Available online at www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2016; 8(5): 322-325

ISSN- 0975 1556

Research Article

Comparative Study of the Results of Capillary Blood International Normalized Ratio on Coagucheck XS POC and Conventional Coagulation Blood Test

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Available Online:1st May, 2016

ABSTRACT

Millions of patients worldwide are taking anticoagulants like acenocumarol and warfarin for prevention of serious thrombotic complications as stroke or heart attack. The coumarins or vitamin K antagonists (VKAs) have been the mainstay of oral anticoagulant therapy for more than 50 years. In clinical practice VKAs are challenging to use, because they reveal considerable variability in dose response among different patients, resulting from genetic mutation and drug and diet interactions. Because of this they require frequent laboratory monitoring which is time consuming and discomfort for the patients. The development of point-of-care (POC) devices enables International normalized ratio (INR) to be obtained in outpatient as well as at home setting at the moment. Some earlier studies have shown statistically significant differences between values from clinical laboratory and POC meters, because of which the accuracy of these meters remain still controversial. The aim of this study was to evaluate the results of INR on the CoaguChek XS meter relative to chronometric assay on laboratory coagulometer Sysmex S 2000i.

Keywords: coagulation analyzer, point-of-care testing, prothrombin time, INR

INTRODUCTION

Cardio-vascular and cerebro-vascular diseases are leading cause for morbidity and mortality worldwide[1,2]. Atherothrombosis is underlying cause of these diseases. It is a generalized and diffuse progressive process that affects multiple vascular beds and its clinical consequences include acute coronary syndrome, ischemic stroke, ischemic cardiomyopathy, peripheral arterial disease which are potentially life-threatening conditions. Major role in the prevention and treatment of these diseases and its complications is the anticoagulant treatment[3,4]. For more than 50 years, Vitamin K antagonists (VKAs) are still the most wildly used oral anticoagulant drugs[5]. They demonstrate considerable variability in dose response among different patients, resulting from genetic mutation and drug and food interactions[6]. As a result they require regular INR monitoring for dose adjustment, because sub therapeutic anticoagulation can lead to increased thromboembolic risk, while anticoagulation above the therapeutic range places the patient at risk of haemorrhage[7]. Frequent testing of prothrombin time (PT) and INR (internationally normalized ratio) measurement are critical for maintenance of therapeutic anticoagulation[7-10]. Laboratory testing of PT/INR requires a visit of the patient in haematology clinic and venous blood collection by venepuncture from qualified personnel. Blood is placed into citrate tubes and after centrifuging platelet –poor plasma is loaded on to coagulation analyser. The time taken, from the time patient walks in to the laboratory to reporting, is at least 25–30 min[11]. Control of anticoagulant treatment by INR measurement can be facilitated if testing could be performed with less frequent visits to the laboratory and with a relatively easier method.

For this reason, in the early 1990s POC devices for INR measurement were introduced[12]. Point of Care (POC) PT/INR monitoring is less invasive, requires only finger prick capillary blood and product results for less than 2 min. It can be used in outpatient as well as at home setting and enables self-dose adjustment of the anticoagulation dose at the moment by patients[10]. The CoaguChek XS portable INR monitor (Roche Diagnostics, Basel, Switzerland) was released in October 2005. This system detects the activity of thrombin, instead of detecting a clot by mechanical or optical methods. The test strip contains reagents - human recombinant tissue factor and a peptide substrate (Electrocyme TH), which reacts with thrombin to generate an electrical signal. The human recombinant tissue factor used in the CoaguChek test strip has international sensitivity index (ISI) of 1[12]. Such monitors need to be accurate over the full therapeutic range of the INR and require an acceptable independent evaluation. A number of studies have proved comparability between CoaguChek XS and laboratory techniques[13-18]. whereas others have questioned the reliability of POC test INR

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Figure 1: Coagucheck SX POC device

Figure 2: Laboratory testing of INR with analyser CS Sysmex 2000i.

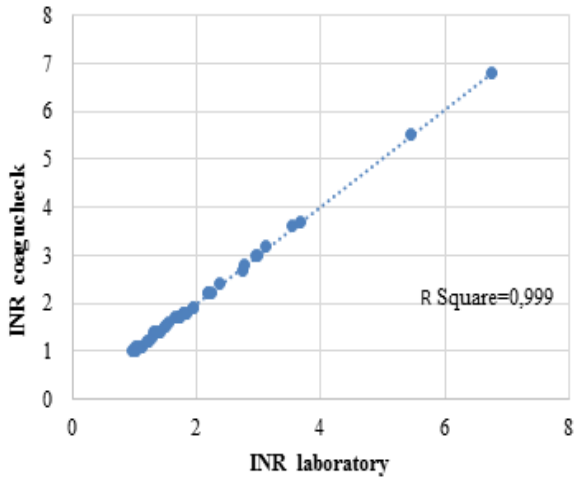

Figure 3: Correlation between INR values from Coagucheck XS and laboratory**.**

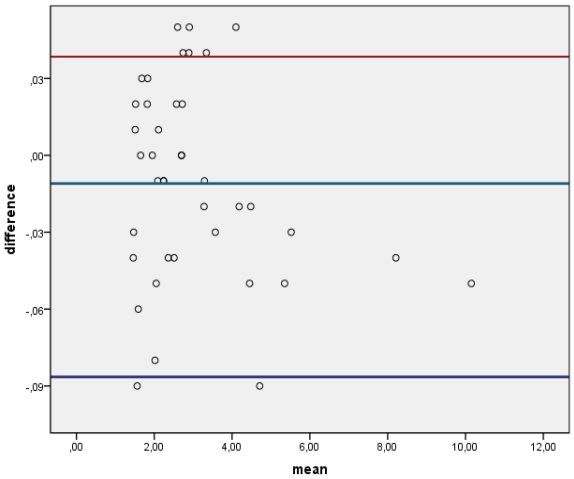

Figure 4: Bland-Altman plot for agreement between INR from CoaguCheck XS and Sysmex CS 2000i

results[19,20]. The aim of the present study was to evaluate the INR results obtained with Coaguchek XS (Roche Diagnostics Ltd, USA) with the INR obtained on laboratory coagulometer Sysmex CS 2000i with an International Sensitivity Index (ISI) of 1.06.

MATERIALS AND METHODS

The study was performed in the Centre of clinical laboratory of Medical University of Plovdiv, Bulgaria in the period 10.2015 – 02.2016. INR was obtained through 2 different methods: whole capillary blood samples for in vivo testing with Coaguchek XS and venous sample for coagulometric laboratory testing with Sysmex CS 2000i analyser. Patients included in the study were receiving VKA acenocumarol (Sintrom, Novartis Pharma S.pA) once daily for at least past 6 weeks.

Prothrombin time was determined as INR in capillary blood and platelet-poor plasma. For this aim capillary blood was taken until 10 o'clock in the morning from 40 patients up to 12 hours after the last administration of acenocoumarol by finger prick of the ring finger with individual lancets and placed on CoaguCheck XS test strip and INR was obtained amperometric (electrochemical) of the CoaguChek XS system. The principle of the method using a capillary whole blood is based on the amperometric determination of prothrombin time by INR after activation of coagulation with human recombinant thromboplastin. For this purpose is needed 8 µl capillary blood. A drop of blood is dripped onto the test strip and the result is displayed on the screen of CoaguChek XS. The linearity of the method of INR: 0. 8 - 8.0, reproducibility in time CV = 4.5%. Quality control is automatically performed for each test strip. It displays the result in approximately one minute and can be configured to display results in INR, seconds, or % Quick. The CoaguChek XS PT test strips are manufactured with a human recombinant tissue factor and

have an International Sensitivity Index (ISI) of 1.0. (Figure No 1). Simultaneously from the patients was taken venous blood through venepuncture as blood was drawn into tubes with an anticoagulant sodium citrate and INR was determined in the laboratory with coagulometer CS Sysmex 2000i. (Figure No 2). Collection, processing and storage of blood samples for testing of prothrombin time as INR was carried out under standard conditions, to eliminate variation of results of factors in preanalytical stage. Laboratory coagulometer analysis is made with platelet-poor plasma, obtained after centrifugation of venous blood with anticoagulant sodium citrate at a ratio of 1 part 3.8% sodium citrate to 9 parts of venous blood. Centrifugation was performed at 3000 × g for 10 min. Plasma was centrifuged within 1 hour of blood sample taking and analysis was carried out within 2 hours. The method is based on coagulation of the platelet-poor plasma after adding thromboplastin in excess in optimum calcium amount. It shows the extrinsic coagulation pathway by mixing50 µl patient plasma with 100 µl reagent. Clot formation is measured after 100 seconds. Used reagent is Dade Innovin Reagent, containing purified recombinant human tissue factor, synthetic phospholipids (tromboplasitin) and calcium. The results are reported on a coagulometer CS Sysmex 2000i. The activity is determined by pre-set calibration curve. The results are presented

ET in seconds

Prothrombin ratio R

INR

prothrombin activity%

For calibration was used calibration plasma. Linearity of the method of INR: 0.8 - 10.0, reproducibility: CV in a series of 3-5%, CV at a time by 5-8%, D% from -3.58 to + 3.24%.

RESULTS

In the study were included 31 male (77.5%) and 9 (22.5%) female patients, as the youngest patient was 45 years old and the oldest 83. The average age of enrolled patients was 70, 70 ± 1,42. From the laboratory results of INR, obtained from 40 patients with analyser CS Sysmex 2000i, the lowest measured value was 0.96 and the highest 6.75 (average 2,03 ± 0,18). From the results obtained by an INR testing with Coagucheck XS device lowest measured value was 1 and the highest 6.8 (average 2,04 ± 0,19). Figure 1 shows the comparison of the CoaguChek XS System results to the laboratory results. They show significant correlation between the values of INR, obtained by two methods.

Correlation coefficient was 0.99, p = 0.00 (Figure No 3). The mean (standard deviation) difference in the readings of INR (minus laboratory Coagucheck XS) is 0,011 (t = -1,805, df = 39, p = 0, 079) which indicates that the two INR measurements are in very close agreement. The Bland–Altman method calculates the mean difference between two methods of measurement (the 'bias'), and 95% limits of agreement as the mean difference (2 sd) [or more precisely (1.96 sd)]. The graphic analysis of Bland-Altman shows great agreement between two methods with 32 out of 40 samples. In 95% - disposed confidence interval of the difference, the lower limit was: -0, 0233, and the upper: 0,0013. (Figure No 4)

DISCUSSION

In this prospective study, we demonstrate the analytical and clinical effectiveness of CoaguChek XS device for monitoring of treatment with acenocoumarol by testing a wide range of values of the INR. Previous studies on the accuracy of other similar devices have shown increased variability at high levels of INR[19,20]. Recent studies conducted on the CoaguChek XS, however, show improved accuracy even at high values of INR[13-18]. In a study of Berezniki al.[13] demonstrates that CoaguChek XS INR values correlate with the laboratory of INR even in the hands of the patient. In the present study the results obtained by Coagucheck XS device correlated with conventional coagulometric assay. No statistically significant difference between the two methods of research was found. Regression analysis is a measure of correlation values, not accuracy. The high correlation does not automatically mean that there is good agreement between the two methods. Because of this for comparison of the results was used the analysis of the Bland-Altman[21]. The study shows great similarity of results. Even INR was created for standardisation of the results from different analysers it still may have differentINR values being obtained with different reagents and analyzers resulting from different from reagent sensitivities and patient blood chemistries[22].

CONCLUSION

1. CoaguChek XS is very accurate when testing INR, compared with laboratory results. Therefore, it has the potential to become part of the daily practice of physicians, including dentists treating patients receiving VKA.
2. CoaguChek XS is a convenient, portable and easy to use device that provides information on INR values within two minutes, as a result, avoid delay treatment due to wait for laboratory results.
3. Allows assessment of anticoagulant therapy with VKA in an outpatient setting, without the need for specially trained personnel and expensive equipment.
4. CoaguChek XS has built-in quality control for each test strip and provides accurate results of PT / INR real-time monitoring of patients treated with oral VKA.
5. Most patients prefer having a small drop of blood by finger prick (only 8 µl) beside blood from a vein - which enables the doctor and the patient to monitor the treatment at any time.

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