# New oral anticoagulants in the prevention of stroke

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**Abstract**

Atrial fibrillation is associated with a few folds higher risk of stroke. Traditional vitamin K antagonists used in the prevention of stroke in patients with non-valvular atrial fibrillation are often not efficient enough due to their interactions with a broad range of substances including medicines or food ingridients and problems with monitoring the treatment. New oral anticoagulants pose an alternative for the vitamin K antagonists. They are equally efficient in the prevention of stroke, but are safer and have no requirement for routine coagulation monitoring. We present a case of a patient with atrial fibrillation, high risk of tromboembolism and recurring episodes of hemorrhages. Considering the possible complications, rivaroxaban was administered.

## Introduction

Atrial fibrillation, occurring in about 1–2% of the population, is the most common type of sustained heart arrhythmia [1, 2]. The number of patients afflicted with atrial fibrillation has doubled during the last 50 years and is still growing, owing to the expanding life expectancy and the decrease in the level of mortality caused by heart diseases especially among men after 75 years old. Atrial fibrillation confers a 5-fold risk of stroke and about 20% of strokes are attributed to atrial fibrillation [1–3]. Ischaemic strokes caused by atrial fibrillation are often fatal and the patients who survive suffer from a greater disability and have a higher risk of another stroke. Oral vitamin K antagonists are effective in the prevention of stroke but are more inconvenient in use. The necessity of individual dose adjustment and their interactions with a large number of substances often impair the quality of treatment [4–7]. According to many clinical studies less than a half of the patients have the correct level of international normalized ratio (INR) [8].

We present a case of a patient with atrial fibrillation treated with rivaroxaban.

## Case report

A 77-year-old woman with coronary heart disease, hypertension, heart failure, with rheumatoid arthritis, after ischaemic stroke and with recurrent episodes of haemorrhages was admitted to a cardiology department due to loss of consciousness. The laboratory tests revealed decreased haemoglobin level (11.4 g/dl), renal insufficiency (estimated glomerular filtration rate (eGFR) 34 ml/min) and a correct level of aminotransferases activity. Moderate heart failure features (ejection fraction (EF) – 45%) and atrial fibrillation with left bundle branch block in the electrocardiogram were present on admission to hospital. Holter ECG monitoring revealed periods of sinusoid rhythm interrupted by atrial fibrillation episodes connected with advanced atrioventricular block. This led to a decision of heart pacer implantation. Due to a high risk of thromboembolic complications the patient required oral anticoagulation. Because of the insufficient control of the INR level and the necessity to modify the dosage of the warfarin over four times during the last 6 months (INR lability), the further use of oral vitamin K antagonist was highly questionable. Considering the necessity of preventing stroke recurrence, and the possible haemorrhagic complications (5 points on the HAS – BLED scale) rivaroxaban was prescribed. Because of the level of GFR the dose was decreased to 15 mg once daily.

## Discussion

Despite thoroughly documented benefits of the anticoagulation treatment, its application is observed to be limited. It has been indicated in American studies that only 40% of patients with a high risk of stroke caused by atrial fibrillation receive oral anticoagulation [9, 10]. Furthermore, according to another multicentre study, not only an insufficient number of patients with atrial fibrillation received oral anticoagulation, but also nearly 60% of them were below the therapeutic range of INR [8, 10, 11]. Maintaining an

appropriate level of INR during less than 60% of the therapeutic time undermines the beneficial aspects of the treatment. There is a number of factors decreasing the efficiency of oral anticoagulation: unsatisfactory cooperation with the patient, lack of sufficient conviction for this method of treatment, and little knowledge of the scientific evidence including false opinions of overestimated danger of hemorrhagic complications of oral anticoagulation [12–14]. Hopefully, implementing new methods of treatment connected with a decreased risk of haemorrhagic complications will improve the situation. In many cases rivaroxaban can be an alternative to oral vitamin K antagonists.

It is a highly selective factor Xa inhibitor which disrupts the blood coagulation pathway preventing both the activation of prothrombin and formation of a thrombus [15–17]. The ROCKET AF study provided confirmation of its non-inferiority regarding the prevention of stroke in comparison to warfarin and a significant reduction of major bleeding, intracranial haemorrhage and fatal bleeding in the rivaroxaban group. The Rocket AF study conclusions and practical aspects of the treatment should convince both the doctor and the patient that rivaroxaban can provide more consistent and predictable anticoagulation than warfarin. In the case of the above-presented patient, problems with individual dosing, INR lability and practical problems with frequent INR monitoring led to the decision of substituting warfarin with rivaroxaban. Shifting from warfarin to rivaroxaban in patients with a stable INR level is highly questionable and should be considered very carefully. The Rocket AF study did not provide evidence for the superiority of rivaroxaban over warfarin in terms of preventing stroke and the number of bleeding incidents was comparable [18, 19]. Thus, implementing rivaroxaban in the case of our patient may not necessarily diminish the risk of nose bleeding episodes, which occurred most frequently during periods of labile INR level. On the other hand, taking into consideration the steroid therapy which our patient was subjected to and its possible interactions with the oral vitamin K antagonists as well as its adverse influence on the digestive system, the risk of major bleeding incidents could be decreased with rivaroxaban. According to clinical studies, dexamethasone used in the therapeutic oral doses can increase the level of warfarin, which would require frequent INR monitoring [20].

Implementing new oral anticoagulants in prevention of stroke for patients with atrial fibrillation appears to be a significant alternative, though it should not be regarded as a solution to all the therapeutic problems. The financial cost of the therapy still poses a serious dilemma, as well as the lack of a selective antidote and difficulties with monitoring the efficacy of the treatment.

## Conclusions

Oral vitamin K antagonists used in the prevention of stroke require frequent INR monitoring, have a wide range of interactions with other substances including food ingredients and may inflict practical problems. Maintaining an inappropriate level of INR during most of the therapeutic time makes the oral vitamin K antagonists inefficient in preventing stroke. Rivaroxaban is non-inferior to warfarin in the prevention of stroke, but reduces the number of major bleeding incidents. Rivaroxaban should be considered for patients controlling the INR irregularly, or with a labile INR level.

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