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Rivaroxaban and Apixaban plasma concentrations at trough in patients with atrial fibrillation

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Background: The direct factor Xa (FXa) inhibitors Apixaban and Rivaroxaban are used for stroke prevention in patients with atrial fibrillation (AF). The FXa-inhibitors do not require routine laboratory monitoring in the same extensive way as warfarin, but as exposure, i.e. plasma concentration, correlate to efficacy and safety and it was important to establish both the methods to monitor when needed and typical exposure intervals.

Aims: The aim of this study is to show the typical exposure range of apixaban and rivaroxaban in real-life patients with AF, and further to evaluate different laboratory methods for these measurements.

Methods: We have included a total of 141 AF patients treated with either apixaban 2.5 mg/5 mg (n=10/60) twice daily or rivaroxaban 15 mg/20 mg (n=10/61) once daily. Trough plasma concentrations were measured by liquid chromatography-tandem mass-spectrometry (LC-MS/MS) and Anti-FXa assays were calibrated with apixaban/rivaroxaban (STA® Liquid Anti-FXa (Diagnostica Stago, Asnieres, France)).

Results: Typical (10th-90th percentiles) exposure intervals were 43-118 ng/ml for apixaban and 13-63 ng/ml for rivaroxaban. The median trough apixaban plasma concentration measured by LC-MS/MS was 75 ng/ml (range 15-186 ng/ml). Patients who were treated with apixaban 5 mg twice daily had significantly higher drug levels than patients treated with the 2.5 mg dose. The median trough rivaroxaban plasma concentration measured by LC-MS/MS was 34 ng/ml (range 5-84 ng/ml). No significant difference in rivaroxaban concentration was seen between the 15 mg and 20 mg doses. Anti-FXa assays correlated strongly with LC-MS/MS for both apixaban and rivaroxaban ($p<0.001$).

Conclusions: Apixaban and rivaroxaban plasma concentrations varied substantially in AF patients. We here describe the range of exposures as well as typical exposure intervals for both drugs. We suggest that these typical exposure intervals may be used for dose guidance.

Biography

Fadiea Al-Aieshy is a certified Pharmacist working at Karolinska University Hospital and a PhD-student in Medical Science at Karolinska Institute in Stockholm, Sweden. The main aim of her research is to evaluate biomarkers for the new oral anticoagulants dabigatran, apixaban and rivaroxaban, to increase safety and efficacy in individual patients.

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