CORRELATION BETWEEN PROTHROMBIN TIME LEVELS OBTAINED USING PROTHROMBIN METER WITH LABORATORY IN NEONATES

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ABSTRACT

Objective: To determine correlation between the Prothrombin time obtained by Prothrombin time meter with Prothrombin time estimation by clinical laboratory in neonates.

Study Design: Cross sectional study.

Place and Duration of Study: Study was conducted in the department of Paediatrics, Combined Military Hospital Lahore, from Feb 2014 to Aug 2014.

Methodology: One hundred cases, comprising of infants between the age from 0 to 28 days of both genders fulfilling the inclusion and exclusion criteria, were included in the study after seeking written informed consent. Blood samples from all selected neonates were obtained from a peripheral vein under strict aseptic conditions. The samples were analyzed on Sysmex Coagulation Analyzer CA-500 from the Pathology Department. Simultaneously a drop of blood was obtained by heel prick and spot checked by Roche Coaguchek Prothrombin Time Meter. SPSS version 17 was used for data analysis. Percentage and frequency were calculated for the qualitative variables; while mean and standard deviation were calculated for the quantitative variables. Data was analyzed by using Pearson's correlation between the values obtained with the meter and the laboratory.

Results: The mean (SD) INR values measured from PT meter was 2.176 (0.94557), while that from laboratory was 2.1467 (0.91013). A useful correlation with a correlation coefficient of 0.984 (r =0.984) was found between the two values.

Conclusion: PT values obtained by PT meter did not differ significantly from the PT estimation by clinical laboratory in neonates.

Keywords: Coaguchek XS, Correlation, Plasma, Prothrombin Time.

INTRODUCTION

Neonatal sepsis which is a life threatening condition with a reported incidence ranging from 49-170 per 1000 live births in the developing countries[1], is the single most common cause of developing life threatening complications like disseminated intravascular coagulation (DIC). Diagnosis and management of DIC would need measurement of Prothrombin time (PT) along with other laboratory parameters. In Asian countries the reported incidence of neonatal sepsis varies from 7.1 per thousand live births to 37.2 per thousand live births[2]. Pakistan now has highest neonatal mortality 46/1000 live births[3]. Sepsis contributes to an overwhelming number of these deaths but we do not have an exact known incidence of neonatal sepsis in our population. The incidence in India is 25 per 1000 live-births[4]. Thrombocytopenia is a common problem in neonates with sepsis, occurring in half of the cases with proven sepsis[5].

Laboratory PT measurement in plasma has been a method of choice since long in cases of sepsis who progress to DIC as a complication. The time taken for the standard laboratory PT test is approximately 25-30 min[6] and requires a significant amount of sample. Both these factors pose a challenge in neonates. The introduction of a point of care potable PT meter has made it possible to accurately monitor PT values in neonatal intensive care units and outpatient clinics[7,8]. It is relatively a less invasive method

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requiring only a heel prick with an ease to use, makes it equally popular.

Coaguchek XS from ROCHE is a relatively recent PT meter which is designed for bedside testing and is available in our country. The accuracy of PT values obtained from a PT meter as against a standard laboratory PT results has not been extensively validated. A few studies have had equivocal results with inadequate consensus drawn[9,10]. The study conducted by Lakshmy *et al*[6], showed that results obtained by PT meter were comparable with the laboratory values with absolute difference, mean ± Standard deviation (SD) between the two being 0.03 ± 0.15 and a *p*-value ≤0.05. A good correlation was also seen with correlation coefficient (r) of 0.94. In another study, the correlation was found to be 0.99[11].

This study was aimed to determine the correlation between PT values obtained by PT meter (Roche Coaguchek Prothrombin Time Meter) with those obtained from laboratory. Our research study would provide essential data regarding the utilization of a PT meter in hospitals of our country.

METHODOLOGY

This was a cross sectional study that was conducted in the department of Paediatrics, Combined Military Hospital Lahore from 18th February 2014 to 17th August 2014. Infants between the age from 0 to 28 days and both genders, requiring the need to measure PT due to any cause were included. Neonates having hematocrit less than 25% as estimated by blood were excluded from the study. 100 neonates fulfilling the inclusion and exclusion criteria which were admitted to the neonatology unit of Paediatric department, Combined Military Hospital Lahore were selected using non probability consecutive sampling. Sample size was estimated using 5% type-I error, 10% type-II error with an expected percentage of correlation as 81% between PT values obtained by PT meter and PT estimation by clinical laboratory. After a formal permission from hospital ethical committee, blood samples from all selected neonates were obtained from a peripheral vein under strict aseptic conditions. Venous blood sample was collected in PT bottle containing citrate. The samples were appropriately labeled and transported to the Pathology Department of Combined Military Hospital Lahore. Plasma from the venous blood sample was analyzed on Sysmex Coagulation Analyzer CA- 500. Simultaneously a drop of blood was obtained by a heel prick and spot checked by Roche Coaguchek Prothrombin Time Meter. Tabulated data collection form was designed and kept in the neonatal unit of Combined Military Hospital Lahore. Name, age, date of admission to NICU, diagnosis, PT values determined by PT meter and results obtained by laboratory were recorded. SPSS version 17 was used for data analysis. Percentage and frequency was calculated for the qualitative variables like gender; while mean and standard deviation were calculated for the quantitative variable like age. Data was analyzed by using Pearson's correlation between the two values obtained, one by PT meter and other from laboratory. The *p*-value of ≤0.05 was considered significant.

RESULTS

A total of 100 neonates requiring the need to measure PT were included in this cross sectional study conducted in the Paediatric department of Combined Military Hospital Lahore between 18th February 2014 to 17th August 2014. There was no missing values as all the enrolled indoor patients were studied. The mean age of the neonates was 14.62 with a standard deviation of ± 5.310 days. Range was 20 days. Sixty (60%) were male and forty (40%) were female. The INR values measured from PT meter ranged from 1.10 to 6.50, the mean being 2.176 with a standard deviation of ± 0.94557. Similarly 100 serum samples sent to laboratory for PT estimation revealed values between 1.10 and 5.60 with a mean of 2.1467 having a standard deviation of ± 0.91013. A Scatter diagram of PT meter values and laboratory PT values was plotted. It showed useful correlation between the two values with a correlation

coefficient of 0.984 (figure). The *p*-value calculated was 0.01, which was highly significant.

DISCUSSION

A major proportion of patients getting admitted in our neonatal intensive care units are suffering from serious conditions like neonatal sepsis which as a complication may lead to coagulopathy. Hence it is important to have results of prothrombin time and INR available as soon as possible for the prompt management of these neonates. Moreso a prothrombin time is also mandatory for prevention of bleeding complications and the need to transfuse plasma. Thus any device to assess the level of prothrombin time should be accurate, non-invasive and valid. For this purpose PT meters are widely used in the developed countries and at the same time are being subjected to continuous research in regard to their comparison with serum PT estimation[12]. Use of PT meter is still not widely prevalent in our country and we frequently rely on laboratory PT measurements needing a greater quantity of blood and a significant delay in getting results. Repeated sampling is also unduly expensive for a majority of our population. It may also lead to development of anemia in our already malnourished population.

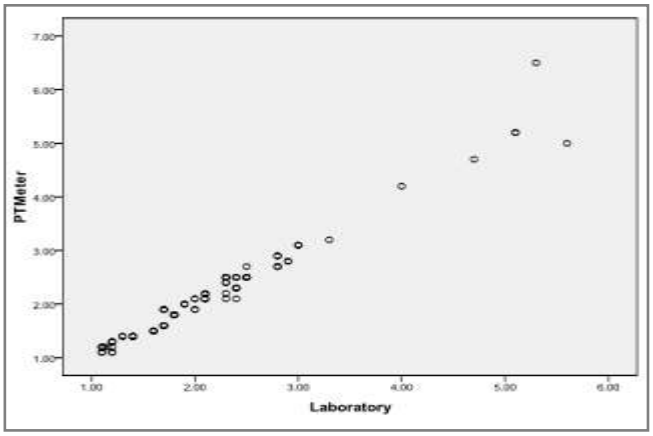

Figure: Scatter plot showing comparison between PT meter and laboratory serum Pt estimation.

The CoaguChek XS System is a third-generation portable point of care monitor used for prothrombin time (PT) testing. It is intended to evaluate the PT/INR. The monitor uses a lot-specific code chip and takes a single drop of capillary or venous whole blood. It displays the result in approximately one minute, and can be configured to display results in INR. The CoaguChek XS PT test strips are manufactured with a human recombinant tissue factor and have an International Sensitivity Index (ISI) of 1.0. This device, despite its limitations (cost and availability) has shown a good correlation with serum PT values. The CoaguChek XS system was specially designed for use at point of care clinical settings, rather than limited for patient self testing only[13].

Several studies have evaluated the clinical use of the CoaguChek XS Plus system in a variety of clinical settings using different laboratory based tests, but not a single study was carried out in comparison with Sysmex CA 500 series coagulation analyzer. Keeping in view the variability of results and limited literature in this context, our study focused on the correlation between Coagu Chek XS and Sysmex CA 500 which is readily available and used in our laboratories. The purpose was to ensure that the results are reliable enough for monitoring the patients without being confirmed with the laboratory.

Lakshmy and Kumar 6 concluded a similar study showing that Coaguchek XS INR meters are reliable and accurate and can be used by patients for monitoring of anticoagulation therapy. They compared the efficacy of CoaguChek XS INR meter in 42 patients requiring the need to measure PT with laboratory levels. Comparative results showed a fairly good correlation of 0.94, which is close to our results. Likewise, Bereznicki *et al*[14] carried out a similar research and revealed a good correlation between PT meter and laboratory values with a coefficient of correlation 0.91 as against our value of 0.98. Greenway and his associates[15] in their study indicated a correlation coefficient of 0.90. Kako *et al*[16] showed a correlation coefficient of 0.69. Vazquez *et al*[17] in their study concluded that correlation coefficient between point of care devices and laboratory methods were in the range of 0.96-0.98. In another study carried by Mina *et al*[18], it was

shown that the correlation of INR measurements between CoaguChek XS and STAR coagulation analyzer was excellent with a correlation coefficient of 0.964. Most studies are in agreement to the fact that the PT meter values do not correlate well with serum laboratory values at a higher level of INR. Our results are in concordance with these findings that show an increased INR difference at higher INR values[19-21]. These parameters thus remain a subject of further research in neonatology.

Recently, new portable device have been reported that use battery operated optical sensor that can rapidly quantify PT/INR within seconds by measuring alterations in the viscoelastic properties of a drop of whole blood following activation of coagulation with thromboplastin[22].

Despite the common perception of PT meter being costly, it has been observed that its use is actually quite cost effective. Single strip costs around 500 rupees whereas the PT test from laboratory costs around 600 rupees. Although the net difference in cost between the two is minimal but keeping in view the frequency of the tests and its readily availability, use of CoaguChek PT/INR meters add to extra care and timely management of such critically ill patients. Sharma *et al*[23] and Phibbs *et al*[24] suggested that use of portable devices in monitoring, and management of anticoagulation status appears cost-effective when combined estimates of clinical effectiveness are applied.

Another argument is that the use of portable meters in neonatal intensive care units can result in transmission of blood borne pathogens if preventive and control measures are not meticulously taken. McGoldrick[25] has suggested that appropriate cleaning and disinfection by using 70% isopropyl alcohol or 10% sodium hypochlorite solution for a minimum of 1 minute contact time can significantly reduce the odds of transmitted infections.

In light of our results we would like to emphasize that Coaguchek XS from ROCHE is a good PT meter for the measurement of PT values and can be efficiently used in monitoring and management of neonates. There is a limitation in our study that it has been conducted in neonates only. Unlike in older patients, these neonates are not subjected to oral anti-coagulants. Thus, the use of this meter in assessment of PT/INR on elderly patients on regular basis cannot be established.

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CONCLUSION

Coaguchek XS from ROCHE was a useful PT meter for measurement of prothrombin time. A good correlation (coefficient of correlation 0.984) was found between PT meter and prothrombin time estimated through standard laboratory techniques. Its use in our neonatal intensive care units would avoid repeated blood sampling and will give instant results that will be beneficial in prompt monitoring and timely management of neonates.

CONFLICT OF INTEREST

This study has no conflict of interest to be declare by any author.

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