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Neonatal seizures in Nigerian infants*

[1]A.A. ASINDI, [2]O.E. ANTIA-OBONG, [2]E.O. IBIA and [2]J.J. UDO
[1]*Neurology and* [2]*Neonatal Units, Department of Paediatrics, University of Calabar Teaching Hospital, Calabar, Nigeria.*

Summary

Nigerian newborns presenting with convulsion in University of Calabar Teaching Hospital, Calabar during the period January 1989 to December 1990 were prospectively studied to determine the aetiology and pattern of their seizures. There were 60 patients representing 4% of admissions into the Newborn Unit during the period. Birth asphyxia, infections and hypoglycaemia were the important identifiable aetiological factors which operated either singly (48% of cases) or in concert (in another 48%) of the infants. Detectable infections included meningitis and septicaemia caused predominantly by coliforms and *Staphylococcus aureus*. Hypocalcaemia and electrolyte imbalance did not feature. There was an unusually high prevalence (63% of cases) of the generalised type of seizures probably due to the high frequency of mixed aetiology. The mortality rate of 50% encountered appears to be related to the underlying aetiology and prematurity. Detectable causes of neonatal seizures in our environment appear to be potentially preventable by improved obstetric and neonatal care. There is dire need also to provide modern facilities for investigating newborn seizures in order to improve upon the diagnostic yield.

Résumé

Les noveaux-nés Nigérians ayant la convulsion, présentés au Teaching Hospital de l'Université de Calabar pendant la période du janvier 1988 au décembre 1990 étaient étudiés prospectivement pour déterminer l'étiologie et l'exemple des bouleversements. Il y en avaient soixante, soit quatre pourcent des malades admis dans la section des nouveaux-nés pendant cette période. L'asphyxie de naissance, les infections et l'hypoglycaemie étaient les facteurs étiologiques importants qui agissaient soit isolement (48% des cas), soit de concert (encore 48%) sur les enfants. Les infections qui peuvent se détecter comprennent la meningite et la septicaemie causées d'une manière prédominante par les coliformes et le *Staphylococcus aureus*. Un déséquilibre entre l'hypocalcaemie et l'électrolyte n'a pas figuré. Il y avait une prédominance peu commun des types généralisés d'attaques (63%) due probablement à une haute fréquence d'étiologie mixte. Le taux de la mortalité de 50% recontré semble lié à l'étiologie et à la prématurité fondamentales. Il paraît que les causes discernables des attaques néo-natales chez nous peuvent être virtuellement empêchées par des soins obstétrique et néo-natal améliorés. Urgent est le besoin de fournir des facilités modernes pour l'investigation des cas des nouveaux-nés afin d'améliorer le rendement diagnostique.

Introduction

Neonnatal seizures and their long-term sequelae have been extensively studied[1-5]. An important aetiological factor identified with infant seizures is predominantly post-asphyxial hypoxic-ischaemic encephalopathy[1,2]. Others include metabolic disturbances, central nervous system trauma and malformation, sepsis and withdrawal of maternal drugs. Eriksson and Zetterstrom[3] have shown that neonatal seizure is associated with increased mortality, severe psychomotor retardation, epilepsy and cerebral palsy. Repeated seizure activity per se may be damaging to the brain. However, the outcome of neonates with seizures is mostly dependent on the underlying aetiology of the convulsion and the extent of cerebral insult. The early onset and asphyxia-induced seizures appear to carry the worst prognosis[4].

In Benin-City, Nigeria, Omene *et al.* [5] reported an incidence of 3.5 per 1000 hospital live-births with perinatal asphyxia and hypoglycaemia as the

* Correspondence: A.A. Asindi, P.O. Box 3642, Unical Post Office, Calabar, Nigeria.

principal aetiological factors (1974-1979). The aetiologic and clinical spectrum of this condition has not yet been described in infants in many other part of Nigeria. It is therefore desirable to carry out an up-dated survey on this important subject in order to determine the pattern in the Nigerian infants, particularly regarding its aetiology and incidence. The data can be used to determine possible preventive measures.

We report here our two-year experience with 60 cases of neonatal seizures in Nigeria newborn infants admitted into the University of Calabar Teaching Hospital, (UCTH) Calabar and prospectively studied to determine the predisposing factors, pattern of seizures, and the early outcome.

Patients and methods

During the period January 1989 to December 1990, newborn infants suspected of having convulsive movements were admitted into the Special Care Baby Unit (SCBU) of the University of Calabar Teaching Hospital (UCTH) and prospectively studied. The determination of a seizure was made clinically if any abnormal movements, either localised or generalised, were repetitive, stereotyped and accompanied with abnormal eye deviation. Before any infant was fully enrolled, at least one of the authors and an experienced senior nursing staff must have observed some of the episodes. Neonatal tetanus and mere jitteriness were not included.

Investigations included precise details of pregnancy, labour and delivery history with particular interest on possible birth asphyxia obtained from the mother, her relations or case notes. Lumbar puncture, blood glucose, calcium, electrolytes' estimations and blood culture were undertaken. Due to lack of facilities it was not possible to perform electroencephalography (EEG), modern neuro-imaging techniques, viral studies and estimate blood and urine amino acids. The hospital has no machine for monitoring the foetal or neonatal blood Ph and blood gases.

Treatment measures included the use of diazepam to terminate active seizures and phenobarbitone for maintenance. These drugs are easily available and popular in our unit. We are not quite familiar with the use of phenytoin sodium in neonatal seizures hence, it was not used. Other modalities of management included an attempt to treat the possible or definitive cause of the seizures, for example the correction of metabolic anomalies, and the use of antibiotics for infections.

Because of strong taboo in the community against post-mortem examination, autopsy was carried out in only three infants. All information collected were entered into a pro-forma form. Since a large number of patient suffered from a multiplicity of factors we attempted to identify and classify some causative factors as being primary to others. For instance, if an infant was asphyxiated at birth, and became hypoglycaemic or infected, the asphyxia was regarded as primary cause while the latter were regarded as secondary or as complications. Also, infection as primary problem could be complicated by hypoglycaemia. This mode of classification was entirely arbitrary just for ease of data analysis. Also all infants born in the UCTH, general hospitals and private practitioners clinic were classified as hospital-born, while those born outside such establishments eg. private houses, churches, road etc. were regarded as home-born.

Birth asphyxia following home delivery was determined if we could elicit a history that the baby had failed to cry and was gasping for a prolonged period after birth, combined with inability to suck in the first days of life. In hospital delivery, significant birth asphyxia was based on Apgar scores less than 4 in 5 minutes. Blood glucose of 1.6mmol/L or less in term infants and 1.1mmol/L or less in infants weighing 2,500g and below during the first 72 hours of life, or below 2.2mmol/L in infants aged above 72 hours was considered as hypoglycaemia. Septicaemia was diagnosed in an ill infant with bacteriologically positive blood culture.

Results

During the two-year period, a total of 60 infants exhibited abnormal movements which were identified as seizures. These were made up of 34 males and 26 females giving a M:F ratio of 1.3:1. During the period under review there were 1,452 neonatal admissions, thus making the incidence of neonatal seizure in our centre 4.1%. Fifty-one infants (85%) were term, 7 (11.7%) preterm (gastational age ranging from 30 to 35 weeks (mean 32.3 weeks), and the remaining 2 were post-term. Birthweights ranged from 1.6 to 4.4kg. Thirteen infants had birthweights ranging from 1-2.5 kg; 38 from 2.6-3.5 kg, and 5 were above 3.5 kg. The smallest infant in the series weighed 1.55 kg. The birthweights of 4 infants could not be determined becuase they were born at home

(all term) and brought in after 48 hours of delivery. Only 2 infants were light-for-date weighing 2.0 and 2.2kg. respectively at 40 weeks each.

The delivery of the 60 infants were conducted in the following places: 29 in UCTH, 4 in private practitioners' clinics, 22 in private homes, 4 in the church and 1 on the road side while approaching the hospital. Thus 33 (65%) infants were hospital-born, and 27 (45%) were home-born (Table 1).

Table 1: Mortality figure related to age of onset of seizures (n=60*)

Age of onset (days)	No. of Patients	No. of Deaths	Mortality Rate (%)
< 1	30	11	36.7
1-3	9	5	55.6
4-6	7	6	85.7
7 and above	8	5	62.5
Total*	54	27	50

* 6 of the 60 infants had left hospital against medical advice.

Aetiology of seizures

The cause of seizure could not be identified in 2 infants. Twenty-nine infants (48.3%) had only one detectable cause each while in another 29 (48.3%) the identifiable causes were multiple — 2 factors in each of 22, 3 in 5, and 4 in 2 infants.

Perinatal asphyxia was the most common cause of seizures in our series with 36 infants involved (Table 2). Of these 36, 13 were complicated with hypoglycaemia, another 13 with infection (meningitis or septicaemia or both) while 5 were both infected and hypoglycaemic. Prolonged obstructed labour was the dominant cause of asphyxia.

Infections which included meningitis (8 cases), septicaemia (4 cases) or both (4 cases) were identified as the primary diagnosis in 16 (26.7%) of the 60 newborns and 4 of the 16 were complicated by hypoglycaemia. The organisms isolated from infected infants were largely coliforms and Staphylococcus pyogenes.

There were 4 cases of isolated hypoglycaemia one of which was delivered on the road. In two infants the seizures was related to congenital malformation of the central nervous system. One had an open thoracic myelomeningocoele which was continuously leaking spinal fluid, and he died on the second day of life. The other who was identified to have Edward syndrome had severe birth asphyxia, hypoglycaemia, staphylococcal meningitis and convulsed repeatedly from birth up to 10 days when it succumbed while on phenobarbitone 5mg/kg/day in 2 divided doses following a loading dose of 20mg/kg given intravenously and diazepam 0.3mg/kg/dose given intravenously for break-through seizures.

Table 2: Age of onset of seizures related to primary diagnoses

Age of onset (days)	Diagnoses (No. of patients)					
	Asphyxia	Infection	Hypogly.	Cong Abn	Unknown	Total
< 1	29	0	3	2	0	34
1-3	6	2	0	0	2	10
4-6	0	6	1	0	0	7
7 and above	1	8	0	0	0	9
Total	36	16	4	2	2	60

A summation of the causative factors in each of the 60 infants shows that there were 37 cases of birth asphyxia, 28 of infection, 21 of hypoglycaemia and 2 of congenital malformation of the central nervous system. Three infants had severe hyperbilirubinaemia — 2 in association with hypoglycaemia, 1 with sepsis, the three had exchange blood transfusions. The infact with sepsis had exhibited classical features of kernicterus in between seizure episodes before the exchange.

Forty-eight infants had their serum electrolytes levels estimated and all had sodium values over 120 and below 150mmol/L (range 122-147mmol/L). The lowest serum calcium level recorded was 2mmol/L in two infants. There were no detectable cases of skull bone birth injuries, neurocutaneous syndromes and maternal drug withdrawal.

Pattern of seizures

A majority of the infants (34 of 60 or 56.7%) presented with seizures within the first 24 hours of life (Table 2). Considering causes of diagnosis, the 2 infants with congenital anomalies, 3 or 4 with isolated hypoglycaemia, and 29 (80.6%) of 36 with both asphyxia, convulsed within 6 hours of birth. Seizure due to infection manifested from the 5th day of life. Curiously, there was a male with uncomplicated birth asphyxia who convulsed only on the eleventh day of life.

Seizures were observed to be mixed (focal and generalised) in 38 (63.3%) infants, consistently focal in 19 (31.7%) while in 3 (5%) the pattern could not be classified. Of the 38 cases with mixed seizures 25 were of multiple and 13 of single aetiology while the 19 cases with pure focal seizure were made up of 4 with multiple, and 15 with single factors.

Table 3: Mortality related to cummulative diagnoses made in 60 newborns

Diagnoses (No. of Cases)	Mortality (No.)	Mortality rate (%)
Asphyxia (37)	15	40.5
Infection (28)	14	50
Hypoglycaemia (21)	9	42.9
*Cong. Abn. (2)	2	100

*Congenital abnormality

Outcome

The immediate outcome was analysed in relation to causative factors, onset of seizures and gestational age of the infants. Six of the infants had left the hospital against medical advice and therefore could not be fully evaluated. Of the remaining 54 patients, 27 (50%) died. Of the perinatal factors associated with the seizures, infants with sepsis had the highest fatality (50%) followed by hypoglycaemia (42.9%) with asphyxia coming third (40.5%) (Table 3). The mortality rate was lowest (36.7%) in infants whose seizures were observed from the first day but highest (86%) among those whose seizures commenced between the 4th and 7th day of life (Table 3). Five (71.4%) of the 7 preterm, 21 (41.2%) of 51 term, and 1 (50%) of 2 post-mature infants were among the dead. Follow-up studies are in progress to evaluate the long-term neurological sequelae on the survivors.

Discussion

In this study we were limited to determining every seizure entirely by clinical judgement without the aid of an encephalography, thus there was a possibility of missing out infants with very subtle convulsions since 42% of infant seizures can occur without obvious clinical manifestations[4]. On the other hand there was a possibility of including artefacts by enlisting infants whose movements were non-convulsive. However, since abnormal eye movement was made a necessary diagnostic criterion, and all the high-risk infants in our Newborn Unit were observed by both medical and specially trained nurses, we believe that our number is real and approximately accurate.

The overall frequency of neonatal seizures in our centre was 4% which compares favourably with the 3% reported by Ment *et al* [1]. But Connell *et al* [2] whose study was confined to high-risk admissions observed a frequency of as high as 25% by continuous monitoring. We had no facilities for continuous monitoring and a number of the infants in our unit were admitted only for observation. This included infants of elective caesarean section, hence our incidence rate is not as high.

The present study has identified birth asphyxia, infections and hypoglycaemia, in order of decreasing frequency, as the major aetiological factors associated with neonatal seizures in our centre. Birth asphyxia has been identified as the single most common cause of neonatal seizure in several other reviews[1,3-9]. In the evaluation of all our 60 patients, this entity was involved in about 62% of the cases. This falls within the wide range of 30% to 70% observed by Omene *et al* [5], Volpe[10] and

other workers[11,12]. However, while improvement in obstetric and neonatal care has caused a steep decline in birth asphyxia in the developed countries, deliveries in the Third World countries are still fraught with the risk of severe hypoxic-ischaemic encephalopathy[7,13].

The existence of mixed aetiology in neonatal seizures is not unknown but is rare in the series from technologically advanced countries whereas in our series 48% of the infants convulsed from two or more adverse factors operating concurrently. Mixed aetiology was also the experience (13%) in the series from Benin- City[5]. More than 70% of deliveries in Nigeria take place outside medical facilities and prolonged, obstructed and infected labour is a very common consequence[14]. Unfortunately, going by the data available from out study, hospital delivery does not appear to guarantee against any of the adverse factors so identified. Most of the asphyxiated infants delivered in UCTH were products of prolonged obstructed labour. Again, it can be assumed that the dearth of facilities to maintain strict asepsis during resuscitation and incubation predisposes high-risk infants born in hospitals in the developing countries to neonatal infections. However, the observation that the frequencies of birth asphyxia, infection and hypoglycaemia of hospital-born babies are so closely comparable with those of infants born at home, is rather misleading. It is more likely that a much greater proportion of home-born infants are vulnerable to these factors but a majority of such cases would have perished without records or before reaching hospital.

Our experience concurs with that of Omene *et al* [5] that neonatal hypocalcaemia and electrolyte imbalance do not appear to be common causes of seizures in our environment. This finding is at variance with Volpe's series[6] in which hypocalcaemia-related neonatal seizures was found to be 13%. This higher incidence may be related to the ingestion of cow's milk with a high phosphate content. The majority of our infants were breast-fed.

The incomplete glial proliferation, myelination and dendritic connection in neonates may explain why epileptic electrical discharges are incomplete, thus producing fragmentary or localised activity which is the experience in most series[1-4] including that of Benin-City[5].

The unusually high prevalence of generalised seizure (63%) encountered in the present study may be related to the mixed aetiology involving a comparatively large number (48%) of our cases. These adverse factors acting simultaneously could probably excite the brain more extensively, thus producing a rather aggressive electrical discharge to manifest a generalised instead of a consistently focal pattern.

The age of onset of seizures in this series in relation to the aetiology is not different from what previous authors have observed. Hypoxic-ischaemic encephalopathy, hypoglycaemia and nervous system malformation were responsible for seizures in the first 24 hours in a majority (57%) of patients. With infections alone most patients convulsed towards the end of the first week of life.

The outcome of neonates with seizures is known to be influenced by the aetiology, age of onset, duration and the extent of brain damage, all of which are interrelated. In this study the overall mortality rate was 50% which is four times that recorded (13%) by Eriksson and Zetterstrom[3]. The death rate was relatively higher (86%) in infants whose seizures commenced between the 4th and 6th day of life which coincides with when infection, as a related course, was most rampant. Infection therefore appears to be an unfavourable factor as 71% of the preterm involved perished. Prognosis for neonates is steadily improving in tune with better obstetrical management and intensive neonatal care[15] in well equipped centres. The lack of essential facilities for managing both the term and preterm infants in our care made it difficult to improve the chances of the potentially salvageable neonates in the series. However, without facilities for brain scan and with a very low autopsy rate, the role of intracranial haemorrhage in causing death among this category of infants is most probably being underscored.

It is likely that more revelations could have been made if all the infants were subjected to full investigation. Without facilities for extensive biochemical screening, imaging techniques and viral studies, it has been impossible to determine the role of some disease conditions which have not featured in our series. For example, we were unable to exclude a wide array of metabolic aberrations including in-born errors of metabolism, TORCH syndrome, or satisfactorily rule out cerebral dysgenesis and peri/intraventricular haemorrhages amongst others factors.

In spite of all these limitations, the study has served as a pointer as to what constitute the aetiology and the general pattern of neonatal seizures in our

environment. It should alert those who are involved in obstetric and neonatal services of what action to take to prevent or reduce the incidence of this potentially damaging condition in Nigerian newborns.

More diagnostic and therapeutic facilities should be provided to enhance accurate identification and prevention and possible treatment of the causative factors. More health educational efforts need be directed at expectant mothers who should be encouraged to use the available health establishments for ante-natal care and safe delivery. High-risk pregnancies should be monitored at tertiary level of care and concerted effort made to prevent birth asphyxia, prematurity and limit infection, all to save the infants and their young brains.

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