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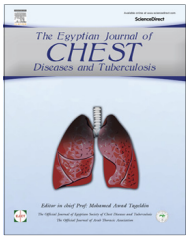

ORIGINAL ARTICLE

A study on the role of rivaroxaban in management of venous thromboembolism

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KEYWORDS

Rivaroxaban;
Anticoagulant;
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Abstract *Background:* Over 50 years the research work all over the world was concerning to find out a novel oral heparin to avoid the side effects of conventional anticoagulants as warfarin which requires changes in diet and lifestyle, regular checkup, and has a risk of severe hemorrhage. Rivaroxaban offers such advantages as oral mode of administration, more predictable anticoagulant response, greater specificity with no need for routine checkup and patient monitoring and has a uniform dose. When switching patients from warfarin to rivaroxaban, warfarin is discontinued and rivaroxaban is started as soon as INR is below 3.0 to avoid periods of inadequate anticoagulation.

Aim of the work: To study the role and suitability of oral rivaroxaban therapy in management of venous thromboembolism in Egyptian patients.

Patient and methods: This work was done over 120 mild or minor pulmonary embolism patients, divided into 2 groups, *group I* included 100 patients received oral rivaroxaban for 1 week, continued with warfarin for 6 months guided with INR measurement, *group II* included 20 patients who are financially supported and can continue with rivaroxaban for 6 months. The following was done for all patients. Clotting time (CT), D Dimer, INR, APTT, platelet count, complete liver and kidney functions, digital X ray Chest, multi-slice CT angiogram in some cases, and ECG, CK MB and troponin when needed.

Results: Our patients were divided into 2 groups, *group I* included 100 patients 54 males and 46 females with a mean age of 48.3 ± 15.43 and a mean body weight of 84.7 ± 16.4 *group II* included 20 patients 11 males and 9 females with a mean age of 45.6 ± 12.21and a mean body weight of 85.2 ± 12, the recorded side effects were minor bleeding in 11% of the cases of group I and 10% of the cases of group II, headache in 6% of the cases of group I and 5% of the cases of group II, GIT upset in 5% of the cases in both groups, dizziness in 4% of the cases of group I and 5% of the cases of group II with no statistical significant differences between the 2 arms of the study.

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Conclusion and recommendation: Rivaroxaban is a rapid onset of anticoagulant that can be given in fixed doses without routine monitoring. It can replace injectable anticoagulants as an initial treatment in management of patients with mild venous thromboembolism as it is suitable as regard the economic and the health status of the Egyptian patients.

Introduction

There is a clinical need for safe new oral anticoagulants, as the currently available anticoagulants such as vitamin K antagonists [1] and low-molecular-weight heparins (LMWHs) [2], are not targeted, which means that they inhibit more than one enzyme in the coagulation cascade. In recent years, new anticoagulants targeting single component of the coagulation cascade have been developed.

The use of warfarin reduces the rate of thromboembolic stroke in patients with atrial fibrillation but requires frequent monitoring and dose adjustment as its response is modified by genetic and environmental factors that can influence its absorption, pharmacokinetics, and pharmacodynamics. Rivaroxaban, is the first bioavailable orally administered direct factor Xa inhibitor, which may provide more consistent and predictable anticoagulation than warfarin [3], as it selectively and reversibly blocks the active site of factor Xa and does not require a cofactor (such as Anti-thrombin III) for activity. Activation of factor X plays a central role in the coagulation cascade. As factor Xa acts at the junction of the external and internal pathways of coagulation, rivaroxaban prolongs both PT and aPTT, which is dose dependent [4].

Rivaroxaban maximum plasma concentration is 30 min to 3 h, and its half-life has been reported to be 3–9 h. Rivaroxaban provides high potency and selectivity and dose-dependent inhibition of factor Xa. Two thirds of the drug is metabolized to inactive metabolites in liver, half of which is excreted by kidneys and other half is excreted via fecal route. CYP3A4, CYP345, and CYP2J2 catalyze the hepatic metabolism of rivaroxaban [5]. The other one-third is excreted unchanged by kidneys. As a significant portion of rivaroxaban is excreted via kidneys, renal impairment is expected to increase the concentration of the drug, with increasing severity of renal impairment causing more retention of the drug. Mild renal impairment (creatinine clearance 50–80 mL/min) increases the concentration (AUC) of the drug by 44%, moderate impairment (Cr CL 30–49 mL/min) by 52%, and severe impairment (Cr CL 15–29 ml/min) by 64% that is associated with more inhibition of factor Xa and more prolongation of PT. The drug is contraindicated in patients with severe renal impairment with CrCl < 15 mL/min to avoid excessive drug accumulation and bleeding [6], liver impairment (dabigatran does not undergo hepatic metabolism and may be safe in patients with hepatic disease), as well as those who are pregnant (category C drug), breastfeeding should not take rivaroxaban [7].

Aim of the work

To study the role and suitability of oral rivaroxaban therapy in management of venous thromboembolism in Egyptian patients.

Methodology

This work was done in Chest department, Tanta University, Egypt from March 2012 to December 2013 over 120 mild or minor pulmonary embolism patients divided into 2 groups, *group I* included 100 patients who received oral rivaroxaban for 7 days, in a dose 10–20 mg twice daily according to the hepatic and renal status of the patient, warfarin was added from the third day, after 1 week rivaroxaban was withdrawn, and warfarin continued for 6 months guided with INR measurement. Initial INR was done before starting warfarin, then repeated after 1 week, 2 weeks and then monthly to adjust warfarin dosage, *group II* included 20 patients who are financially supported and can continue with rivaroxaban for 6 months. The following was done for all patients: Thorough history taking, complete physical examination, clotting time (CT), D Dimer, INR, APTT, platelet count, urea and creatinine, SGPT, SGOT, direct and indirect serum bilirubin, digital X ray Chest P/A and lateral view, multi-slice CT angiogram in some cases, and ECG, CK MB and troponin when needed.*Inclusion criteria* were patients with mild or minor pulmonary embolism, haemodynamically stable, with normal O2 saturation, refusing hospitalization. *Exclusion criteria* were patients with recent or known bleeding disorders, severe heart-valve disorder, stroke within 14 days or severe stroke within 6 months, uncontrolled hypertension, severe renal dysfunction with creatinine clearance < 30 ml/min, recent gastrointestinal bleeding due to ulceration or esophageal varices, active liver disease and pregnancy or breast-feeding.

Results

This work was done over 120 mild or minor PE patients, divided into 2 groups, *group I* included 100 patients 54 males and 46 females with a mean age of 48.3 ± 15.43 and a mean body weight of 84.7 ± 16.4 *group II* included 20 patients 11 males and 9 females with a mean age of 45.6 ± 12.21 and a mean body weight of 85.2 ± 12 .The main symptoms of our patients were dyspnea in 74.1%, chest pain in 65%, haemoptysis in 33.3%, cough in 19% and wheeze in 15%, the main risk factors for VTE were obesity in 51.6% dyslipidemia in 49.1%, smoking in 26.6%, hormonal contraceptives in 25.8% DM in 24.1%, hyper-tension in 18.3%, hypervitaminosis k in 16.6% and other cardiac disorder in 15%, the recorded side effects were minor bleeding in 11% of the cases of group I and 10% of the cases of group II, headache in 6% of the cases of group I and 5% of the cases of group II, GIT upset in 5% of the cases in both groups, dizziness in 4% of the cases of group I and 5% of the cases of group II with no statistical significant differences between the 2 arms of the study.