SHORT COMMUNICATION

Adherence in patients with atrial fibrillation treated with dabigatran

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INTRODUCTION

According to the 2003 definition proposed by the World Health Organization, adherence is the degree to which a patient's behaviour follows the medical recommendation obtained from a healthcare professional. This is an active process wherein the patient is a partner in the development of a therapy plan [1]. Failure to follow the physician's instructions is a serious threat to the patient's health as well as a source of increased healthcare costs. It is particularly difficult to maintain adherence in chronic and asymptomatic diseases [2–4].

The measurement of the drug's blood concentration is the most reliable way to verify the patient's self-report on adherence. However, in the case of non-vitamin K antagonist oral anticoagulants (NOACs), it is an expensive method and is available only in a few medical research centres in Poland. There is also the risk of inaccurate evaluation of adherence due to individual variations in metabolism rates and possible drug interactions that influence plasma drug concentrations [3, 5].

Atrial fibrillation (AF) is one of the most common heart arrhythmias. It increases the risk of death due to cardiovascular causes and of other events, predominantly stroke. The first-choice drugs for the prevention of thromboembolic events are NOACs, including dabigatran [6]. Therefore, adherence to treatment with NOACs is becoming a particularly important issue, given the lack of an objective and easily accessible verification method in clinical practice.

METHODS

Forty consecutive patients with AF treated with dabigatran were enrolled in the study. Samples to determine concentrations of dabigatran were taken from 2 to 12 h after last dose. Plasma concentrations of dabigatran were determined in the Division of Clinical Pharmacology of Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Torun, Poland, by plasma-diluted thrombin time, using the Hemoclot thrombin inhibitor assay (Hyphen BioMed, Neuville-Sur-Oise, France). Descriptive statistics were performed using STATISTICA (StatSoft Inc., 2014).

RESULTS AND DISCUSSION

All patients enrolled in the study reported taking dabigatran at a dose of 2×110 mg (n = 13) or 2×150 mg (n = 27). The mean age of patients was 70.45 ± 13.28 years, 72.5% of the patients were men, and 67.5% of the study population were admitted to hospital as planned. The mean CHA_2DS_2VASc score was 3.95 ± 1.78, and the HAS-BLED score, 2.28 ± 1.13. The mean estimated glomerular filtration rate, calculated according to the Modification of Diet in Renal Disease formula, was 71.63 ± 21.99 mL/min/1.73 m². The dabigatran concentration in the study group ranged from 0 ng/mL to 481.78 ng/mL (median: 119.86 ng/mL; mean: 131.11 ± 118.54 ng/mL). In 27.5% of patients plasma dabigatran levels were below the optimal therapeutic concentration (< 40 ng/mL). The optimal therapeutic concentration (i.e. 40–200 ng/mL) was observed in 50% of patients. Dabigatran concentrations above this range but not associated with a significant increase in the risk of bleeding complications (i.e. 201–400 ng/mL) were noted in 17.5% of patients. Dabigatran concentrations above 400 ng/mL, which is the level associated with a significant increase in bleeding risk, occurred in 5% of patients. Patients with plasma dabigatran concentrations lower than 40 ng/mL were included in the non-adherent group because the only explanation for such low levels is failure to take the drug.

Similar results were obtained in several recent studies assessing the level of adherence to NOACs in patients with AF. A retrospective analysis by Xiaoxi et al. [7] included 6461 American citizens with AF treated with warfarin (59.1%), dabigatran (15.7%), rivaroxaban (19.1%), or apixaban (6.0%). The authors analysed the proportion of days covered (PDC) and classified patients with a PDC of 80% or higher as adherent. The percentage of adherent patients during the initial six months of follow-up was below 50%: 47.5% for NOACs versus 40.2% for warfarin (p < 0.001).

In a study by Shore et al. [8], including 5376 patients with non-valvular AF, 27.8% of the population were non-adherent in the first year of dabigatran therapy. A similar result was shown in a retrospective study by Borne et al. [9], including 2882 patients with non-valvular AF and a CHA_2DS_2VASc score of two or more. Those patients were tested for adherence within a year of introducing dabigatran (72.7%), rivaroxaban (19.8%), or apixaban (7.5%). The percentage of non-adherent patients (PDC < 80%) was estimated at 27.6% for the entire group.

A study by Maura et al. [10] included 22,267 French patients with non-valvular AF treated with dabigatran (11,141 individuals) or rivaroxaban (11,126 individuals). During over a one-year follow-up, the authors estimated the percentage of adherent patients at only 53.3% for dabigatran and 59.9% for rivaroxaban.

The reasons for non-adherence in patients with AF treated with NOACs include, among others, economic considerations and side effects of therapy or fear thereof. Patients may also misunderstand medical recommendations or not be convinced about the necessity of therapy [3, 4].

In the case of NOACs, higher adherence can be expected for rivaroxaban, which is taken once daily, as opposed to dabigatran and apixaban, which are applied every 12 h similarly to other long-term cardiovascular therapies [11, 12].

Andrade et al. [13] assessed the preferences of Canadian doctors (n = 178) and patients (n = 266) as well as doctor-patient cooperation regarding NOAC treatment. The authors showed better compliance for patients taking once-daily drugs (rivaroxaban and warfarin). Patients taking apixaban and dabigatran, dosed twice a day, missed their doses during the seven preceding days, and on average 30% of them were taking the wrong doses, for example, once a day [13].

Good patient-doctor communication is the key to improving adherence. It essentially involves a clear explanation of the disease and the need for treatment, as well as learning about the patient's lifestyle, along with his or her physical and financial capabilities and preferences. The decision about anticoagulant therapy should involve the patient, which leads to a better understanding and acceptance of therapy goals [2, 11].

Improving adherence to treatment with NOACs will be a great challenge for medical community in the near future because NOACs have become the drugs of choice in thromboembolic prophylaxis in patients with non-valvular AF.

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