Evaluation of the QMS[®] Teicoplanin Immunoassay (ThermoFisher Scientific) on Cobas[®] 8000 System (Roche Diagnostics) and Comparison to Fluorescence Polarization Immunoassay for the Determination of Teicoplanin Concentrations in Human Plasma

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Background: The performances of the QMS[®] Teicoplanin immunoassay recently developed on Cobas[®] 6000/8000 systems were evaluated and compared to a fluorescence polarization immunoassay (FPIA) [Teicoplanin Innofluor[®] Assay (Thermo Fisher Scientific, Indianapolis, IN)] on FLX analyzer (Abbott Laboratories, Abbott Park, IL). **Methods:** The validation was performed according to the Cofrac (French Accreditation Committee) document SH GTA 04. For the comparison, 48 plasma samples were analyzed by FPIA and QMS assays. **Results:** The QMS assay is accurate (intra assay and inter assay inaccuracy $\leq 2.4\%$)

and precise (intra assay and inter assay imprecision $\leq 10.2\%$). A linear relationship [$QMS = 1.0319 \times FPIA - 2.8518$, $r^2 = 0.9246$ ($P < 0.001$)] between FPIA and QMS was found. In the Bland–Altman plots, no systematic bias was found even if QMS results trends to be lower (mean of the ratio QMS concentration/FPIA concentration = 0.91). **Conclusion:** These results between QMS and FPIA are consistent, which indicates that QMS[®] Teicoplanin immunoassay on Cobas[®] 8000 System is an alternative to FPIA. J. Clin. Lab. Anal. 27:96–98, 2013. © 2012 Wiley Periodicals, Inc.

Key words: antibiotic; therapeutic drug monitoring; FPIA

INTRODUCTION

Teicoplanin is a glycopeptide antibiotic used in the treatment of infections caused by gram-positive strains of bacteria (1). Teicoplanin is composed of a mixture of compounds, the main components are A2 (from A2–1 to A2–5), which represents 90–95% of the Teicoplanin mixture and A2–2 is the most active compound and constitutes about 50% of the mixture (2). Therapeutic drug monitoring of Teicoplanin has been recommended by various reports to maintain adequate trough plasma concentration (≥ 10 – 15 mg/l or ≥ 20 – 40 mg/l, regarding the measurement method and the infection severity) (3). Measurement of Teicoplanin plasma concentration can be carried out using liquid chromatography procedures for quantitative determination of each Teicoplanin component (4–7). These methods are time consuming and

immunoassays are used more commonly. Until recently, only a fluorescence polarization immunoassay (FPIA) was available on the market (TDxFLx[®] analyzer; Abbott Laboratories, Abbott Park, IL). However, Thermo Fisher Scientific has developed a homogeneous turbidimetric immunoassay that utilizes the Quantitative Microsphere System (QMS) technology on HITACHI[®] 917 System (8). This assay was recently adapted for the Cobas[®] 8000 modular analyzer series (Roche Diagnostics, Basel,

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Received 16 August 2012; Accepted 19 November 2012

DOI 10.1002/jcla.21567

Published online in Wiley Online Library (wileyonlinelibrary.com).

Switzerland). The aims of this work are to evaluate analytical performance of QMS assay according to the Cofrac (French Accreditation Committee) document SH GTA 04 (9) and to compare plasma concentrations of Teicoplanin in human plasma measured with QMS[®] Teicoplanin Immunoassay (Thermo Fisher Scientific, Indianapolis, IN) on COBAS[®] 8000 System and fluorescence polarization immunoassay on FLX analyzer.

MATERIALS AND METHODS

Teicoplanin plasma samples were collected over a 3-month period from patients treated by Teicoplanin. Spiked plasma samples (3, 4, 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100 mg/l) were prepared by mixing teicoplanin solution in drug free plasma. Teicoplanin was obtained from Sigma (Saint-Quentin Fallavier, France). These samples were first analyzed by FPIA and then stored at -20°C for QMS assay.

FPIA was performed using Teicoplanin Innofluor[®] Assay (Thermo Fisher Scientific) on FLX analyzer (Abbott Laboratories) according to the manufacturer's guidelines.

The QMS assay is a homogenous particle-enhanced turbidimetric immunoassay based on competition between drug in the sample and drug coated onto a microparticle for antibody binding sites of the Teicoplanin antibody reagent. This assay was first developed on HITACHI[®] 917 System and then adapted to Cobas[®] 6000/8000 C501/C502 module of according to the results of correlation study between HITACHI[®] 917 System and Cobas[®] 6000 C501 module.

Inaccuracy and imprecision were determined from the analysis of 32 replicates on 19 separate days (inter assay inaccuracy and imprecision) and 30 replicates in the same run (intra assay inaccuracy and imprecision) of the quality controls (low level, medium level, and high level). Inaccuracy is defined as the percentage of deviation from the nominal level and imprecision as the coefficient of variation within a single run (intra assay) and between different runs (inter assay).

Method comparisons were carried out according to Bland–Altman procedures and linear regression.

RESULTS

The results of the intra assay and inter assay inaccuracy and imprecision are presented in Table 1. Although only 48 samples (32 patients, 3 internal quality controls of the Innofluor[®] assay system, and 13 spiked plasma samples) were analyzed, a large range of plasma concentration was covered [from 3.3 mg/l to 67.3 mg/l for patients samples (QMS assay)]. A linear relationship [$\text{QMS} = 1.0319 \times \text{FPIA} - 2.8518$, $r^2 = 0.9246$ ($P < 0.001$)] between FPIA

TABLE 1. Analytical performances of the QMS assay

Level (nominal concentration)	Intra assay ($n = 30$)		Inter assay ($n = 32$)	
	Inaccuracy	Imprecision	Inaccuracy	Imprecision
Low level (9.63 mg/l)	−1.24%	8.9%	+2.6%	10.2%
Medium level (32.2 mg/l)	−1.95%	1.9%	+2.41%	7.5%
High level (71.4 mg/l)	−0.43%	1.7%	+4.2%	5.6%

Fig. 1. Relationship between QMS assay and fluorescence polarization immunoassay (FPIA) by linear regression ($n = 48$)

Fig. 2. Relationship between QMS assay and fluorescence polarization immunoassay (FPIA) by Bland–Altman procedure ($n = 48$)

and QMS was established (Fig. 1). In the Bland–Altman plots, no systematic bias was found even if QMS results tends to be lower (mean of the ratio QMS/ FPIA = 0.91) (Fig. 2).

CONCLUSION

According to the Cofrac (French Accreditation Committee) document SH GTA 04, the evaluation of the QMS assay was limited to the imprecision, the inaccuracy, and a comparison with the method previously used in the laboratory since the new QMS assay is CE-marked (The letters CE stand for “Conformité Européenne” which means “European Conformity”) on the Cobas[®] 6000/8000 systems. The limit of quantitation (3 mg/l) and the specificity were not checked. The QMS assay is accurate (intra assay and inter assay inaccuracy $\leq 4.2\%$) and precise (intra

assay and inter assay imprecision $\leq 10.2\%$). The results of Teicoplanin concentrations in human plasma measured by FPIA (Teicoplanin Innofluor[®] Assay) or QMS[®] Teicoplanin immunoassay on Cobas[®] 8000 C502 module were consistent between both assays even if QMS results trends to be slightly lower.

FPIA is a widely used and very convenient method. However, the FLX analyzer may not be available indefinitely and is not available worldwide. Since the results of Teicoplanin Innofluor[®] Assay on FLX analyzer and QMS[®] Teicoplanin immunoassay on Cobas[®] 8000 C502 module are consistent, QMS[®] Teicoplanin immunoassay constitutes an alternative method to FPIA, appropriate for routine therapeutic drug monitoring of Teicoplanin.

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