Rivaroxaban – an oral, direct Factor Xa inhibitor is currently used in clinical practice for the prevention and treatment of thromboembolic disorders. Routine coagulation monitoring is not required, but a quantitative determination of rivaroxaban exposure might be useful in certain clinical circumstances (e.g., prior to urgent surgery).

Because of its mode of action, rivaroxaban prolongs the prothrombin time (PT), but the results vary depending on the assay reagents; the international normalized ratio (INR) correction used for monitoring the vitamin K antagonists cannot be used for rivaroxaban.

To evaluate the suitability of the PT assay for the measurement of rivaroxaban plasma concentrations (ng/ml) using rivaroxaban calibrators and controls, and to assess the inter- and intra-laboratory precision of the measurements.

Evaluations were carried out over 10 days by each laboratory using its own PT reagents. Results are presented as median values ± standard deviation (N=18). The intra-laboratory CV was 2.7–34.1% (for 19 ng/ml), 1.1–7.9% (160 ng/ml).

Further validation of this method is required in clinical settings.

The control plasma samples were diluted with calibrator containing 0 ng/ml rivaroxaban where the values were greater than the calibration range.

The local PT assay results were expressed as rivaroxaban concentrations (ng/ml) using the conventional INR, which cannot be used for the measurement of rivaroxaban plasma concentrations (expressed in ng/ml) using the PT combined with rivaroxaban calibrators and controls, in contrast to the conventional INR which cannot be used.

Owing to the variability of the measurements observed (in particular at low rivaroxaban plasma concentrations), more specific and sensitive methods (i.e., anti-Xa factor Xa chromogenic assays) (please see poster CPC049) are a better alternative when more precise measurements of rivaroxaban exposure are required.

Rivaroxaban is a direct Factor Xa inhibitor and is currently used in clinical practice for the prevention and treatment of thromboembolic disorders.

Methods

Participating laboratories in Europe and North America were provided with sets of rivaroxaban calibrators (0, 41, 219 and 643 ng/ml) and pooled human plasma controls containing 19, 160 and 643 ng/ml of rivaroxaban. The concentrations of rivaroxaban in the pooled human plasma controls were unknown to the participating laboratories.

Conclusions

The results of this field trial suggest that it is feasible to measure rivaroxaban plasma concentrations using calibrated and controlled results of a multicentre field trial.

Table 1. Local PT reagents and instruments used by the participating laboratories

Table 2. Local PT reagents and instruments used by the participating laboratories

References


Prothrombin time assay for measuring rivaroxaban plasma concentrations using calibrators and controls: results of a multicentre field trial

CPC047

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Introduction

Central PT reagent:

- There was less inter-laboratory variation when the central PT reagent was used (CV 2.0–7.5%; undiluted samples; expressed as rivaroxaban concentrations) compared with local PT reagents; however, measured rivaroxaban concentrations were higher than the actual values (Figure 2; Table 2), as with local PT reagents.

The intra-laboratory CV was 4.5–19.3% (for 19 ng/ml), 1.2–8.3% (160 ng/ml), and 0.9–5.0% (463 ng/ml).

- The CV of the calibrators was 4.4–6.5% for the central PT reagent compared with 12.5–27.2% for local PT reagents (Table 2).

Objective

- To evaluate the suitability of the PT assay for the measurement of rivaroxaban plasma concentrations (ng/ml) using rivaroxaban calibrators and controls, and to assess the inter- and intra-laboratory precision of the measurements.

Method:

Participating laboratories in Europe and North America were provided with sets of rivaroxaban calibrators (0, 41, 219 and 643 ng/ml) and pooled human plasma controls containing 19, 160 and 643 ng/ml of rivaroxaban. The concentrations of rivaroxaban in the pooled human plasma controls were unknown to the participating laboratories.

Results

- Local PT assay results were expressed as rivaroxaban concentrations (ng/ml) using the conventional INR, which cannot be used.

The intra-laboratory CV was 13.6–29.7%. Less variation was found when the results were expressed as rivaroxaban concentrations (ng/ml, CV 3.9–15.5%; undiluted samples), although over-estimation was observed (Figure 1; Table 2).

- The inter-laboratory CV was 2.7–34.1% (for 19 ng/ml), 1.1–7.9% (160 ng/ml) and 1.1–8.6% (643 ng/ml).

Conclusions

- The results of this field trial suggest that it is feasible to measure rivaroxaban plasma concentrations (expressed in ng/ml) using the PT combined with rivaroxaban calibrators and controls, in contrast to the conventional INR which cannot be used.

- Owing to the variability of the measurements observed (in particular at low rivaroxaban plasma concentrations), more specific and sensitive methods (i.e., anti-Xa factor Xa chromogenic assays) (please see poster CPC049) are a better alternative when more precise measurements of rivaroxaban exposure are required.

- Further validation of this method is required in clinical settings.