

Oral Anticoagulants in Orthopaedic Surgeries Comparison of Rivaroxaban and Standard-of-Care

Dr. Sanjay Khot, Dr. Sunil Kant Kamra*

Assistant Professor Department of Anaesthesiology Chandulal Chandrakar Memorial Medical College,
Kachandur, Durg (Chhattisgarh) 490024



Address for Correspondence

Dr. Sunil Kant Kamra

Assistant Professor Dept. of Anaesthesiology

Chandulal Chandrakar Memorial Medical College, Kachandur, Durg (Chhattisgarh) 490024

Abstract

Background: Venous thromboembolic (VTE), deep vein thrombosis (DVT) and pulmonary embolism (PE), cause significant morbidity, mortality and healthcare costs. Direct oral anticoagulant which has been demonstrated in clinical trials, anaesthetists need to be careful of how to minimize the risks of bleeding complications when treating patients who are taking an anticoagulant. Rivaroxaban, non-vitamin K antagonist direct oral anticoagulants (DOACs), was shown to be more effective regimens for the prevention of VTE after orthopaedic surgery. **Aims and objectives:** To look for the influence of timing of the first thromboprophylactic dose and clinical outcomes in patients undergoing orthopaedic surgery. **Method:** Patients aged ≥ 18 years, with planned orthopaedic surgery or fracture-related orthopaedic surgery and in whom thromboprophylaxis has been indicated. Out of 324 patients selected for the study 164 received rivaroxaban 10 mg once daily and 160 received standard-of-care (SOC) pharmacological prophylaxis. Incidences of symptomatic thromboembolic events and bleeding events were analysed. Bleeding events and thromboembolic events recorded and calculated for the rivaroxaban and SOC groups. **Results:** Overall major bleeding events observed in rivaroxaban group was 9 (5.49%) was much lower than the SOC group which was 13 (8.13%). The percentage of patients using mechanical methods alongside pharmacological thromboprophylaxis was slightly higher in the rivaroxaban as compared to SOC groups (64% and 55%). Overall thromboembolic effect was lower in rivaroxaban as compared to SOC group. **Conclusion:** Comparison of rivaroxaban & SOC shows the effectiveness and safety of rivaroxaban in patients undergoing major orthopedic surgery in clinical practice. Major bleeding events & thromboembolic with rivaroxaban were less as compared to SOC group.

Introduction

The use of direct oral anticoagulants which includes apixaban, rivaroxaban, and dabigatran, are approved for several therapeutic indications, can simplify perioperative and postoperative management of anticoagulation. American Society of Regional Anesthesia (ASRA) and the European and Scandinavian Societies of Anaesthesiology published guidelines for regional anaesthesia in 2010 for patients on anticoagulants.^[1] Various new oral anticoagulants have been approved by the US Food and Drug Administration (FDA) like dabigatran, rivaroxaban and ticagrelor and apixaban and are approved for the prevention of Venous thromboembolism (VTE) after elective knee or hip replacement surgery, for the prevention of stroke in patients with non-valvular AF, and the treatment of VTE and prevention of recurrent VTE.^[2]

Venous thromboembolism (VTE), deep vein thrombosis (DVT) and pulmonary embolism (PE), cause significant morbidity, mortality and healthcare costs.^[3,4] The risk of VTE is particularly high in patients who undergo major orthopedic surgery like total knee or hip replacement hence these patients should routinely receive anticoagulants for short-term perioperative and postoperative prophylaxis.^[5,6] Additionally, the use of regional neuraxial anesthesia poses a risk of hematoma in patients who are receiving anticoagulants, during insertion and removal of the needle and catheter.

In Europe, rivaroxaban is also indicated for co-administration with acetylsalicylic acid (ASA) alone or with ASA plus clopidogrel or ticlopidine for the prevention of atherothrombotic events after acute coronary syndrome with elevated cardiac biomarkers. The Study Group in France on thrombosis and haemostasis in surgery suggested adjustments to the interval between discontinuation of the drugs and performance of neuraxial procedures, based on the degree of risk of thrombosis.^[7]

In spite of the clinical evidence on the safety and efficacy profile of direct oral anticoagulants which has been demonstrated in clinical trials, anaesthetists need to be careful of how to minimize the risks of bleeding complications when treating patients who are taking an anticoagulant and are due to undergo surgery with regional anesthesia.

Rivaroxaban, a non-vitamin K antagonist direct oral anticoagulants (DOACs), was shown to be more effective than enoxaparin regimens for the prevention of VTE after orthopedic surgery.^[8]

It has been shown that the timing of the first postoperative dose of thromboprophylaxis agent and the type of anesthesia used either general or neuraxial, during orthopaedic surgery may affect the clinical outcomes in patients undergoing surgery.^[9] Neuraxial anesthesia was shown to significantly reduce mortality and the occurrence of pulmonary embolism and deep vein thrombosis.^[10]

Aims and Objectives

Study was carried out to look for the influence of timing of the first thrombo prophylactic dose on clinical outcomes in patients undergoing orthopedic surgery

Patients and methods

Patients aged ≥ 18 years, with planned orthopaedic surgery or fracture-related orthopedic surgery and in whom thromboprophylaxis has been indicated. Written informed consent was taken from all the patients included in the study. The study protocol was approved by the Ethics Committee of the institute.

The type, dose, and duration of thromboprophylaxis were decided by the physician treating the patient. Total 324 patients were selected for the study for a period of 1 year at CCM Medical College and hospital Kachandur, Durg.

Out of 324 patients selected for the study 164 received rivaroxaban 10 mg once daily and 160 received standard-of-care (SOC) pharmacological prophylaxis which includes low-molecular-weight heparins and dabigatran. Incidences of symptomatic thromboembolic events and bleeding events were analysed and recorded according to timing of the first postoperative thromboprophylactic dose and use of type of anaesthesia. Use of mechanical prophylaxis like elastic stockings and intermittent pneumatic compression was also recorded.

Table 01

Timing of first dose after surgery	Rivaroxaban (%)	Standard-of-care (SOC) (%)
< 6 hours	74 (45.12)	70 (43.75)
>6 to ≤ 12 hours	54 (32.93)	51 (31.87)
>12 to ≤ 24 hours	36 (21.95)	39 (24.38)
Total	164	160

Out of 164 patients received rivaroxaban 74 (45.12%) received first dose in < 6 hours, 54 (32.93%) received first dose between >6 to ≤ 12 hours and 36 (21.95%) received their first dose in >12 to ≤ 24 hours. In SOC group first dose given at < 6 hours was 70

Bleeding events occurred during and after surgery were differentiated as major and non-major bleeding events. Major bleedings were clinically overt bleeding that was fatal occurring in critical organ which necessitated reoperation or was outside of the surgical site, and bleeding warranting treatment cessation and surgical-site bleeding events associated with a fall in hemoglobin of ≥ 2 g/dl.^[11]

Analysis

Incidences were calculated for the rivaroxaban and SOC groups. Bleeding events were those who presented as treatment-emergent events and thromboembolic events were those that occurred within 3 months of surgery.

Data was analysed according to the timing of the first postoperative dose of rivaroxaban and SOC and type of anesthesia used like general, spinal, combination, neuraxial, peripheral etc. mechanical prophylaxis used was also recorded

Results

All patients started antithrombotic therapy within 24 hours of surgery.

324 patients were selected for the study out of which 164 received rivaroxaban 10 mg once daily and 160 received standard-of-care (SOC) pharmacological prophylaxis

(43.75%), patients who received first dose in >6 to ≤ 12 hours was 51 (31.87%) and 39 (24.38%) received their first dose in >12 to ≤ 24 hours.

Table 02

Adverse Events	Timing of first dose after surgery	Rivaroxaban	% (n=164)	standard-of-care	% (n=160)
Major bleeding events	< 6 hours	2	1.22	3	1.88
	>6 to ≤ 12 hours	4	2.44	6	3.75
	>12 to ≤ 24 hours	3	1.83	4	2.50
	Total	9	5.49	13	8.13
Thromboembolic events	< 6 hours	1	0.61	3	1.88
	>6 to ≤ 12 hours	2	1.22	4	2.50
	>12 to ≤ 24 hours	4	2.44	4	2.50
	Total	7	4.27	11	6.88

In < 6 hours group, patients who received rivaroxaban major bleeding events was observed in 2 (1.22%) cases. While in SOC group major bleeding events was observed in 3 (1.88%). In >6 to ≤ 12 hours group, patients major bleeding events was observed in 4 (2.44%) cases who received rivaroxaban, while in SOC group major bleeding events was observed in 6 (3.75%). In >12 to ≤ 24 hours groups major bleeding events for patients receiving rivaroxaban and SOC group was 3 (1.83%) and 4 (2.50%) respectively.

Thromboembolic events < 6 hours group, patients who received rivaroxaban was 1 (0.61) as compared to SOC group it was high 3 (1.88%). Also in >6 to ≤ 12 hours group patient who received rivaroxaban thromboembolic events was 2 (1.22%) while in SOC group it was high 4 (2.50%). But in >12 to ≤ 24 hours group thromboembolic events was near about same in patients receiving rivaroxaban 4 (2.44%) and SOC group 4 (2.50%). But the overall thromboembolic effect was lower in rivaroxaban as compared to SOC group.

Overall major bleeding events observed in rivaroxaban group was 9 (5.49%) was much lower than the SOC group which was 13 (8.13%).

The percentage of patients using mechanical methods alongside pharmacological thromboprophylaxis was slightly higher in the rivaroxaban as compared to SOC groups (64% and 55%).

Discussion

Venous thromboembolism, comprising deep vein thrombosis cause significant morbidity, mortality in patients after orthopaedic surgery. The direct oral anticoagulants like apixaban, rivaroxaban, and dabigatran are approved for the prevention of VTE after orthopaedic surgery. Rivaroxaban which is direct inhibitors of Factor Xa has half-life of 5-13 hours. Elderly patients are at increased risk of thromboembolic disorders are more likely to be receiving anticoagulants.^[12]

Earlier studies shown that timing of the first dose of thromboprophylaxis may have an impact on bleeding and thromboembolic events. Fondaparinux in a study was associated with the incidence of major bleeding events.^[13] While starting rivaroxaban 6–10 hours after surgery when hemostasis has been established is recommended.^[14]

In our study major bleeding incidence was observed when rivaroxaban or SOC was given >6 to ≤ 12 hours i.e. 4 (2.44%) and 6 (3.75%). In SOC group it was higher as compare to the rivaroxaban group. Overall major bleeding events were more in standard-of-care group 13 (8.13%) as compared to rivaroxaban group which was 9 (5.49%).

Thromboembolic events in patients receiving rivaroxaban was 7 (4.27%) which was less than the SOC group 11 (6.88%). In both the group overall thromboembolic effect in patients who received prophylaxis in < 6 hours was less while in other group it was slightly higher.

These data suggest that in certain situations a slight delay in initiating rivaroxaban may not compromise the effectiveness of rivaroxaban in preventing thromboembolic events in these patients also use of mechanical thromboprophylaxis did not appear to further reduce the risk of thromboembolic events.^[15]

Type of anaesthesia used may potentially influence clinical outcomes. Patients receiving anticoagulants and undergoing neuraxial anaesthesia may have an increased risk of spinal hematoma.^[16] In a study it was shown that rivaroxaban showed a favourable benefit–risk profile compared with SOC irrespective of the type of anaesthesia used. Some earlier studies have showed that neuraxial anaesthesia was associated with a lower incidence of VTE.^[17]

Conclusion

Comparison of rivaroxaban & SOC shows the effectiveness and safety of rivaroxaban in patients undergoing major orthopaedic surgery in clinical practice. Major bleeding events & thromboembolic with rivaroxaban were less as compared to SOC group. However owing to the small patient numbers in study group definitive conclusion cannot be drawn and further large studies are required for confirmations.

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