Neonatal convulsions—a 10 year review

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SUMMARY The incidence and aetiologies of neonatal convulsions within a hospital population were reviewed over 10 years (1971–80 inclusive). Three periods, 1971–4 (12 904 live births), 1975–7 (13 304 live births), and 1978–80 (14 849 live births) during this decade are compared. The overall incidence of neonatal convulsions rose from 2·6/1000 and then to 8·6/1000 live births. Most convulsions were associated with cerebral hypoxia and ‘fifth day fits’. Increasingly thorough investigations reduced the number of infants in whom no cause was identified to 11%. Although there was an appreciable overall reduction in mortality associated with convulsions, mortality among babies whose fits were caused by cerebral hypoxia remained over 50%.

More intensive care and observation of the newborn has been accompanied by an appreciable increase in the incidence of convulsions within the first weeks of life. There has been growing awareness that although the prognosis for these infants varies widely, it is closely associated with the underlying cause. An appreciation of changing patterns may be a guide to preventive measures, and a more accurate diagnosis enables a more confident prognosis to be given.

Methods

The diagnosis of a definite neonatal convulsion has always been difficult. All infants suspected of having fits both in the postnatal and special care nurseries of this hospital were assessed by a consultant paediatrician. Infants were included in this series only if their seizures met the criteria outlined by Volpe.¹ Credence was given to well documented reports of nursing or medical staff, whereas vague, isolated or unsubstantiated episodes were excluded. The infants were coded for medical records and from 1978 a special register was kept. The case histories of all infants recorded as having convulsions over the 10 year period were reviewed by the author.

For the period 1971–4 the diagnosis of cerebral hypoxia was made on the clinical picture alone. For the subsequent periods the diagnosis had to be supported by evidence of cerebral oedema or haemorrhage, or both, on either computed tomography (CT) or ultrasonography. Fifth day fits have been accepted as a specific clinical group.² In this series they were defined as normal term infants of appropriate size for gestational age who

developed short lived and otherwise unexplained convulsions towards the end of the first week of life.

Throughout the period of the study the infants underwent increasingly thorough laboratory investigations. By the final three year period investigations included: full blood examination; blood sugar; serum sodium, calcium, phosphate, and magnesium; acid base estimations; serum proteins; serum IgM; metabolic screen of blood and urine; microscopic examination and bacterial culture of cerebrospinal fluid (CSF); and skull radiograph. A full antenatal and perinatal drug history was recorded, together with a postnatal drug and feeding history of both mother and baby. Viral culture of CSF, blood, urine, and faeces was performed where there was a clinical suggestion of viral infection. Ultrasonography and CT were used to confirm the diagnosis of cerebral oedema, haemorrhage or structural abnormality, or where another diagnosis could not confidently be made. If clinically indicated further elucidation of metabolic abnormalities was made. Several infants had a trial of pyridoxine, without success. CSF zinc values were estimated on a selected number of infants.³

When babies fitted from more than one cause only the most important was listed. For example, three babies who had transient convulsions caused by hyponatraemia subsequently had persistent fits after cerebral hypoxia and haemorrhages. They have been listed only under this second category. The neonatal period was defined as up to 28 days after birth. Therefore, several babies who fitted after this time, although still preterm on dates, have been omitted. One infant who was readmitted fitting on day 23, after discharge from hospital on day 9, has been included. Infants who died after the neonatal

period have not been included in the mortality tables. This hospital acts as a referral centre for both obstetric and neonatal problems. To minimise referral biases, babies who were born elsewhere and transferred here for neonatal care have been excluded from the study.

Results

The periods reviewed were 1971–4 (12 904 live births), 1975–7 (13 304 live births), and 1978–80 (14 849 live births). The number of infants with neonatal convulsions was 27, 80, and 128 for these periods, showing a rise in incidence from 2 to 6/1000 and then to 8.6/1000 live births. The major aetiologies are listed in Table 1 and are shown in both absolute numbers and in percentages of the total number of babies with fits during that period. Two groups predominate—those with convulsions ascribed to cerebral hypoxia and fifth day fits. In the first period the numbers of babies with convulsions diagnosed as caused by cerebral hypoxia are probably falsely high, as the criteria for inclusion in the group were not as strict as in the subsequent periods. Some of these might have been more properly included in the 'unknown' category. The basic trend has been towards a notable and persistent increase in the number of infants with convulsions due to cerebral hypoxia, fifth day fits, meningitis, and hyponatraemia. Prematurity (born before 37 weeks of gestation) was strongly associated

Table 3 *Other causes of convulsions (1971–80)*

<i>Aetiology</i>	<i>No</i>
Cerebral haemorrhage after birth trauma	4
Cerebral haemorrhage after parental abuse	1
Cerebral haemorrhage after antenatal motor car accident	1
Zellweger's syndrome	1
Intrauterine CMV	1
Uraemia	1
Congenital hydrocephalus	1
Overdose of intralipid	1
Hypernatraemia	1

CMV = cytomegalovirus.

with cerebral hypoxia and meningitis, particularly in the later years of the study. Table 2 shows the number as a fraction (and then percentage) of preterm babies in each of the aetiological categories. Other individual causes of convulsions recorded over the period are listed in Table 3.

Selected case details. One infant in whom convulsions were associated with birth trauma developed fatal disseminated intravascular coagulation after massive cephal haematomata, and cerebral haemorrhage secondary to a fractured skull sustained during a forceps delivery.

Cerebral haemorrhage after parental abuse was noted in an infant brought back to the hospital on day 23 having been home for two weeks. Investigations showed multiple skull fractures together with bruising, and other bony injuries of varying ages.

Convulsions, ascribed to cerebral haemorrhage after an antenatal motor car accident, occurred in an infant born at 35 weeks of gestation. The mother had been in a car accident at 32 weeks of gestation. A severe antepartum haemorrhage occurred but the pregnancy continued. At delivery a large organised retroplacental clot was seen. The infant was microcephalic and CT showed massive bilateral intraventricular haemorrhages (IVH). It was suggested that the IVH followed a period of intrapartum cerebral hypoxia associated with the antepartum haemorrhage at the time of the accident.

An overdose of intralipid was recorded when an infant received a bolus dose of 25 ml of 10% intralipid over 50 minutes, rather than the prescribed 24 hours. Fortunately there were no permanent sequelae and the child is developing normally at 4 years of age.

The incidence of neonatal convulsions related to the age of the infant at the time of onset is detailed for the major categories over the last three year period in the Figure. This shows that most of the cerebral hypoxic group presented within the first two days and that hypoxia was the most important cause of fits at this time. The peak due to fifth day fits is clearly illustrated, although there are a variety of other aetiologies presenting towards the end of the first week. Relatively few babies present with convulsions between days 8 and 28.

The neonatal mortality of infants with fits, related to the aetiology of their convulsions, is shown in Table 4. The death of the infant who

Table 1 *Neonatal convulsions*

<i>Aetiology</i>	<i>1971–4</i> <i>No (%)</i>	<i>1975–7</i> <i>No (%)</i>	<i>1978–80</i> <i>No (%)</i>
Fifth day fits	8 (29)	30 (37)	48 (38)
Cerebral hypoxia	11 (41)	23 (30)	38 (30)
Unknown	2 (7)	14 (17)	14 (11)
Hypocalcaemia	1 (4)	4 (5)	8 (6)
Hyponatraemia	—	1 (1)	5 (4)
Meningitis	1 (4)	3 (4)	7 (5)
Hypoglycaemia	3 (11)	1 (1)	1 (1)
Others	1 (4)	4 (5)	7 (5)
Total	27 (100)	80 (100)	128 (100)

Table 2 *Neonatal convulsions related to prematurity. Numbers born before 37 weeks of gestation*

<i>Aetiology</i>	<i>1971–4</i> <i>No (%)</i>	<i>1975–7</i> <i>No (%)</i>	<i>1978–80</i> <i>No (%)</i>
Fifth day fits	0/8 (0)	0/30 (0)	0/48 (0)
Cerebral hypoxia	4/11 (36)	14/23 (60)	27/38 (71)
Unknown	1/2 (50)	2/14 (14)	0/14 (0)
Hypocalcaemia	1/1 (100)	2/4 (50)	2/8 (25)
Hyponatraemia	—	1/1 (100)	5/5 (100)
Meningitis	0/1 (0)	1/3 (33)	5/7 (71)
Hypoglycaemia	1/3 (33)	0/1 (0)	1/1 (100)
Others	0/1 (0)	1/4 (25)	3/7 (43)
Total	7/27 (26)	21/80 (26)	43/128 (34)

Figure Incidence of neonatal convulsions according to age at onset 1978-80.

Table 4 Neonatal mortality according to aetiology of fits

Aetiology	1971-4		1975-7		1978-80	
	No	(%)	No	(%)	No	(%)
Cerebral hypoxia	5/11	(45)	14/23	(61)	20/38	(53)
Hypoglycaemia	1/3	(33)	0/1	(0)	0/1	(0)
Meningitis	1/1	(100)	0/3	(0)	2/7	(29)
Zellweger's syndrome	1/1	(100)	—	—	—	—
Congenital hydrocephalus	—	—	—	—	1/1	(100)
Unknown	1/2	(50)	0/14	(0)	0/14	(0)
Birth trauma	—	—	0/3	(0)	1/1	(100)
Total	9		14		24	
As % of total number with fits	33.5%		17.5%		18.5%	

fitted from hypoglycaemia was caused by subsequent septicaemia. Although mortality when expressed as a percentage of the total number of infants fell from 33%–18% during this period, mortality among infants fitting from cerebral hypoxia remained around 50%.

Discussion

The development of this hospital as an obstetric referral centre together with the introduction of a neonatal intensive care unit in 1974 probably accounts for most of the trends noted. The net result was an increase in the number of preterm and sick infants, particularly in those surviving more than a few hours. Babies that might have died quickly were now surviving with ventilatory support and it was in this group that many of those fitting from cerebral hypoxia were found.

The problems that all neonatal intensive care units have with infections, together with the rising incidence in group B streptococcal infection is reflected in part by the increase in the numbers with meningitis. The growing incidence of symptomatic hyponatraemia followed an increase in the number of infants with birthweight below 1000 gm and

Table 5 Comparative series

Year	Source	Incidence per 1000 live births	Aetiology unknown (%)	Mortality (%)
1959	Leeds	—	47	42
1969	Gothenburg	3.7	31	13.5
1970	Boston	—	27	—
1972	Edinburgh	14	56	10
1979	Stockholm	1.5	29	13
1974	Melbourne	2.0	7	33.5
1977	Melbourne	6.0	17	17.5
1980	Melbourne	8.6	11	18.5

greater dependence upon parenteral nutrition. This problem was not fully appreciated until the 1978-80 figures were reviewed. Close biochemical monitoring and subsequent changes in regimens have virtually eliminated this problem. The rise in the number of fifth day fits has not been explained and is currently being investigated.

Comparisons with other published series⁴⁻⁹ are difficult because of differing populations, diagnostic criteria, and advances in laboratory investigations. Table 5 compares some of these series with this current review. Each series covered a slightly different time span varying from the first 8 to the first 28 days of life. As most fits occurred within the first week, this variation is of little importance. Only one series⁶ clearly related the incidence of occurrence to the time of onset of the fits. This showed similar curves to those in our Figure, with a peak caused by cerebral hypoxia in the first two days and a second peak, which was labelled 'metabolic', towards the end of the first week.

A major trend has been the growing number of infants in whom an aetiological diagnosis could be made. This has been shown to be of therapeutic and prognostic benefit.

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