Establishment of reference intervals of tests used to screen for immunoassay interferences: The example of polyethylene glycol precipitation procedure

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%Recovery was found between %95–103 for serum and %98–102 for saliva samples. Results of the developed LC-MS/MS method showed a good correlation with the results of commercial CLIA and ELISA kits ($R^2 = 0.98$ and 0.95) respectively for serum and saliva samples.

Conclusions

The developed method has high sensitivity, short measurement time and shows good correlation with commercial ELISA and CLIA kits.

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M110

Quantitative measurement of biotin by LC-MS/MS in human serum and the effect of multivitamin and renal function on biotin concentration

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Background-aim

Biotin, also known as vitamin B7 is water-soluble vitamin which acts as coenzyme of metabolism. Its deficiency is known to be rare, however, excess of biotin from exogenous intake have been reported to make interference on several analytical systems using biotin-streptavidin immunoassay. This study is to develop a reliable quantitation method of serum biotin using liquid chromatography tandem-mass spectrometry, and to measure the serum level of biotin in patients with chronic kidney disease (CKD) and general population and predicting its potential effect on immunoassay.

Methods

Samples were extracted using internal standard dissolved acetonitrile and reconstituted in 3% acetonitrile. LC separation of biotin was performed on Ascentis® Express F5, 2.7 Micron HPLC Column 2.1 mm × 100 mm, 2.7 μm (Sigma-Aldrich, St Louis, MO, USA) and detected by 1200 series infinity system and 6490 Mass Spectrometer (Agilent Technologies, Santa Clara, CA, USA) on positive electrospray ionization mode. Analytical performance of the developed method was analyzed based on standard protocols. Serum biotin levels from patients with chronic kidney disease who taking or not taking the multivitamin containing 300 μg of biotin, and those under health checkup were compared.

Results

Precision of low- and high-concentration controls showed coefficient of variations (%) of <10%. Linearity was satisfied with first degree polynomial model. Lower limit of quantification was 3 ng/mL. Ionization suppression was observed in serum in matrix effect evaluation. Biotin concentration decreased regardless of storage temperature and number of storage days. Biotin concentrations in >98% of samples exceeded the 10 ng/mL which is the lowest known threshold for biotin interference in frequently used immunoassay system. In the non-dialysis CKD group, the patients who were administered the multivitamin had a higher biotin concentration than those who were not ($P = .011$).

Conclusions

This method is eligible for detect the level of biotin level which is able to evaluate the biotin interference. Clinical laboratorians should be alerted of high concentration of biotin in non-dialysis CKD patient and its possible interference.

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M111

Establishment of reference intervals of tests used to screen for immunoassay interferences: The example of polyethylene glycol precipitation procedure

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Background-aim

The identification of immunoassay interferences is essential to avoid potential harmful clinical consequences. However, tests used to screen for interference (polyethylene glycol (PEG) precipitation procedure, heterophilic blocking tubes, streptavidin-coated beads, or dilution tests) themselves can have an impact on the assay results. The PEG precipitation procedure is commonly used to screen for macro-prolactin (macro-PRL) and macro-thyroid stimulating hormone (macro-TSH). Therefore, reference intervals (RIs) after treatment of samples considered being free from interferences must be established in order to decide whether or not an interference could be excluded or suspected. The aim of this study was to establish such RIs for PEG precipitation procedure for some common immunoassay parameters.

Methods

Ten heparinized plasma and serum samples from healthy volunteers were collected. Samples were promptly spun and the supernatant discarded into different aliquots. The following parameters were then analyzed (Cobas® 8000 analyzer, Roche-Diagnostics) in order to obtain baseline values: TSH, free T4 (FT4), free T3 (FT3), thyroxine (T4), triiodothyronine (T3), follicle-stimulating hormone (FSH), luteinizing hormone (LH), PRL, testosterone (T), dehydroepiandrosterone sulfate (DHEA-S), sex hormone binding globulin (SHBG), and 25-OH vitamin D (25(OH)D). Next, samples were treated with the PEG (25%, 6000 *w*/w) precipitation procedure. Results obtained after the test were compared to baseline results with Bland-Altman plots to establish RIs.

Results

The following RIs for the different parameters were obtained: a mean bias of 20.9% (CI95% 12.5 to 29.3) for TSH; −62.7% (CI95% -65.8 to −59.7) for FT4; −47.4% (CI95% -51.6 to −43.3) for FT3; −22.4% (CI95% -27.2 to −17.6) for T4; −54.6% (CI95% -57.5 to −51.6) for T3; −31.8% (CI95% -58.3 to −5.2) for FSH; 72.0% (CI95% 55.6 to 88.4) for LH; 27.7% (CI95% 21.9 to 33.5) for PRL; −58.4% (CI95% -90.3 to −26.4) for T; −56.7% (CI95% -59.5 to −53.8) for DHEA-S; 38.2% (CI95% 23.9 to 52.3%) for SHBG; and of 20.1% (CI95% 10.6 to 29.5) for 25(OH)D.

Conclusions

The establishment of RIs for interference testing, as provided in this study for PEG precipitation procedure, is mandatory to objectively assess and report the presence of interferences.

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M112

An LC-MS/MS based candidate reference method for the quantification of androstenedione in human serum and plasma

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Background-aim

Accurate measurement of androstenedione in human serum and plasma is required for steroid profiling to assure the appropriate diagnosis and differential diagnosis of hyperandrogenism.

Methods

In this work, we introduce a validated LC-MS/MS candidate reference measurement procedure for the quantification of androstenedione in human serum to be used for the standardization and harmonization of routine assays. Sample preparation is based on protein precipitation with zinc sulfate followed by purification with solid phase extraction. As a standard, certified reference material from NMIA was used, which was characterized by qNMR in-house. A $^{13}C_3$-labeled analyte was used as internal standard.

Results

The method allows the measurement of androstenedione in the range of 0.05 ng/mL to 12 ng/mL with an LOD and LOQ of 0.04 ng/mL and 0.13 ng/mL, respectively. Imprecision of interday-assay and intraday-assay were δ 4.4% and δ 3.8%, whereas the accuracy ranged between 91% and 105%.

Conclusions

This protocol describes a robust and reliable method which is suggested as reference measurement procedure for the standardization and harmonization of routine assays for the quantification of androstenedione.

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M113

Empowerment of diabetic patients: Development of a remote monitoring and management system

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Background-aim

Daily monitoring and appropriate patient-specific empowerment can positively influence lifestyle behaviour of patients with diabetes and significantly reduce complications. As personal face-to-face coaching is costly and hard to scale, mobile applications and web services have now become a key driver for chronic disease self-management. We aimed to improve the diabetic patients care path and bridge the gap between them, physicians and laboratories by developing a pilot Diabetes Remote Monitoring and System.

Methods

The system uses an open-source MEAN software development stack as well as Bootstrap components, supporting fast prototyping and multi-platform deployment. We follow agile software development methods and User Experience (UX) engineering which increase the quality of user-friendly interactive systems. Iterative and frequent lab-tests involving four type 1 diabetes patients were conducted in early design phases to detect and fix usability issues. Patients were asked to perform a set of tasks and to answer questions about their UX with the system. Late design phases included recorded remote user testing with ten patients diagnosed with type 1 diabetes.

Results

The resulting system (https://goo.gl/8hF5cY) offers two interfaces. The patient's view includes a customizable dashboard; it provides a variety of tools aiming at the empowerment of diabetic patients. Among others, widgets allow to efficiently monitor glycaemia, diet, medications intake and physical activities. It also provides educational “Tips and Tricks”, reminders, HbA1c estimation, insulin bolus assistant and is furthermore interoperable with wearable fitness trackers and Wi-fi connected scales. A diabetic patient and two diabetologists have informally validated the Bolus Calculator algorithm. The physician's view includes medical support decision tools, online appointments, teleconsulting module, and allows to easily share adapted treatment plan based on detailed patient's ambulatory glucose profile.

Conclusions

Our digital solution has the potential to improve self-management and empowerment of patients with diabetes, as well as enhancing the contact with healthcare professionals. Furthermore, the evaluation of a deeper interoperability with sensors, wearables, IoT devices and electronic health records is ongoing.

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M114

Comparison of two automated assays for the determination of cobalamin in serum. Which one to choose?

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Background-aim

Cobalamin measurement is routinely performed for the screening of vitamin B12 deficiency. Unfortunately, there is no consensus on