

## Methods for Detection of Direct Oral Anticoagulants and their Role in Clinical Practice

Katrina Pukite, Ketija Apsite, Irina Pupkevica, Ilze Cernevska, Oksana Boichuk, Janis Meisters, Dagnija Straupmane, Inga Urtane, Aivars Lejnicks and Oskars Kalejs

Riga Stradins University, Clinical Pharmacist, Latvia

Riga Stradins University, Faculty of Medicine, Latvia

Riga Stradins University, Department of Pharmaceutical Chemistry, Latvia

Riga Stradins University, Department of Internal Medicine, Latvia

Pauls Stradins Clinical University Hospital, Center of Cardiology, Latvia

Pauls Stradins Clinical University Hospital, Department of Laboratory, Latvia

E-mail: [katrina.pukite89@inbox.lv](mailto:katrina.pukite89@inbox.lv)

Abstract:

**Introduction:** Atrial fibrillation (AF) is the most common arrhythmia that increases by age, doubles for every decade after age of 50 years and reaches about 10% patients  $\geq$  80 years. Despite direct oral anticoagulants (DOACs') predictable pharmacokinetics and pharmacodynamics, the laboratory tests are necessary for effective and safe medical treatment, also for prediction and detection of thrombotic and bleeding events, as well as in situations when temporary discontinuation could be desirable.

**Aim:** of this study was to identify and analyze the need of coagulation tests for AF patients with high cardiovascular risk in clinical practice.

**Methods:** Quantitative, analytic, cross-sectional clinical trial, during the period from October 2016 till June 2017, was performed at Pauls Stradins Clinical University Hospital, Center of Cardiology, Latvia. There were collected data about patients with non-valvular AF, under anticoagulative therapy  $\geq$  3 months, defined as a high-risk group by CHA2 DS2 -VASc score-more or equal to 2 or 3, men and women respectively. Data were analyzed using SPSS.

**Results:** There were collected data about 143 patients of whom 46.2% (n=66) were male; the mean age was 69.7 (SD  $\pm$  9.9) years. About 2/3 (73.1%) of all patients the AF were longer than 1 year. The mean CHA2 DS2 -VASc score was 4.2 (SD  $\pm$  1.5). The most common comorbidities were arterial hypertension (65.0%; 93), chronic heart failure (48.3%; 69), coronary artery disease (32.9%; 47), diabetes mellitus

(24.5%; 35), and dyslipidemia (25.9%; 37). Almost half of patients (46.2%; 66) used DOACs, 31.5% rivaroxaban and 14.7% dabigatran respectively; furthermore, 1.4% patients used DOACs' with antiaggregants. 49.7% (71) patients had increased risk of possible drug-drug interactions, most frequently with proton pump inhibitors (16.8%; 24), amiodarone (24.5%; 35), antiinflammatory drugs (49.0%; 70). The use of DOACs and possible drug-drug interactions increases by risk score, reaching the maximum score 3 (16.1%; 23) and the mean frequent score 4.4 of 86 (60.1%) AF patients respectively.

**Conclusion:** Coagulation tests were applicable more than half of patients (60.1%) to detect DOACs concentration in plasma. Despite DOACs' expected pharmacokinetics and pharmacodynamics, the anticoagulant tests are necessary for effective and safe medical treatment, also for prediction and detection of thrombotic and bleeding events, as well as in situations when temporary discontinuation is desirable.

Keywords:

Pharmacokinetics; Cardiovascular; Pharmacology; Drug

Abbreviations

DOACS: Direct Oral Anticoagulants; AFIB: Atrial Fibrillation; AXF: Anti-Xa Factor; DTI: Direct Thrombin Inhibitors; DI: Drug-drug Interactions; CHA2DS2: VASc Risk Score.

Introduction:

As the world population ages, the burden of AFib (atrial fibrillation) and venous thromboembolism disease is expected to increase, and prescriptions for long-term anticoagulation will climb [1- 3]. Anticoagulated patients are vulnerable to spontaneous, traumatic and perioperative bleeding. Warfarin is a vitamin K antagonist that has been used for decades to prevent and treat arterial and venous thromboembolism [4]. But due to the need of regular monitoring, non-vitamin K antagonists/oral anticoagulants are now widely used as alternatives to warfarin for stroke prevention in atrial fibrillation and management of venous thromboembolism. These are dabigatran etexilate (Pradaxa, Boehringer Ingelheim, Germany)

Conclusion:

DOACs' usage correlates with CHA2DS2-VASc score with mean frequent score 4.4 of 86 (60.1%) AFib patients respectively. From all high-risk AFib patients (score  $\geq$  3) 47.7% had potentially moderate or major risk of drug-drug interactions. According to data by HASBLED score, it is shown that 72.7% (104) patients had increased risk of bleeding. In summary, for 60.2% AFib patients appropriate monitoring of anticoagulative therapy should be considered.

Anticoagulative laboratory testing for patients on high-risk group could prevent safer anticoagulative therapy for patients with AFib.

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