International Journal of Surgery 44 (2017) 324–328

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

Original Research

Safety and effectiveness of argatroban versus heparin for preventing venous thromboembolism after lumbar decompressive surgery☆

Ying Guo [a, b], Zhongwen Zou [b], Lianshun Jia [a, *], Zhi Huang [b], Xiong Yun [b], Guo Xing [b]

[a] Department of Spine Surgery, Changzheng Hospital of Second Military Medical University, Shanghai, PR China
[b] Department of Orthopedic Surgery, NO.187 Hospital of CPLA, Haikou, Hainan, PR China

HIGHLIGHTS

- In this work, we evaluated the safety and effectiveness of argatroban for the prevention of venous thromboembolism (VTE) after posterior lumbar decompressive surgery.
- The result of our study showed that the incidence of DVT is relatively low in Chinese patients undergoing posterior lumbar surgery.
- The therapeutic efficacy of argatroban is similar to LMWH for preventing postoperative VTE on posterior lumbar surgery.
- To the best of our knowledge, this is one of the few articles about use argatroban as an antithrombotic drug after spine surgery.

ARTICLE INFO

Article history:
Received 25 April 2017
Received in revised form
4 July 2017
Accepted 5 July 2017
Available online 8 July 2017

Keywords:
Argatroban
Heparin
Lumbar vertebrae
Venous thromboembolism

ABSTRACT

Background: To evaluate the safety and effectiveness of argatroban for the prevention of venous thromboembolism (VTE) after posterior lumbar decompressive surgery.
Methods: Included in this retrospective study were 556 patients who underwent posterior lumbar decompressive surgery for trauma and degenerative diseases. They were divided into two groups: argatroban group (n = 274), and low molecular weight heparin (LMWH) group (n = 282). The occurrence of postoperative venous thrombosis and complications including hemorrhage and allergic reaction was compared between the two groups. Neurological and clinical outcomes in terms of Visual Analogue Scale (VAS) and the Oswestry Disability Index (ODI) were assessed before operation and at 6 and 12 months after operation.
Results: Postoperative venous thromboembolism (VTE) occurred in seven patient. No pulmonary embolism (PE) occurred in any patient. Thrombosis occurred in 3 cases (1.0%) and bleeding in 1 case (0.04%) in argatroban group vs. 4 (1.4%) and 4 (1.4%) in LMWH group, showing no significant between the two groups ($P > 0.05$). There was significant reduction in the severity of back and leg pain (VAS $P < 0.05$) and significant improvement in the patient quality of life (ODI, $P < 0.05$) 6 months and 1 year after operation, showing no significant difference between the two groups ($P > 0.05$).
Conclusions: Argatroban proved to be equally effective as LWMH for anticoagulation therapy. Both drugs exhibited a similar preventive effect against postoperative VTE after posterior lumbar spine surgery, without increasing the risk of postoperative bleeding. The neurological and clinical outcomes are satisfactory and similar between the two pharmacological methods.

1. Introduction

Venous thromboembolism (VTE) is a significant cause of postoperative morbidity and mortality following orthopedic surgery, especially joint arthroplasty. However, little is known about VTE in spine surgery. Although the clinical incidence of VTE and complications is relatively low with spine surgery, special attention needs to be paid to the primary prevention of VTE to avoid serious consequences [1]. Although several pharmacological and mechanical methods have achieved good clinical outcomes, there are no consensus guidelines for anticoagulant therapy after spine surgery. Low molecular weight heparin

☆ This work was fulfilled by Department of Orthopedic Surgery, NO.187 Hospital of CPLA.

* Corresponding author. No.415, Fengyang Road, Huangpu District, Shanghai, PR China.
E-mail address: 7638555@qq.com (L. Jia).

http://dx.doi.org/10.1016/j.ijsu.2017.07.031
1743-9191/

(LMWH) is considered the gold standard and recommended by the American College of Chest Physicians (ACCP) for spine surgery [2], but some serious adverse effects such as heparin-induced thrombocytopenia (HIT) have limited its use. Argatroban is a synthetic thrombin inhibitor, but its efficacy for spine surgery and assessment on postoperative safety has rarely been reported. The objective of this study is to compare LMWH and argatroban for preventing VTE after lumbar decompressive surgery, and then evaluate the safety and effectiveness of argatroban for the prevention of VTE.

2. Materials and methods

This study was approved by the Institutional Review Broad of the hospital. Written informed consent was acquired from each patient. A total of 556 patients who underwent lumbar surgery and needed spinal decompression due to trauma and degenerative diseases between August 2013 and June 2016 were included in this study. The exclusion criteria were: 1): patients with deep vein thrombosis (DVT) before surgery; 2) patents using anticoagulants such as aspirin and warfarin for other diseases; 3) patients younger than 18 years; and 4) patients with a history of hepatic impairment, renal/liver insufficiency, acute infections, active tuberculosis and malignant tumors. Accordingly, the 556 included patients were divided into two groups: argatroban group (n = 274), and LMWH group (n = 282). The initial time of medication was 6–8 h after surgery. From the first day after surgery, patients in argatroban group were treated with intravenous infusion of 10 mg argatroban within 2 h bid with a micro-pump. Patients in LMWH group received subcutaneous injection of 2125 U LMWH 6 h after surgery followed by 4250 U qd. The treatment in both groups lasted 7–14 days until the patients were able to ambulate independently. Besides, all patients wore thigh-high compression stockings with a sequential compression device (SCD) after surgery, and they were also told to do active dual straight-leg-raising exercise, or passive exercise for patients who suffered nerve impairment.

Doppler ultrasound on the bilateral deep veins of the lower extremities was performed before surgery, at 7 and 14 days after surgery, and at 4 weeks after ending of the treatment. Patients were monitored daily for symptoms and signs of DVT or pulmonary embolism (PE), including pain and swelling of the lower extremity, and difficulty in breathing. A definite diagnosis of DVT was made by Duplex ultrasound, and CT was also used to evaluate suspected PE events after surgery.

Bleeding was classified as two types: severe and non-severe. Severe bleeding was defined as fatal bleeding, bleeding in inflow critical organs, such as the posterior peritoneum, intracranium, intraocular and intraspinal canal, bleeding-induced reoperation, or clinically significant bleeding outside the surgical site with a $\geq$20 g/L decrease in hemoglobin (Hb) level or the need for $\geq$2 units of whole blood or packed red blood cell transfusion. Non-severe bleeding contained other bleeding events that were not evaluated as severe bleeding, such as skin bruising, fecal occult blood, gastrointestinal bleeding and urine erythrocytes.

The following baseline data were collected, including age, gender, hospital day, operation time, blood loss during surgery, blood drainage, time for clear drainage, and bedtime after surgery. If patients experienced increased neurological symptoms, lumbar MRI would be performed. Neurological and clinical outcomes in terms of Visual Analogue Scale (VAS) and the Oswestry Disability Index (ODI) were assessment before operation and at 6 and 12 months after operation. All patients were evaluated by an independent observer not involved in the surgical procedure.

3. Statistical analysis

Quantitative data are presented as mean ± SD. The Mann-Whitney *U* test was used for numerical data (ex, age, operation time and blood loss). Chi-square test or Fisher exact test was employed for comparing the male to female ratio and the incidence of complications between the two groups. For comparison VAS and ODI score, *t*-test was used between groups, and one-way analysis of variance followed by Dunnett-t test was used within the group. SPSS ver. 21 software (IBM Co., Armonk, NY, USA) was used for statistical analysis. Statistical significance was defined as $P < 0.05$.

4. Results

A total of 556 patients (252 men and 304 women) met the criteria and were enrolled into this study. Among them, 282 patients received LMWH for anticoagulation, and the other 274 patients were treated with argatroban. VTE occurred altogether in seven patients, all in the form of postoperative DVT. No PE occurred in any patient. In argatroban group, postoperative DVT occurred in three patients (1.0%), including one patient with symptomatic anterior tibial vein embolism, and two patients with asymptomatic posterior tibial vein thrombosis. In LMWH group, postoperative DVT occurred in four patients (1.4%), including two patients involving the bilateral venous plexus of the calf muscle, one involving the popliteal vein, and one involving the posterior tibial vein. All of them were asymptomatic. Of the seven patients who developed postoperative DVT, each group had a case as for fracture reduction decompression intra-fixation and overhauling operation. One patient in argatroban group and two patients in LMWH group underwent posterior lumbar interbody fusion (PLIF). No postoperative DVT occurred in any patient who underwent intervertebral foramen approach vertebral interbody fusion (TLIF). There was no significant difference in VTE occurrence between the two groups ($P > 0.05$) (Table 1).

In argatroban group, bleeding occurred only in a 72-year- old woman (0.04%) who underwent three-level (L3/L4, L4/L5 and L5/S1) PLIF for lumbar spinal stenosis. She developed incisional bleeding after removal of the drain tube 2 days after surgery, devoid of neurological dysfunction. The bleeding situation was improved 7 days after surgery, when the anticoagulation drug was discontinued. In LMWH group, bleeding occurred in four cases, including large subcutaneous ecchymosis in one and incisional bleeding in two, which were all improved after discontinuation of the anticoagulation drug. Symptoms of neurological dysfunction occurred in one patient, including increased pain and numbness of both lower limbs. A spinal epidural hematoma in the surgical area was confirmed by MRI examination in this patient. After removal of the pressurized material through a second surgery, the patient soon recovered. There was no significant difference in the bleeding rate between the two groups ($P > 0.05$).

Allergic reactions occurred in two cases in LMWH group, and no in argatroban group. Seeing that the two patients only presented a decreased platelet count 7 days after surgery without any other abnormalities detected to explain this phenomenon, heparin-induced thrombocytopenia was the initial consideration, and LMWH was immediately replaced by argatroban for 10 and 15 days respectively in the two patients before they were discharged from the hospital. However, the platelet count in the two patients failed to increase to the normal range at the time of discharge. The platelet count in one patient became normal without bleeding or thrombosis when she came back to the hospital three months after discharge. The other patient was lost to follow-up after discharge.

There was no significant difference in age, gender, hospital day, operation time, and anticoagulation time between the two groups,