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Research Article

A study of nucleated red blood cell count as a marker of severity of hypoxic ischemic encephalopathy

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ABSTRACT

Background: Encephalopathy is a term used to describe central nervous system dysfunction. Neonatal encephalopathy associated with perinatal asphyxia is called hypoxic ischemic encephalopathy. Birth asphyxia and subsequently developing Hypoxic Ischemic Encephalopathy (HIE) is one of the major causes of perinatal mortality and morbidity especially in developing countries like India. The present study will be carried out to analyse nucleated red blood cell count and to find out a relationship between this and severity of HIE.
Methods: A prospective (case control) study was undertaken between august 2011 and October 2013 in the neonatal intensive care unit, the study population was consisted of 50 full term infants with asphyxia (group-1) and 50 healthy new-born (group-2).
Results: The average absolute nRBC count (nRBC/mm^3) for the control group was 38.6/mm^3. It is 426.55/mm^3 in the first period with SD of 203.99 & a SEM of 48.08 (in HIE Gr-I). It increases with time in 2nd period and again decreases in the third time period. However the average value is always higher than the control group ($p<0.001$). In case of HIE Gr-II the average nRBC count is 498.45 with SD of 214.72 and a SEM of 56.8 whereas these are 412.43, SD of 202.54 & SEM of 48.32 in case of HIE Gr-III. So there is a positive correlation between the absolute number of nRBC count and HIE, but there is no linear correlation between the nRBC count and the severity of HIE.
Conclusions: Nucleated red blood cell count (nRBC) count increases in all grades of HIE, but there is no linear correlation between nRBC count and the severity of HIE.

Keywords: Hypoxic ischemic encephalopathy (HIE), Nucleated red blood cell (nRBC)

INTRODUCTION

Birth asphyxia is estimated to account for 920000 neonatal deaths every year and is associated with another 1.1 million intrapartum stillbirths. The WHO also estimates that globally, 29% of neonatal death are caused by birth asphyxia.[1]

More than a million children who survive birth asphyxia develop problems such as cerebral palsy, mentalretardation, learning difficulties, and other disabilities.[2,3]

Encephalopathy is a term used to describe central nervous system dysfunction. Neonatal encephalopathy associated with perinatal asphyxia is called hypoxic ischemic encephalopathy (HIE). Multiorgan systems involvement is a hallmark of hypoxic-ischemic encephalopathy.[4] Apart from brain involvement organ system involved following a hypoxic-ischemic events include the following: heart (43-78%), lungs (71-86%), renal (46-72%), liver (80-

85%), hematologic (32-54%). Because the present indices of asphyxia are unhelpful in the diagnosis and prediction of the severity of asphyxia, we wished to investigate the relationship between nRBC count and the severity of HIE.

METHODS

The study population was consisted of 50 full term infants with asphyxia (group-1) and 50 healthy new-born (group-2). All the new-borns were delivered at our hospital, dept. of obstetrics & gynaecology, and admitted in NICU of dept. of paediatrics, BMCH will be evaluated regarding their eligibility to be included or excluded in the study.

Inclusion criteria

1) Newborn suffering from birth asphyxia and subsequently developing hypoxic ischaemic encephalopathy.

2) Newborn who fulfil the case definition criteria.

3) Gestational age (37-40) weeks [assessed GA].

4) Birth weight 2.5- 3.5 kg.

5) Neonates surviving more than 24 hrs.

Exclusion criteria

1) Newborn with sepsis, major congenital anomalies, birth trauma.

2) Any bleeding infant.

3) Premature infant.

4) Newborn borns to mothers having major diseases like malaria DM, severe anaemia, preeclampsia/eclampsia, thyroid disorder, idiopathic purpura, placental disorder like vascular thrombosis, abruption placenta.

5) H/o maternal intake of any drugs causing bone marrow suppression/thrombocytopenia.

6) Newborn with congenital leukaemia, necrotising enterocolitis, those having exchange transfusion.

The new-borns whose APGAR score[5,6] at 5th minutes was 5 or below and arterial blood pH. During birth or a few hours after birth below 7.2, and had the findings of HIE were accepted as having perinatal asphyxia. Patients were recorded according to the HIE staging of the Sarnath and Sarnath.[7] The blood samples were collected in asphyxiated infants in three different times named as period. The same tests were performed in control infants in three different times after parental consent was obtained. The first period was within 48 hours after birth, the second was between the third and the sixth days after birth, and the third period between the seventh and the fourteenth days after birth. All asphyxiated babies had coagulation work-up including Prothrombin Time (PT), partial thromboplastin time (PTT), fibrinogen and fibrin degradation products to rule out Disseminated Intravascular Coagulation (DIC). Trans fontanel and abdominal ultrasonographic examination were performed to evaluated intracranial haemorrhage and renal vein thrombosis in the asphyxiated new-borns. The mechanism responsible for the thrombocytopenia was investigated by measuring MPV. The platelet count and MPV was assessed on EDTAant coagulated specimens using a coulter-S+ counter (Coulter STKS, coulter electronics Ltd North well drive, England).

RESULTS

Asphyxiated and control groups were not different for matched features, which includes birth weight and gestational age. However a major difference between the two groups was the APGAR score.

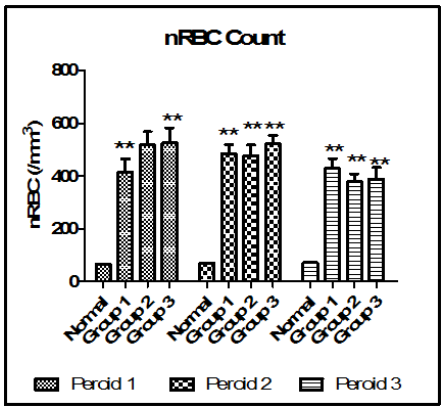

Figure 1: Comparison of nucleated RBC among various stages of HIE and normal control. Values are expressed as mean ± SEM. Statistical analysis (One way ANOVA; Dunnett compare all vs. control) was performed using Graph Pad Instat Software. $^{**}p<0.01$ when all the groups compared with normal.

Table 1: Comparison of nucleated RBC among various stages of HIE and normal control.

Parameters	Avg.	SD	SEM
nRBC P1 G1	426.55	203.99	48.08
nRBC P1 G2	518.25	218.72	48.90
nRBC P1 G3	526.08	219.58	63.38
nRBC P2 G1	484.22	214.83	50.63
nRBC P2 G2	477.05	214.14	47.88
nRBC P2 G3	389.41	221.40	63.91
nRBC P1 G1	375.54	217.57	51.28
nRBC P1 G2	381.10	194.16	43.41
nRBC P1 G3	150.13	186.42	53.81

The average absolute nRBC count (nRBC/mm^3) for the control group was 38.6/mm^3. It is 426.55/mm^3 in the first period with Standard Deviation (SD) of 203.99 & a SEM of 48.08 (in HIE Gr-I). It increases with time in 2nd period and again decreases in the third time period. However the average value is always higher than the control group ($p<0.001$). In case of HIE Gr-II the average nRBC count is 498.45 with SD of 214.72 and a SEM of 56.8 whereas these are 412.43, SD of 202.54 & SEM of 48.32 in case of HI Gr-III. So there is a positive correlation between the absolute number of nRBC count and HIE, but there is no linear correlation between the nRBC count and the severity of HIE.

DISCUSSION

Few studies have been performed to find a relationship among platelet count and the grade of hypoxic ischemic encephalopathy. But most of the studies have been carried out in animals. The present study will be carried out to analyze the hematological parameter and to find out a relationship between this and severity of HIE. These hematological parameters with a cut of value can be a useful marker and may serve as a guide for grading. Moreover these parameters may be used to assess short term prognosis. It will help us in better understanding of the problem and will be helpful in the development of post insult therapy.

Hassan et al.[8] showed in their study; the NRBC/100 WBC and absolute nucleated red blood cell levels in the blood of newborns in the control group were 3.87 ± 5.06 and 58.21 ± 87.57/mm^3, respectively; whereas the corresponding values in the cases were 18.63 ± 16.63 and 634.04 ± 1002/mm^3, respectively ($p<0.001$). A statistically significant negative correlation existed between nucleated red blood cell level and indicators of the severity of perinatal asphyxia, first minute APGAR score and blood pH ($p<0.001$), respectively. A positive correlation was demonstrated between these parameters and severity of asphyxia, acidosis, and poor outcome ($p<0.05$). The NRBC/100 WBC and/or absolute nucleated red blood cell are simple markers for assessment of severity and early outcomes of perinatal asphyxia.

Joseph et al.[9] said that in HIE the nRBC counts peaked between 6 and 8 hours of age and fell to normal levels by 36 to 72 hours of age (56% had values >1860×10^6/L). The characteristics haematological changes found are attributable to asphyxia insult, not to brain injury. Because of inconsistent changes, hematologic counts can not be used on their own to time asphyxia insults.

CONCLUSION

The study was carried out to analyze the hematological parameter (nRBC) and to find out a relationship between this and severity of HIE, at dept. of pediatrics, Burdwan medical college from Aug-2011 to Oct-2013. It involved 50 cases suffering from birth asphyxia and subsequently developing hypoxic ischemic encephalopathy. The specific objective of this study is: To evaluate nRBC count as a marker of severity of HIE. The study revealed a positive correlation between the absolute number of nRBC count and HIE, but found no linear correlation between the nRBC count and the severity of HIE.

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Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

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