Effect of different types of anticoagulants in the prevention of venous thrombosis in the operation of knee joint bone operation

Wensheng Xu[1,2], Tao Zhang[3], Zenghua Yang[2] and Lin Nie[1*]
[1]Qilu Hospital of Shandong University, Jinan City, Shandong, China
[2]First Affiliated Hospital of Baotou Medical College, Baotou City, Inner Mongolia, China
[3]Baotou Medical College, Baotou City, Inner Mongolia, China

Abstract: Deep venous thrombosis is one of the common complications after major surgery in the Department of Orthopedics. The selective knee replacement of the lower extremities is more likely to cause the occurrence of DVT. The most commonly used anticoagulants in the Department of Orthopedics now include low molecular weight heparin (LMWH), Rivaroxaban, ordinary heparin, aspirin and warfarin. At present, the clinical application of low molecular weight heparin is the most, and the effect is the most accurate. This study compared the efficacy and safety of three commonly used anticoagulants such as aspirin, LMWH and Rivaroxaban in preventing VTE after hip and knee arthroplasty, so as to provide a theoretical basis for selecting suitable anticoagulant drugs in clinic. It has been proved that LMWH has good efficacy and safety in the prevention of VTE after hip and knee arthroplasty and is a priority anticoagulant. Rivaroxaban can effectively control the occurrence of DVT and the drug is convenient, but it will increase the risk of bleeding and should be used carefully.

Keywords: Anticoagulant, Rivaroxaban, low molecular weight heparin, venous thrombosis, orthopedics operation.

INTRODUCTION

Deep vein thrombosis (DVT) is one of the common complications after major operation in Department of Orthopedics. Selective hip and knee replacement surgery on the lower extremities is more likely to cause the occurrence of DVT in the lower extremities, which mainly causes pain and swelling of limbs, and affects activities (Abdul *et al.,* 1993; Khaleel *et al.,* 2001). The important thing is that most of the pulmonary embolism is caused by the abscission of the DVT embolus, which is seriously endangering the patient's life. DVT and pulmonary embolism (PE) are collectively referred to as venous thromboembolism (VTE). The incidence of DVT in traumatic patients was 5%~56%. The clinical doctors have different experience and attention to the prevention and treatment of DVT, and often give experiential anticoagulant therapy (Ilizarov *et al.,* 1991; Hou *et al.,* 2015). However, it is not clear whether the routine use of preventive anticoagulant therapy should be used in patients with single fracture and good body condition. At the same time, the increase of bleeding volume and infection caused by anticoagulant can not be ignored. Deep vein thrombosis can occur abruptly. The most common symptoms are swelling, pain and increased soft tissue tension. Symptoms are aggravated after exercise, and can be relieved by rest or limb lifting (Delloye, 1992). There is a local press for pressure pain. If the deep vein thrombosis falls off, it can enter the dirty cavity through the inferior vena cava and then enter the lung with blood flow, leading to the pulmonary artery clots, leading to corresponding pulmonary embolism symptoms, such as refractory hypoxemia, chest pain, hemoptysis, dyspnea and so on. But it should be noted that most of the deep venous thrombosis and pulmonary embolism do not show obvious clinical symptoms (Chen *et al.,* 2009). Therefore, more than half of the patients with venous thromboembolism are missed.

Currently, the most commonly used anticoagulants in Department of Orthopedics include low molecular weight heparin (LMWH), Lev Shaaban, heparin, aspirin and warfarin (Chen *et al.,* 2015). At present, LMWH (low molecular weight heparin) is the most widely used in clinic, and the effect is the most precise. Rivaroxaban and Apixaban tablets are both direct Xa factor agents, and more and more in clinical application (Frierson *et al.,* 1994). Rivaroxaban has been proved to be effective and safe in the prevention of deep venous thrombosis after the replacement of the myeloid knee joint. Aspirin, as a traditional anticoagulant drug, has been found to have antiplatelet effect in a very early study, so it has a long history for anticoagulant therapy in Department of Orthopedics. In the current study, most of the new drug is mainly used to prevent deep venous thrombosis in artificial joint replacement patients.

Artificial joint replacement surgery, as a common joint surgery, especially in the pulp, the knee joints for pressure operation, patients with very high risk of venous thromboembolism (Kojimoto *et al.,* 1988; Konakondla *et al.,* 2017). There are reports in the literature, if not normal pressure during the perioperative period of anticoagulant therapy, the incidence of deep venous thrombosis after a week or two of the rate of 40%-60% and the conventional

**Corresponding author:* e-mail: xwsoye@126.com

pressure anticoagulation in patients within 3 months, there are still 1.3%-10% of the patients with deep venous thrombosis (Michaelf *et al.,* 1994; Lee *et al.,* 2015). Through the application of anticoagulant drugs, VTE (venous thrombosis) the incidence rate has been significantly reduced, but it has been reported that application of potent anticoagulant drugs can increase the risk of bleeding, hematoma, incision infection and even lead to reoperation and death, so anticoagulant ideal drug should be both efficacy and safety (Nishihira *et al.*,1998). This study compared the efficacy and safety of three commonly used anticoagulants such as aspirin, LMWH and Rivaroxaban in preventing VTE after hip and knee arthroplasty, so as to provide a theoretical basis for selecting suitable anticoagulant drugs in clinic.

MATERIALS AND METHODS

Cinical data

This study collected data of 190 patients with hip / knee replacement during hospitalization in 2016. There were 89 males and 101 females, the average age of 60.2±5.4. 126 cases of hip joint, including 41 cases of femoral neck fracture, 35 cases of femoral head necrosis, 32 cases of dysplasia of the hip, 18 cases of other diagnoses, 64 cases of knee joint, including 50 cases of osteoarthritis and 16 cases of rheumatoid arthritis. All patients were approved by Ethics Committee of our hospital and signed on the informed consent.

Admission criteria

Patients undergoing hip and knee arthroplasty for various reasons (including total hip, artificial femoral head replacement, total knee and Dan Wei replacement, initial replacement, refurbishment, etc.); The sex, age, weight and so on are not limited; There was no venous thrombotic disease before operation. Exclusion criteria: The history of thromboembolic disease, currently receiving anticoagulant therapy; Hemorrhagic disease or major bleeding history (such as Dunnei bleeding or gastrointestinal bleeding requiring transfusion; Severe liver disease; Coagulation dysfunction or anticoagulant contraindication.

Surgical methods

All knee arthroplasty was performed by an experienced joint surgeon. Hip replacement is performed by lateral approach. Total knee arthroplasty is performed by anterior median incision and anterolateral parolateral approach (Ferro *et al.,* 2011). Knee joint replacement is performed by anteromedial approach. Total knee arthroplasty is used for tourniquet (Ilyas *et al.,* 2017). The drainage tube was placed after the operation.

Grouping and data collection

The same basic preventive and physical precautions were taken in all patients. According to the use of anticoagulants, the patients were randomly divided into 3 groups. Aspirin group 61 cases, 12 hours after the operation, Aspirin Enteric-coated tablets 100mg, 2 times a day, for 6 weeks. Low molecular weight heparin (enoxaparin sodium) group of 69 cases, 12 hours after injection of enoxaparin endothelial 4000IU, 1 times / day for 12 consecutive days. Rivaroxaban group 60 cases, 12 hours after the operation, oral Rivaroxaban10mg, 1 times /day, for 12 days (Bousse *et al.,* 2007). The lower limbs, bleeding complications, including local complications such as incisional spots, hematoma and other complications, digestive system, cardiovascular and cerebrovascular system, urinary tract bleeding and bleeding after operation were observed. Color Doppler ultrasonography or lung scan was used to identify thrombus in suspected or possible patients (Ferro *et al.,* 2010). The follow-up was 6, 9, and 12 weeks after the operation.

STATISTICAL ANALYSIS

The statistical software SPSS was used to analyze it. The measurement data to mean standard deviation ($x\pm s$), Variance analysis was used in the group. The count data were expressed as percent and X^2 test was used among groups. The test level was $\alpha=0.05$ and $P<0.05$ was statistically significant.

RESULTS

General information

The analysis of general information on patients was shown in table 1. The difference of sex, age and body mass index between the three groups was not statistically significant and it was comparable.

The occurrence of DTV and PE

A total of 10 patients were diagnosed as DTV (Deep Vein Thrombosis), accounting for 5.2% of the total number of patients, 15 cases had swelling and pain of the lower extremities and no thrombus was found in color Doppler. All DTV patients were diagnosed with symptomatic PE (Pulmonary Embolism) in 2 cases and the incidence of 1% was not fatal. The 10 DTV patients received aspirin, patients in 5 cases, accounting for 8.1% of the patients received aspirin; low molecular weight heparin group 2 cases of DTV and symptomatic PE, without the occurrence of fatal PE; group Rivaroxaban DTV occurred in 3 cases, accounting for 5% of the patients received Rivaroxaban. There was no significant difference in the incidence between the three groups. There were 1 cases of symptomatic PE in the low molecular heparin group, and no PE patients in the other two groups. Due to the limitation of the number of cases, no statistical analysis could be done. Further large-scale clinical studies were needed.

Hemorrhage complication

A total of 17 cases of bleeding complications occurred in

Table 1: General clinical data

Group	Gender		Age	BMI (Body Mass Index)
	Male	Female		
Aspirin group (n=61)	15	46	68.2±9.5	21.5±3.2
Low molecular weight heparin group (n=69)	22	47	65.3±10.3	22.2±3.3
Rivaroxaban group (n=60)	17	43	67.5±12.4	22.8±2.9
F-measure	0.230		1.152	0.286
P	0.791		0.243	0.251

Table 2: The number of deep venous thrombosis after operation

Group	Cases	Proportions
Aspirin group (n=61)	5	8.1
Low molecular weight heparin group (n=69)	2	2.8
Rivaroxaban group (n=60)	3	5.0

Table 3: The number of pulmonary embolism after operation

Group	Cases	Proportions
Aspirin group (n=61)	0	0
Low molecular weight heparin group (n=69)	1	1.4
Rivaroxaban group (n=60)	0	0

Table 4: Complications of bleeding

Group	Incisional burnout	Proportion
Aspirin group (n=61)	3	0
Low molecular weight heparin group (n=69)	4	1.4
Rivaroxaban group (n=60)	6	0

Table 5: Loss of flow rate and hemoglobin

Group	Flow rate(ml)	Hemoglobin decline (g/L)
Aspirin group (n=61)	342.8±107.4	25.4±12.5
Low molecular weight heparin group (n=69)	375.1±149.6	26.7±11.6
Rivaroxaban group (n=60)	383.6±198.2	24.3±10.8

all patients, the incidence rate was 7.8%, of which 13 cases were located in the incisional spots, accounting for 6..8% of the total number of patients, 4 cases of bleeding events (2 cases of gastrointestinal bleeding, 1 cases of urinary tract bleeding, 1 cases of phlegm), the incidence rate was 2.1%. The aspirin group had 3 peri incisional speckles, which accounted for 4.9% of the patients receiving aspirin. In the low molecular weight heparin group, there were 4 cases of peri incisional speckles, the incidence of which was 5.7%. In group Rivaroxaban, 6 cases of burnout around the incision accounted for 10% of the group, and the difference in the incidence of bleeding complications between the three groups was statistically significant. See table 4. The decline in flow rate and hemoglobin is shown in table 5

DISCUSSION

Deep venous thrombosis (DVT) is a common serious complication in the Department of orthopedics, especially after hip and knee arthroplasty. Although the DVT itself shows only limb swelling and pain, it may endanger the patient's life if the embolus fall off and form in the lungs (Wang, 2015). Effective thromboprophylaxis for hip and knee replacement patients can reduce the overall incidence. The main purpose is to reduce the incidence of symptomatic DVT and PE and the morbidity and mortality caused by it. And the study confirmed that it could reduce the cost of medical care (Stanitski *et al.*, 1996; Shim *et al.*, 2010). Because of the high incidence of hip and knee replacement surgery after VTE, so VTE

active prevention is essential, but how to choose a safe and effective preventive measures, the problem is always ankle surgeons have to face, especially the use of potent anticoagulant drugs (such as low molecular weight heparin and Rivaroxaban) may increase the risk of bleeding and bleeding incidence of death. Therefore, preoperative DVT risk assessment is very important for every joint replacement patient (Simpson *et al.,* 2001). Through DVT risk factor assessment, we can identify high-risk patients who use strong anticoagulant drugs after operation, and choose mild anticoagulant drugs such as aspirin for low risk patients, so as to reduce the risk of bleeding.

Preoperative and postoperative factors affect the three conditions of thrombosis and progression. Hip prophylaxis should be carried out throughout the perioperative period, rather than relying solely on drug action (Wagner, 1977). It mainly includes basic prevention, physical prevention and drug prevention. Basic preventive measures: Preoperative training of active and passive effectively Du flexion and dorsiflexion of ankle joint, active and passive knee flexion hip joint; surgical operation to soft, fine, avoid intimal injury; minimize the duration of hip flexion compression femoral vein during operation; regulate the use of tourniquet; post operatively (Zhang *et al.,* 2016). Lift high limb, prevent deep venous reflux disorder. Physical precautions: intermittent pneumatic compression device, plantar vein vegetable and gradient pressure elastic stockings, etc., using mechanical pump principle to accelerate blood flow of lower limb vein, reduce blood stasis and reduce incidence of postoperative lower extremity (Delloye, 1992). Expert recommendation and drug prevention combined application, the use of physical prevention alone is only suitable for patients with abnormal coagulation disorders and high-risk bleeding risk (Ilizarov *et al.,* 1991; Hou *et al.,* 2015). It is still recommended to combine with drug prevention after bleeding risk reduction. For patients with or without physical prophylaxis, it can be prevented on the contra lateral side.

Drug prevention: At present, the main anticoagulants include Low-molecular-weight heparin (LMWH), warfarin, Rivaroxaban, dabiga group, aspirin and so on. The strong anticoagulants include LMWH, Rivaroxaban, dabiga group and so on and aspirin is a mild anticoagulant drug. In recent years, the study found that in the effective prevention and potent anticoagulant drugs tend to increase the incidence of bleeding complications and causes of death (Abdul *et al.,* 1993; Khaleel *et al.,* 2001; Vivakaran *et al.,* 2012). So the Department of orthopedics physicians must pay attention to evaluation of risk factors for bleeding, at the same time through the preoperative assessment of risk factors and risk factors of hemorrhage, guide the postoperative rational use of anticoagulant drugs, so as not to cause serious complications, prolong the hospitalization time, increase of medical expenses (Chen *et al.,* 2009). Although aspirin has been proven effective in preventing ischemic heart disease and cerebrovascular artery disease, its pharmacological mechanism is mainly to prevent platelet thrombosis in the artery, and to protect against venous thrombosis. In general, there is still a lot of controversy over whether aspirin can be used as a routine medication for the prevention of joint replacement (Zhang *et al.,* 2016). The anticoagulant effect of LMWH is affirmative, quick onset, constant dose and bioavailability of 90%. LMWH is currently recognized as a clinically recommended anticoagulant drug with good efficacy and safety (Simpson *et al.,* 2001). Until other patients are combined with severe renal insufficiency, other anticoagulants are selected. The clinical application of Rivaroxaban in the short time, few clinical reports, its effectiveness, safety and other related adverse reactions still need a large sample prospective clinical study on further study, and the drug needs to be imported, the price is relatively expensive, so it is widely used by certain restrictions.

CONCLUSION

Anticoagulants are recognized as the main VTE methods for prevention, and there are more options for anticoagulant prevention, but the preferred anticoagulants are not the same. So before starting VTE, it is necessary to assess the risk factors of DVT and the risk of bleeding, and strictly screens the taboos, so as to formulate effective and safe anticoagulant prevention programs, and closely monitor the corresponding signs and laboratory indicators in the course of drug use, in order to avoid serious consequences. This study shows that low molecular weight heparin has good efficacy and safety in the prevention of VTE after hip and knee arthroplasty, and is the first recommended anticoagulant. But it is not convenient to use outside the hospital, and the course of treatment is relatively insufficient. Preoperative assessment of patients with no high risk factors for DVT, and no contraindications to aspirin, can be used as anticoagulant. It is convenient, low price, long-term and relatively safe. Overall, Rivaroxaban can effectively control the occurrence of DVT and facilitate administration, but it will increase the risk of bleeding and should be used with caution.

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