

Occasional Survey

Epidemiology and Prognosis of Childhood Epilepsy in Hong Kong: Literature Review

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Abstract

The present study summarises relevant articles on the epidemiology of childhood epilepsy in the local scene published over the past twenty years. We performed a search of the Medline and a manual search of Hong Kong Medical Journal, Hong Kong Practitioner, Hong Kong Journal of Paediatrics, Chinese Medical Journal using the key words 'epilepsy', 'children' and 'Hong Kong'. Overall, the prevalence of childhood epilepsy in Hong Kong can be estimated and the natural history of seizures in our patients can be better determined. Disorders using International League Against Epilepsy classifications, such as Lennox-Gastaut syndrome, benign childhood epilepsy with centrotemporal spikes, childhood absence epilepsy and juvenile myoclonic epilepsy are increasingly being recognised in Hong Kong. Aetiologies of epilepsies could be delineated in a great proportion of patients. Early predictors of medical intractability were identified. CNS infection and perinatal hypoxic-ischaemic encephalopathy were common causes of remote symptomatic epilepsy and the resulting seizures were often medically intractable.

Key words Children; Epilepsy; Hong Kong

Introduction

Epilepsy is one of the most common neurologic disorders in childhood. It is defined as two or more unprovoked seizures more than 24 hours apart in a child over 1 month of age.¹ In the past, epilepsy was considered to be a progressive, non-remitting disease. Gowers, who studied epileptic patients seen in tertiary referral centers, once mentioned: "The tendency of the disease is towards self-perpetuation; each attack facilitates the occurrence of another

by increasing the instability of the nerve elements.... The cases in which the best results are obtained... are precisely, those who are never heard again."² In his brief comment, Gowers identified the important role played by epidemiology in the study of epilepsy. Guidelines had been developed by the International League Against Epilepsy for the classification of seizures and epilepsy syndromes, as well as for epidemiologic research in epilepsy.^{1,3,4} Over the past two decades, studies have expanded our understanding of the epidemiology and prognosis of seizures, which is at times contrary to long-held beliefs. This article reviews data on the epidemiology and prognosis of childhood epilepsy in the local scene.

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Methods

We performed a search of the electronic database Medline using the key words "epilepsy", "children" and "Hong Kong". We also conducted a manual search of Hong Kong Medical Journal, Hong Kong Practitioner, Hong Kong Journal of Paediatrics, Chinese Medical Journal between 1986 and 2006. All original articles were reviewed.

Inclusion and Exclusion Criteria

Children with only febrile seizures, acute symptomatic seizures, isolated seizures and neonatal seizures were excluded. Adult-based studies of epilepsy were also excluded if the major proportion of patients studied were adults.

Results

The number of relevant articles on epidemiology and prognosis of childhood epilepsy in Hong Kong was twelve.⁵⁻¹⁶ Specific aspects of these studies were reviewed and presented as follows:

Frequency Measure

The prevalence rate of active epilepsy for children under 15 years of age was reported by Kwong et al to be 1.52/1000 on July 1, 1997. Prevalence rates increased with age and were higher in boys. Age of seizure onset was observed to be highest in the first year of life and declines thereafter.⁵ According to another study conducted in a teaching hospital, the period prevalence rate of epilepsy in 1997 was estimated to be 4.5 per 1000 children less than 19 years of age.⁶ A figure of 1.54 per 1000 had been reported in a territory-wide survey among adult epileptic patients.¹⁷ Direct comparison of data derived by the above studies was difficult because of different sources of patient referral and methodologies.

Aetiology

Epilepsy is a heterogeneous group of disorder from both clinical and aetiological points of view. Idiopathic epilepsy accounted for 40% of childhood epilepsies.⁵ Discrepancy was observed in the proportion of cryptogenic and symptomatic epilepsies. The frequency of cryptogenic epilepsy was reported to be 0.9% in a cohort of epileptic children according to a study conducted in a teaching hospital, a much lower figure when compared to 16.8% in another survey in a regional hospital.^{5,6} Sources of patient referral could partly explain such a difference. According to important overseas studies published during recent years. The percentage of cryptogenic epilepsies ranges between 20.7-44.4%. Aetiologies in symptomatic epilepsy could be traced in 30-61% of cases, but these figures were not fully comparable.¹⁸⁻²⁰ It is possible that the yield of aetiologies could have been much higher if neuroimaging, especially MRI brain, had been performed in all children. The causes were prenatal in 27%, perinatal 28% and postnatal 45%.⁵

The three most common causes were CNS infections, CNS malformations and perinatal hypoxic-ischaemic encephalopathy.^{5,6}

Seizure Types and Epileptic Syndromes

In the past, it was generally believed that childhood epilepsies were mostly generalised, but more recent studies published overseas have shown that this is not the case. Newer data indicate that the majority of seizures and epileptic syndromes are partial.^{18,20,21} Furthermore, more benign epileptic syndromes, such as benign childhood epilepsy with centrotemporal spikes and childhood absence epilepsy, account for a substantial proportion of childhood epilepsies in community-based samples.^{20,22} Disorders using International League Against Epilepsy classifications, such as Lennox-Gastaut syndrome, benign childhood epilepsy with centrotemporal spikes, childhood absence epilepsy and juvenile myoclonic epilepsy are increasingly being recognised in Hong Kong.⁷ Generalised tonic-clonic seizures and partial seizures secondarily generalised were the most frequent seizure subtypes. The proportion of partial epilepsies and generalised epilepsies was almost equal as reported in one study.⁵ Benign childhood epilepsy with centrotemporal spikes was observed in 7% and childhood absence epilepsy in 6% of epileptic children aged less than 15 years in one study.⁵

Epilepsy and Neurodevelopmental Impairments

The association between epilepsy and cerebral palsy and/or mental retardation is well recognised. According to overseas publications, about 15-30% of childhood-onset epilepsy is associated with these conditions.^{19,23} Conversely, epilepsy is a common co-morbid condition in children with developmental disabilities. Additional neuroimpairments were observed in 36% of our epileptic children in one study, in which mental impairments were more common than motor disability.⁶ Epilepsy occurred in 37% of children with cerebral palsy.⁸ The frequency was highest in spastic tetraplegia. Factors associated with development of epilepsy in children with cerebral palsy were mental subnormality.⁸ When compared to neurologically normal children with epilepsy, children with cerebral palsy had a higher incidence of epilepsy with onset in the first year of life, status epilepticus, polytherapy, persistent seizures and multiple seizure types.⁸ Wong found that 7.6% of children with autistic spectrum disorders have recurrent seizures.⁹ Kwong & Wong had reported that only 2 (1.6%) of the 124 children with Down's syndrome had epilepsy, a percentage much lower than other case series reported.¹⁰ Children with

infantile spasms were associated with a poor neurodevelopmental outcome, multiple disabilities were observed in 15%, cerebral palsy in 21% and mental retardation in 90% of patients.¹¹ Epilepsy was the comorbidity in 48% of patients with tuberous sclerosis.¹² Factors associated with development of infantile spasms in tuberous sclerosis were tubers in parietal and occipital regions.¹²

Status Epilepticus

A retrospective review of 37 children admitted to a teaching hospital with the diagnosis of status epilepticus from 1986 to 1993 showed that the mortality was 11%. Mortality was attributed to the underlying causes. Neurological sequelae was observed in 27% of survivors and recurrent status epilepticus developed in 12% of patients. Acute CNS insults accounted for 60% of status epilepticus. This is followed by idiopathic aetiology in 11%, previous CNS insults 13% and febrile illness 5% of cases.¹³ The same author in another study of status epilepticus observed that symptomatic aetiology and refractory status epilepticus were associated with adverse outcomes. Young age at status epilepticus (<12 months) and duration of seizures more than 60 minutes tended to be more frequent among those with poorer outcome.¹⁴ Rectal diazepam given before hospital arrival was only observed in one sixth of patients.¹⁴ Prompt use of rectal diazepam by caretakers or paramedical should be encouraged may help to prevent refractory status epilepticus.

Remission

Wong reported 54% of the cohort with epilepsy had complete seizure remission.⁶ Epilepsy in children with neuroimpairments had less favorable outcome. Only 37% of children with cerebral palsy had good seizure control, i.e. seizure-free for at least 2 years.⁸ Factors associated with seizure-free status among children with cerebral palsy were normal intelligence, single seizure types, seizure responsive to monotherapy and spastic diplegia.⁸ In a cohort of children with benign childhood epilepsy with centrotemporal spikes, none of the patients experienced seizures beyond 15 years of age.⁷

Medical Intractability

Lack of remission was not synonymous as intractability. Patients not in remission include those with infrequent seizures owing to non-compliance with medications, or infrequent seizures not being treated. Medical intractability was defined as uncontrolled seizures occurring with an

average frequency of at least 1 seizure per month over an observational period of 2 years or more despite treatment with at least 3 different antiepileptic drugs, singly or in combination.^{23,24} Fourteen percent of a cohort of local epileptic children experienced medically intractable epilepsy.¹⁵ Early predictors of intractability were identified in that study were as follows: high initial seizure frequency, remote symptomatic aetiology, infantile spasms, mixed seizure types, history of status epilepticus, history of neonatal seizures and early breath-through seizures after treatment initiation. Independent predictors of intractability were abnormal neurodevelopmental status, remote symptomatic aetiology and lack of early response to treatment.¹⁵ The risk of medical intractability was highest among the symptomatic localisation group. Among children with intractable epilepsy, CNS infections accounted for 24% and 28% of cases. Neuroimaging was essential in the evaluation of intractable epilepsy. Abnormalities were detected in two-third of patients.¹⁵

Psychosocial Impacts

According to a local questionnaire survey among parents with epileptic children in a regional hospital, the main family concerns were seizures, school performance and side effects of medications.¹⁶ Half of the patients complained that their children were more restless and short-tempered. Half of them worried that epilepsy was incurable. One-fifth thought that swimming should be prohibited even if seizures were controlled and 15% were afraid that their children would die during the seizure attacks. The majority of parents requested more information about epilepsy and closer communication between teachers and physicians.¹⁶

Discussion

Research pursuits within the epidemiology of epilepsy have come a long way from the days of simply counting how many people had seizures. By combining improvement in classification systems, diagnostic technology and methods for case ascertainment, our understanding of epidemiology was strengthened. Local epidemiological data on childhood epilepsy are important in order to assess the magnitude of this problem and to target resources to patients who are most in need. Besides, identification of the aetiology of epilepsy can hopefully result in possible prevention of this common disorder. The findings are also important for paediatricians in determining an effective course of treatment, as well as communicating the illness,

recurrence rates, and long-term prognosis to parents. This review summarised the recent data on epidemiology and prognosis of childhood epilepsies in the local population.

Review of the literature on epidemiological studies shows that the prevalence of epilepsy ranges from 4-7 per 1000 population.^{23,25,26} Incidence rates are typically between 30 and 50 per 100,000 population per year.^{23,25,26} A bimodal incidence of unprovoked seizures was observed at the extremes of age.^{25,26} According to studies conducted in other Chinese communities, the prevalence is 4 to 7 per 1000 population.²⁷⁻³⁰ Our prevalence rate is somewhat lower than that reported in other epidemiological studies. Factors such as geographic origins, socio-economic situations, study designs and methodology are of importance in accounting for the differences. Some studies include neonates and patients with single unprovoked seizures. The majority of patients could be classified according to the International League Against Epilepsy classifications of epileptic seizures and epileptic syndromes. Neuroimaging had been widely used in the evaluation of epilepsy. CT scan was performed in 69% and MRI 54% in a cohort of epileptic children.⁶ This figure of neuroimaging was highly comparable to some of the studies carried out in the western countries. Neuroimaging was performed in 75% of epileptic children and out of which 85% had MRI according to a recent study reported by Larsson & Eeg-Olofsson.³¹ Whereas in another study by Endziene et al, CT scan brain was performed in only 16% of patients.³² The three most common causes of childhood epilepsy identified in the local population were CNS infections, CNS malformations and perinatal hypoxic-ischaemic encephalopathy. Studies in Taiwan and South Korea similarly identified perinatal hypoxic-ischaemic encephalopathy, congenital brain anomalies and tuberous sclerosis being the commonest aetiologies for infantile spasms.^{33,34} There is some evidence suggesting that the incidence of epilepsy may have declined in the last decades. If one analyses the causes of epilepsy, probably more effective vaccines against pathogens causing meningitis and improved perinatal care could have decreased our disease burden.

The proportion of children who experienced medically intractable epilepsy was comparable to a multi-institutional study on intractable epilepsy in Japan, in which the frequency was 13%.³⁵ Ten percent of the cohort reported by Berg et al met the criteria of intractability early in the course of their disorders.³⁶ The discrepancy in frequency can be explained by the true differences in various socioeconomic and geographical situations. The variability also reflects the lack of a standard and well-accepted

definition of intractable epilepsy. Early identification of patients who are at high risk of developing intractable epilepsy is essential in parental counselling and selecting patients for more intensive investigations and treatment, such as epilepsy surgery. Almost all the associations of intractability included aetiology, age of onset under 1 year and with abnormal neurology was explained by the syndromic grouping.^{24,37} Regarding the aetiology, CNS infection and perinatal hypoxic-ischaemic encephalopathy was identified to be the most important causes of intractable epilepsy according to our local data. Similarly, in a study of infantile spasms conducted in Taiwan, the prognosis of West syndrome was heavily dependent on whether the aetiology was cryptogenic or symptomatic.³⁸ In Casetta's series of intractable epilepsy, perinatal brain injuries predominated, while the most characteristic finding of underlying causes in intractable localisation-related epilepsy was CNS infection in Ohtsuka's study.^{37,39} In the acute stage of CNS infection and perinatal hypoxic-ischaemic encephalopathy, patients often experienced repeated status epilepticus or frequent seizures requiring intensive care. Seizures in the acute stage often originate from several different regions of the brain in the individual patient, and multifocal seizures continue after the acute stage. These patients are often resistant to medication. Whether improvement in prevention of acute CNS infection and perinatal care can result in decreasing the proportion of intractable epilepsy awaits further studies.

Half of the families of our children with epilepsy worried that epilepsy was an incurable disease and one-sixth were afraid of death due to seizures. This negative attitude was also observed in Korea and some parts of China.⁴⁰⁻⁴² On the other hand, the attitude towards epilepsy was more favorable in Taiwan.⁴³ Parental anxiety outweighed the physical factors in determining quality of life in childhood epilepsy. Public health education is urgently needed in order to improve the quality of life among children with epilepsy. In summary, our studies have provided useful information on the prevalence of childhood epilepsy in the local population and the natural history of seizures. Knowledge gaps clearly exist in many aspects of childhood epilepsy. For instance, although current data suggests the prognosis of childhood-onset epilepsy is relatively favorable in terms of seizure remission, we need data on its long-term impact on education and social outcomes. There are various reasons that made these outcomes unclear. Social and academic limitations may be attributable not only to natural course of epilepsy, but also to medications, underlying disease and/or, inaccurate and inappropriate social stigmatisation

about epilepsy. It is clear that the optimal treatment of childhood epilepsy needs to encompass the child's entire well-being and not limit solely to achieving seizure control.

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