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Analyses of Tumor markers and its Precision, Constancy and Replication: Comparison of two, separately operated-Pre and Intra-analytical-LRS integrated Cobas e411 iECL analyzers

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Abstract *Background:* Recent developments in tumor assays and its basic requirements for performance and analysis also requires lab to manage and pursue standardized SOPs for pre-intra and post analytical steps. *Aim:* Present study was undertaken to compare and implement (where necessary and applicable) precision, constancy and replication status of two, separately operated-Pre and Intra-analytical-LRS integrated Cobas e411 iECL analyzers (Roche, Basil). *Materials and Methods*: PreciControl TM1 (Lot # 405821) controls of CEA, CA 19-9, AFP, CA 15-3 (Roche Diagnostic, Basil) were used, and analyzed 25 times each on cobas e411 A and e411 B, both operated by separated group of trained Lab technologists. All four analytes were determined by standard established methods as per documented protocols. *Results*: R^2 regression data showed significant correlation ranging from 0.9666 to 0.9923, thus exhibiting efficiency, accuracy and precision of 96.66% to 99.23%. Regression correlation analyses and linear plot equations were CEA = R^2 = 0.9851 y 1.0018 x -0.0393; AFP = R^2 = 0.9923 y 1.0786 x -0.5199; CA 19-9 = R^2 = 0.9794 y 0.8751 x + 2.5033 and CA 15-3 = R^2 = 0.9666 x + 0.9903. *Conclusion:* Generated data and resultant observations noted that accuracy, reproducibility, precision are 99.6% to 99.23% in both separately operated instruments. In addition, analytical performance attributes of two separate groups of staff was also comparable and compatible to each other. Such standardization, homogeneity, consistency and exactitude ensure quality assured services to end-users, clinicians, and most importantly patients.

Keywords Tumor markers, iECL technology, immunoassay analyzers

Introduction

For many solid tumor malignancies, serum tumor markers play a pivotal role and provide significant diagnostic and prognostic. Even for histopathological and radiological diagnoses, tumor markers estimation facilitates further confirmation of metastasis and any difference between remission and progression [1,2]. Moreover, tumor markers are commonly used in clinical practice to monitor response to therapy and prediction for treatment regiments and any sign of relapse [3]. However, generally, not all clinical laboratories could perform or analyze tumor markers such as CEA, AFP, CA 15-3, CA 19-9, CA 72-4, because of strict requirements of control, standardization of analytical techniques, precision, accuracy, reproducibility etc [3,4]. Recent advancement in tumor assays and it's prerequisites for performance and analysis also requires lab to control and follow standardized SOPs for pre-intra and post analytical steps [5,6]. In addition, it's simply impossible to assume or provide assurance that results of one

type of instrument (model, make) is same as the results of other type of instruments; same goes for analytical procedures or even staff who is performing these analyses [6-8]. It was noted earlier that inherent predicament for standardizing immunoassays for tumor makers is because of availability of various types of assays (iECL, ELISA, MEIA, RIA etc), use of different standards or antigen/antibody with variable affinities, and frequency or testing (alternate days, one day, 12 hour cycle or SOS) [6,7]. Therefore present study was undertaken to compare and implement (where necessary and applicable) precision, constancy and replication status of two, separately operated-Pre and Intra-analytical-LRS integrated Cobas e411 iECL analyzers (Roche, Basil).

Materials and Methods

Previously described protocol was followed for comparative precision analyses of tumor markers and standardization of skills and instrumentations [2,9]. PreciControl TM1 (Lot # 405821) controls of CEA, CA 19-9, AFP, CA 15-3 (Roche Diagnostic, Basil) were used, and analyzed 25 times each on cobas e411 A and e411 B, both operated by separated group of trained Lab technologists. All four analytes were determined by standard established methods as per documented protocols [9]. Reference ranges for PreciControl TM1 were; CEA = 3.86-5.90 ng/ml (Mean 4.88), CA 19-9 = 15.7-27.3 U/ml (mean 21.5), AFP = 6.63-10.20 IU/ml (mean 8.39) and CA 15-3 = 17.5-26.9 U/ml (mean 22.2). The data was compared statistically by using SPSS ver 20.0 (USA), regression correlation R2 analysis and considered significant when $P < 0.05$.

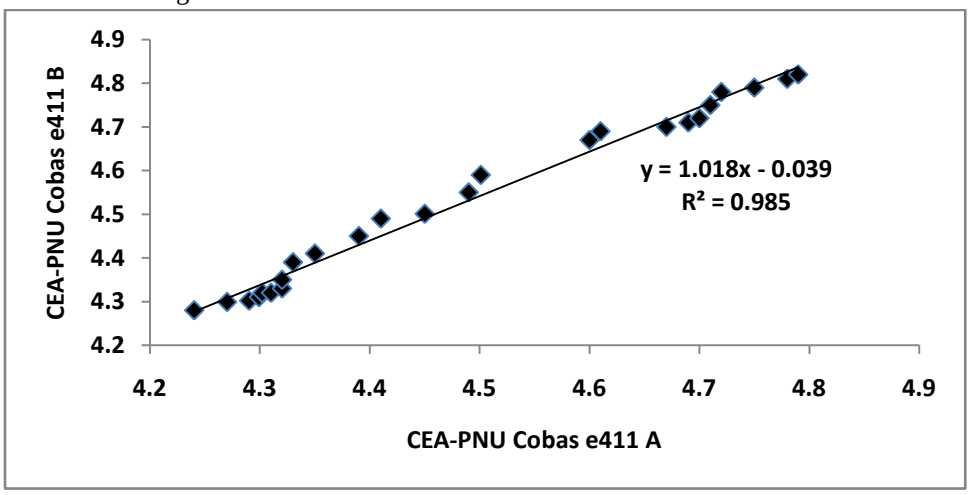

Figure 1: Precision analysis of CEA PNU on two separately operated Immunoassay analzyers Cobas e411 A & B

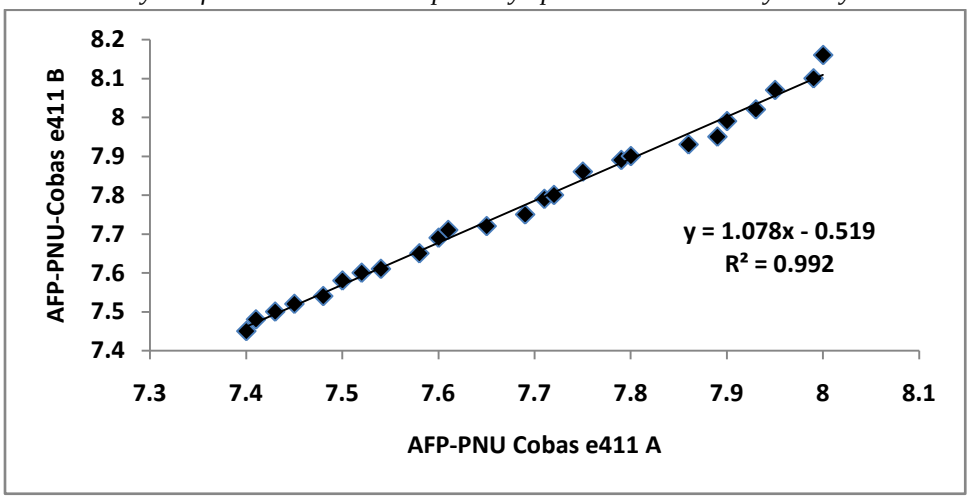

Figure 2: Precision analysis of AFP PNU on two separately operated immunoassay analyzers Cobas e411 A & B

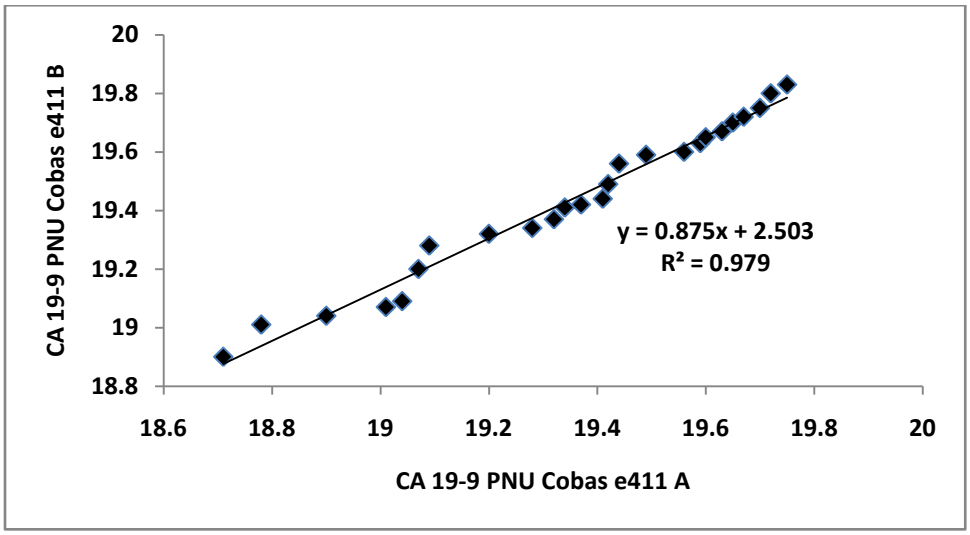

Figure 3: Precision analysis of CA 19-9 PNU on two separately operated Immunoassay analyzers Cobas e411 A & B

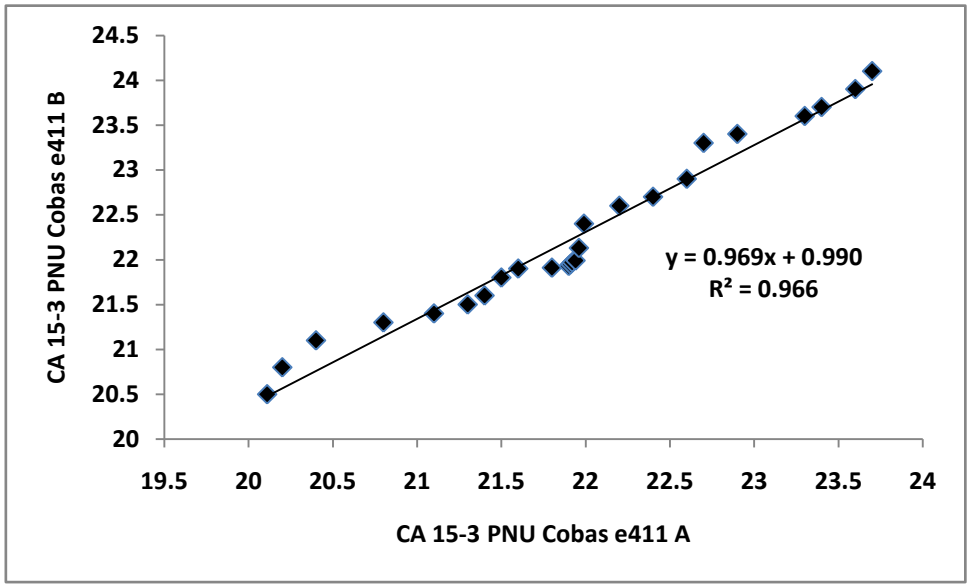

Figure 4: Precision analysis of CA 15-3 PNU on two separately operated Immunoanalyzers Cobas e411 A & B

Results

Results are summarized in Fig 1 to 4. Regression correlation analyses of four tumor markers, CEA, AFP, CA 19-9 and CA 15-3 was performed to evaluate precision, reproducibility, accuracy and compatibility of staff and two separate instruments. PreciControl TM1 (Lot # 405821) was used to complete the task and was run on two independently operated iECL technology Cobas e411 (Roche-Basil), separately conducted by 2 sets of trained and skilled technologists, mostly in 12/12 hours cycle on daily basis. R2 regression data showed significant correlation ranging from 0.9666 (Fig 4: CA 15-3) to 0.9923 (Fig 2: AFP), thus exhibiting efficiency, accuracy and precision of 96.66% to 99.23%. Regression correlation analyses and linear plot equations were CEA = R^2 = 0.9851 y 1.0018 x -0.0393; AFP = R^2 = 0.9923 y 1.0786 x -0.5199; CA 19-9 = R^2 = 0.9794 y 0.8751 x + 2.5033 and CA 15-3 = R^2 = 0.9666 x + 0.9903. Generated data and resultant observations noted that although analytical performance was evaluated on 2 separately managed instruments, however, its accuracy, reproducibility, precision are 99.6% to

99.23% comparable to each other. Moreover, analytical performance attributes of two separate groups of staff was also comparable and compatible to each other. Such standardization, homogeneity, consistency and exactitude ensure quality assured services to end-users, clinicians, and most importantly patients.

Discussion

Serum tumor markers are mostly very significant entity for facilitation in diagnosis, staging, treatment arrangement and assessment in follow-ups of cancer patients [3]. However, availability of several category of tumor markers, analysis techniques, instrumentation make and model and the staff itself who performs these analysis, repeatedly makes it problematic and sometimes unethical for the end-users (clinicians, oncologists) and the patients themselves [3-6, 8]. Therefore, College of American Pathologist (CAP), American Association of Clinical Chemistry (AACC), International Federation of Clinical Chemistry (IFCC), frequently emphasized continual evaluation and reevaluation of accuracy, principles, instrumentations, quality assurance measures, technologists skills and abilities, for the parameters to be measured and their intended use [3-5, 7, 8, 10]. Correlation of cut-off values (reference ranges included), clinical justification, rationale for requesting serum tumor tests, sensitivity and specificity of the test itself are some of the arguments, that needed to be look into and resolved [5,6]. Thus present study that was undertaken to compare and implement (where necessary and applicable) precision, constancy and replication status of two, separately operated-Pre and Intra-analytical-LRS integrated Cobas e411 iECL analyzers (Roche, Basil), showed significant compatibility regarding exactness, reliability and reproduction of multiple runs. A previous study also noted appreciable correlation amongst several tumor markers, more notably CEA and AFP, regarding standardization and calibrations [1]. It was argued that concordance among analyzers might be variable, depending upon technology, principles and techniques, antibodies used for coupling reactions, chemical and buffers concentration and even technologists who are actually performing the tests.

Conclusion

R^2 regression analysis performed on two iECL immunoassay analyzers showed significant correlation and efficiency, accuracy and precision of 96.66% to 99.23%. Resultant observations manifested that two separately operated instruments, if managed through strict standardization and SOPs, will produce best accuracy, reproducibility, precision upto 99.0% which is comparable to each other. Consequently, analytical performance of two separate groups of staff was also noted to be compatible to each other, ensuring standardization, homogeneity, consistency of the services which ensures quality assured services to end-users, clinicians, and most importantly patients.

Reference

[1]. Bhatnagar S, Lim MCF, Abelardo AD (2015). Evaluation of Four Tumor Markers (CEA, AFP, CA125 and CA19-9) on Sysmex HISCL- 5000 Immunoassay Analyzer. Annals of Clinical and Laboratory Research. 3 (3): 32-37.

[2]. Burtis CA, Ashwood ER, Bruns DE (2013) Tietz Textbook of Clinical Chemistry and Molecular Diagnostics (5th edn). St. Louis: Elsevier saunders.

[3]. Rahman M, Haque M, Mian M, Shahi M, Rahman SJR. (2014). Tumor Markers: Precision, Accuracy, Validity and Statistical Matters of Concern. Chattagram Maa-O-Shishu Hospital Medical College Journal. 13. 10.3329/cmoshmcj.v13i2.21080.

[4]. Schrohl AS, Holten-Andersen M, Sweep F, Schmitt M, Harbeck N, Foekens J, Bru¨ nner N, on behalf of the European Organisation for Research and Treatment of Cancer (EORTC). (2003). Receptor and Biomarker Group. 2003. Tumor Markers. From laboratory to clinical utility. Molecular & Cellular Proteomics 2.6. The American Society for Biochemistry and Molecular Biology, Inc. 378-387

[5]. Qin D, Jiang X, Mo G, Feng J, Yu C, Deng B. (2019). A Novel Carbon Quantum Dots Signal Amplification Strategy Coupled with Sandwich Electrochemiluminescence Immunosensor for the Detection of CA15-3 in Human Serum. Clin Lab. 22; 4(2):504-512. doi: 10.7754/Clin.Lab.2018.180930.

[6]. Yin-Yu M, Fu-Yi X, Fei-Bo W, Ri-Yi Z, Xiao-Lin Y. (2019) Performance Evaluation of an Enzyme-Linked Immunosorbent Assay for Seven Autoantibodies in Lung Cancer. Clinical Laboratory, 65(4) DOI: 10.7754/clin. lab.2018. 180930 PMID: 30969073

[7]. Geurts-Moespot J, Leake R, Benraad TJ, Sweep C G (2000). Twenty years of experience with the steroid receptor external quality assessment program—the paradigm for tumour biomarker EQA studies. On behalf of the EROTC Receptor and Biomarker Study Group. *Int. J. Oncol*. 17, 13–22

[8]. Sweep C G, and Geurts-Moespot J. (2000) EORTC external quality assurance program for ER and PgR measurements: Trial 1998/1999. European Organisation for Research and Treatment of Cancer. *Int. J. Biol. Markers* 15, 62–69

[9]. Sultana I, Alam JM, Ali H, Noureen S. (2018) Correlation analysis of thyroid antibodies (anti-thyroid peroxidase AntiTPO and anti-thyroglobulin Anti TG) with thyroid stimulating hormone (TSH), Thyroid hormones (T3, T4) and disease status in selected population. *Chemistry Research Journal*, 3(3):16-20.

[10]. Mongia SK, Rawlins ML, Owen WE, Roberts WL (2006) Performance characteristics of seven automated CA 125 assays. Am J Clin Pathol 125: 921-927.

[11]. Hotakainen K, Tanner P, Henrik A, Haglund C, Stenman UH (2009) Comparison of three immunoassays for CA19-9. Clin Chim Acta 400: 123-127.

[12]. Deinzer M, Faissner R, Metzger T, Kaminski WE, Löhr M, et al. (2010) Comparison of two different methods for CA19-9 antigen determination. Clin Lab 56: 319-325.