Intraventricular haemorrhage and periventricular leukomalacia in Nigerian infants of very low birth weight

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Summary

Transfontanelle ultrasound scans were performed on 93 very low birth weight neonates admitted at the University of Ilorin Teaching Hospital (UITH), Ilorin, Nigeria, between January 1992 and April 1994, to ascertain the pattern and determinants of intraventricular haemorrhage and periventricular leukomalacia. Forty-seven percent of the infants had normal ultrasound; 22% had mild intraventricular haemorrhage (IVH), 7.5% had moderate to severe IVH and 23% had periventricular leukomalacia (PVL) and a 3.5 fold increase in IVH. Infants with apgar scores ≤ 3 at 5 minutes had a 6-fold increase in IVH and 2-fold increase in PVL. There was no association with birth weight, gestational age, respiratory distress and place of delivery. Our study suggests that antepartum events proximate to delivery and the immediate post partum events play significant roles in the development of IVH and PVL in this population. Improvement in antenatal, labour and delivery, and immediate newborn care; including provision of basic resuscitation equipment and skills to midwives in the rural maternity centers will reduce the incidence and severity of IVH and PVL.

Keywords: ***Intraventricular, Haemorrhage, Periventricular, Leukomalacia, Prematurity, Ultrasound.***

Résumé

Les échographies trans fontanelles étaient opérées chez 93 néonates hospitalisées au centre hospital-universitaire d'Ilorin UITH, Nigeria entre janvier 1992 et avril 1994, afin de déterminer la tendance et facteurs déterminants d'hémorragie intra ventriculaire et la leucomaklacie péri ventriculaire. 47% des enfants avaient l'échographie normale, 22% avaient l'hémorragie intraventriculaire légère (IVH), 7,5% avaient IVH modéré au niveau élevé et 23% avaient leucomalacie péri ventriculaire (PVL) et en 3,5 parties d'augmentation en IVH. Des enfants avec Score Apgar ≤3 pendant 5 minutes avaient une augmentation en six parties en IVH et augmentation en 2 parties en PVL. Il n'y a pas une association avec poids de naissance, âge de gestation, douleur respiratoire et lieu d'accouchement. Notre étude évoque que des événements antépartum à proximité d'accouchement et des événements post partum immédiat qui jouent des rôles importants dans le dévéloppement de IVH et PVL dans cette population. Amélioration anténatale, accouchement et des soins d'urgence pour les nouveaux nés y compris presentation de matériel de réanimation de base et connaissances pour des sages-femmes dans les maternités rurales et suveillance de naissance traditionnelle vont baisser la fréquence et la gravité de IVH et PVL.

Introduction

Intraventricular Haemorrhage and Periventricular leukomalacia (PVL), constitute antecedents of acute and long term neuromorbidity in Very Low Birth Weights infants (VLBW)[1-3]. In developed countries, cerebral palsy (CP) occurs 25 – 31 times more common among infants who weigh less than 1500gm at birth than in full sized newborn (8% vs 0.25%); and babies whose birth weight is less than 2500gm account for one third of all children with CP. The most reliable predictors of CP and other developmental disabilities in these low birth weight infants are cystic PVL, Grade IV IVH and persistent ventriculomegaly[4]. In developing countries with higher overall perinatal/neonatal morbidity and mortality, and specific neurologic morbidity and mortality[5-7], the contribution of IVH and PVL to these higher rates have not been well defined; primarily because of the paucity of data.

The pathogenesis of IVH and PVL are multifactorial and different combinations of factors may be operative in different populations of patients[1]. These factors are further modulated by geographical location due to different obstetric and neonatal practices. Racial differences in the pattern and magnitude of various neonatal problems (e.g) disparity in the prevalence of respiratory distress syndrome (RDS) among white and black infants[8] and geographical ddifference in bacterial aetiology of neonatal sepsis also play a role[9]. Therefore this study was done to determine the pattern and possible determinants of IVH and PVL in a defined group of VLBW infants at the University of Ilorin Teaching Hospital (UITH), Ilorin, Nigeria.

Methods

Setting and subjects

The study was carried out prospectively between January 1992 and April 1994. The UITH has the only neonatal unit within an area of about 50 square kilometers (Km), hence most premature babies who survive the immediate post partum period are invariably transported over long distances to UITH. The UITH had no facilities for mechanical ventilation, blood gas analysis or pulse oximeter during the period of the study. Infants were nursed in incubators or with radiant warmers, and given oxygen when indicated for respiratory distress.

One hundred and ninety-six neonates ≤ 1500gm at birth were eligible for the study. One hundred and three babies were not scanned because 73 of them died within 72 hours or there were logistical problems, remaining 93 babies for the study. Transfontanelle ultrasound scanning through the anterior fontanelle was done by an experienced radiologist (D.A.N) using a real time sector scanner (Siemens Sonoline SX) with a 5.0 MHz transducer. Scans were done when the machine was operational during normal working hours and the infants were deemed stable enough for transport to the Radiology department (a distance of 5km). Initial scans were done at 8± 3 days (range 2 – 16 days) of age. The findings were classified as normal, IVH, and PVL. IVH was graded according to the method of Papile et al[10], i.e.

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Grade 1: Subependymal haemorrhage; Grade II: Intraventricular haemorrhage without ventriculomegaly; Grade III: Intraventricular haemorrhage with ventricular dilatation; and Grade IV: Intraventricular haemorrhage with parenchymal extension. We did not attempt to quantitate the size of periventricular echo densities. Follow-up scans were performed in 2 weeks for infants with IVH Grade III and IV, or as soon as feasible in any infant, following a clinically significant deterioration. To identify risk factors associated with these neurosonographic findings, the following clinical information were documented: Birth weight, Gestational age using the Ballard score[11], weight for gestational age classification, using the Colorado chart (i.e. small for gestational age if < 10th percentile or appropriate if 10 – 90th)[12], place of delivery, apgar scores and the presence of respiratory distress.

Data analysis

Only infants who had head ultrasound scans were included in the analysis. The highest grade of IVH in either ventricle was used. The infants were grouped into 4; normal, mild IVH (Grade I and II), moderate to severe IVH (Grades III and IV), and PVL. There was no infant with combined IVH and PVL on the initial scans. Because of the high number of babies born outside UITH there were a lot of missing apgar scores data. The IVH groups were combined for analysis involving apgar scores. Group comparisons of independent means were done by one way analysis of variance. For discrete variables, comparisons were carried out using the log likelihood ratio statistics (G-statistics)[13] or Fisher's exact test. Whenever the null hypotheses were rejected, pairwise comparisons were done to identify the source of the difference, and odds ratio with 95% confidence intervals were calculated.

Results

Ninety-three infants formed the basis for the results in Table 1. Forty-seven percent of the infants had a normal ultrasound; 22% had mild IVH, 7.5% moderate to severe IVH, and 23% had PVL. There was no association between ultrasound findings and gestational age or birth weight, weight for gestational age classification, sex, respiratory distress and place of delivery.

There were significant associations between abnormal scans and apgar scores ≤ 3 at 1 and 5 minutes. Infants with apgar scores ≤3 at 1 minute were five times more likely to have an abnormal scan (OR = 5.2; 95% CI =1.3 – 20; P<0.025). There was a 10–fold increase in the incidence of PVL (OR =10.4 (1.1 – 97); (P<0.025) and a 3.5–fold increase in IVH (OR = 3.5 (0.7 – 17); P>0.05). Infants with apgar scores ≤ 3 at 5 minutes were four times more likely to have an abnormal scan (OR = 3.9; 95% CI = 1–16; P<0.05). They had a 6-fold increase of IVH (OR =5.7 (1.1–28); P < 0.05) and a 2-fold increase in PVL (OR =2.4 (0.4 – 14); P>0.05).

On follow-up scanning, two infants, both with bilateral Grade III IVH developed cystic PVL, and persistent ventriculomegaly respectively

Most of the infants were asymptomatic. However one infant with Grade III IVH had apnea with seizures, another with Grade I had apnea, and two infants (Grade II and III) developed bilirubin encephalopathy that could not be attributed to any other aetiology.

Discussion

In developed countries, IVH and PVL each has a current incidence of about 20% in VLBW infants. These rates are expected to fall with continued improvement in obstetric and neonatal care[1]. The few studies from developing countries have reported figures ranging from 50% in South Africa and Hong Kong, to almost 100% in Malaysia[14-16]. The data from developing countries are difficult to compare with one another or with data from developed countries because of the differences in neonatal practices as a result of the prudent utilisation of limited resources e.g. in Baragwanath Hospital, South Africa,

Table 1 Neuro sonographic findings and perinatal variables

Ultrasound findings	Normal (43)*	I/II(2)*	III/IV(7)*	PVL(22)*
Gestational age (Wks)	30.9± 1.7	31.2 ± 1.5	31.3 ± 1.0	30.7 ± 1.6
< 32 weeks	27	9	3	14
32 – 34 weeks	16	12	4	8
Birth weight (Gm)+	1228 ± 184	1176 ± 153	1250 ± 173	1143 ± 227
BW for GA Class:				
SGA	8	6	1	5
AGA	35	15	6	7
Sex(M/F)	19/24	9/12	3/4	6/16
Age at U/S (days)+	8± 3.5	9.1 ± 3.7	7.3 ± 1..5	8.9 ± 3.7
Respiratory Distress	7	6	3	6
Duration of 0_2 (hrs)+	43 ± 33	21 ± 17	19 ± 15	21 ± 18
Apgar scores	23*	(8)*	(3)*	(9)*
1 minute ≤ 3	10	6	2	8
> 3	13	2	1	1
5 minutes**≤ 3	4	4	2	3
> 3	19	4	1	6
Place of Delivery:				
Inborn	23	10	6	7
Outborn	20	11	1	15

**=n (group size)* ***P value <0.05*
+ = mean ± SD **** P value < 0.025*

the cut-off weight limit for ventilatory assistance was 1000g, and in the Malaysia study, the authors stated that "the shortage of nursing staff and neonatal facilities was very severe, and the annual deliveries of 25,000 – 26,000 very high". Our study also suffers from the biases inherent in the natural selection process that would prevail under such conditions of inadequate or limited resources.

Prima facie, the 30% incidence of IVH from the present study would seem comparable to studies from developed countries and lower than the figures from developing countries. However, this is a highly selective group of infants – the least sick of our VLBW population. Thirty-seven percent of babies died mostly within the first 75 hours of severe respiratory compromise. Considering the known association between severe respiratory illness and IVH, these babies would, most probably have had severe IVH.

In contrast to most studies, there were no associations between IVH and gestational age or birth weight and respiratory distress in our study. This can be explained by the extreme natural selection in which babies at the very immature end of spectrum would have died from severe compromise, hence not scanned and included in the analysis. This is corroborated by the small variances in birth weight and gestational age, and the small number of infants with respiratory distress among the survivors. The association between abnormal neurosonographic findings and apgar scores ≤ 3 at 1 and 5 minutes is somewhat interesting. Although, infants with 1 and 5 minutes apgar scores have similar odds of having abnormal scans, the association at 1 minute was due to an increase in the incidence of PVL, while at 5 minutes the association was attributable to an increase in incidence of IVH.

Non survivors had worse apgar scores (data not shown) and based on the severity of their respiratory illness, would have had neurosonographic abnormalities, and hence strengthen the association. Therefore, although apgar scores constitute weak proxy evidence of ante and intra partum distress, these findings suggest that the antepartum events proximate to delivery and the immediate post partum events play significant roles in the development of IVH and PVL in our population of VLBW infants. This is consistent with our earlier report that the 2nd born twin (more prone to peripartum distress) is more likely to develop IVH than first twin[17]. Consequently, the incidence of IVH and PVL in surviving infants can be reduced by improvement in antenatal, labour and delivery, and immediate newborn care. Since most of the deliveries take place outside the Teaching Hospital, basic resuscitation equipment and skills should be provided to midwives in the rural maternity centers.

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