

Anticoagulant effects of Rivaroxaban after surgical fixation of spinal fracture

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Abstract: In recent years, the concept of treatment after surgery in the department of orthopedics has changed from hemostasis to anticoagulant. This article analyses the safety and effectiveness of anticoagulants for prophylactic anticoagulants after spinal fractures. By analyzing the incidence of bleeding and VTE in 2 weeks after operation, there was no significant difference between the 2 groups ($P>0.05$), but the incidence of VTE in rivaroxaban group was significantly lower than that in control group. In conclusion, the rivaroxaban oral anticoagulants are stable, safe and easy to use. It significantly reduced the incidence of VTE after spinal fracture and nerve injury, and did not increase the risk of bleeding. It is an ideal type of prophylactic anticoagulant after the operation of spinal fracture, which is worthy of further clinical study.

Keywords: Rivaroxaban, anticoagulant drugs, spinal fractures, venous thromboembolism.

INTRODUCTION

With the development of medical science, the understanding of disease in the medical field is constantly deepening and changing (Ilizarov, 1989; Chen *et al.*, 2015). In recent years, the Department of orthopedics surgery treatment concept has been transformed into hemostasis by anticoagulation, clinicians are also using a variety of methods to prevent perioperative venous thromboembolism (VTE), physical measures such as stretching exercise, limb muscle pressure pump base (Ilizarov, 1969; Khaleel *et al.*, 2001). Drug measures such as low molecular weight heparin, warfarin, and new oral dosage forms of rivaroxaban, Apixaban and so on (Liu *et al.*, 2015). These measures is to reduce the incidence of VTE, improve the safety of clinical treatment, has been recognized and recommended especially department of orthopedics trauma and joint professional scholars (Ilizarov, 1990; Liu *et al.*, 2017). But because of concerns about the risk of bleeding after spinal operation anticoagulant potential to a certain extent, compression injury (Kojimoto *et al.*, 1988; Wang, 2015), epidural hematoma formation concerns will cause the nerve so standardized treatment after spinal surgery is not required prophylactic anticoagulation, and after spinal surgery should be preventive anticoagulation is still a need for further researches

As a new type of oral anticoagulant, rivaroxaban has been paid more and more attention to by more and more clinicians because of its own characteristics (Michael *et al.*, 1994). Its application in preventing deep vein thrombosis after joint replacement has achieved good clinical effects and patient satisfaction (Wagner *et al.*,

1977). However, the application of it after spinal surgery is still lack of large sample clinical confirmation (Khaleel *et al.*, 2001). In this paper, 120 cases of spinal fracture and nerve injury in our hospital in 2016 were taken as an example. We studied the effect of anticoagulation therapy, and analyzed the safety and efficacy of anticoagulant drug rivaroxaban for postoperative anticoagulation after spinal fracture surgery.

MATERIALS AND METHODS

General information

A retrospective study of 120 cases of thoracolumbar fracture with nerve injury in our hospital during the above period was reviewed. Inclusion criteria: (1) Spinal fracture with different degree of nerve injury, no other combined injury. (2) There was no history of anticoagulant drug use in the past, the function of coagulation before operation was normal, and VTE was excluded by color Doppler ultrasound of lower extremity. (3) The posterior vertebral decompression fracture was treated with pedicle screw fixation (4) Rivaroxaban anticoagulant or no anti-coagulant of any drug was taken after operation. (5) The data of color Doppler ultrasound of 10~14 D two lower limbs were obtained. The cases in the group were divided into group rivaroxaban and control group according to whether oral rivaroxaban was taken after operation. All patients were approved by Ethics Committee of our hospital and signed on the informed consent.

Exclusion criteria

Patients had previous history of varicose veins or thrombosis. Preoperative ultrasound examination of the lower extremities is abnormal, such as venous thrombosis or venous insufficiency. Preoperative blood indexes were

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abnormal, such as platelet count or liver function abnormality. Patients refused to attend for personal reasons. After oral rivaroxaban, the patient developed nausea, vomiting, anorexia, abdominal pain and other obvious digestive system reactions. Patients had subcutaneous fatigue spots, bleeding of silver teeth and black stools. During the test, patients died or voluntarily demanded to quit because of personal reasons. According to the principle of randomization, it was divided into the control group and the experimental group. According to the actual completion of the experiment and the above selection criteria, 112 effective cases were finally obtained, including 57 cases in the rivaroxaban experimental group and 55 cases in the blank control group.

Experimental method

After admission, the patients were tested for their coagulation function, cardiopulmonary function and two lower extremity venous color Doppler ultrasound. In the admissions since 4~6 h surgical treatment, were treated with posterior laminectomy fracture with pedicle screw fixation, intertransverse fusion with. The 2 groups were treated with routine intravenous drip of antibiotics 24~48 h after operation, and the drip into dexamethasone injection 10 mg 1 times /day, a total of 3day (D), and the incision drainage tube was removed on the third day after operation. The active drug control in the perioperative period of patients with hypertension and diabetes was stable.

VTE prevention programs: rivaroxaban group 6~10 h after operation to 10 mg oral rivaroxaban 1 /d to 14 d after surgery, withdrawal, early active and passive limb exercise guidance after surgery, lower extremity muscle strength allows the tube after start wearing a brace ambulation removed 3 D drainage after operation, at the same time with 2 times a day the pneumatic pump trousers treatment. The control group did not use any anticoagulant drugs, and the other measures were the same as those in the rivaroxaban group. The 2 groups were examined by 10~14 d after 10~14 lower extremity venous color Doppler ultrasound screening.

Observation index includes: (1) The time of operation and the amount of bleeding during the operation; (2) The rate of blood transfusion and the amount of blood transfusion (red blood cell and plasma) during the perioperative period; (3) Incision drainage, surgery after 3 D of the total flow; (4) The incidence of postoperative bleeding, including epidural hematoma, incision subcutaneous hematoma, incision bleeding, skin ecchymosis and mucosal bleeding, gastrointestinal bleeding, limb muscle hemorrhage, intracranial hemorrhage; (5) The incidence of VTE at 2 weeks after operation included double superficial veins, deep veins and venous thrombosis and pulmonary embolism.

STATISTICAL ANALYSIS

The data were processed by SPSS 18 statistical software. The data were expressed as $\bar{x} \pm s$. T test was used for comparison between groups. The percentage data was expressed by percentage. χ^2 test was used for comparison between groups and the difference was statistically significant between $P < 0.05$.

RESULTS

Comparison of operation conditions

The operation was completed successfully in all 2 groups. There was no significant difference between the 2 groups of operation time, intraoperative bleeding, intraoperative blood transfusion rate and intraoperative blood transfusion ($P > 0.05$), and table 1. Bleeding events in rivaroxaban group occurred first days after incision bleeding in 2 cases, after second days subcutaneous hematoma occurred in 1 cases, the control group after first days of incision bleeding in 3 cases, second days after surgery incision bleeding in 2 cases, incision hemorrhage were treated with incision compression bandage, subcutaneous hematoma give a syringe of hematoma after bandaging and treatment effect were good. The 2 groups had no epidural hematoma, skin ecchymosis and mucosal bleeding, gastrointestinal bleeding, limb muscle hemorrhage, intracranial hemorrhage.

VTE occurrence

There was no symptomatic VTE in group rivaroxaban. In the control group, there were 1 case of chest pain and chest pain after seventh days of operation. Blood oxygen saturation 72.4% and oxygen partial pressure 71mm Hg (1 mm Hg = 0.133k Pa) were found in the arterial blood gas analysis. The pulmonary artery CTA (Computed Tomography Angiography) confirmed the right inferior pulmonary embolism. The left femoral deep vein, the posterior tibial vein, the right popliteal vein and bilateral intramuscular venous thrombosis were found by bedside ultrasound. In the control group, 1 cases of left leg and left foot swelling occurred on the ninth day after operation, and the left femoral deep vein, the posterior tibial vein, the fibula vein and the double calf intermuscular venous thrombosis were examined by vascular color Doppler ultrasound and the anticoagulant, antiplatelet and blood stasis removing stasis were given, and the thrombus was rechecked after 6 weeks. For the patients without VTE symptoms, 10~14 d after surgery was used to screen the two lower extremities venous color Doppler ultrasound: in group rivaroxaban, 1 cases were formed by intermuscular venous thrombosis in group rivaroxaban, 2 cases of fibula thrombosis and 3 cases of intermuscular venous thrombosis in the control group.

Postoperative flow rate

There was no significant difference in the incidence of

Table 1: Comparison of operation conditions

Group	Operation time /min	Amount of bleeding /m L	Blood transfusion/case	Plasma /m L	Erythrocyte transfusion /IU
Experimental group (n=57)	118.5±21.4	550.6±81.2	21(57)	0~42(168.1±51.2)	0~6(1.4±0.3)
Control group (n=55)	115.3±25.6	562.2±91.5	18(55)	0~550(142.3±65.7)	0~6(1.5±0.2)

Table 2: Postoperative flow rate

Group	Postoperative flow rate /m L	Hemorrhagic event	VTE
Experimental group (n=57)	431.7±65.4	3	4
Control group (n=55)	451.5±53.2	2	8
p value	0.574	0.945	0.014

Table 3: Numerical comparison of prothrombin time after operation

Prothrombin time	Experience group	Control group	t value	p value
Preoperative	9.54±1.21	9.64±1.22	0.65	0.41
1 day after the operation	9.12±1.03	9.46±1.18	0.89	0.56
6 days after the operation	10.47±1.56	9.84±1.47	2.14	0.03
12 days after the operation	10.55±1.84	9.05±1.63	2.56	0.01

Table 4: Comparison of fibrinogen value after operation

Fibrinogen	Experience group	Control group	t value	p value
Preoperative	3.17±1.02	3.58±1.55	0.87	0.41
1 day after the operation	4.58±1.56	5.47±1.28	0.51	0.58
6 days after the operation	4.51±1.27	6.51±1.40	0.41	0.03
12 days after the operation	4.14±1.15	6.47±1.64	0.47	0.01

Table 5: Comparison of D-Dimer values after operation

D-Dimer	Experience group	Control group	t value	p value
Preoperative	154.27±55.6	164.3±45.17	0.34	0.74
1 day after the operation	1551.3±417.6	1357.6±426.7	1.25	0.34
6 days after the operation	1378.6±322.4	1579.2±347.5	1.57	0.05
12 days after the operation	1157.2±304.5	1467.3±308.2	2.45	0.01

bleeding events and the occurrence of VTE after operation, the incidence of postoperative bleeding and bleeding events between the 2 groups ($P>0.05$), but the incidence of VTE in group rivaroxaban was significantly lower than that in the control group ($P<0.05$). There was no significant difference in the incidence of VTE (table 2).

DISCUSSION

In the application of prophylactic anticoagulation after spinal surgery is still a controversial issue, supporters consider high-risk and high mortality of perioperative VTE (Abdul *et al.*, 1993), especially pulmonary embolism of deep vein thrombosis secondary to fall off, the event often leads to the death of the patient, so after the operation should be timely use of preventive medicine at the same time with anticoagulation, physical measures to reduce the risk of VTE (Frierson *et al.*, 1994; Fang *et al.*, 2017). While opponents consider anticoagulation itself is

a potential risk of bleeding, worried after spinal surgery using drug anticoagulation may lead to intraspinal hemorrhage, incision hemorrhage or hematoma (Dong *et al.*, 2016), mucosa or gastrointestinal bleeding, limb muscle bleeding, especially worried about the hematorrhachis formation of epidural hematoma. Due to spinal cord and cauda equina or nerve root compression, irreversible damage, so that after spinal operation only by physical measures to prevent VTE Against the preventive use of anticoagulants (Ilizarov *et al.*, 1991; Delloye 1992). Based on the above arguments, this study observed the clinical curative effect of 2 kinds of scheme of thoracolumbar spine with nerve injury patients after fracture prevention of VTE, analyzes the necessity of using spinal fracture after operation, preventive anticoagulation efficacy and safety, hoping to provide some reference for the formulation of anti coagulation scheme after spinal surgery (Eralp *et al.*, 2004).

The three major risk factors for VTE are hypercoagulable state of blood, injury of blood vessel wall and stagnation of venous blood flow, and large surgery in Department of orthopedics is a very high risk factor (Paley *et al.*, 1991). The operation of the thoracolumbar fracture with nerve injury is not only a major operation in the Department of orthopedics, but also with the injury of bone and soft tissue (Wang *et al.*, 2015). There is a high risk of VTE after the operation (Simpson *et al.*, 2001). As (1) Trauma and surgical trauma of spinal fractures cause the body to be in stress state. The adhesion and aggregation of platelets increase significantly, and the coagulation system is activated, resulting in hypercoagulable state of blood.(2)Fracture trauma and surgical trauma caused damage to the vertebral vein system and the intramuscular vessels in the paravertebral muscles, and the normal structure of a large number of vascular walls was destroyed.(3)Posterior spinal surgery is mostly prone position. Chest and abdominal compression leads to increased intrathoracic and intraperitoneal pressure and caval pressure. Prone position pads also have certain compression on the iliac fossa and groin, resulting in obstruction of venous return in the pelvic cavity and the lower extremities.(4)Spinal fracture and nerve injury patients weakened limb muscles, muscle vein pump function also weakened or lost, and postoperative bed rest, patient pain is not willing to exercise, resulting in venous circulation slowed down or stasis.(5) Thoracolumbar fractures of posterior surgery more domestic general anesthesia, but anesthesia can cause postoperative blood viscosity increased, and significantly increase the incidence rate of VTE. Therefore, the thoracolumbar spine fracture complicated with nerve injury postoperative prophylactic anticoagulation is necessary, and the study found that only the use of physical measures to prevent thrombosis of the control (Stanitski *et al.*, 1996) group after 2 weeks, the incidence rate of VTE was significantly higher than that in group rivaroxaban prophylactic anticoagulation, the only physical prevention measures is also insufficient, it is necessary at the same time using preventive medicine anticoagulation.

CONCLUSION

As a typical representative of anticoagulants in the new oral dosage form, rivaroxaban has its own unique advantages. Its pharmacodynamics is stable, its metabolites are not bioactive, and have little interaction with non steroidal anti-inflammatory drugs and platelet aggregation inhibitors. No obvious bleeding time is prolonged after clinical observation, but it is still not recommended for postoperative thrombosis prevention. In a word, rivaroxaban and other new oral dosage anticoagulant efficacy stability, high safety, convenient use, can significantly reduce the thoracolumbar fracture complicated with nerve injury. The incidence of postoperative VTE, and did not increase the risk of

bleeding is a kind of prophylactic anticoagulation spinal fracture postoperative ideal, worthy of further study.

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