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New procalcitonin point-of-care test meets analytical performances to stratification of infectious syndrome

Dear Editor,

With the increase of laboratories grouped into platforms, located away from clinical departments, and the need to meet demand faster, the use of point-of-care tests (POCTs) is growing, especially in emergency or intensive care units (ICU). In these departments as well as in outpatient departments, fever in infants/children/adults is the leading cause of presentations. However, a majority of infectious syndrome did not require antibiotics immediately and procalcitonin (PCT) may help to differentiate mild or severe infections [1]. As a consequence, POCTs offering biomarkers of infections including PCT, may improve this challenge to avoid unnecessary invasive testing. However, POCTs have to meet several requirements: providing the quantitative measurement of PCT in whole blood, taking into account the haematocrit; the assay must be accurate, easy to use and correlate with the BRAHMS PCT (ThermoScientific, BRAHMS AG, Hennigsdorf, Germany), which, in absence of standardization, is considered a surrogate reference method including cut-off values. Currently, few available POCTs meet all these requirements as recently reported [2]. Among POCT available to measure PCT on whole blood, the PATHFAST instrument (Biosynex-Theradiag, Marne La Vallée, France) has implemented PCT assay using common antibodies and/or calibrators from BRAHMS GmbH.

The aim of our study was to evaluate the analytical and clinical performances of the PATHFAST BRAHMS PCT assay in comparison with the BRAHMS PCT sensitive KRYPTOR kit on KRYPTOR GOLD analyzer (ThermoScientific, BRAHMS AG, Hennigsdorf, Germany).

PCT was measured on plasma using the BRAHMS PCT sensitive KRYPTOR kit on KRYPTOR GOLD analyzer considered, in our study, as the reference method. PCT was measured on whole blood and on plasma with the PATHFAST BRAHMS PCT assay, which is based on non-competitive chemiluminescence enzyme immunoassay (CLEIA) combined with MAGTRATION© technology on PATHFAST analyzer. The analyzer allows the determination on whole blood taking into account hematocrit percentage of each sample, and also on plasma with a detection of matrix.

Imprecision studies, and the determination of the limit of blank (LoB) and of the limit of detection (LoD) were based on the CLSI protocols [3,4]. A plasma pool with PCT concentration of 12μg/L was used to test the low-end linearity of the assay. Analytical performances (imprecision, LoB, LoD, and linearity study) of the PATHFAST assay are presented in Table 1. The within-run coefficients of variation (CV) was twice as high (around 10%) than manufacturer claimed (around 5%) probably because using whole blood, and plasma as CV closed to 5% were obtained when using Quality Control (QC) material. The intermediate precision CV ranged from 5% to 9%, remaining acceptable according to the Jaffe's recommendations. [5], which state that assays with an imprecision up to a 20 % CV may reasonably be useable and acceptable for a POC system. The LoB (0.002μg/L) and LoD (0.02μg/L) were slightly different to that obtained by the manufacturer (0.004 and 0.007 μg/L, respectively). The PATHFAST BRAHMS PCT assay displayed acceptable linearity over the most clinically relevant range for PCT concentrations with a gradual decrease in recovery from 100.0% (assigned value 12 μg/L) to 83.3% (assigned value 0.037 μg/L). The CUSUM test did not show significant deviation from linearity.

The comparison study was performed on 160 plasma samples vs 160 corresponding whole blood samples and on 182 plasma samples on both analyzers from consecutive patients ranging from 0.03 to 92μg/L admitted to the Emergency and the ICU departments of Lapeyronie Hospital (Montpellier, France). First, the tests were performed from heparinized tubes on the PATHFAST instrument on whole blood upon receipt of the tubes at the central laboratory. Then, the tubes were centrifuged 10 min at 2000g and the PCT was simultaneously determined on the plasma on both KRYPTOR analyzer and PATHFAST instrument. Only KRYPTOR PCT values were used for the clinical diagnosis. Agreement between whole blood PCT vs plasma PCT, was estimated using the Passing Bablok regression analysis, and Bland-Altman plots using XLSTAT® software, version 2016.06.35661 (NY, USA). Clinical concordance using different cut-off values (PCT values < 0.25, $0.25 <$ PCT values < 0.50, $0.5 <$ PCT values < 2, and $2 <$ PCT values < 10 μg/L) between the methods with disease state was assessed using Cohen's κ-test [6]. We observed a trend to a very slight underestimation of PATHFAST BRAHMS PCT vs. KRYPTOR PCT values in all measuring ranges. However, the PATHFAST BRAHMS PCT assay exhibited good correlation in the working range of 0.03–92 μg/L and an acceptable concordance with results from KRYPTOR with a bias of −0.19 (±4.63)

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Table 1
Analytical performances of PATHFAST BRAHMS PCT assay on the PATHFAST© instrument.

	Data from our study			Data from manufacturer	
	Mean, µg/L	CV, %		Mean, µg/L	CV, %
Repeatability precision (n = 20)					
Low whole blood sample	0.11	10.11	Control level 1	0.09	4.4
High whole blood sample	0.95	11.60	Control level 2	2.02	5.2
			Control level 3	36.1	5.1
Intermediate precision (n = 25)					
Control level 1	0.22	5.25	Control level 1	0.09	6.9
Control level 2	8.93	6.14	Control level 2	2.02	5.6
Plasma pool	0.24	9.00	Control level 3	36.1	5.8
LoB	0.002			0.004	
LoD	0.020			0.007	

Linearity	
Theoretical values, µg/mL	Mean of observed values with PATHFAST BRAHMS PCT assay, µg/L (% of mean recovery)
12.0	12 (100)
6.0	6.3 (105)
3.0	3.15 (105)
1.5	1.575 (105)
0.75	0.81 (108)
0.375	0.39 (104)
0.18	0.17 (94.4)
0.09	0.075 (83.3)
0.045	0.037 (83.3)
0.022	0.012 (54.5)
0.009	0.0015 (16.6)

CV, coefficient of variation; LoB, limit of blank; LoD, limit of detection.

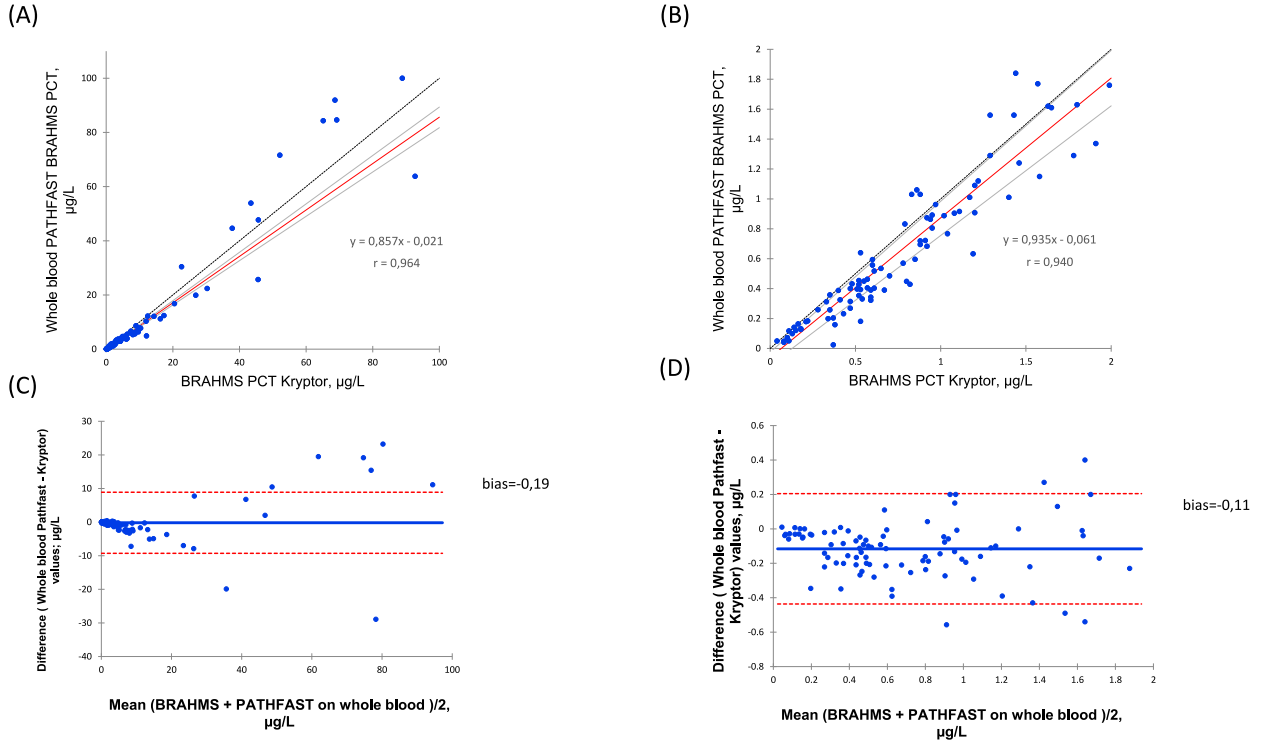

Fig. 1. (A) Passing-Bablok regression analysis on plasma samples in the range (A) 0.02–100 µg/L and (B) 0,02-2 µg/L of BRAHMS PCT Kryptor against whole blood PATHFAST PCT values. Bland-Altman analysis between BRAHMS PCT vs PATHFAST PCT values on (C) all measuring range and (D) on <2 µg/L values.

μg/L (Fig. 1). In the low range (PCT values < 2 μg/L), the underestimation was lower than for higher values and the agreement in PCT measurements was quite satisfactory (r > 0.93 with a bias of −0.11 (±0.16) μg/L (Fig. 1). The Kappa coefficient was determined to be 0.87 (95% CI, 0.812 to 0.934) and consequently, the strength of agreement is considered to be almost perfect between the two methods (see Table A in supplemental appendix). The discrepancies at the cut-off of 0.5 (n = 9) between the two assays with the final diagnostic were listed in Table B (supplementary table). Values of PATHFAST BRAHMS PCT were lower than values obtained with KRYPTOR, however the values all remain higher than 0.25 μg/L which is considered, according to the Hamade study [7]; as the emergency alert threshold. As a result, for patients with values between 0.25 and 0.5 μg/L, it is recommended to repeat a PCT 24–48 hours later [7]. However, since PCT measurement is not a diagnostic test, it should be used only to supplement and not to replace clinical judgement [8]. In addition, no reference methods for PCT quantitation are yet available, and comparison studies could be difficult to interpret [9].

The same comparison study was performed on 182 plasma samples comparing values of PCT determined on KRYPTOR and PATHFAST (supplementary Figure A). The PCT assay on PATHFAST exhibited good correlation in the working range of 0.02–100 μg/L and an acceptable concordance with a bias of −0.41 (±3.90) for plasma sample measurements on both instruments. The same acceptable agreement was observed on low plasma values (<2 μg/L) with a bias of −0.15 (±0.17) (supplementary Figure A).

We measured on the PATHFAST, external quality assessment (EQA) specimens stored at −80 °C (n = 15) from the 2021 to 2022 ProBioQual EQA program (ProBioQual, Lyon, France) and we compared values KRYPTOR vs PATHFAST as well as vs others manufacturers, which used common antibodies and/or calibrators from BRAHMS GmbH (Abbott, Biomérieux, Roche, Siemens). For the values < 10 μg/L, the results were close to those of Kryptor, beyond the values > 10 μg/L, the results are more dispersed with higher values compared to Kryptor values values but similar to other systems (see supplementary Figure B). Even if they are the same antibodies and calibrators as Kryptor, the values remain different, probably due to the matrix effect, to the measurement methods but also to the lack of standardization of calibration between methods.

Overall, the analytical performances of the PATHFAST BRAHMS PCT assay were acceptable with a good imprecision (CV close to 10%), good linearity and LoD largely lower than 0.25 μg/L. The slight underestimation remains acceptable at the clinical level. The few discordant results as well as the differences in EQA determinations highlighted the urgent need of standardization since the implementation of this dosage on new platforms and in decentralized laboratories using POCT is constantly growing. The bias is acceptable for a device intended to be relocated. It could allow faster clinical decision, a triage of patients and to provide sufficient diagnostic discrimination either to diagnose or exclude serious infection especially in pediatrics units.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.plabm.2024.e00372.

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