CASE REPORT

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Managing mechanical mitral valve on warfarin therapy with gross hematuria: A case report with unfractionated heparin as a bridging therapy

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ABSTRACT

A dilemma can happen to a physician when managing bleeding case on a patient with mechanical heart valve with anticoagulant therapy. Major bleeding on anticoagulant treatment usually affects gastrointestinal tract (40-60 %) and urinary tract (15%). To manage the bleeding, vitamin K was restrictedly used in a patient with a mechanical heart valve and only can be used if there is major bleeding. The hypercoagulable state also must be considered when reinitiating warfarin therapy, once the bleeding already stopped. A 51-year-old female with St Jude Medical mechanical mitral valve replacement for 13 years and on regular warfarin therapy came with gross hematuria. INR level was 5.6, and nothing was found that can be the cause of the bleeding from the urinalysis, Urology ultrasonography, and CT scan. Warfarin was stopped for 3 days, and bleeding still occurred. Unfractionated heparin then was given to the patient to prevent thromboembolism event and as a bridging therapy. On the sixth day, hematuria was stopped, and hemoglobin was reduced only by 2 mg/dL. No rebleeding was found from the patient until 3 months later.

Key Words: Mechanical mitral valve, warfarin, bridging therapy, hematuria, unfractionated heparin

Introduction

Managing bleeding case, e.g., gross hematuria, on a patient with mechanical heart valve is so challenging and sometimes becomes a dilemma to the physicians because the patient is on anticoagulant therapy to prevent thromboembolism event that can happen to the patient. Procoagulant therapy is routinely used for most of bleeding case, but for patients with a mechanical heart valve, procoagulant therapy is still a controversy.

Case Report

A 51-year-old female with St Jude Medical mechanical mitral valve replacement for 13 years and on regular warfarin therapy came to the cardiology clinic at Badung Hospital with gross hematuria for 3 days. She was hospitalized to investigate the cause of the hematuria. Urinary tract infection was found from urinalysis result, right hydronephrosis grade I-II with no visible opaque stone from Urology USG result, and Urology CT-Scan result is within normal limit. The INR level on the 1st day of hematuria was 5.6 (therapeutic target INR 2.5), and warfarin stopped for 3 days until INR level reached 1.08, but gross hematuria did not stop. To prevent thromboembolism events, the patient was given unfractionated heparin as a bridging therapy with aPTT target range 50-70 seconds. On the 6th day from the onset, hematuria stopped, and 2 days later the patient was restarted to get warfarin overlapped with unfractionated heparin until INR level >2. During 6 days of hematuria, hemoglobin was reduced by 2 mg/dL. No rebleeding was found from the patient until 3 months later.

Discussion

It is a dilemma when a physician must treat bleeding complication while patients with mechanical heart valve need anticoagulant therapy. Major bleeding usually affects GI tract (40-60 %), urinary tract (15%), and followed by ICH/SDH and retroperitoneal/abdomen compartment syndrome. Bleeding complication can happen because of narrow therapeutic index, difficulty in predicting the biological response, multiple interactions to particular food and drug, and other patient-related factors.[1,2]

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Bleeding is a more common complication in older adult patient. During chronic therapy, bleeding can be prevented by reducing INR level between 2 -3. INR values up to 9 (without bleeding) can be managed with drug omission and the restarted again with a lower dose. If bleeding more significant or INR level more than 9, Vitamin K_1 should be given to reduce the INR level within 24-48 hours. In patient with prosthetic valve administration of Vitamin K should be avoided because of the risk of valve thrombosis, unless there was a major bleeding.[3]

Immediately stopping warfarin until INR level reaches to normal is the initial management. American College of Cardiology/American Heart Association (ACC/AHA) does not recommend Vitamin K in patients with mechanical heart valve because Vitamin K will induce hypercoagulable state and increase the risk of prosthetic valve thrombosis and thromboembolism events. High dose vitamin K also will increase the risk of warfarin resistance as an impact of Vitamin K accumulation in liver and higher doses of warfarin are needed to reach the INR target level. ACC/AHA recommend Fresh Frozen Plasma to manage bleeding on mechanical heart valve (MHV) patient compared to a high dose of vitamin K. However, low dose of vitamin K can still be considered with FFP combination.[4]

European Society of Cardiology (ESC) Guidelines suggests low dose Vitamin K (1 mg/2mg) can be used if INR level > 6 with and higher dose (5 mg) if INR level >10. The oral route is preferable than intravenous to minimalize anaphylaxis reaction. Immediately reversed anticoagulation effect can only be done if there is major bleeding.[5] The International Society of Thrombosis and Hemostasis definitions of major bleeding in non-surgical and surgical patients are as follows: fatal bleeding and/or symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intraarticular or pericardial, or intramuscular with compartment syndrome and/or bleeding causing a fall in hemoglobin level of 2 g/dL (1.24 mmol/L) or more, or leading to transfusion of two or more units of whole blood or red cells.[6] ESC recommends using intravenous phrothrombin complex concentrate if available than using FFP because phrothrombin complex concentrate has short half-life.[5]

In this case, patient's gross hematuria was not a major bleeding because patient's hemoglobin level was reduced 2 mg/dL only and besides that, patient INR was 5.6 before warfarin was stopped. So, in this case, no procoagulant therapy was given to the patient. Because of no procoagulant therapy (e.g., Vitamin K) was given to the patient, gross hematuria continued until it was stopped on day 6 by itself. The long duration of gross hematuria was a stressful moment for the patient. However, with decent communication and education to the patient that immediate reversal anticoagulation effect can increase the risk of prosthetic valve thrombosis and thromboembolism events, the patient could accept her condition.

There are many complications associated with mechanical heart valve. These include thromboembolism, acute thrombotic occlusion, complications of long-term anticoagulation, prosthetic valve endocarditis, periprosthetic leakage, chronic hemolysis and reoperation. Acute thrombotic occlusion occurs primarily in patients with suboptimal anticoagulant therapy, which usually results when treatment is stopped or interrupted for a surgical procedure or medical condition. An acute obstruction is a life-threatening complication of mechanical valve prosthesis, and is caused by the formation of fresh clot or fibrous tissue overgrowth (pannus), or both. Ekim, et al. researched thrombosis on the prosthetic mitral valve. In this study about 83% of prosthetic mitral valve thrombosis was caused by thrombus only and the others caused by pannus formation and thrombus.[7]

When restarting warfarin therapy, the hypercoagulable state could be considered to occur in this patient. Bridging therapy with heparin is sometimes preferable to manage a hypercoagulable state that theoretically can happen when restarting warfarin therapy. In this case, the patient was given unfractionated heparin 3 days after stopping warfarin to prevent thromboembolism event because INR level's patient was quite low and as a bridging therapy when initiated warfarin again. Unfractionated heparin was chosen because it has the shortest half-life and protamine sulfate was available as its antidote. Neutralization of low molecular weight heparin (LMWH) is incomplete.[8]

Warfarin will reduce thrombin formation by intervening coagulation factor related to Vitamin K. However, warfarin also inhibits anticoagulation factor like Protein C and Protein S. Protein C has half-life for 6 hours but factor II and X for 72-96 hours so warfarin initiation will make an imbalance between procoagulation and anticoagulation factors in the blood. Higher warfarin doses will deplete Protein C but Factor II

and X have not yet reduced optimally. Therefore, it is critical to do overlap therapy or bridging therapy with unfractionated heparin or LMWH at least 48 hours until INR target is reached to prevent hypercoagulable state.[9,10] There were some thromboembolism case reports when initiating warfarin therapy. Binyim, et al. present a case with thromboembolism event happened on a patient with atrial fibrillation when starting warfarin as stroke prevention. On the 3rd day, warfarin dose was increased to quickly reached INR target, but unfortunately, this condition induced deep vein thrombosis in the patient. The patient did not use unfractionated heparin or LMWH as bridging therapy.[11] Other case reported by Charokopos, et al. there was a thrombosis on prosthetic aortic valve 2 days after initiating warfarin (4 mg/day) without using unfractionated heparin or LWMH as a bridging therapy.[9]

Procoagulant therapy should be given to mechanical heart valve patient if only there were a major or serious bleeding. When restarting warfarin, patient should be given bridging therapy to prevent hypercoagulable state.

References

1. Prashanth Panduranga, Mohammed Al-Mukhaini, Muhanna Al-Muslahi, Mohammed A Haque, Abdullah Shehab. Management dilemmas in patients with mechanical heart valves and warfarin-induced major bleeding. World J Cardiol 2012; 4: 54-59.
2. Radaelli F, Dentali F, Repici A, et al. Management of anticoagulation in patients with acute gastrointestinal bleeding. Dig Liver Dis 2015; 47: 621-627.
3. Opie LH and Gersh BJ. 2013. Drugs For The Heart. Elsevier Saunders: Philadelphia.
4. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2014; 129: 2440-2492.
5. Baumgartner H, Falk V, Bax JJ, 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J 2017; 38: 2739-2791.
6. Schulman S, Kearon C. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. J Thromb Haemost 2005; 3: 692-694.
7. Ekim H, Akbayrak H, Başel H, et al. Management of prosthetic mitral valve thrombosis. Eastern Journal of Medicine. 2005; 10: 10-14.
8. Katzung BG and Trevor AJ. 2015. Basic & Clinical Pharmacology 13th Ed. McGraw-Hill Education: San Fransisco.
9. Charokopos N, Antonitsis P, Artemiou P, et al. Acute mechanical prosthetic valve thrombosis after initiating oral anticoagulation therapy. Is bridging anticoagulation with heparin required? Interact Cardiovasc Thorac Surg 2009; 9: 685-687.
10. Rehman HU. Paradoxical Increased Risk of Thrombosis after Initiation of Vitamin K Antagonists in Thromboembolic Disease. J Clin Case Rep 2013; 3: 121.
11. Khalid A Binymin, Magda Nasher, and Dipti Patel. Warfarin-induced deep vein thrombosis. Int Med Case Rep J 2014; 7: 123-125.