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Periprocedural Off-label Use of Rivaroxaban in Patient with Atrial Fibrillation and a Persistent Left Atrial Appendage Thrombus Despite Standard Anticoagulation Therapy: A Case Report

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ABSTRACT

Atrial fibrillation (AF) is a common cardiac arrhythmia characterized by irregular and rapid heart rates, which may lead to various complications, such as stroke, heart failure, and thrombus formation. One particular complication, the development of a left atrial appendage thrombus, increases the risk of thromboembolic events, posing significant health risks to affected individuals. Patients with atrial fibrillation with a left atrial appendage thrombus should receive oral anticoagulation with a non-vitamin K antagonist oral anticoagulant (NOAC), such as rivaroxaban in a standard dose of 15 mg or 20 mg, according to creatinine clearance. However, these guidelines do not provide clear instructions on managing patients with a left atrial appendage thrombus who have already been anticoagulated with 20 mg rivaroxaban for 21 days without thrombus resolution prior to cardioversion. In light of this, we attempted an off-label treatment approach by administering a double dose of rivaroxaban (15 mg twice daily) to a patient presenting with AF and a persistent left atrial appendage thrombus. This case report explores this innovative off-label treatment approach, emphasizing the importance of effective management strategies to mitigate the associated complications and improve patient outcomes. This case report describes a patient with atrial fibrillation and a left atrial appendage thrombus who underwent successful cardioversion after receiving 15 mg of rivaroxaban twice daily as an off-label treatment. The patient well tolerated the increased frequency of administration. This case report suggests that using 15 mg of rivaroxaban twice daily for 14-21 days as an off-label treatment may be viable for patients with atrial fibrillation and a persistent left atrial appendage thrombus despite standard anticoagulation therapy. Clinicians should consider this approach when developing treatment plans for these patients, especially when traditional management strategies have proven ineffective and while keeping in mind the findings of the X-VERT study.

INTRODUCTION

Atrial fibrillation (AF) is a prevalent cardiac arrhythmia affecting approximately 1-2% of the general population. It is associated with significant morbidity and mortality, primarily due to the increased risk of stroke and other thromboembolic events. Current treatment strategies for AF patients focus on reducing this risk, with direct oral anticoagulants (DOACs) such as rivaroxaban emerging as effective therapeutic options for managing AF. Specifically, a standard dose of Rivaroxaban 15 mg or 20 mg according to the Creatinine clearance regimen has been widely adopted for stroke prevention in AF patients before cardioversion. Numerous clinical trials, such as the ROCKET AF[1] and X-VeRT[2] studies, have demonstrated the efficacy and safety of rivaroxaban in AF patients. In the ROCKET AF trial, [1] rivaroxaban displayed noninferiority to warfarin, with a 21% relative risk reduction in stroke or systemic embolism. The X-VeRT trial[2] further supported the use of rivaroxaban in patients undergoing cardioversion, showcasing a 2.1% event rate for rivaroxaban-treated patients compared to a 2.0% event rate for those on vitamin K antagonists. In cases where a left atrial appendage thrombus is present before cardioversion, guidelines recommend adequate anticoagulation therapy. However, they do not specifically address the management of patients whose thrombus does not resolve after receiving the standard 20 mg once-daily rivaroxaban regimen for three weeks. This case report examines the potential benefits of an alternative rivaroxaban dosing regimen for a patient with atrial fibrillation and left atrial appendage thrombus before cardioversion. This experimental approach involves administering 15 mg of rivaroxaban twice daily for three weeks, a regimen used in the EINSTEIN study[3] for treating pulmonary embolism (PE). The EINSTEIN study[3] demonstrated the efficacy and safety of rivaroxaban in patients with PE, showing a 2.1% recurrence rate for rivaroxaban-treated patients compared to a 1.8% rate for those on standard anticoagulation therapy (noninferiority $p<0.001$). Building upon the established efficacy of the 20 mg once-daily treatment and the success of the EINSTEIN study, we explore the potential of the 15 mg twice-daily

rivaroxaban regimen as a practical approach for managing left atrial appendage thrombus in patients with atrial fibrillation who are undergoing cardioversion. Further research is needed to assess the safety and efficacy of this alternative dosing regimen in this specific patient population.

CASE PRESENTATION

The 61-year-old obese (BMI=30 kg/m2) male patient was admitted to the Tbilisi Heart Center (Tbilisi, Georgia) with symptoms of exertional chest discomfort and a medical history of essential hypertension, type 2 diabetes mellitus, atrial fibrillation (diagnosed one year before admission) and heart failure (NYHA class 2). The patient's medication regimen included bisoprolol 5 mg QD, rosuvastatin 10 mg QD, torsemide 20 mg QD, rivaroxaban 20 mg QD, and potassium 250 mg BID.

The coronary angiography revealed no signs of atherosclerotic coronary occlusion or other abnormalities. This finding was reassuring and suggested that the chest pain may be related to atrial fibrillation rather than coronary artery disease. Therefore, the medical team decided to perform a cardioversion procedure, and transesophageal echocardiography was conducted to exclude the presence of a left atrial appendage thrombus. However, the echocardiogram revealed the presence of hyperechogenic thrombotic masses.

In this case, the decision was made to deviate from the standard treatment approach for atrial fibrillation with clot dissolution prior to cardioversion. Typically, patients with atrial fibrillation and a detected thrombus would be treated with anticoagulants, such as warfarin or a direct oral anticoagulant (DOAC) like rivaroxaban, to reduce the risk of stroke before attempting cardioversion. The medical team carefully discussed the treatment strategy, possibly switching the patient from rivaroxaban to warfarin. This vitamin K antagonist has been the traditional choice for anticoagulation in patients with atrial fibrillation. However, it requires frequent monitoring of the international normalized ratio (INR) and dose adjustments based on various factors, such as diet and concomitant medications.

On the other hand, rivaroxaban, a factor Xa inhibitor, offers a more predictable anticoagulant effect and does not require routine monitoring. The patient was on rivaroxaban 20 mg once daily for atrial fibrillation management.

After weighing the pros and cons, the decision was made to use an off-label approach and increase the dose of rivaroxaban to 15 mg twice daily, as demonstrated in the EINSTEIN study for 21 days.[3] This decision was based on the potential benefits of maintaining the patient on a regular medication with a more predictable anticoagulant effect, despite the lack of established guidelines for this specific dosing regimen in this context.

After ten days of anticoagulation, repeated imaging investigations revealed the resolution of the left atrial appendage thrombus. Therefore, there were no significant adverse events during the off-label dosage of rivaroxaban. After that the patient was successfully treated with cardioversion procedure.

DISCUSSION

This case report discusses the off-label use of rivaroxaban 15 mg twice daily for left atrial appendage thrombus resolution prior to cardioversion. This approach was utilized to manage a patient with persistent atrial fibrillation and detected left atrial appendage thrombus, which did not resolve with the standard 20 mg rivaroxaban once daily. Based on its efficacy in treating venous thromboembolism, this dosing regimen could effectively prevent thrombus formation in the left atrial appendage prior to cardioversion. Rivaroxaban, a factor Xa inhibitor, is effective in treating deep vein thrombosis (DVT) and pulmonary embolism (PE). In the EINSTEIN-DVT[4] and EINSTEIN-PE[3] studies, rivaroxaban was compared to standard therapy (enoxaparin followed by vitamin K antagonist) in patients with acute symptomatic DVT and PE, respectively. Rivaroxaban was found to be non-inferior to standard therapy in terms of efficacy and had a similar safety profile in both studies. Based on the success and safety profile observed in the EINSTEIN-DVT[4] and EINSTEIN-PE,[3] we hypothesize that off-label rivaroxaban 15 mg twice daily may effectively prevent left atrial appendage thrombus formation prior to cardioversion. The patient was treated with this off-label dosing regimen, and the cardioversion was successful. In addition, the patient did not experience significant bleeding or complications, per the safety profile reported in the abovementioned studies.

In conclusion, this case report demonstrated promising results in the off-label use of rivaroxaban 15 mg twice daily for left atrial appendage thrombus prevention prior to cardioversion. The evidence from the EINSTEIN-DVT,[4] EINSTEIN-PE,[3] and EINSTEIN Extension studies suggests that factor Xa inhibitors may effectively manage thrombotic events. Clinicians should consider this off-label dosing regimen when standard anticoagulation therapy has proven ineffective, considering the need for further research to confirm these findings and establish safety and efficacy in a larger population.

CONCLUSIONS

The patient's favorable response to treatment and the manageable adverse effects highlights the potential viability of this off-label use of Rivaroxaban, particularly in situations where standard treatment may not be appropriate or has failed.

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