Analysis of the interaction of anticoagulants on points of care (POC) tests for urine from patients on therapy with dabigatran and rivaroxaban

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Background: The amount of new oral anticoagulants (NOACs) such as dabigatran and rivaroxaban may be necessary to determine in specific patient populations. Point of care (POC) methods were currently developed to analyse direct thrombin (international patent application No. PCT/EP2012/002540) and direct factor Xa inhibitors (international patent PCT/WO2012/069139A1) in urine. NOACs as well as conventional anticoagulants (except vitamin K antagonists) are excreted into the urine. Interactions of the anticoagulants may occur on the POC tests for dabigatran and rivaroxaban. POC test have the advantage over tests from plasma to be non-invasive, repetitive and rapid. They show when the NOAC is not any more on board and help to decide when to start or when to increase the dose the conventional anticoagulant.

Aim: We aimed to quantify the interaction of heparin, low-molecular-weight heparin (nadroparin), hirudin, and argatroban of the thrombin and factor Xa specific POC tests using urine samples on treatment with dabigatran or rivaroxaban.

Background: Urine samples were obtained from patients on treatment with 2 × 110 mg or 2 × 150 mg dabigatran (all \( n = 15 \)) daily, 10 mg od rivaroxaban \( (n = 15) \), from 30 patients on treatment with low-molecular-weight heparin nadroparin (LMWH), and from five controls. All studies were accepted by the local university ethical board and patients gave written informed consent prior to participation. Urine samples of patients with dabigatran and controls were spiked with 0.0, 0.1–1.0 units of unfractionated heparin (UFH), 0.0 0.1–1 mg/mL hirudin and up to 6 mg/mL argatroban. From these samples the POC test for dabigatran was performed. Urine samples of patients with rivaroxaban or controls were spiked with similar concentrations of nadroparin and fondaparinux. Samples with UFH, nadroparin and fondaparinux were analysed without and with addition of 1 IU antithrombin/mL (AT) per mL urine. The POC test for rivaroxaban was performed from all these samples and from urine samples of patients under therapy with LMWH. The urine samples were incubated for 15 min in the POC device and the colour of the samples were judged as positive or negative.

Results: The POC tests for dabigatran and rivaroxaban were positive in all patients on therapy and negative in controls. UFH, LMWH, and fondaparinux did not indicate any interaction in all experimental settings. The POC test for rivaroxaban was negative in all patients on treatment with LMWH without addition of AT and was positive in some patients after addition of AT. High concentrations of hirudin and argatroban showed some interaction with the POC test for dabigatran.

Conclusion: The specificity of the POC assays for dabigatran and rivaroxaban in urine is high and no interactions occur in the absence or presence of AT for all heparins and heparin derived anticoagulants in patients on treatment with LMWH. Only for patients receiving hirudins and argatroban the POC test for dabigatran should not be used.

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