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WILL STANDARDIZATION BE A NEW APPROACH TOWARDS EVIDENCE BASED MEDICINE?

Biochemistry

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ABSTRACT

Harmonization and standardization are important when disease is defined by clinical biochemistry results. Evidence based medicine is the conscious, explicit and judicious use of current best evidence in making decisions about the care of individual patients. There are very few studies proving standardisation and it's application in laboratory medicine. The objective of this study is to verify the trueness and portability of patient reports by standardization of glucose estimation using two different methods in two different analysers. Methods of estimation compared are hexokinase and GOD-POD. Instruments used are Abbott Architect c8000 and ERBA XL-640 respectively. After the analysis, the results obtained are comparable and methods are traceable and therefore can be used interchangeably for patient report evaluation. Through this experiment we conclude that standardization enables uniform interpretability, which is important in integrating health systems into modern clinical environment

KEYWORDS

Standardization, Harmonization, Evidence-based medicine, Traceability.

INTRODUCTION

Evidence based medicine is the conscious, explicit and judicious use of current best evidence in making decisions about the care of individual patients. Standardization is development of a system that allows comparability of test results, independent of measurement method. Whereas harmonization refers to the process of establishing comparable results among measurement procedures for the given analyte. Harmonization and standardization are especially important when disease is defined by clinical biochemistry results, for example, the diagnosis of diabetes based on plasma glucose determinations. Therefore, the analytical quality in this instance becomes very critical for a correct evaluation. In this study we are verifying the trueness and portability of patient reports by standardisation of glucose estimation using two different methods in two different analysers. [1,2]

METHADOLOGY AND MATERIALS

Fifty patient plasma samples (free of hemolysis, Lipemic) with glucose concentration of varying ranges between 50mg/dL to 500mg/dL were run over the course of five days at Clinical Biochemistry Laboratory, B.J. Medical College and Civil hospital, Ahmedabad. Samples were processed by two methods Hexokinase and GOD-POD methods in instruments Abbott Architect c8000 and ERBA XL-640 respectively.

A set of data was generated from patient samples by both the methods, which is then mathematically compared using linear regression and Bland-Altman plot. Further properties of repeatability, variability and the traceability of two methods were analysed. Hexokinase method used a single, liquid, ready to use kit of Architect company was used. GOD-POD Reagent – Ready to use reagent kit of Enzopak, Reckon diagnostics P. LTD.

RESULTS AND DATA ANALYSIS

The glucose concentration results are pooled to obtain data set that is used to prepare linear regression and Bland -Altman plots.

A) Linear regression curve was plotted to analyse the degree of association between the measurements as shown in graph below:

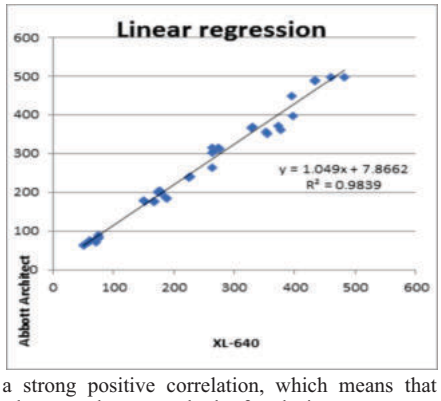
Graph 1. Linear regression graph with outliers

Method A	HEXOKINASE
Method B	GOD-POD

METHOD	HEXOKINASE	GOD-POD
1	103	101
2	102	101
3	103	102
4	103	101
5	102	101
MEAN	102.6	101.2
SD	0.55	0.45
CV	0.53	0.45
1	176	174
2	175	174
3	176	173
4	176	175
5	175	174
MEAN	175.6	174
SD	0.55	0.71
CV	0.31	0.41

B) Calculating correlation coefficient

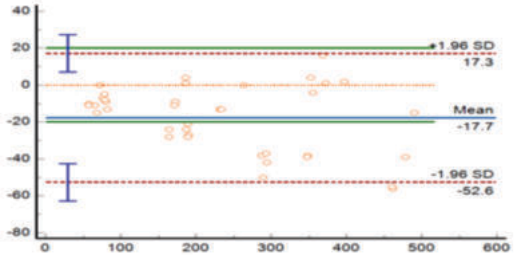
Correlation coefficient obtained here is r = 0.9919.



This is a strong positive correlation, which means that there is corelation between the two methods of analysis.

C) Measuring agreement.

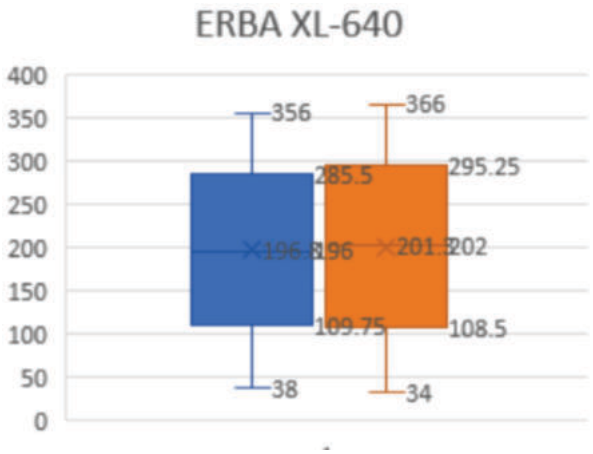
Using correlation and regression analysis is no guarantee of agreement between two methods, therefore, here we use Bland-Altman plot.



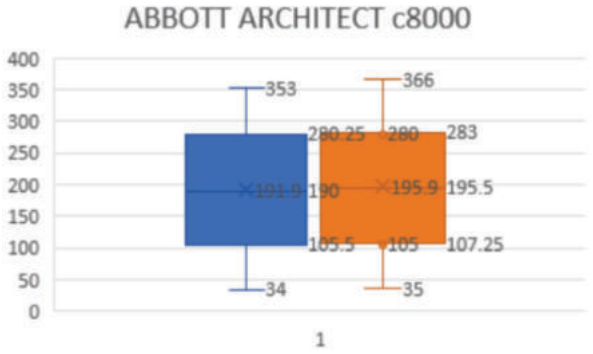
Provided differences within d±2s would not be clinically important, we could use the two measurement methods interchangeably. These

are referred to as limits of agreement.

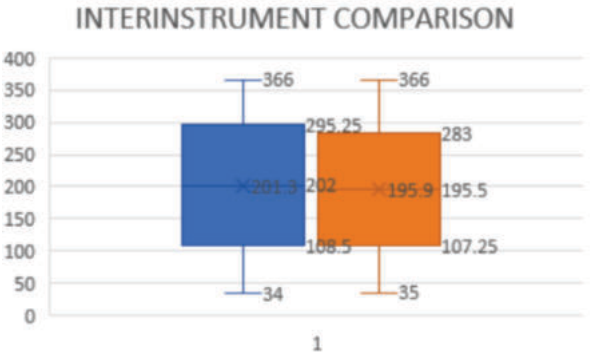
D) Measuring repeatability
Provided differences within d ± 2s would not be clinically important, we could use the two measurement methods interchangeably — i.e., there is no considerable variation in repeated measurements on the same subject in both methods.



E) Measuring bias and variability from target.
This can be done by comparing external quality control results by both methods using samples of three levels of concentration. This comparison will help to detect instrumental bias if any. The material used is RIQAS (Randox International Quality Assessment Scheme).



Total bias =2.2 %



Total bias = 2 %

The variability observed in both methods are negligible.

Total allowable error is within range as per CLIA criteria Therefore total bias is within acceptable limits. Hence both methods and instruments are accurate and comparable.

F) Traceability of methods.
The traceability of calibration techniques used in both methods is given as follows:

	HEXOKINASE	GOD-POD
CALIBRATOR	8P60/1E65-Multiconstituent Calibrator	CAL2350 CAL2351
Reagent list no	7P55/3L82	
Analyte	Glucose	Glucose
Reference Material	NIST SRM 965	NIST SRM 965 NIST SRM 917
Reference Method	ID-GC/MS	ID-GC/MS
Target / nominal value	Level 1: 5.55 mmol/L Level 2: 24.84 mmol/L	Level 2: 6.65 mmol/L
Total uncertainty	Level 1: 0.149 Level 2: 0.666	Level 2: 0.54

Therefore, both methods are metrologically traceable to one reference method.

DISCUSSION

In this study we describe the quantitative evaluation of plasma glucose by glucose oxidase-peroxidase method and hexokinase method. (i.e.) we compare the two automated enzymatic methods to understand and familiarize the principles of method selection and evaluation. Particular emphasis was placed on widely used instrumental adaptations of these methods that were available although none of the methods studied here was proposed as a reference method in its present form, the comparative results obtained would be useful in establishing the basis for additional investigations. The plan of this inter-instrument comparison included determination of values for serum glucose by one hexokinase-based and one glucose oxidase-based procedures. Also, we have compared of two methods of glucose estimation traceable to the same reference method using two different analytical instruments.

Trueness of a test is one of the biggest concerns of a clinical laboratory but it is often forgotten that trueness should be independent of the analytical platform and the analytical procedures used.

Different test methods often produce divergent test results, making it necessary to implement method specific reference intervals for their interpretation. This in turn prevents portability of patient records. It also prevents realization of common reference intervals and decision limits, thereby, hampering the benefits from interval studies and their contribution to evidence-based medicine. Standardization process ensures that the procedure and results are consistent with expectations, therefore can be interpreted more accurately and high-quality records of the patient can be maintained.

According to Vocabulary of Metrology (VIM), traceability is the property of result of a measurement or the value of standard whereby it can be related to stated references, usually national or international standard, through an unbroken chain of comparisons, all having stated uncertainty. However, traceable calibration does not necessarily produce traceability of results. For that we need to establish and strictly adhere to value transfer protocol, use commutable, serum based secondary reference materials and ensure analytical specificity and sensitivity to interference of comparison method. For non-specific methods which are not traceable, the concept of harmonization could be followed, which is typically based on distribution among laboratories of commutable secondary reference materials with arbitrarily set target values. Therefore, “harmonized” remains a term that can be used whenever results measured by any clinical laboratory procedure are equivalent irrespective of the process used to achieve that condition.

This experiment was performed in an optimized environment. Both analytical methods and instruments were selected and implemented after proper evaluation as per (CLSI) NCCLS guidelines. In this analysis, we independently proved the linearity and correlation between two methods, it's repeatability along with inter- and intra-day precision, verified accuracy and trueness of two methods of glucose estimation using two different analyzers confirming it's commutability and then authenticated its traceability to a common reference method as per ISO 17025 & 15195, approved and listed by JCTLM WG2 thereby proving that results obtained from both methods can be used interchangeably for patient report evaluation. [3,4,5,9]

CONCLUSION

Through this experiment we conclude that standardization enables uniform interpretability, which is important in integrating health systems into modern clinical environment. This approach will help in universal portability of records and to eliminate existing confusions regarding interpretations based on different methods of analysis.

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