INTRODUCTION

Oversuse of antibiotics treatments and the continuous emergence of multidrug resistant organisms has posed a threat to public health. A lack of diagnostic and prognostic biomarkers for bacterial infection has led to inappropriate use of antibiotics, increased opportunity for antibiotic resistance, toxic side effects of antibiotics to patients which consequently increases mortality and is a cost burden on the NHS.

Within secondary care, worry over clinical deterioration paired with an attempt to balance risk of poor clinical outcome results in over-prescription of antibiotics (Jee et al., 2018). Worry of patients potentially having an underlying and undiagnosed infection consequently results in a further increase in bacterial resistance (Tsangaris, I., et al., 2009) whilst simultaneously increasing the risk of unnecessary prolonged exposure to antibiotics which can inadvertently affect a patient’s overall clinical outcome. A reliable and immediate way of mitigating these challenges is the introduction of a rapid diagnostic and prognostic test—procollatinon (PCT) assay.

Procalcitonin (PCT) is a 116 amino acid peptide that belongs to the calcitonin (CT) family and plays a role in the homeostasis of calcium (Vijayan et al., 2017). Under normal physiological conditions, healthy individuals have low levels of PCT (<0.05 ng/mL) and elevated levels of PCT are reported in patients with bacterial infections (Assicot et al., 1993).

PCT has been reported to be a superior pro-inflammatory biomarker with favourable biokinetics over CRP, for early diagnosis and monitoring of bacterial infections. PCT is detectable within 4-6 hours of onset of bacterial infection and peaks within 24 hours; in contrast to CRP which gradually rises and peaks within 48 hours of infection (Leslie et al., 2015). PCT has a half-life of 24 to 35 hours thus immediately indicating efficacy of antibiotics treatment and has been evidenced to have a high negative predictive rule out value (99% at a cut-off value of 0.2 ng/mL) (Pibarot and Vincent, 2010) thus making it an ideal marker to rule out sepsis. Currently within the UK, PCT has not been approved for use parallel to clinical judgement for procollatinon-guided antibiotic stewardship as the data is insufficient.

The intended use of this verification and use of assay is to aid in assistance that the presumed infection is specifically bacterial, prompting for a more accurate diagnosis and tailored appropriate antibiotic treatment plan, which is the fundamental principle of antibiotic stewardship.

METHODS

1. Measurement of Trueness - 11 Venas EQA samples were assayed for Accuracy and evidence were supplied using slope and intercept and bias as well as calculating trueness bias was done using Bland Altman plot.

2. Method Comparison - 31 samples were analysed for PCT method comparison. The Pearson’s correlation co-efficient was used for PCT quantification method agreement and linearity between MKLUH Access DXi800 and Morocome Bay Hospital’s DX800.

3. Measurement of Precision - Mean, standard deviation and cv% of 10 replications of 3 levels of RANDOQ Speciality IQC.

4. Linearity - The limit of detection (LoD), and the Limit of Quantification (LoQ) was performed to achieve a cv >20% and LoQ quoted by Beckman of 0.02ng/mL.

RESULTS

Measurement of Trueness

A significant significantly higher negative bias of 32.39% was seen on the ALT against MKLUH results. Negative bias can be explained by method difference. The WESAS and RAGAS EQA samples processed do not have results for Access PCT as it is not a part of their scheme. The ALT is for BIAIMS PCT methods and results used where referenced as a non-specific immunoassay.

Method Comparison

The desirable specification for measurement of precision for PCT is <10% across all ranges.

Measurement of Precision

The intra-batch imprecision quoted by Beckman is 6.86% CV at concentrations ≤1.15 ng/mL. The intra-batch CVs are all acceptable.

Linearity

The inter-batch CV quoted by Beckman is 8.09% CV at concentrations ≤1.15 ng/mL and the inter-batch CVs tabulated are within both the Beckman range and acceptable.

CONCLUSION

The use of PCT and the clinical interpretation of concentrations relies on assay sensitivity. The cut off value adopted that rules out suspected bacterial infection and discouragement of antibiotic treatment is ≤0.25 ng/mL (Schuetz et al., 2019) whilst further monitoring being encouraged. The access PCT method passed with a limit of detection of 0.60 ng/mL and limit of quantification was 0.018 ng/mL at CV of 15.9% which is acceptable and within the Beckman quoted limits < 20% CV at 0.02 ng/mL (Beckman Coulter, 2019a).

Owing to Access assay sensitivity, PCT can be used as a prognostic biomarker to guide continuation, de-escalation, and importantly discontinuation and discosuragement of treatment thus aiding in Antibiotic Stewardship. However, the bias evidenced between two measurements on the same samples, using a similar assay but different machines, evidenced that PCT is not a suitable diagnostic marker for sepsis.