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Original article:

COMPARISON OF PT/INR RESULTS BETWEEN AUTOMATIC SELF-MONITORING COAGULATION ANALYZER DEVICE AND LABORATORY METHOD IN PATIENTS ON ORAL ANTICOAGULATION

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ABSTRACT

Background- Warfarin and Acitrom are commonly used oral anticoagulants in preoperative and postoperative period in patients with cardiovascular diseases which needs frequent dose modification depending on INR values in specialized biochemistry laboratories. Nowadays newer self-monitoring devices are available to assess the INR values.

Objective- To compare the INR values obtained by self-monitoring coagulometer with the standard laboratory method.

Methods - Total 200 patients underwent INR estimation by both conventional laboratory method and self-monitoring coagulometer. Correlation between the methods was analyzed by pearson correlation coefficient and Bland-Altman analysis was used to assess mean difference.

Results- The mean INR values by standard laboratory test was 2.72±1.25 and 2.92 ±1.35 by self-monitoring coagulometer. There was a strong correlation between both the methods and mean difference was 0.2±0.1

Conclusion- There was good consistency between INR values by both methods showing rapid and reliable analysis by self-monitoring coagulometers.

Key words- laboratory method, PT-INR, self-monitoring device, point of care

Introduction

Diseases of the heart valves constitute a major cause of cardiovascular morbidity and mortality worldwide with an enormous burden on healthcare resources. Rheumatic heart disease (RHD) continues to be the dominant form of heart valve disease in developing nations.1 The mean age of patients with valvular diseases in India are young and over 98% of them receive mechanical cardiac valves. After mechanical cardiac valve replacement surgery patients require lifelong anticoagulation therapy. Vitamin K antagonists (VKAs), such as warfarin, have been the drugs of choice for oral anticoagulation for a long time.

The anticoagulant effect of VKAs can be monitored by the prothrombin time or the international normalized ratio (INR). Limited therapeutic index of warfarin requires regular INR testing to adjust the dose of anticoagulation and prevent complications of both higher and lower levels.

Conventional methods of INR testing require patients to visit a professional medical institutuion, which is time consuming costly, and many patients fail to follow up on regular basis. In recent years, several portable coagulometers using capillary blood for INR analysis have been developed. These instruments, known as point of care (POC), have eliminated the need for whole blood collection and plasma separation by centrifugation and, thus, facilitate easy fast and accurate monitoring of VKAs therapy. Although they were originally developed for home use, POC monitors have become very useful in hospital and outpatient clinics due to the practicality and speed in obtaining results. However, there are limited studies in the literature regarding the consistency of their results with standard laboratory methods. The purpose of this study is to analyze the safety accuracy and cost effectiveness of INR testing by portable coagulometers as compared to conventional testing in patients of mechanical heart valve replacement surgeries.

Material and Methods

The study was conducted in department of CTVS and dept. of Biochemistry of G B Pant institute of postgraduate medical education and research, Delhi.

Inclusion Criteria

- Patients receiving oral warfarin or Acenocoumarin therapy after mechanical valve replacement surgery
- Patients without coagulopathy disorder
- Patients having good compliance

Exclusion criteria

- Patients with coagulopathy disorder
- Non compliant patients
- Patients on warfarin or acenocoumarin therapy without cardiac valve replacement

Methods

To examine the coagulation functions of these patients, conventional lab testing methods and self testing methods are used in parallel to check and record the INR values of the patients.

Standard Laboratory Procedure

Blood samples were collected by a clean puncture of an ante- cubital vein in the blood collection room. Peripheral venous blood of about 3 cm^3 was collected by laboratory staffs, and added into a blood collection tube containing 3.8% buffered sodium citrate. Then, the tubes were transferred to the labora- tory where they were centrifuged at 2500 □ g for 20 minutes at room temperature. The plasma obtained after centrifugation were analyzed with a STAGO STA-R (Diagnostica Stago, France) automatic coagulometer using STA-R Hepato Quick kit (Diagnostica Stago, SAS) with an ISI value of 0.91.

Point-of-Care Procedure

The CoaguChek XS (Roche Diagnostics, Basel, Switzerland) system consists of a small and portable coagulometer and dis- posable test strips. It measures the INR in whole blood obtained by finger prick, using recombinant human thromboplastin, and has an international sensitivity index (ISI) value of 1.0.

All measurements were performed simultaneously in the blood collection room when venous blood samples were taken for standard laboratory tests. About 0.01 cm^3 blood at the end of capillary of finger was collected from all patients by the same physician and added into corresponding area on the dry reaction test strip and tested with a portable CoaguChek XS coagulometer.

Study Protocol

A total of 200 patients with median age who visited the CTVS OPD of G.B. Pant hospital were enrolled in this study who were previously operated (Valve replacement surgery) and were taking warfarin/acitrom therapy and were in regular follow up.

Patients underwent INR testing by both conventional method as well as coagucheck device. Values obtained by both these methods were compared considering the conventional laboratory testing as standard of care. By comparing the values off all patients the accuracy of self monitoring device is compared to the standard method. Cost per test is also calculated for both the methods of testing and cost effectiveness is compared. Turnaround time was calculated for both the methods and was also compared.

RESULTS

The INR value of all 200 patients were collected for analysis. Table 1 shows the list of indications for oral vit-k antagonist anticoagulant therapy. The INR values tested by standard laboratory procedure ranged from 0.8 to 11.7 with mean 2.72 and standard deviation (SD) 1.25. The INR self-tested by patient by CoaguCheck XS system ranged from 0.9 to 12.3 with mean 2.92 and SD 1.35. The mean INR

difference between the 2 methods was 0.20 ±0.10. In Bland- Altman analysis, the INR values by Coaguchek XS system exhibited bias of -0.024 with a standard error of 0.316. Pearson correlation coefficient

(r) obtained by comparing INR levels of these two methods was

0.948 (p value <0 .001 and 95% confidence interval 0.901-0.997). The agreement of INR measurements between CoaguChek XS and STA-R was further analyzed according to INR categories as Subgroup INR<2, Subgroup INR 2-3.5, Subgroup INR>3.5. Pearson correlation coefficients (r) obtained at subgroups INR < 2.0, INR 2.0-3.5, and INR > 3.5 ranges were 0.901 (95% CI:0.871-0.980, P < .001), 0.945 (95% CI: 0.870-0.991, P < .001), and 0.916 (95% CI: 0.832-0.982, P < .001), respectively. The mean differences in the INR measurements in subgroups were 0.31 ± 0.3 0.43 ± 0.34, and 0.55 ± 0.49, respectively. The overall differences of INR values by 0.5 between both the methods were 20% with 17.3% cases in subgroup INR<2, 21.1% cases in subgroup INR 2.0- 3.5 and 32.3% cases in subgroup INR>3.5.

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Table 1 List of indications for oral anticoagulation therapy

Disease	No. of patients	percentage
prosthetic valve replacement	146	73
Preop patient with intracardiac thrombus	29	14.5
Deep vein thrombosis	14	7
Preop patient in atrial fibrillation	11	5.5
Total	200	

Table2- Summary of Accuracy Analysis Between the 2 Methods

RESULTS	STAGO STA-R	CoaguChek
Total participants(n= 200)		
INR, mean±SD	2.72±1.25	2.92±1.35
Difference, mean + SD	0.31±0.3	
95% CI limits of difference	0.963- 0.985	
Difference of 0.5, n (%)	40 (20%)	
Subgroup, INR<2 (n=52, 26%)		
INR, mean±SD	1.66±0.44	1.72±0.49
Difference, mean + SD	0.43±0.34	
95% CI limits of difference	0.871- 0.980	
Difference of 0.5, n (%)	9 (17.3%)	
Subgroup, INR 2-3.5 (n= 114)		
INR, mean±SD	2.15±0.34	2.32±0.39
Difference, mean + SD	0.37±0.40	
95% CI limits of difference	0.870- 0.991	
Difference of 0.5, n (%)	20 (21.1%)	
Subgroup, INR>3.5 (n= 34)		
INR, mean±SD	4.89±0.94	
Difference, mean + SD	0.55±0.49	
95% CI limits of difference	0.832-0.982	
Difference of 0.5, n (%)	11 (32.3%)	

Table 3 Performance Criteria Results

STAGO STA-R INR (mean + SD)	2.72±1.25
CoaguChek XS INR (mean + SD)	2.92 ± 1.35
Difference (mean + SD)	0.38 ± 0.53
95% CI Limits of difference	0.44 to 1.14
Magnitude of difference Number of Patients (%)	
<0.5	142 (71%)
0.5-1.0	36 (18%)
>1.0	22 (11%)

Discussion

This observational study in our tertiary care hospital enrolling 200 patients on oral anticoagulation therapy showed that INR results of portable CoaguChek XS system correlates well with traditional laboratory testing (STAGO STAR) in majority of patients. CoaguChek XS coagulometer provides rapid and reliable INR analysis for clinical management of the patients who are on oral anticoagulant therapy. Oral anticoagulants are widely used for the treatment of many cardiovascular diseases, such as AF/flutter, preoperative valvular heart disease, after prosthetic valve replacement and venous/arterial thromboembolism. Although newer oral anticoagulants provide efficient prevention of thromboembolism in patients with many patients, warfarin and acenocoumarin are still commonly used for many patients, particularly for those with rheumatic heart diseases and prosthetic valves.

Although the number of patients receiving oral anticoagulants has consistently increased, the therapeutic success is highly dependent on the requirements to maintain the INR within a narrow target range, which includes frequent testing and appropriate dose adjustments. The risk of hemorrhagic and thromboembolic complications associated with the use of oral anticoagulants necessiates the routine INR monitoring mandatory for patient safety. Oral anticoagulation therapy should be managed in a systematic, regular and precise fashion, incorporating patient education, systematic INR testing, followup, and good patient communication of results and compliance for dose adjustments. Laboratory methods for INR testing needs adequate amount of whole blood collection and plasma separation by centrifugation, which requires a considerable amount of time and work load. Portable CoaguCheck coagulometers are increasingly being self-used by patients at home and their health care providers. The Coaguchek XS system is the third generation of devices produced by Roche Diagnostics for portable INR monitoring. The first Coaguchek model was launched in 1994, followed by the CoaguChek S in 2000. The sample size required for these CoaguCheck devices is much smaller (10 μL) and easier to obtain as compared with standard laboratory methods with advantage immediate availability of results, better accessibility and reduced economic strain on patients . Patients can have their test result managed by their health care provider (patient self-testing), or they can interpret their INR result and adjust their own dose of anticoagulant accordingly (patient self-management).

Previous systematic reviews showed that self-monitoring is a safe intervention, which gives rise to significant reduction in thromboembolic events while reducing the risk of death. Additionally, patients spend more time in the therapeutic range of INR than they would without self-monitoring. (3,4,5) However,there have been several documented limitations regarding the accuracy of these devices, including differences compared with a standard plasma-based laboratory method, especially in supretherapeutic INR ranges(6). In our study the comparison between INR results of the CoaguChek XS coagulometer and a standard laboratory method (STAGO STA-R) found considerably high correlation between these methods and Pearson's coefficient for the correlation between INR values was very high at 0.948 with $p<0.01$.

Correlation coefficients greater than 0.7 indicate strong correlations between two variables and 1.0 is the highest degree of correlation possible. We also observed that the mean difference of INR measurements tended to increase as the mean INR values increased. Similar results were obtained by Kalcik M et al. (7) Similar findings were observed in a study carried out by Donaldson et al which demonstrated that the greater the INR value, the lower the correlation was detected between the methods studied(8). The reason increasing discrepancy between the methods in patients with higher INR remained unknown, and urges to double check the results with the laboratory findings in patients with INR values >5.0. Several studies suggest that both methods can be considered comparable as long as both INRs are within the therapeutic range or if both present a maximum difference of 0.5 INR units, regardless of the oral anticoagulation level.(9,10) Our study demonstrated that the mean difference of INR obtained by CoaguChek XS compared to the standard laboratory testing was of 0.31. Meneghelo et al. conducted a study with 219 INR samples, finding correlation coefficients of 0.91 for INR < 2; 0.85 for INR of 2 - 3.5; and 0.71 for INR >3.5. The percentage of agreement between the two methods for all ranges was 88.5%.(11) Williams et al. published a study in 2007, based on 97 INR samples from patients in a pediatric age group, in which the Coaguchek XS device had been used and reported that 19% of the samples had variation greater than 0.5 INR points, which matches with our finding of same in 20% INR values.

We found that in the target therapeutic range of INR 2.0-3., the CoaguCheck device showed greater precision for measurement of values which is important for clinical management and monitoring anticoagulation therapy doses. The THINRS Trial found that 80% of a population of 3,644 individuals were eligible for self-management of anticoagulation, after adequate training but did not find changes to the risk of major bleeding or death in the anticoagulation self-management group (12). DeSantis et al. found that 73.9% of values were within the therapeutic window, which is superior to the mean of 63.2% found in six other randomized clinical trials (13). The possibility should therefore be considered that the ease of measuring INR makes it more likely for patients to remain within their therapeutic ranges for longer periods of time. The 2012 ACCP Guideline recommends self-management of anticoagulation combined with normal outpatients monitoring, with a recommendation level of 2B, for patients on vitamin K inhibitors who demonstrate both the motivation and competence for anticoagulation self-management, using the portable device.(14)

CONCLUSION

The determination of INR using the CoaguChek XS device is very satisfactory compared with the standard laboratory (STAGO STA-R) method. It gives consistent results, improves monitoring frequency and correlates well as compared with the laboratory methods though very high results needs to be confirmed before any intervention for management. Along with reducing the economic burden on patients for frequent INR testing, it also helps in early identification and prevention haemorrhagic or thromboembolic complications of non-compliant anticoagulation therapy. The self-monitoring devices have potential widespread utility among the patients taking anticoagulation as an alternative to conventional laboratory methods though further large scare multicenter randomized studies are required.

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