Effect of safflower injection on lower limb fracture healing as well as blood viscosity and blood coagulation function

Ya-Zhong Wang¹, Yun Wen²

¹Department of Orthopaedics, Beijing Fengsheng Special Hospital of Traditional Medical Traumatology and Orthopaedics, Beijing, 100140, China
²Orthopaedics Department No. 2, Xiangdong District People’s Hospital of Pingxiang City Jiangxi Province, 337016, China

Abstract

Objective: To analyze the effect of safflower injection on lower limb fracture healing as well as blood viscosity and blood coagulation function. Methods: A total of 118 patients with fracture of lower limb were randomly divided into observation group and control group (n=59), control group received conventional surgical treatment, observation group received surgery + postoperative safflower injection treatment, and then differences in serum content of bone turnover indexes and bone metabolism indexes as well as levels of thrombelastogram parameters and blood coagulation function indexes were compared between two groups after 1 month of treatment. Results: Bone turnover indexes sBAP, PINP and BGP content in serum of observation group after 1 month of treatment were higher than those of control group while sCTX, sTAP and TRAP-5b content were lower than those of control group; bone metabolism indexes Ca²⁺ and 25-OH-VitD content in serum were higher than those of control group while P, PTH and β-Ca²⁺ content were lower than those of control group; thrombelastogram parameters R time and K time were longer than those of control group while MA value, G value and angle level were lower than those of control group; blood coagulation function indexes PLT, FIB and D-D content in serum were lower than those of control group while PT, APTT and TT levels were higher than those of control group. Conclusions: Safflower injection can promote postoperative fracture end healing in patients with fracture of lower limb, and also plays a positive role in reducing blood viscosity and optimizing blood coagulation function.

1. Introduction

Fracture of lower limb is the most common clinical type of fracture, there is the risk of postoperative poor blood supply in fracture end and slow fracture healing, and meantime, as a result of the surgical stimulation and lower limb immobility, the incidence of postoperative deep venous thrombosis and embolic events of important organs increases[1,2]. The timely treatment of promoting blood circulation and reducing blood viscosity after fracture operation can furthest accelerate fracture healing, avoid thromboembolism and other accidents. Safflower injection is the common Chinese patent medicine for prevention of thrombosis, has the effect of activating blood circulation and stimulating meridians as well as removing blood stasis and easing pain, and modern research has also confirmed that the active components of safflower injection can inhibit platelet activation and inhibit thrombosis[3]. At present, some scholars recommend the application of safflower injection in postoperative adjuvant treatment of patients with fracture, but there is still not much research about its specific effect. In the study, safflower injection was added in postoperative treatment of patients with fracture of lower limb in our hospital, and its roles in promoting patients’ fracture healing, regulating blood viscosity and the body's blood coagulation function and other aspects were mainly observed.

2. Materials and methods

Corresponding author: Yun Wen, Orthopaedics Department No. 2, Xiangdong District People’s Hospital, Pingxiang City, Jiangxi Province, 337016, China.
Tel: 010-66067455; 13651094835
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2.1. General information

A total of 118 patients with lower limb fracture who received surgical treatment in my hospital between January 2014 and January 2016 were included, and the inclusion criteria were: (1) with clear fracture under X ray; (2) with fracture for the first time in last six months; (3) < 70 years old; (4) patients signed informed consent. Exclusion criteria were: (1) with chronic fracture of lower limb; (2) with severe liver and kidney dysfunction; (3) with blood coagulation disorders; (4) those who took drugs that led to osteoporosis for a long time. 118 patients were included in the study and divided into observation group and control group (n=59) according to random number table. Control group included 31 male cases and 28 female cases, they were 24-68 years old and (45.93±6.12) years old in average, and the types of fracture were: 24 cases with fracture of tibia, 19 cases with fracture of fibula and 16 cases with fractures of both tibia and fibula; observation group included 33 male cases and 26 female cases, they were 22-69 years old and (44.76±6.09) years old in average, and the types of fracture were: 25 cases with fracture of tibia, 20 cases with fracture of fibula and 14 cases with fractures of both tibia and fibula. The two groups of patients showed no statistically significant difference in the distribution of gender, age and types of fractures (P>0.05) and they were comparable.

2.2. Treatment methods

Both groups of patients received open reduction and internal fixation for fracture, the control group received routine postoperative antibiotics for 2-3 d to prevent infection, and patients with severe pain could receive reasonable anti-inflammatory analgesic drugs according to the degree of pain. Observation group received routine + postoperative safflower injection therapy, specifically as follows: safflower injection (Tonghua Guhong Pharmaceutical Co., LTD., approved by Z22023866) 30 mL in 250 mL of normal saline, intravenous drip, 1 time/d, 2 weeks as a course of treatment, for at least two courses of treatment. Anti-infection and analgesia therapy were the same as those of control group.

2.3. Observation indexes

2.3.1. Serum indexes

After 1 month of treatment, 3 mL of fasting cubital venous blood was collected from two groups of patients and centrifuged at high speed to get supernatant and cryopreserve it in -80 °C refrigerator for test, and the specific detection indexes were as follows: (1) bone turnover indexes: bone-specific alkaline phosphatase (sBAP), C-terminal telopeptide of type I collagen (sCTX), total alkaline phosphatase (sTAP), N-terminal propeptide of type I tropocollagen (PINP), osteocalcin (BGP) and tartrate-resistant acid phosphatase-5b (TRAP-5b). (2) Bone metabolism indexes: full-automatic biochemical analyzer was used to determine serum calcium (Ca²⁺), phosphorus (P), 25-hydroxy-vitamin D (25-OH-VitD), parathyroid hormone (PTH), β-collagen degradation product (β-CTX) content. (3) Blood coagulation indexes: semi-automatic coagulometer was used to detect the platelet (PLT), fibrinogen (FIB), D-dimer (D-D), prothrombin time (PT), activated partial thromboplastin time (APTT) and thrombin time (TT).

2.3.2. Thrombelastogram

After 1 month of treatment, 2 mL of peripheral venous blood was collected from patients, thromboelastography was used to obtain thrombelastogram, and the R time, K time, MA value, G value, angle and other main parameter values were recorded.

2.4. Statistical methods

Data in the study was input in software SPSS23.0, measurement data comparison between two groups was performed by t test and P<0.05 indicated statistical significant differences.

3. Results

3.1. Bone turnover indexes

sBAP, PINP and BGP content in serum of observation group were significantly higher than those of control group while sCTX, sTAP and TRAP-5b content were significantly lower than those of control group (P<0.05), shown in Table 1.

3.2. Bone metabolism indexes

Ca²⁺ and 25-OH-VitD content in serum of observation group were significantly higher than those of control group while P, PTH and β-CTX content were significantly lower than those of control group (P<0.05), shown in Table 2.

3.3. Thrombelastogram

R time and K time of observation group were significantly longer than those of control group while MA value, G value and angle level were significantly lower than those of control group (P<0.05), shown in Table 3.

3.4. Blood coagulation indexes

PLT, FIB and D-D content in serum of observation group were significantly lower than those of control group while PT, APTT and TT levels were significantly higher than those of control group (P<0.05), shown in Table 4.
4. Discussion

Fractures of lower limb are clinically common, and the most common treatment for them is open reduction and internal fixation. At present, many studies have found that different postoperative interventions can directly influence the fracture healing and internal environment in patients\[4,5\]. Traditional postoperative fracture intervention is only using antibiotics to prevent infection, and providing analgesic drugs according to the pain degree in patients only when necessary, but postoperative blood supply obstacles in fracture end and difficult fracture healing still occur in many patients. Safflower injection is the current popular Chinese patent drug that can promote blood circulation to remove blood stasis as well as relieve swelling and pain. The study of Liu et al\[6\] shows that safflower injection can contribute to the postoperative rehabilitation of patients with multiple fractured ribs. Therefore, some scholars propose to add the drug in postoperative routine intervention in patients with fractures, but the proposal has not been clinically popularized at present. In order to define the exact effect of safflower injection in promoting postoperative rehabilitation of patients with fracture, safflower injection was early applied in patients with fracture of lower limb in our hospital after operation, and the study was mainly conducted from three aspects: fracture healing, blood viscosity and blood coagulation function.

Fracture end healing is affected by osteoclast/osteoblast balance and a variety of serum factors, the levels of bone turnover and bone metabolism factor in the blood circulation can intuitively reflect the healing process of patients with fracture, their changes are before bone mineral density, their specificity and sensitivity are both higher than those of bone mineral density, and they are the widely accepted clinical indexes to know the conditions of fracture healing\[7,8\].

In the study, serum levels of bone turnover and bone metabolism indexes of two groups of patients were studied at first after one month of treatment. BAP, sCTX, sTAP, PINP, BGP and TRAP-5b are the bone turnover factors studied in depth at present, and it was found in the study that sBAP, PINP and BGP content in serum of observation group were higher while sCTX, sTAP and TRAP-5b content were lower after 1 month of treatment. SBAP and BGP are the important markers reflecting osteoblast activity, and PINP is positively correlated with the bone mineral density in the body. With the increase of bone resorption, sCTX concentration rises, sTAP and TRAP-5b are released by osteoclasts, and they are one of the specific markers of the bone resorption\[9,10\]. The above results indicate that postoperative adjuvant safflower injection therapy can accelerate the osteogenic activity and promote fracture healing in
patients with fracture. In respect of bone metabolism indexes, Ca\(^{2+}\) and 25-OH-VitD content in serum of observation group were higher while P, PTH and \(\beta\)-CTX content were lower after operation. Ca\(^{2+}\) and 25-OH-VitD are the necessary materials for osteogenesis, it is known that PTH can lower blood calcium levels and improve blood phosphorus levels, and high level of \(\beta\)-CTX indicates that bone resorption increases\(^\text{[11,12]}\). The research results show that the postoperative application of safflower injection can promote the fracture end healing in patients with lower limb fracture. Lower-extremity deep venous thrombosis is the most common complication in patients with lower limb fracture, and it mainly caused by surgical trauma stress and postoperative long-term immobility-induced blood viscosity increase, etc. Lower extremity deep venous thrombosis is an important cause of pulmonary embolism, cerebral infarction and so on, and therefore, optimizing coagulation system function and reduce the blood viscosity in time is quite necessary for patients with fracture\(^\text{[13]}\). Thrombelastogram is a “gold standard” that can objectively reflect the patients’ blood coagulation state and predict the occurrence of long-term thromboembolic events\(^\text{[14,15]}\). It was found in the study that peripheral venous blood thrombelastogram parameters R and K time of observation group were longer while MA value, G value and angle level were lower after 1 month of treatment, which is consistent with the effects of anticoagulant drugs reported in previous literatures, and indicates that the postoperative application of safflower injection can play a positive role in regulating patients’ blood viscosity and inhibiting the lower-extremity venous thrombosis. Further detection of blood coagulation function indexes PLT, FIB, D-D, PT, APTT and TT levels showed that PLT, FIB and D-D content in serum of observation group were lower while PT, APTT and TT levels were higher after treatment, they prove the anticoagulant effect of safflower injection once again, and related research shows that it may be related to their anti-platelet aggregation function\(^\text{[16]}\).

To sum up, it is concluded as follows: Safflower injection can promote postoperative fracture end healing in patients with fracture of lower limb, also plays a positive role in reducing blood viscosity and optimizing blood coagulation function, and is worth popularization and application in clinical practice in the future.

References


