Case report

Rivaroxaban 10 mg/d in severe renal failure does not prevent ischemic events in premorbid neurologic disease

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1. Introduction

Stroke prevention in atrial fibrillation (AF) by the direct oral anticoagulants (DOAC) dabigatran, rivaroxaban and apixaban was investigated in patients with no or only moderate renal failure [1–3]. Renal failure is frequent in AF-patients [4–6]. All DOAC are eliminated at least partly by the kidneys, and dose reduction is recommended for patients with a creatinine-clearance of 30–50 ml/min. Patients with severe renal impairment, defined by a creatinine clearance <30 ml/min were excluded from the rivaroxaban-investigating trials [3]. Limited clinical data for patients with severe renal impairment (creatinine clearance 15–29 ml/min) indicate that rivaroxaban plasma concentrations are significantly increased. It is unknown if further dose reductions in more severe renal failure will be efficient and safe. We observed a patient with AF and recurrent ischemic strokes, the last occurring under “low dose” rivaroxaban.

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2. Case report

An 82-years old Caucasian female, 53 kg weight, with arterial hypertension, diabetes mellitus, renal insufficiency and hyperlipidemia underwent pulmonary-vein isolation in June 2013 because of paroxysmal AF. In the following weeks AF recurred. In October 2013, she was hospitalized because of a left-cerebral occipital ischemic stroke and 3 non-recent ischemic lesions right frontal, occipital and parietal. Carotid duplex-sonography showed bilateral arteriosclerotic plaques without stenosis. Transthoracic echocardiography did not show any cardiac thrombi or valvular abnormalities. Because the international normalized ratio (INR) was 1.7, the stroke was assumed by admitting physicians as due to “non-adjustable INR”, although the patient’s records showed that in the previous months her INR values were constantly 2.0–3.0. The vitamin-K-antagonist-therapy with phenprocoumon was changed to rivaroxaban. Because of renal failure with a creatinine clearance of 32 ml/min a dosage of rivaroxaban 10 mg/d was given. She was discharged with a medication comprising molsidomin, candesartan, amlodipine, spironolactone and hydrochlorothiazide.

Eleven days after initiation of rivaroxaban she was re-hospitalized because of acute onset of right-sided weakness of the upper and lower limbs. Blood tests showed severe renal failure (Table 1). Clinical neurologic investigation showed a mild right-sided facial and hypoglossus palsy, mild right-sided hemiparesis, and right-sided hypotonia and cerebral-magnetic-resonance-imaging an ischemic left-sided thalamic lesion. She was discharged with candesartan, amlodipine, escitalopram, linaclotide, simvastatin, trazadone and, despite persisting renal insufficiency, rivaroxaban 15 mg/d.

3. Discussion

This case reports about a fallacy leading to a dilemma resulting in recurrent stroke. The fallacy: DOAC were initiated because of “non-adjustable INR”. Instable INR values may be due to several reasons like impaired cognition, depressed mood, or inadequate health literacy [7]. Instead of investigating the reason for the low INR-value which had presumably contributed to the stroke, the treating physicians changed from vitamin-K-antagonists to DOAC without clarifying and solving the underlying problem.

The dilemma: Rivaroxaban 10 mg/d was chosen because of renal insufficiency. The dose chosen was not based on any clinical trial data. Although the blood tests indicated that the coagulation system was influenced by rivaroxaban, the recurrent stroke indicates that the anticoagulant therapy was not effective. A higher dose, however, might increase the bleeding risk. Patients with a creatinine-clearance <30 ml/min were excluded from the rivaroxaban-investigating trial [3]. Renal insufficiency may develop rapidly due to infection, change in co-medication, fluid losses or lack of fluid intake. Renal function should be estimated by calculating the creatinine-clearance by the Cockcroft-Gault-formula [1–3]. Other formulae may overestimate renal function (Table 1) [8,9].

It has been shown recently that inappropriate use of DOAC in patients with AF is frequent and possibly leads to adverse events [10].

4. Conclusion

In cases of stroke, renal failure and inadequate anticoagulation it is not useful to change from vitamin-K-antagonists to “low dose” DOAC. Diligent investigations for the cause of INR instability and continuation of vitamin-K-antagonist therapy seem to be more effective and safer since there is the opportunity of monitoring therapy and to avoid under- as well as over-dosage.

Conflict of interest

None declared.

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The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

REFERENCES