogenicity and atrial fibrillation must be between 2,5 and 3,5 [7]. But in our case, using heparin with severe thrombocytopenia was risky.

On the other hand, Fondaparinux a factor Xa inhibitor used for venous thromboembolism prevention and treatment [1] has low affinity for platelet factor 4, making it an alternative agent to unfractionated heparin (UFH) and low-molecular weight heparin (LMWH) and a plausible consideration for patients with a history of heparin-induced thrombocytopenia (HIT) with decreased platelets and hypercoagulable state [2]. The use of fondaparinux as a bridging therapy in patients with mitral mechanical heart valve replacement and severe thrombocytopenia due to chemotherapy has never been discussed before in the literature but this case was like a HIT situation where balance between bleeding and thrombosis was needed.

While both unfractionated heparin and low-molecular weight heparin are also options but carries a risk for HIT when binding to platelets and endothelial cells, therefore, both UFH and LMWH are most often avoided in this case. Fondaparinux binds specifically to antithrombin and has minimal affinity for platelet factor 4, making it an alternative agent to UFH and LMWH. However, the use of fondaparinux in patients with mechanical heart valve replacement and a thrombocytopenia induced by chemotherapy has never been reported in the literature.

Furthermore, thrombocytopenia by itself may increase bleeding risk, but it does not protect against venous thromboembolic events or stroke that was very risky in this patient with a high CHADVASC score and HASBLED score and on chemotherapy for cancer. Thus, caring for patients with both thrombocytopenia and an indication for anticoagulation can be challenging. It is generally when platelet counts <50,000/microL that severe spontaneous bleeding is most likely as in this case [8]. However, there is not a good linear correlation between the platelet count and bleeding risks in these situations. In addition, the risk of VTE is greatest in the setting of a strongly prothrombotic risk as active chemotherapy [9].

There are no randomized trials comparing different approaches to reducing the risks of VTE, stroke and mechanical valve thrombosis in people with cancer and thrombocytopenia and mortality from VTE and other thromboembolic events may be greater than mortality from bleeding in most populations. That is why we need to shed the light on these issues and further studies need to be done so that new guidelines would take into consideration this subpopulation.

Conclusion:

We report a case of a patient with a mechanical mitral heart valve replacement and thrombocytopenia chemotherapy induced with a successful bridging with fondaparinux. While there is currently no literature for the use of fondaparinux in patients with mechanical heart valves, this drug may offer an option for bridging of such patients who cannot use heparin due to severe thrombocytopenia and high thrombosis risk concomitantly. However, further randomized trials are warranted to confirm both the safety and efficacy of this agent in this population.

Conflict of interest:

The authors declare that *there is no conflict of interest* . All authors have been personally and actively involved in substantial work leading to the paper and will take public responsibility for its content. The authors have not received any funding for this article.

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