



MANAGEMENT OF PT-INR IN PATIENTS OF MECHANICAL VALVE REPLACEMENT

Medical Science

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ABSTRACT

All patients with a mechanical valve replacement need lifelong anti-coagulation therapy with Warfarin. Some patients of Bioprosthetic valve also may require Warfarin therapy. 100 patients who underwent mechanical valve replacement at GSMC & KEM hospital, Mumbai since January 2017 till February 2019 and followed up in the outpatient department of the hospital were included in the study. Warfarin was started 48 hours post-surgery in all patients of valve replacement at 3mg/day. After 24 hours 5 ml of peripheral blood was collected and sent to the laboratory for PT (Prothrombin time) & INR (International normalized ratio) detection. During the period of study of 100 patients of mechanical valve replacement from January 2017 till February 2019 the PT-INR ranged from 1.2 to 6.5. No cases of thromboembolism were encountered during the period of follow up. Major bleeding episodes were seen in 3 patients (3%) during follow-up, 1 case of cerebral bleeding and 2 cases of gastrointestinal bleeding. Minor episodes of bleeding (subcutaneous bleed, epistaxis, gingival bleed) were seen in 21 cases. The American college chest physicians (ACCP) recommends VKA (Vitamin K Antagonist) therapy with a target INR of 2.5 (range 2.0 to 3.0) for mechanical aortic valves and target INR of 3.0 (range 2.5 to 3.5) for mechanical mitral valves.

KEYWORDS

Mechanical Valve replacement, Warfarin, Prothrombin time, International normalized ratio, Bleeding

INTRODUCTION

All patients with a mechanical valve replacement need lifelong anti-coagulation therapy with Warfarin. Some patients of Bioprosthetic valve also may require Warfarin therapy. Thrombotic and embolic complications and anticoagulation-related bleeding are by far the most prevalent contributors to morbidity and mortality after surgery for Valvular heart disease (VHD).^{1,2} The risk of thromboembolic complications is greatest during the first three months after surgery for both mechanical and bioprosthetic devices, with persistent life-long risk for patients with mechanical valves.^{3,4} The American college chest physicians (ACCP) recommends VKA therapy with a target INR of 2.5 (range 2.0 to 3.0) for mechanical aortic valves and target INR of 3.0 (range 2.5 to 3.5) for mechanical mitral valves. For patients who are at low risk of bleeding, the ACCP recommends adding an antiplatelet agent such as low-dose aspirin (50 to 100 mg/day) to VKA therapy.

The ACC/AHA Guidelines for the management of Patients with Valvular Heart Disease recommend VKA therapy with a target INR of 2.5 for patients with mechanical aortic valves, if no additional risk factors are present. Additional risk factors are defined as atrial fibrillation, prior thromboembolism, left ventricular dysfunction, or hypercoagulable state. For patients with mechanical mitral valves, older generation mechanical aortic valves, or risk factors in addition to any type of mechanical aortic valve, a target INR of 3.0 is recommended. Antiplatelet therapy at a dose of 75 to 100 mg/day is recommended in addition to warfarin for all patients with mechanical valves.

An estimated 100,000 patients worldwide undergo cardiac valve replacement due to diseases including rheumatic heart valves and degenerative valves.⁵ Warfarin effectively inhibits the synthesis of vitamin K cyclase, which is the most commonly used as anti-coagulant drug for patients after cardiac valve replacement.^{6,7}

MATERIALS AND METHODS :

100 patients who underwent mechanical valve replacement at GSMC & KEM hospital, Mumbai since January 2017 till February 2019 and followed up in the outpatient department of the hospital were included in the study. Aortic valve replacement (AVR) was done in 30 cases (19 males, 11 females), Mitral valve replacement (MVR) was done in 58 cases (30 males, 28 females) and Double valve replacement (DVR) was done in 12 cases (5 males, 7 females). The cases included 99 patients with rheumatic heart disease and 1 patient with infective endocarditis.

Age of patients operated ranged from 18 to 53 years. Mean age at operation was 32.74 years and ranged from 18 to 53 years. Valves implanted were 24 St. Jude Medical valves (SJM Valves 19-25 mm), 18 Medtronic ATS valves (ATS Valves 16-26 mm) in the Aortic position and 42 SJM valves (25-31 mm), 24 ATS valves (25-31 mm) and 4 Sorin valves in the mitral position.

Warfarin was started 48 hours post-surgery in all patients of valve replacement at 3mg/day. After 24 hours 5 ml of peripheral blood was collected and sent to the laboratory for PT-INR detection. The dosage of warfarin was adjusted according to the PT-INR values, as per guidelines given by ACC/AHA. The PT-INR test was repeated after 5 days, at time of discharge, 15 days later in the outpatient department and monthly thereafter if the dosage of warfarin is adjusted and PT-INR values are stable.

The patients were divided into a normal group who developed no warfarin related complications, those with bleeding episodes and embolism related complications.

Table 1:

Cases of bleeding, embolic complications and PT-INR		
Complications	Number of patients	PT-INR
Thromboembolic	0	-
Major bleeding episodes (cerebral, GIT bleed)	3	3.7 2
Minor bleeding complications (epistaxis, gingival bleed, subcutaneous bleed)	21	2.9 1.1
No complications	76	2 0.5

All the 100 patients were followed after mechanical valve replacement, 3 patients developed major bleeding episodes (3%), 21 had minor bleeding episodes (21%) and 76 patients had no complications (76%).

Table 2:

Patient characteristics			
Parameter	Normal	Bleeding	Thromboembolism
Gender			
Male	54	7	-
Female	46	17	-

Level of education			
Less than 10 th and	53	16	-
10 th std pass & more	47	8	-
Place of residence			
Urban	38	5	-
Rural	62	19	-

Statistical analysis Continuous variables are expressed as a mean $\pm$ standard deviation. Differences between groups were assessed by student t test or chi square test. P values < 0.05 were considered statistically significant.

RESULTS:

During the period of study of 100 patients of mechanical valve replacement from January 2017 till February 2019 the PT-INR ranged from 1.2 to 6.5. No cases of thromboembolism were encountered during the period of follow up. Major bleeding episodes were seen in 3 patients (3%) during followup, 1 case of cerebral bleeding and 2 cases of gastrointestinal bleeding. Minor episodes of bleeding (subcutaneous bleed, epistaxis, gingival bleed) were seen in 21 cases. Bleeding complications were seen in 6(20%) out of 30 cases of AVR, 15(25.86%) out of 58 cases of MVR and 3(25%) out of 12 cases of DVR. Bleeding episodes were seen in 7(12.96%) out of 54 males and 17(36.95%) out of 46 female patients. Bleeding episodes were commonly seen in patients whose level of education was less than 10th standard (30.18%) compared to those whose level of education was 10th standard or more (17.02%). Bleeding episodes were more commonly seen in people staying in rural areas who didn't have access to regular PT-INR monitoring (30.64%) as compared to people staying in urban areas with access to regular PT-INR testing (13.15%). PT-INR in 24 patients with bleeding episodes ranged from 1.9 to 6.7. The PT-INR in patients with major bleeding ranged from 3.7 ± 2 and in patients with minor bleeding episodes 2.9 ± 1.1 . The patients who did not develop bleeding or thromboembolic complications the PT-INR ranged between 2 ± 0.5 . A statistically significant difference was found between patients no bleeding complications and patients with minor bleeding complications.

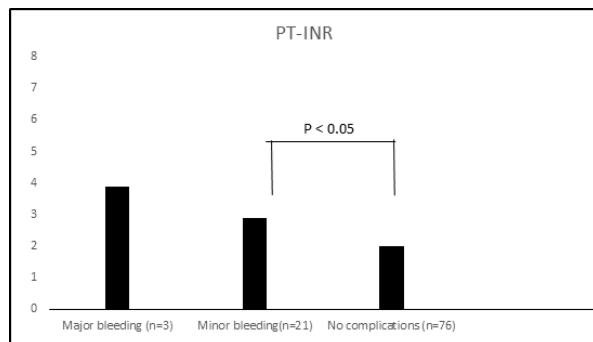


Figure 1 : PT-INR average values at the time bleeding complications developed

DISCUSSION

Rheumatic heart disease is one of the most common types of heart disease, the major causative factor of which is the valve damage caused by inflammation, which leads to problems in the process of transfusion of blood in the patient's heart, including ventricular hypertrophy and dyspnoea, while the severe form of the disease may pose a threat to the life of affected patients.^{8,9} Today, replacement of a diseased heart valve with a mechanical prosthesis is a routine procedure with a low perioperative morbidity and mortality. However, the potential risk of thromboembolism postoperatively is still a major concern for mechanical heart valve patients.¹⁰ Thromboembolism and bleeding complications account for approximately 75% of all the postoperative complications observed in mechanical heart valve patients. Warfarin treated patients are closely monitored, through measurements of their international normalized ratio (INR). An INR of > 3 (and especially > 4) often results in bleeding, while inadequate anticoagulation (INR < 2) enhances the risk for thrombotic events.¹²

The appropriate warfarin dose is influenced by numerous variables, including the vitamin K load in the patient's diet, hepatic function, comorbidities, concurrent medications, and CYP2C9 polymorphisms. Other factors limiting the use of warfarin are unpredictable and patient-specific dose responses, a delayed onset or delayed cessation of

action, the need to monitor anticoagulation, and many drug-drug and drug-food interactions.^{13,14,15} It has been shown that the risk of bleeding is directly proportional to the intensity of anticoagulant therapy and the amount of time the international normalized ratio (INR) is outside of the therapeutic target range.^{16,17} There are many drugs (i.e., sulfapyrazone, cimetidine, amiodarone) that inhibit the metabolic clearance of warfarin, thereby increasing the warfarin concentration. Poor fat absorption, hepatic dysfunction, fever and hyperthyroidism impair the synthesis/consumption balance of vitamin K-dependent coagulation factors. Cephalosporins enhance warfarin effect by inhibiting circulatory interchange of vitamin K without affecting the plasma level of warfarin. Anabolic steroids, clofibrate, isoniazid, tamoxifen, phenytoin and acetaminophen also increase the anticoagulant effect of warfarin due to an unknown mechanism.¹⁸ The PT-INR as preferable clinical indicators of anti-coagulant effects are able to reflect the degree of blood agglutination in patients, providing a basis for clinicians to propose treatment plans for patients.¹⁹

The risk of thromboembolic complications is greatest during the first three months after surgery for both mechanical and bioprosthetic devices, with persistent life-long risk for patients with mechanical valves. Furthermore, the presence of atrial fibrillation, a common arrhythmia in patients with valvular heart disease (especially if involving the mitral valve), also requires lifelong anticoagulation in the majority of patients.^{3,4}

The benefits of VKA therapy after mechanical valve placement are marked. When compared with no antithrombotic therapy in a 1994 meta-analysis, VKA therapy showed statistically significant reductions in the rate of major systemic embolization (from 4.0 to 1.0 events per 100 patient-years), total thromboembolism risk (from 8.6 to 1.8 events per 100 patient-years), and risk of valve thrombosis (from 1.8 to 0.2 events per 100 patient-years).²¹ VKA therapy was also superior to aspirin therapy alone for total thromboembolism risk (1.8 events per 100 patient-years; 95% confidence interval [CI], 1.7 to 1.9 versus 7.5 events per 100 patient-years; 95% CI, 5.9 to 9.4) and risk of valve thrombosis (0.2 events per 100 patient-years; 95% CI, 0.2 to 0.2 versus 1.0 events per 100 patient-years; 95% CI, 0.4 to 1.7).²¹

The risk of major bleeding in patients with mechanical valves treated with VKA therapy was found to be 1.2 to 2.6 events per 100 patient-years.^{10,20}

CONCLUSIONS:

PT-INR is useful for monitoring the dosage of Warfarin therapy in patients with mechanical and biological valve replacement, to adjust the dosage or stoppage of warfarin therapy in case of adverse complications like bleeding and thromboembolism.

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