

Coagulation profile in healthy Nigerian neonates

*M.A. Okunade and E.M. Essien

Department of Haematology, University College Hospital, Ibadan, Nigeria

Summary

A study of some coagulation factors were carried out in preterm and term infants on the first day of life. Screening coagulation tests – prothrombin time (PT), partial thromboplastin time with kaolin (PTTK) and the concentrations of Factors VIII: C and fibrinogen were determined in 100 normal newborn infants classified into three groups according to their gestational ages: 28 to 30 weeks, 31 to 36 weeks, 37 to 42 weeks. The respective values were compared with those of six-month-old infants as well as adults. The mean values of the screening coagulation tests, PT and PTTK, Factor VIII: C and fibrinogen were significantly different in all the three gestational age groups of neonates when compared with those of six-month-old infants and adult Nigerians. This suggests that a relative hypocoagulable state exists among newborn infants and could be responsible for increased bleeding tendencies in these groups of infants. This is the first documented report of coagulation profile in Nigerian neonates, and the range obtained in this study can thus be regarded as standard for healthy Nigerian neonates. The body of data should therefore provide a basis for evaluating newborn neonates with bleeding problems.

Keywords: Pre-term, term infants, coagulation, PT, PTTK.

Résumé

Une étude de certains facteurs de coagulation a été faite sur less enfants nés avant terme et ceux nés à terme au premier jour de leur naissance. Les tests de coagulation de: temps de prothrombine (PT), la temps partiale de Prothormbine avec du Kaolin (PTTK) et les taux de acteurs VIII: C et de fibrinogenes ont été déterminé chez 200 nouveaux nés normaux et classifiés en 3 groupes par rapport à leur ages gestationels (28 a 30 semaines, 31 a 36 semaines, 37 a 42 semaines). Les valeurs respectives ont été comparés à ceux des enfants de 6 mois et à ceux des adultes. Les valeurs moyennes de tests de coagulation PT et PTTK les facteurs VIII: C et fibronogenes ont été prolongé de maniere significative dans les groupes d'ages gestationelle, l'orsque compares à ceux des enfants ages de 6 mois et des adultes Nigerians. Ceci suggere q'un état hypocoagulable relatif existe entre les enfants nouveaux nés et pourrait etre responsable de la tendance croissante de saignement parmi les enfants de ces groupes. Ceci est le premier rapport documenté sur le profile de la coagulation chez les nouveaux nés Nigerians. Les valeurs obtenues dans cette étude pourvaient par consequent etre considerés comme standard chez les nouveaux nés Nigerian en sante. Ces données purraient aussi donne une base pur l'évaluation des nouveaux nes presentant les problemes de saignement.

Introduction

In Nigeria as well as in many other developing countries, there are no available data on the components of the coagulation system during the first week of life. Related

information on other childhood periods are equally scarce. The need to establish such values in our environment cannot be over-emphasised as ranges in other countries may not apply to our communities. Also many other biological values have been reported to be significantly different in Nigerians compared of premature infants especially.

Until recently, the prognosis of premature infants especially the extremely premature (i.e., gestage < 30 weeks) has been very poor. Premature infants frequently develop haemorrhagic and/or thrombotic complications which contribute significantly to high mortality and morbidity rates in this age group [1,2]. Difficulties arise in the management of these babies because of lack of data on physiological values of coagulation parameters. A knowledge of the values of the components of the coagulation system is necessary, particularly when dealing with the haemorrhagic complications. The primary objective of this study was to establish normal values for some known blood coagulation factors in preterm and term infants. A secondary objective was to attempt to use these data to explain the observed increase in the incidence of haemorrhagic and or thrombotic complications among these infants.

Patients and methods

Infant population

A. All neonates who were delivered by spontaneous vaginal route at the University College Hospital, Ibadan, Nigeria were used. All babies who required instrumentation at delivery or had history of birth asphyxia, evidence of sepsis or congenital anomaly at birth were excluded from the study.

A total of 100 infants were studied between January 1990 and June 1991. Informed consents were obtained from their mothers. Their gestational ages range between 28 and 42 weeks. These infants were classified into three (3) gestational age groups accordingly:

Group 1 – Extremely premature, but healthy infants with gestational ages of 28 to 30 weeks.

Group 2 – Older premature infants with gestational ages of 31 to 36 weeks.

Group 3 – Full-term infants with gestational ages of 36 to 42 weeks.

B. Ten six-month-old babies and ten adults matched for their ages were used for comparison in this study.

Sample collection

Free flowing venous blood (1.8ml) was collected from the antecubital or dorsal veins within 24 hours of delivery and added to plastic tube containing 0.2ml of 3.2% trisodium citrate at a ratio of 9:1 (v/v) for blood coagulation studies. The anticoagulant blood ratio was altered for babies with packed cell volume (PCV) greater than 55% [3]. Plasma was separated after centrifugation at 1200g for 15 minutes.

All samples were stored at -70°C for batch analyses within 3 months of collection.

Laboratory method

The plasma was used for determination of PTT [4], PTTK [5], Factor VIII assay [6] and fibrinogen concentration [7]. The

Correspondence: Dr. M.A. Okunade, Department of Haematology, University College Hospital, Ibadan, Nigeria

results are expressed as mean values standard error and were analysed statistically using unpaired student t-test and correlation coefficient and the significant values were set at $P < 0.05$.

Results

100 infants satisfied the criteria for selection (i.e., no history of birth asphyxia, evidence of intrauterine infection or congenital anomaly).

Table 1: Values of coagulation parameters studied in the different age groups

		Group 1 (28-30 wks gestation) (n = 18)	Group 2 (31-36 wks gestation) (n = 34)	Group 3 (37-42 wks gestation) (n = 48)	6/12 infants (n = 10)	Adults (n = 10)
Prothrombin time (sec)	Range	18 ± 1.0 17 - 20	15.5 ± 1.0 15 - 18	15.2 ± 0.9 14 - 17	14.2 ± 1.5 12 - 16	13 ± 0.5 11 - 14
Partial thromboplastin time with kaolin (sec)	Range	53 ± 2.0 51 - 58	49.5 ± 1.5 42 - 52	47 ± 2.0 41 - 50	42 ± 1.5 40 - 45	37 ± 5.0 35 - 45
Factor VIII: C (% activity)	Range	60 ± 15 50 - 95	80 ± 10 60 - 105	90 ± 15 65 - 110	105 ± 10 90 - 120	100% 95 - 115
Fibrinogen (mg/dl)	Range	210 ± 20 150 - 280	250 ± 30 200 - 300	285 - 35 230 - 300	385 - 25 315 - 365	295 - 30 250 - 345

Discussion

The values of the coagulation parameters presented in this study are those healthy term and preterm infants on the first day of life. The mean of all parameters studies were significantly prolonged in the three gestational groups of neonates when compared with six-month-old infants and adults.

Results of the screening coagulation tests, were prolonged and the extent of the prolongation was related to the gestational ages of the infants. Barnard et al [8] in their review of the coagulation system in extremely premature infants concluded that such a finding indicated lack of intrauterine maturation of coagulation system. Andrew et al [9] also found low levels of contact factors, Factors XII and XI, prekallikrein and high molecular weight kinninogen at birth; the values gradually increasing to adult values by the sixth month of life. These findings probably contributed to the observation of prolonged PTTk reported during the first six months of life among infants, though, there is no evidence of clinical bleeding in individuals with deficiencies of the contact factors.

Factor VIII: C activity in the study, correlated well with the gestational age of the infants (r value = 0.571). Factor VIII: C increased with gestational age because of the increase in the number of maturation sites of Factor VIII: C synthesis with advancing age of the foetus [11]. Similarly, the finding of gestational age dependence of fibrinogen concentration has been noted by others [11, 12]. The existence of foetal fibrinogen, the synthesis of which lasts 7 to 8 days, has been previously documented. Foetal fibrinogen differs from adult fibrinogen in its characteristically high sialic acid and AP peptide content, and high phosphorus level. These distinguishing characteristics are more marked in the preterm infants (28-36 weeks) than in full term, and predisposes the preterm infant to more haemorrhagic and or thrombotic complications.

The definition of the normal values of any parameter in a single population is a difficult task. This problem is further complicated in the neonate because these parameters are constantly developing and are dependent on gestational as well as postnatal ages of the infants. The major setback in this study, in preterm infants was in obtaining adequate blood samples to perform various tests. The necessity of using carefully designed microtechniques to perform these various tests cannot be overemphasised.

Table 1 shows the summary of all results obtained in the study. Extremely premature infants had significantly prolonged coagulation screening tests (PT and PTTK), low levels of Factor VIII and concentrations of fibrinogen.

As expected, all values were below adult level in all the infant groups except those of the six-month-old infants: in these the highest level of Factor VIII and fibrinogen concentrations were recorded.

The findings of a significantly prolonged PT and PTTK, low levels of factor VIII: C and fibrinogen concentration in term and preterm infants (when compared to six-month-old infants and adults) is compatible with a state of relative hypocoagulability among them as such consideration must be given to those values when evaluating infants with coagulation problems.

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