

Comparison between two automated immunoassay methods for TSH: Architect ci8200[®] versus Cobas e411[®]

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ABSTRACT

The purpose of this work is to present the results of a comparative study between the Abbott's ci8200[®] automated thyroid stimulating hormone (TSH) assay and Roche's Cobas e411[®] automated system.

Keywords: Thyroid stimulating hormone; immunoassay; methods; comparison.

INTRODUCTION

310 venous blood samples were randomly selected among the prescriptions of the various departments of Mohammed VI Hospital of Oujda. The TSH assay was performed on Abbott's Architect ci8200[®] controller and Roche's Cobas e411[®] controller on the same day. The data were divided into three groups according to the biological reference interval (BIR) as indicated by the Architect kit: Group A (n = 25), with values 4.94 µIU / mL, depending on the values obtained by Architect. In the three study groups, the values obtained by Cobas e411[®] were generally higher compared to those obtained by Architect ci8200[®]. The statistical analysis of the results shows a good correlation between the two methods. Our study shows a good concordance of TSH assay results between Architect ci8200[®] and Cobas e411[®]. The inter-technical variability of the TSH assay requires an assay in the same laboratory for the follow-up of the patients; this attitude will make it possible to avoid erroneous interpretations of the results. Dysthyroidism is one of the most common endocrine disorders. Biological diagnosis and monitoring of thyroid diseases such as hypo and hyperthyroidism are based on the measuring of thyrotropin or thyroid stimulating hormone (TSH) with thyroxin (T4) and triiodothyronine (T3). The introduction of radioimmunology in the early 1970s disrupted thyroid exploration with the introduction of serum thyrotropin (TSH) assays. More recently, non-isotopic immunometric methods have considerably

improved the sensitivity and specificity of the assays. This has made the TSH assay a test of thyroid status (hyperthyroidism, hypothyroidism, euthyroidism) that is widespread in medical biology laboratories. TSH is currently considered as a reference test and the best marker of thyroid dysfunction, associated to T4 in the case of a pathological result and in some circumstances to T3 determination. The dosage of TSH is essential since it is from this result that the rest of the medical investigation depends. [1,2]. TSH is a glycoprotein with a molecular weight ~ 28 kDa, synthesized by thyrotropic (basophilic) cells of the anterior lobe of the pituitary gland. Its main function is the regulation of the synthesis and release of thyroid hormones. Its secretion follows a day/night cycle. TSH is made up of two non-covalently linked subunits, designated alpha and beta. The alpha subunit of TSH is common to luteinizing hormone (LH), follicle stimulating hormone (FSH) and human chorionic gonadotropin (hCG) but beta subunits of these glycoproteins are specific to each hormone, conferring to them their biological and immunological specificity. Therefore, the anti-TSH antibodies used for the TSH assay are directly routed against its beta specific subunit [3-8]. The aim of this study is to compare the TSH values measured by two immunoassay machines, Architect ci8200[®] of Abbott and Cobas e411[®] of Roche.

MATERIALS AND METHODS

This method comparison study was realized at the Central Laboratory of the Mohammed VI Teaching Hospital of Oujda during 03 months from October to December 2017. The study was conducted in accordance with the Declaration of Helsinki. 310 venous blood samples were randomly selected from our routine TSH testing requests. Blood sampling and measurement of serum TSH were done in the morning fasting. Blood samples were centrifuged at 1500 xg for 10 minutes in the first hour after collection. Haemolytic serum samples and samples taken from inadequate tubes or low volume samples were excluded from the study. The sera from the samples were divided into two aliquots that were immediately processed on the following platforms: Architect ci8200 using the chemiluminescent

microparticulate enzyme immunoassay technique, using Abbott's Architect TSH assay reagent [9] and Cobas e411 using the electrochemiluminescence sandwich enzyme immunoassay technique, using the chemiluminescence assay reagent. Elecsys TSH from Roche [10]. The samples were processed in one duplicate lot on each analyzer according to the manufacturer's instructions. The calibration curves (number of points) were constructed using calibrators provided in the kits. All TSH assay results are expressed in $\mu\text{IU} / \text{mL}$. The data obtained was analysed by MedCalc Statistical Software Version 15.1.0. The data was divided into three groups according to the biological reference interval (BIR) as indicated by the Architect kit: Group A ($n = 25$), with values $<0.35 \mu\text{IU} / \text{mL}$; Group B ($n = 260$), with values of $0.35\text{-}4.94 \mu\text{IU} / \text{mL}$ and group C ($n = 25$), with values $>4.94 \mu\text{IU} / \text{mL}$, according to the values obtained by Architect. The statistical analysis of the results evaluated the correlation coefficient for the study of the intensity of the connection which could exist between the results of the two methods, the equation of the Passing-Bablok line for the comparison of the two methods, the Bland-Altman diagram to assess the concordance between the two instruments, and the Mann-Whitney U test, which tests the hypothesis that the data distribution is the same in two methods.

RESULTS

The 310 selected samples came from 198 women and 112 men. In the three study groups, Cobas e411® values were generally higher than those obtained by Architect ci8200® (Figures 1). The statistical analysis of the results shows a good correlation between the two methods studied in the three groups. The correlation coefficient for each group was as follows: group A ($r = 0.989$), group B ($r = 0.9712$), group C ($r = 0.7736$). As for the equation of the straight line of Passing-Bablok, Passing-Bablok, we find for each group (Figure 1):

- Group A: $Y (\text{Architect ci8200}^{\circledR}) = 0.8504 X (\text{Cobas e411}^{\circledR}) + 0.0005651$;

- Group B: $Y (\text{Architect ci8200}^{\circledR}) = 0.7765 X (\text{Cobas e411}^{\circledR}) + 0.06195$;

- Group C: $Y (\text{Architect ci8200}^{\circledR}) = 0.6098 X (\text{Cobas e411}^{\circledR}) + 1.4645$.

The Bland-Altman diagram shows that most of the points are in the agreement limits (Mean + 1.96 SD) and that for each group are: 88% of the points for group A, 95% for group B and 92% for group C, with an average difference between the two methods of the order of (0.007) (0.34) and (6.19) $\mu\text{IU} / \text{mL}$ for the study groups respectively. The results of the Passing-Bablok regression show a negligible constant significant difference, but with a significant proportional deviation from the Y axis. For the Mann-Whitney U test it was not significant for the A group ($p = 0, 1821$), that is, there is no difference between the averages of the results obtained from Architect ci8200® and Cobas e411®. In contrast for group B ($p = 0.0002$), and for group C ($p = 0.0260$) the Mann-Whitney U test was significant, as a result there was a difference between the averages of the results obtained from Architect ci8200® and Cobas e411®.

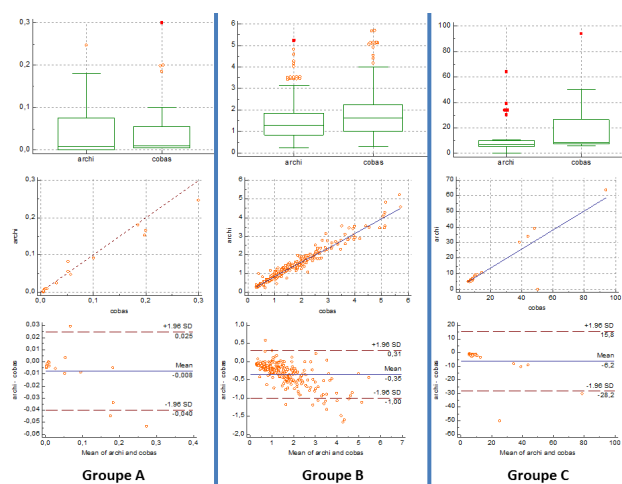


Figure 1: The mean, correlation and comparison of the two methods for the three study groups.

DISCUSSION

Although the measurement of TSH is commonly accepted as reliable, no reference measurement method is well defined. Therefore, routine measurements of TSH have certain limitations. In our study, we found good agreement between two methods of TSH immunoassay. We used latest-generation PLCs available on the Moroccan market, Architect ci8200 and Cobas e411®. The results of our study align with the results of several international studies, such as the studies of Sarkar R [11], Hendriks [12] and Rawlins [13]. In the Sarkar R study, the two TSH, Architect i2000 SR and Cobas 6000 immunoassay analyzers were compared on 1615 samples, the results of which were comparable to those of our study, either for the Passing-Bablok regression or for Mann-Whitney P test that was not significant for group A ($P = 0.0053$), and significant for group B and C ($P < 0.0001$). In the Hendriks study, the comparison involved two methods of assaying TSH, the AxSym automated system that uses fluorescence polarization immunoassay (FPIA) and Elecsys 2010 using (eCLIA) on 50 patient samples, the Passing-Bablok regression objected a slope of 1.37 and interception of -0.02. Rawlins focused on the lower limit of quantification by determining the respective functional sensitivities, but also included a method comparison study between Immulite 2000 (comparable to Architect) and E170 (an earlier version of Cobas) using 104 patient samples, which objected a Passing-Bablok regression with a slope of 1.33 and an interception of 0.01.

From the results of the statistical analyzes of the data, it can be deduced that there was a systematic difference between the TSH values measured by Architect and Cobas. The average value of Cobas was higher than that of the architect on all data with significant Mann-Whitney P values for groups B and C. The analysis of the Bland-Altman plots shows that most points in all three groups were within agreed limits. So according to these results, we can say that there is a good agreement between the two methods.

In our study, both tested automaton operate as closed systems and use barcode calibrators. It is suggested that the

differences observed between the two methods are most often produced by the presence of a wrong amount of the substance in the calibrator, if the calibrator contains less analyte compared to what is labelled, all measurements would be deviated to higher values. In the other side, a negative error can be observed if the analyte is higher than what is labelled. It is clear that this form of error can be eliminated by using the same calibrator for both methods, but the Hendriks study [12] mentioned that even calibration with the same standard does not automatically guarantee consistency between methods. Differences generally occur in two situations, the first when consolidating a method, since despite the fact that the same recombinant TSH molecule is used as a standard, the monoclonal or polyclonal antibodies directed against this molecule are variable differently depending on the manufacturers who recognize the different epitopes of recombinant TSH with different avidity. The second situation is when TSH occurs in human serum in different forms of glycoforms depending on the state of health or disease of the individual, and which are recognized differently by the antibodies during the assay, which may cause heterogeneity of results [14,15].

In thyroid diseases, recommendations for good practice are not lacking, concerning the diagnosis and biological monitoring of hypothyroidism and hyperthyroidism. It is of great importance to guarantee the continuity of these follow-ups by performing these assays using the same technique and / or the same automaton [16]. Accreditation bodies require laboratories to determine their analytical performance criteria to ensure that the quality of the laboratory examinations they perform is in line with that required for the care of their patients. The validity of published good practice recommendations is generally based on evidence obtained through systematic reviews of the literature or professional consensus of good methodological quality [17].

The medical biology act is part of a preventive, diagnostic, prognostic and therapeutic approach. The biologist assumes responsibility for this act which includes the entire analytical macro-process with all pre-analytical, analytical and post-analytical steps, from prescription to validation and transmission of results. The standards NF EN ISO 15189 and NF EN ISO / CEI 17025 define the general requirements concerning the quality and the competence of the laboratories of medical biology and the laboratories of test. This is why the quest for quality must be an essential and constant concern of the biologist and all the laboratory staff [18]. The central laboratory of the Mohammed VI University Hospital of Oujda is engaged in a quality policy that includes a process verification method according to scope A, and an accreditation process. This type of study will provide a solid basis for the establishment of a procedure for accreditation of tests used in our laboratory.

CONCLUSION

Our study shows a good concordance of the results of the TSH assay between the Architect ci8200® and the Cobas e411®, the immunological methods can give variable results, therefore the laboratory professionals must be aware of these problems during the modification methods in their work routine and

comparison of the results obtained from different platforms, through the various validation tests and in the development of its own reference values. The inter-technical variability of the TSH assay requires an assay in the same laboratory for the follow-up of the patients, this attitude will make it possible to avoid erroneous interpretations of the results.

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