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Sequelae of neonatal convulsions

Study of 112 infants

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Keen, J. H., and Lee, D. (1973). *Archives of Disease in Childhood*, **48**, 542. **Sequelae of neonatal convulsions: study of 112 infants.** Of 112 infants who had a convulsion during the first 28 days of life, 105 survived the neonatal period. During follow-up of 83 (80%), 14 were detected as having motor handicap, a further convulsion, or an intelligence assessment below 85. In the 45 infants whose convulsions were associated only with hypocalcaemia, 2 had an intelligence assessment below 85 and 1 had a further convulsion, but none had evidence of motor handicap during the follow-up period.

Birth trauma continued to be the commonest recognized cause of neonatal convulsions until the second half of the last decade when a number of papers were published in which the transient metabolic disturbances, especially hypocalcaemia and hypoglycaemia, were implicated with increasing frequency (Tibbles and Prichard, 1965; Paine, 1968; McInerny and Schubert, 1969).

The prognosis in convulsions with onset later in the neonatal period has, in published series, been less sinister than in those occurring in the first 3 days, and in particular those due to metabolic causes have been relatively benign (Brown, Cockburn, and Forfar, 1972). It is against this background that details are presented of the sequelae of neonatal convulsions in a series of 112 infants seen in the period January 1967 to March 1970.

Material and methods

The 112 infants included in this study presented with convulsions in Crumpsall Hospital, Manchester.* Infants were included when they were observed to have had generalized clonic movements with or without a tonic phase, or when there were clonic movements of a single limb or of facial muscles. The aim was to include all infants delivered in the study period who had fits within the first 28 days of life; however, in only one case did the first convulsion occur after initial discharge from hospital, and it is therefore possible that the figures are an underestimate.

The obstetric unit of the hospital handled 9165 live births in the 39 months January 1967 to March 1970; the 112 infants who presented with convulsions thus represented 12·2 per 1000 live births.

In all the infants who convulsed, details were obtained in retrospect of the pregnancy and mode of delivery, as well as of the child's condition at birth, and behaviour and feeding regimens. Term infants of normal birthweight were fed routinely at 4 hours, the first feed being with 5% dextrose and subsequent feeds of Regal evaporated milk 1 part to water 2 parts or of Ostermilk No.1 71 g powder to 540 ml water. Premature or small-for-dates infants were nursed in the Special Care Baby Unit and fed at the same age on Regal evaporated milk.

The following investigations were carried out as soon as possible after the first recorded fit, which in almost all cases was within 4 hours: blood glucose, serum calcium, total inorganic phosphate, plasma protein, blood *p*H, blood and urine amino acid chromatography.

Neither subdural tap nor CSF examination was performed routinely but only where clinically indicated, as was blood culture. EEG was carried out routinely, usually within 72 hours of the onset of convulsions.

Serum calcium was estimated by EDTA chelation with murexide indicator using an EEL photoelectric titrator with a filter peak of 5750–5800 Å (Wilkinson, 1957). Duplicate 0·1 ml samples of serum were used. Control calcium estimations were carried out on 15 infants matched with hypocalcaemic infants for birthweight, age in hours, type of delivery, and feeding (but not for season of delivery or amount of feed taken); a mean of 8·98 mg/100 ml was obtained with SD 0·71 and variance 0·50. In this study a serum calcium level below 7·5 mg/100 ml was accepted as hypocalcaemia (mean −2 SD). The mean calcium level in the hypocalcaemic convulsing infants thus defined was 6·4 mg/100 ml, SD 0·69, variance 0·48. Serum magnesium was estimated by titan yellow titration modified after Neill and Neely (1956).

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*The group of infants whose progress is described here differs from the group of 100 neonates with convulsions described earlier (Keen, 1969) in that the former study included 52 infants born at St. Mary's Hospital, Manchester, who are not included in the present report, and that the present study was extended at Crumpsall Hospital for a further 22 months.

Follow-up assessments were carried out in the Special Care Baby Unit of the hospital, the aim being to see each child 3-monthly during the first year, then at 18 months, and 2, 3, and 4 years. At each visit a medical and developmental history was obtained, particular attention being paid to any febrile episodes and the child's behaviour during them. Neurological examination and an assessment of developmental level was made at each visit. In infants whose initial EEG was abnormal or in whom convulsions recurred, further EEG tracings were made. When clinic testing of hearing did not produce satisfactory results, examination and audiometry were carried out in the Department of Audiology, University of Manchester. Formal developmental or intellectual assessment was carried out in the second year of life or later using the Griffiths Developmental Scale (Griffiths, 1954) or Stanford-Binet LM Scale (Terman and Merrill, 1961). In the few cases in which the child's ability extended beyond the 2-year level but did not reach the 2½-year basal level of the Binet scale, the two levels were combined using the scoring method outlined by Griffiths.

Results

Of 105 infants who survived the neonatal period, 62 (60%) were examined at the age of 2 years or older, while a further 21 (20%) were seen at the age of 12 months but not later. In all, 22 infants (21%) were lost to follow-up, 9 through moving to known addresses outside the Manchester area. 2 of these who were in residential or foster care were examined by paediatricians elsewhere and no neurological abnormality was detected; the parents of 3 other infants wrote giving what appeared normal developmental details at the age of 2 to 3 years. 6 families were lost after removal, often from demolition areas; and 7 others were unwilling to co-operate.

There was a preponderance of males in the series, 69 males to 43 females, and this excess is still apparent if the infants with uncomplicated hypocalcaemia are considered separately—25 males to 20 females. Several authors have mentioned an excess of boys with neonatal tetany; however, the male excess was greater in this series in those without hypocalcaemia (1·90 males to 1 female) than in the group with hypocalcaemia (1·25 males to 1 female). Details of the presumed cause of the neonatal convulsion are given in Table I together with the incidence in each group of three unfavourable features in follow-up: later motor handicap, a developmental (DQ) or intelligence (IQ) assessment below 85, or a return of fits after the neonatal period. 8 of the 14 infants with intracranial haemorrhage or severe intrapartum anoxia died, 7 in the neonatal period and 1, who had a spastic hemiplegia, of pneumonia at the age of 2 years 3 months. The largest group had hypocalcaemia as the only detected cause of the convulsion and among this group there were no deaths.

Table II shows the age at onset of convulsion. The whole group shows two peaks, one in the first 48 hours and a second on the 5th and 6th days (120–143 hours). If the infants with uncomplicated hypocalcaemia are shown separately, a single peak of onset in the second half of the first week is apparent and it is seen that infants without hypocalcaemia do not show a peak of onset after the first 48 hours.

Return of convulsions (Table III). 4 children had further convulsions after the neonatal period. In 1 child who was hypoglycaemic during the

TABLE I

Aetiology and outcome in 112 infants with neonatal convulsions

Aetiology of neonatal convulsion	No.	Later motor handicap	DQ/IQ below 85	Return of convulsion
Cerebral haemorrhage or birth anoxia	14	2	–	–
Congenital cerebral anomaly	1	–	–	–
Hypoglycaemia alone (blood glucose <20 mg/100 ml)	3	2	2	1
Hypocalcaemia alone (serum calcium <7·5 mg/100 ml)	45	–	2	1
Hypoglycaemia with hypocalcaemia	2	–	–	–
Meningitis	1	–	–	–
Other discovered aetiology	7	–	–	–
No cause found	39	3	3	2
Total	112	7	7	4

DQ, developmental quotient.

TABLE II

Age at first convulsion

Age (hr)	Hypocalcaemia (uncomplicated)	Other	Total
0–23	nil	22	22
24–47	nil	16	16
48–71	1	6	7
72–95	2	5	7
96–119	8	5	13
120–143	17	4	21
144–167	8	2	10
168–191	6	5	11
192+	3	2	5
Total	45	67	112

TABLE III

Infants with return of convulsions after neonatal period

Neonatal diagnosis	Description of later fit	Associated handicap
Hypoglycaemia	Repeated *grand mal* from age of 6 mth	Spastic hemiplegia, DQ 49
No cause found	Myoclonus, onset at 5 mth	DQ 76 at 22 mth
No cause found	Single 'febrile' fit at 10 mth; EEG normal	None
Hypocalcaemia	Single 'febrile' fit at 2 yr 7 mth; EEG normal	None

DQ, developmental quotient.

neonatal convulsion the fits recurred at the age of 6 months, by which age he was severely developmentally retarded; the later fits were not associated with further hypoglycaemia. 1 child, in whom no cause was found for the neonatal fit, developed persistent myoclonic fits at the age of 5 months, and at the age of 20 months he had a DQ (Griffiths) of 76. Each of the remaining 2 children had a single convulsion apparently associated with fever, 1 at the age of 10 months, the other at 2 years 7 months. 1 of these children was initially hypocalcaemic; in the other no cause was found for the neonatal fit; both these children had a normal EEG after the later convulsion; a tracing made in the neonatal period from 1 child was also available and was normal.

Infants with subsequent motor handicap (Table IV). 7 infants were detected as having a motor handicap which persisted, 2 being from the group of 3 infants with symptomatic hypoglycaemia, and both showed severe developmental retardation. 2 infants developed motor handicap after intrapartum anoxia, in 1 hypocalcaemia was associated at the age of 12 hours. In the remaining infants with motor abnormality, no cause for the neonatal convulsions was determined.

TABLE IV

Infants with subsequent motor handicap

Clinical findings	Neonatal diagnosis	Age at first fit
Right spastic hemiplegia	Hypoglycaemia	36 hr
Left spastic hemiplegia	Intrapartum anoxia; hypocalcaemia	12 hr
Spastic quadriplegia; myoclonus	No cause found	21 dy
Spastic diplegia	No cause found	18 hr
Spastic quadriplegia	Hypoglycaemia	14 hr
Right spastic hemiplegia	Intrapartum anoxia; abnormal EEG from age 24 hr	1 hr
Spastic diplegia	No cause found	21 hr

In 6 of these 7 children the first convulsion occurred in the first 48 hours of life, the remaining child being admitted with prolonged generalized fits at 21 days—delivery in this child was uneventful and no cause for the fit was discovered.

Developmental testing (Table V). Developmental or intelligence assessments were carried out on 76 children. Measurements made on the same children on separate occasions were available in 3 cases.

The distribution of scores followed a fairly normal curve except for a peak at the low end where three scores fell below 50.

The mean age at the time of assessment was 22 months for the whole group. Those children tested on the Griffiths scale had a mean age of 18 months and those on the LM scale of 38 months.

The mean mental development of this group of 75 infants convulsing in the newborn period was normal (mean DQ/IQ = 101·2, SD 16·3).

TABLE V

Infants with DQ or IQ below 85

Neonatal diagnosis	Age at first fit (hr)	Developmental level
Hypoglycaemia (blood glucose 10 mg/100 ml)	36	49
No cause found for convulsion	132	67
No cause found for convulsion	30	76
Hypocalcaemia (serum calcium 6·3 mg/100 ml)	125	73
No cause found for convulsion	30	84
Hypoglycaemia (blood glucose 14 mg/100 ml)	14	36 and 9
Hypocalcaemia (serum calcium 7·0 mg/100 ml)	169	83

DQ, developmental quotient.

Thirty infants who had convulsions with hypocalcaemia were tested, their mean IQ/DQ was 104 with SD 11·8; the mean age being 22·6 months: this group, therefore, appeared to have a smaller scatter than the group as a whole and to conform to the expected range of scores in the normal population.

In the whole group, 7 infants had a score of less than 85 (Table V), that is, of more than 1 SD below the mean. 2 of these were hypoglycaemic during their convulsion and both developed spastic cerebral palsy. In 3 infants no cause was found to explain the neonatal fit; of these, 2 began to convulse at 30 hours and the other at 132 hours. The 2 remaining infants had neonatal tetany presenting with a generalized convulsion at the age of 125 and 169 hours, respectively; in neither were there unusual clinical features nor a prolonged convulsive episode, and no neurological abnormality was detected during the follow-up period.

EEG. An EEG record was obtained from 79 infants in the neonatal period usually within 72 hours of the onset of convulsions: 54 of these initial records were normal. Further tracings were obtained in 20 of the 25 infants with an abnormal record initially: in 10 of these the records became normal before the age of 6 months. The 45 infants who convulsed with uncomplicated hypocalcaemia are included in these figures; 32 of this group had a neonatal EEG and in 21 the recording was normal; of the 11 with an initial abnormal record, 8 became normal before the age of 6 months. In the 3 infants in the hypocalcaemic group with a persisting abnormal record, progress during follow-up has been normal. 2 have been seen at the age of 3 years or older, while 1 has been lost to follow-up after being seen at 18 months. None of these 3 children has suffered a return of convulsions, and the 2 who have had psychometric assessments recorded scores of 118 and 101.

Discussion

During the past 15 years a decreasing proportion of neonatal convulsions has been attributable to anoxia or cerebral birth injury and an increasing proportion to metabolic conditions, the most common being hypocalcaemia. The present study shows an incidence of 12·2 infants with neonatal convulsions per 1000 live births in a unit for abnormal obstetrics. Authors describing work carried out before 1960 found a lower incidence: Burke (1954) reported 5·3/1000 births and Craig (1960) 8/1000. However, a recent survey of neonatal convulsions from Edinburgh (Brown *et al.*, 1972) described a higher incidence, 14·6/1000 births, and these authors found a high incidence of fits of metabolic origin (57%). The present study is similar in this respect.

It is of interest to compare the incidence and outcome of fits from birth injury or anoxia in the present series with the findings of Burke (1954). In the earlier study, 35 of the 46 infants convulsed as a result of birth injury or anoxia, an incidence from this cause of 4/1000 births; in our study 14 infants convulsed from these causes, 1·5/1000 births. However, despite the interval of 20 years, the mortality from this cause is identical at 43%, and in each series 25% of survivors suffered either major motor handicap or severe mental retardation.

The significance of hypocalcaemia during a neonatal convulsion is difficult to assess and must be viewed against the rapidly falling serum calcium levels of the normal neonate and the differing biochemical techniques which confuse the comparison of studies from varying centres. Gittleman *et al.* (1956) showed that after premature or traumatic delivery, serum calcium levels fall in the first 48 hours below the levels for infants born spontaneously at term. Our experience is in accord with others in finding that infants convulsing with hypocalcaemia in the first 72 hours of life commonly have a separate cause for the fit, the most frequent findings being perinatal anoxia or hypoglycaemia; and in this situation at least, it seems reasonable to regard the hypocalcaemia as coincidental. Infants with hypocalcaemia but without other detected cause for the convulsion comprised the largest group in this study, and with one exception, the onset of convulsions was after 72 hours of age.

In the follow-up of survivors the following may be selected as unfavourable features: motor handicap, DQ below 1 SD from the mean, or a return of convulsions; these sequelae occurred predominantly in infants whose convulsions started within the first 72 hours of life and were infrequent in uncomplicated hypocalcaemia. The prognosis for life and developmental normality after a neonatal convulsion depends to a large extent on the aetiology, and the low incidence of late complications in this series reflects this.

We express our gratitude to Sister Thornley and her staff in the Special Care Baby Unit of Crumpsall Hospital for their help with the study; to Miss P. M. Lockwood who, with her staff, carried out the EEG; and to Professor J. A. Davis for much valued advice.

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