Status Epilepticus in Children

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ABSTRACT: We have prospectively reviewed the data on 52 children who presented with status epilepticus. Thirty-four (65%) of the 52 had not had seizures before. Children who were previously abnormal were more likely to present with partial status epilepticus or to have seizures > 60 minutes than those who were previously normal. The median age (24 months) of those who presented with status epilepticus was the same as that of children with seizures of shorter duration. The causes were equally distributed among the idiopathic, acute encephalopathic and chronic encephalopathic groups. Three children died and 13 (28%) were left with neurological sequelae. The outcome was favorable for those in the idiopathic category.

RÉSUMÉ: L'état de mal épileptique chez les enfants Nous avons revu de façon prospective les données recueillies sur 52 enfants qui consultaient pour un état de mal épileptique. Trente-quatre (65%) des 52 enfants n'avaient jamais fait de convulsions dans le passé. Les enfants qui n'étaient pas normaux antérieurement étaient plus susceptibles de présenter un état de mal épileptique partiel ou d'avoir des convulsions dont la durée excède 60 minutes que ceux qui étaient normaux antérieurement. L'âge médian (24 mois) de ceux qui présentaient un état de mal épileptique était le même que celui des enfants qui présentaient des convulsions de plus courte durée. L'étiologie se répartissait également comme suit: idiopathique, encéphalopathie aiguë et encéphalopathie chronique. Trois enfants sont décédés et 13 (28%) ont présenté des séquelles neurologiques. L'issue a été favorable chez les enfants dont les convulsions étaient d'origine idiopathique.

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Status epilepticus (SE) is a common problem in pediatric practice. There have been few population studies, and none from North America, concerned with the epidemiology and prognostic features of SE in children, since that of Aicardi and Chevrie in 1970.[1-3] Viani[4] et al from Italy recently reviewed 68 children but their study was restricted to those with febrile SE.

Recent advances in diagnosis and treatment may have changed the course of epilepsies in children. We, therefore, present our data on 52 children with SE.

Materials and Methods

Patients and Population

The Children's Hospital of Winnipeg is the only tertiary care pediatric facility between Toronto and Saskatoon. It drains a population of over 1.5 million. The majority, if not all of the children with SE referred to the Hospital are seen by the Pediatric Neurology Service. We prospectively reviewed children aged one month to eighteen years presenting with seizures to the Emergency Department of the Children's Hospital between May 1985 and December 1986.

SE was defined as a seizure or series of seizures lasting at least 30 minutes without consciousness being regained.[5,6] Seizures were classified according to the proposal of the International League Against Epilepsy (1981).[7]

Statistical Methods[8]

Stepwise Logistic Regression was used to identify clinical variables predictive of an abnormal outcome and to obtain a classification function of outcome. The level of significance was set at $p = 0.05$. The clinical variables included were (i) age, (ii) sex, (iii) seizure type, (iv) duration of SE, (v) etiology, (vi) presence or absence of fever, (vii) normal or abnormal development prior to the onset of SE, (viii) previous history of seizures, and (ix) the presence or absence of a family history of seizures.

An abnormal outcome was defined as one in which there was (i) the occurrence of neurodevelopmental dysfunction or (ii) a deterioration of the state in a child with pre-existing abnormality, following the bout of SE. Patients whose neurological state was abnormal prior to the SE but who showed no deterioration were included in those with a normal (unchanged) outcome.

Results

Age and Sex

Four hundred and twelve children presented with seizures. Fifty-two (12.6%) of them had SE. The median age for both groups (those with and those without SE) was two years.

The female to male ratio was 1.7:1.0 for the SE group and 0.8:1.0 for the remaining 360 children. Forty-six percent of the

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Table 1: Seizure Type

Type of Seizure	Number of Patients (%)
GENERALIZED	
Tonic-Clonic	26 (50%)
Tonic	2 (4%)
Myoclonic	1 (2%)
Absence	1 (2%)
TOTAL	30 (58%)
PARTIAL	
Somatomotor	9 (17%)
Partial complex	3 (6%)
Secondary generalization	10 (19%)
TOTAL	22 (42%)

Table 2: Causes of Status Epilepticus

	Number of Patients	Total	(%)
Idiopathic			
Febrile	11		
Non-Febrile	6	17	33%
Acute Encephalopathic			
Infectious			
Encephalitis	5[a]		
Other	2[b]		
Metabolic			
Hypernatremia	4		
Hyponatremia	1	16	31%
Hypoglycemia	1		
Vascular (cerebral infarct)	1		
Toxic Ingestion	2[c]		
Chronic Encephalopathic			
Post-infectious	3		
Hypoxic-Ischemic	7[d]		
CNS Malformation	5	19	36%
Tumor	2		
Degenerative	2		
TOTAL		52	100%

a All Viral infections
b One with shigella, one with undetermined cause
c One theophylline toxicity
One Kwellada ingestion
d Five perinatal events
Two postnatal events

52 children with SE presented before eighteen months of age and 61.5% prior to their third birthday.

Seizure Data

SE was the first ictal manifestation in 34 (65.4%) of the 52. Ten (19%) patients had previously experienced an episode of SE.

Table 1 shows the distribution of seizure types in those with SE. Thirty (58%) had generalized seizures and twenty-two (42%) had partial seizures.

Of the 30 with generalized seizures, the etiology was idiopathic in twelve (40%) and encephalopathic (twelve acute encephalopathic and six chronic encephalopathic) in 18 (60%). Thirteen (43%) of the thirty patients had status lasting greater than 60 minutes, and six (46%) of the thirteen patients were previously abnormal.

The etiology was idiopathic in five (23%) of the 22 with partial seizure SE and encephalopathic (seven acute encephalopathic and ten chronic encephalopathic) in 17 (77%). Eleven (50%) of the twenty-two had status lasting longer than 60 minutes, and seven (64%) of the eleven were previously abnormal. Ten of the 22 (45%) with partial SE had neurodevelopmental dysfunction prior to the episode as did 9 of the 30 (30%) who presented with generalized SE.

Etiology

Causative factors were grouped into idiopathic (no cause found) and "encephalopathic". The latter group was further subdivided into acute and chronic encephalopathic. Those patients with prolonged febrile seizures of undetermined etiology, were included in the idiopathic group.

Cases were divided evenly between the idiopathic, acute encephalopathic and chronic encephalopathic groups. Details are outlined in Table 2.

Three of the six patients with metabolic dysfunction had cerebral infarction, Henoch-Schonlein Purpura and meningitis respectively. In these children, the metabolic cause was felt to be primarily responsible for the S.E.

The type of CNS malformations in our cases included congenital microcephaly (N = 2) and hemimegalencephaly, lissencephaly and Aicardi's syndrome (one each). Both children with neurodegenerative diseases had mitochondrial encephalomyelopathies.

Outcome

Forty-nine of the 52 children were followed for periods of 1 to 18 months. Three died; one child with hemimegalencephaly died of cardiorespiratory arrest following a two week episode of intractable SE. The second had a progressive neurological disorder and also died in cardiorespiratory arrest; she was found to have a mitochondrial encephalomyelopathy at necropsy. The third patient had idiopathic febrile SE and was found dead in bed at home; the brain was normal at necropsy.

Thirteen (28%) of the 46 survivors had neurodevelopmental sequelae. Thirty of the forty-six were previously normal and nine (30%) of them developed sequelae. Four (25%) of the sixteen patients who were previously abnormal experienced a deterioration in their neurodevelopmental status. Only one child with idiopathic SE had neurodevelopmental sequelae.

Sequelae in the nine previously normal patients included developmental delay in all, hemiplegia in 3 and epilepsy in 4.

Neurological sequelae occurred in 60% of those patients presenting before 6 months of age, 30% of those between 6 and 36 months and 30% of those older than 3 years of age.

Statistical relationship of variables to outcome

Nine clinical variables (see methods) were included in the stepwise logistic regression procedure. Of these, only 3 entered the classification function of outcome ($p < 0.03$). The 3 variables were SE duration, past history of seizures and etiology.

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Table 3: Status Epilepticus in Children

Author	Seizure Criteria	# of Patients	Mortality	Morbidity
Aicardi and Chevrie (1970)	>60 Minutes	239	11%	57%
Hayakawa et al (1979)	>60 Minutes	67	3%	—
Fujiwara et al (1979)	>60 Minutes	79	—	50%
Kumanomidose et al (1979)	Not Given	55	7%	—
Maytal et al* (1986)	>30 Minutes	102	2%	28%
Dunn D* (1987)	>30 Minutes	114	7%	16%
Present Study (1987)	>30 Minutes	52	6%	28%

*Abstract only

The remaining 6 were "rejected" because they did not contribute discriminatory information. The equation obtained was:

Pr (abnormal outcome) = 1/{1 + exp – (–2.43 + 1.716 acute encephalopathy + 2.22 chronic encephalopathy –2.147 past history of seizures + 1.709 seizure length > 60 minutes)}.

Treatment

Diazepam or lorazepam was used at the outset and were followed by phenobarbitone, phenytoin and valproic acid in various combinations. Pentobarbital infusion was also used in one child with focal SE that did not respond to conventional treatment. All drugs except valproic acid were given by the intravenous route and drug levels monitored.

Discussion

SE is a common problem among children with seizures. Almost 13% of children presenting to us with seizures had SE, an incidence similar to that of Aicardi and Chevrie (1970)[1] and Fujiwara et al (1979).[2]

The causes of SE were about evenly divided between idiopathic and (encephalopathic) symptomatic groups in other reports.[1,2,8,9] Our own experience differs in that only 1/3 of our cases were idiopathic.

Infectious and metabolic etiologies were the most common causes in the acute encephalopathic group, an experience similar to that of Aicardi and Chevrie. Hypoxic ischemic encephalopathy, CNS malformations, post-infectious encephalopathy and degenerative CNS disease were the most common etiologies in the chronic encephalopathic group.

SE was more common in those under 2 years of age but there was no difference in the median age of patients presenting with SE as compared to those with seizures of shorter duration.

Patients who were previously abnormal were more likely to present with partial seizures or to have seizures lasting 60 or more minutes, than those who were previously normal.

We used the stepwise logistic regression procedure, a multivariate method, rather than a univariate method, to minimize the effect caused by the inter-dependence of clinical variables. Three of the 9 clinical variables (see methods) entered the classification function equation. The probability of an abnormal outcome was increased with, (i) seizure length > 60 minutes (versus < 60 minutes), the odds ratio being 5.5 and (ii) encephalopathic (versus idiopathic) etiologies, with odds ratios of 5.6 and 9.2 for the acute and chronic encephalopathic groups respectively. On the other hand, the risk of an abnormal outcome was reduced with a previous history of seizures, the odds ratio being 0.12. Previous (normal or abnormal) development was rejected from the final predictive equation. Thus, the effect of seizure length was independent of prior neurodevelopmental status. The equation obtained and estimations presented are valid only for the present set of data and may not be applicable to other population sets. A larger data base from several centres may yield a predictive equation that could be applied with greater reliability.

The mortality in children with SE has varied between 2% and 11% (Table 3). The mortality rate in our group was 6%. Twenty-eight percent of 46 survivors who have been followed developed neurodevelopmental dysfunction after the episode of SE but only one with idiopathic status had sequelae. Differences between (i) patient population, (ii) definition of SE, (iii) case groupings and (iv) length of follow-up likely contribute to the slight variations in our data, from those of others.[1,2,9]

Our data and that in recent abstracts [9,10] suggest that the morbidity related to SE may be less than that previously reported, and that patients with idiopathic SE generally have a good outcome. But, despite advances in diagnostic methods and treatment, there has not been a substantial change in the clinical information on SE in children since Aicardi and Chevrie published their paper in 1970.

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