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Original article

Rivaroxaban and early periprostethic joint infection: our experience

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Summary. *Background and aim of the work:* Periprostethic joint infection (PJI) is a severe post-operative complication after Primary Total Hip Arthroplasty (THA). According to the classification of PJI early acute PJI occurs within 4 weeks from surgery. Some authors think that Rivaroxaban is a risk factor in the incidence of early acute PJI. We analyze our experience about this item. *Materials and methods:* We analyze our experience from 1st January 2015 to 31th December 2016. We consider all consecutive hip arthroplasty implants in this period. *Results:* In the 205 patients analysed we not find early acute PJI in Rivaroxaban group nor in the others assuming another kind of thromboprophylaxis. *Conclusions:* In our series there is no evidence of association between Rivaroxaban and early acute PJI. This is a retrospective cohort study, so we need more studies and more robust experimental designs to confirm these results. (www.actabiomedica.it)

Key words: acute early periprostethic joint infection, Rivaroxaban, Total Hip Arthroplasty

Introduction

Periprostethic joint infection (PJI) is a severe post-operative complication after Primary Total Hip Artroplasty (THA) (1, 2). PJI over the hip arthroplasty is a very rare event, but its incidence increased from 1,99% to 2,18% from 2001 to 2009 (3) and we expect that the percentage will increase again according to the rising number of total hip arthroplasty. Culliford et al. estimate that the number of total hip arthroplasty (THA) will increase of 91,75% from 2010 to 2035 in UK (4); similarly, in USA according to the prevision of Kurtz et al. the number of total hip arthroplasty (THA) will increase of 174% from 2005 to 2030 (5).

After Tsukayama (6) and Trampuz (7) classification, recently early periprostethic joint infection has been defined as an infection that occurs within 4 weeks after surgery (8, 9) and usually manifests with acute joint pain, wound inflammation (warmth and erythema), joint effusion, and loss of function (10). Most early PJI is caused by Gram-positive cocci (Staphylococcus aureus and coagulase-negative Staphylococcus) (11, 12).

Instead of late PJI, the treatment of early periprosthetic joint infection can save the implant. The treatment consists in irrigation and debridement including liner exchange and antibiotic therapy. In case of failure of the previous treatment we must proceed more aggressively with one or two stage revision, Girldestone, arthrodesis or amputation in severe cases (13-16).

The most common risk factors of PJI are obesity, low BMI, diabetes mellitus, hyperglycaemia around surgery even in patients without diabetes, rheumatoid arthritis, immunosuppressive therapy, malignancy, distant site infections, elevated ASA score. There are others risk factors linked with intraoperative and

post-operative factors that seems to increase the incidence of PJI, like prolonged time of operation, use of allogenic blood transfusions and especially for acute infection hematoma, superficial surgical site infection, wound complications like drainage and wound dehiscence (17-19).

Among the many risk factors of periprosthetic joint infection, post-surgery anticoagulants may have a role. Routine thromboprophylaxis with anticoagulants after THA is strongly recommended by the national guidelines of The American College of Chest Physicians (20). Nowadays, in orthopaedist surgery, we can choose between different kind of molecules such as low molecular weight heparin (LMWH), Warfarin, Enoxaparin, Fondaparinux, Rivaroxaban, Dabigatran, Apixaban etc.

Rivaroxaban is a direct-acting oral anticoagulant (DOAC). It is the first available orally active direct factor Xa inhibitor. Rivaroxaban inhibits both free factor Xa and factor Xa bound in the prothrombinase complex (21). Inhibition of factor Xa interrupts the intrinsic and extrinsic pathway of the blood coagulation cascade, inhibiting both thrombin formation and development of thrombi. The convenience of oral use and the potential absence of thrombocytopenia adverse effect are the best advantages (22).

Currently the Authors do not agree about a real association between Rivaroxaban and early deep postoperative surgical site infection after primary THA and TKA.

In this study, we wanted to verify if Rivaroxaban has increased the number of early PJI in patients undergone to total hip arthroplasty in our Clinic.

Methods

We analyzed all consecutive patients undergone to total hip arthroplasty (THA) from 01st January 2015 to 31th December 2016. We excluded patients undergone to total knee arthroplasty (TKA) because, according to the rules of our hospital, it is not possible to prescribe this kind of thromboprophylaxis in this kind of surgery for more than 15 days.

Each patient was treated with thromboprophylaxis from 8-12 hours after surgery to 35 days post surgery, according to American College of Chest Physicians guidelines, published in 2012 (20).

Patients collected were treated with Rivaroxaban, Fondaparinux, Enoxaparin, Nadroparin, Calciparin, Dabigatran, Warfarin, Acenocumarol. In patients that took Warfarin or Acenocumarol, our protocol is suspension 5 days before surgery and substitution with single or double dose of Enoxaparin; after surgery, when bleeding is controlled, patients start double therapy with heparin and Warfarin or Acenocumarol: when INR value is greater 2 for two times they could stop heparin.

In our protocol of antibiotic prophylaxis, we use cefazolin 2 g or Clindamycin 600 mg for allergic patients 30 minutes before surgery. After discharge, patients came back after 2 weeks from surgery to remove the suture, and the first clinical and radiological control was after 45 days.

Results

We analyzed retrospectively 205 consecutive patients between 01st January 2015 to 31th December 2016. Among 205 patients operated, 145 were treated with Rivaroxaban, 25 with Fondaparinux, 19 with Oral Anticoagulants (Warfarin or Acenocumarol), 5 with Calciparin, 3 with Dabigatran, 8 with Nadroparin or Enoxaparin.

Mean age was 69,2 years old, 120 were women and 85 men, mean value of Charlson Comorbidity Index was 2,14. The medium length of stay in hospital for these patients was about 5 days.

We divided these patients into 2 groups: the Rivaroxaban group and the control one composed by patients treated with a thromboprophylaxis different from Rivaroxaban (Figs. 1, 2).

Although We used Rivaroxaban in 70,73% of patients, we registered no cases of early PJI in the group treated with Rivaroxaban nor in the control group.

Discussion

In literature, there is a lack of consensus about a real association between Rivaroxaban and early deep

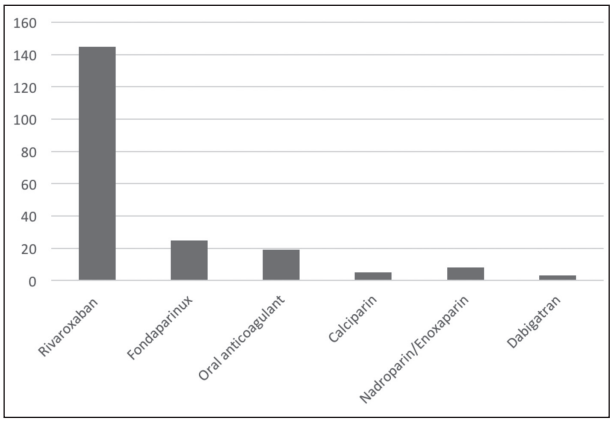

Figure 1. Thromboprophylaxis in our study

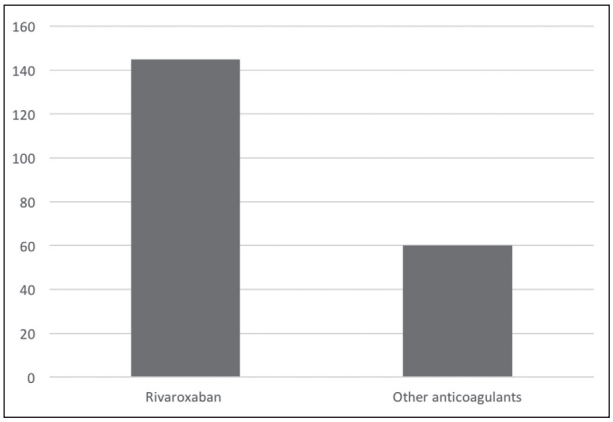

Figure 2. Different use of Rivaroxaban and other anticoagulants

postoperative surgical site infection after primary THA and TKA.

In their study, Brimmo et al. concluded that the use of Rivaroxaban for thromboprophylaxis led to a significantly increased number of deep surgical site infection with an incidence 2.5% in Rivaroxaban group (159 patients) vs 0.2% in the control one (480 patients) (23).

Another study written by Jensen et al (24) confirm this observation. The infection rate in their patients treated with Rivaroxaban after THA and TKA was similar to Brimmo et al. data, with an infection rate of 2.5% in patients treated with Rivaroxaban and 1% in those treated with Tinzaparin. Chahal et al (25) noted an increase from 0.9% to 1.9% in infection rate for 160 patients treated with Rivaroxaban after primary THA and TKA (compared with 227 treated with Enoxaparin), even if this difference did not reach statistical significance.

In their prospective cohort study evaluating postoperative wound healing, Sindali et al (26) noted a 1% deep infection rate in 202 patients who received Rivaroxaban after primary THA and TKA, which is comparable to the overall infection rate reported for primary THA and TKA in the literature (27, 28).

A previous multicenter retrospective study by Jameson et al (29) also reported a low infection rate (17 of 2762; 0.62%) in patients treated with Rivaroxaban, which was not significantly higher than the rate of their Enoxaparin control group (55 of 10,361; 0.53%).

The increased rate of infections observed in patients undergoing THA and TKA in the Brimmo et al. study contrasts with the rate of serious postoperative wound infections observed by Lassen et al (30), who reported a 0.16% rate of postoperative infection in 6183 patients who received Rivaroxaban compared with a 0.27% rate of serious postoperative infection in 6200 patients who received Enoxaparin.

Limit of this study are the retrospective design, the number of patients, the absence of incidence of early deep surgical site infections in both groups evaluated.

Conclusions

Our experience didn't show the same trend we found in some studies in literature (23-25). In our opinion the association between Rivaroxaban and early postoperative deep surgical site infection has not been sufficiently evaluated.

We are not sure about the role of Rivaroxaban among early acute PJI. There is a luck of studies about this item. Rivaroxaban use has increased in the last few years, so further studies are required to verify its association with early periprosthetic infection.

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