A performance evaluation of a novel human recombinant tissue factor prothrombin time reagent

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Introduction

We report on the performance of a novel prothrombin time reagent (NewPT) which utilises human recombinant tissue factor produced by silkworm technology and synthetic phospholipids. Insect systems are widely used to produce proteins from higher eukaryotes because they have a similar pattern of glycosylation, phosphorylation, and protein processing.

The aim of this study was to compare the performance of NewPT with two widely used PT reagents.

Methods

The performance of NewPT (Sysmex Corp. Japan) was compared to that of two commercial PT reagents containing either recombinant human tissue factor (A) or human placental thromboplastin (B) on a fully automated coagulometer. Analyser specific ISI values were determined using Technoclone AK-Calibrant as per SSC guidelines were used. On-board stability and imprecision were assessed using commercial QC preparations. Comparability testing was performed on over 300 normal and abnormal plasma samples.

Results

Normal reference ranges were established in 100 normal healthy donors (Table 1). Excellent between-day imprecision was obtained for all 3 reagents and acceptable on-board stability was observed.

Table 1.

	NewPT	PT reagent A	PT reagent B
Normal range (s) n = 100	9.78-12.89	9.60 – 11.54	11.33 – 13.75
ISI	1	0.97	1.07
Between day imprecision % CV normal QC ; abnormal QC	0.81; 0.83	0.78; 1.55	1.30; 1.24
4 day on-board stability (% of day 0)	-2.1 to -0.8	-4.8 to -0.8	-3.9 to 0.7
Mean INR (Warfarin, n = 130)	3.06	3.02	3.09
Mean INR in warfarin LA plasmas (n = 53)	1.87	1.87	1.62

Good agreement was obtained between methods in 130 samples from patients receiving warfarin. The FII sensitivity of NewPT was similar to reagents A and B but NewPT was more sensitive to FV, FVII and FX. NewPT had similar sensitivity to reagent B for coagulation defects in liver disease and improved sensitivity compared to reagent A.

Fig. 1. INR values for normal controls (n = 100) and patients receiving warfarin (n = 130). PTA vs NewPT

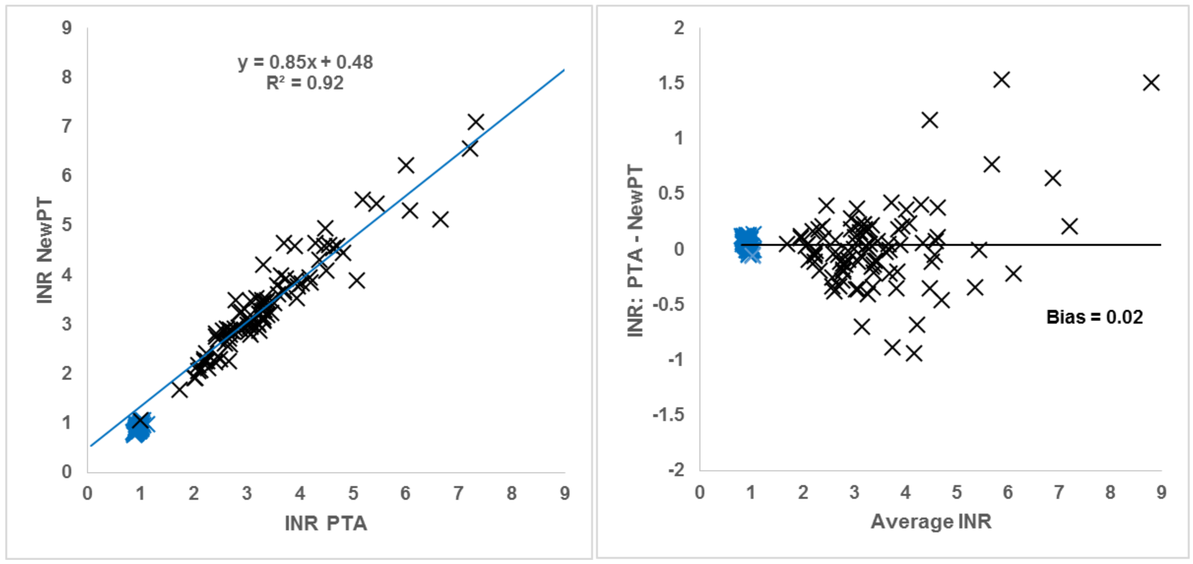
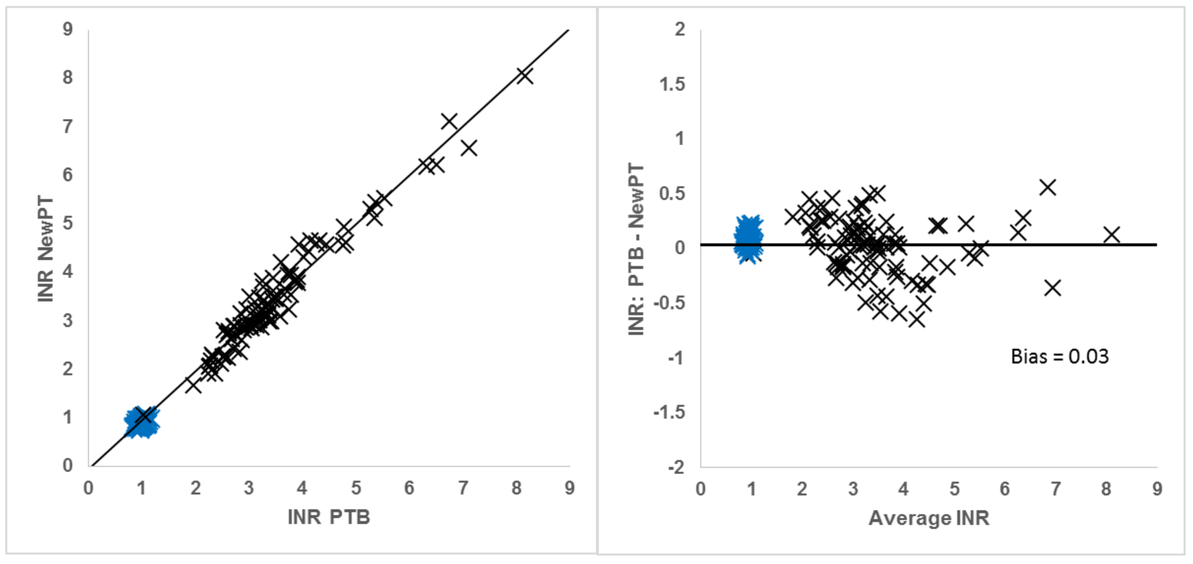


Fig. 2. INR values for normal controls (n = 100) and patients receiving warfarin (n = 130). PTB vs NewPT



No heparin interference was observed in plasma spiked with up to 1.5 IU/mL unfractionated heparin or low molecular weight heparin in NewPT or reagent A both of which contain a heparin-neutralising compound.

The lupus anticoagulant sensitivity of all three reagents was similar. NewPT demonstrated dose responsiveness to Dabigatran, Apixaban and Rivaroxaban with steeper response curves than Reagent A or B.

Conclusions

In a wide range of plasma samples, sbPT demonstrated comparable or improved performance relative to two commercial PT reagents which are suitable for the control of oral vitamin K antagonist therapy and the detection of congenital or acquired deficiency of FII, FV, FVII and FX.