ORIGINAL ARTICLE

The Epidemiology of Infantile Spasms

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ABSTRACT: ***Objective:*** The aim of this study was to estimate population based incidence rates for infantile spasms (IS) and to study our clinical impression that the incidence of IS has recently decreased in the Canadian Provinces of Nova Scotia and Prince Edward Island. ***Methods:*** Birth cohorts from 1978 to 1998, identified through the hospital health records, EEG records and physician computerized databases, were followed for two years for the development of IS. Disease incidence rates were calculated using denominators derived from Statistics Canada's reported annual live birth rates. ***Results:*** The inclusion criteria for IS were fulfilled by 75 patients. The overall incidence of IS was 30.7/100,000 live births (95% CI 24.3, 38.8). Etiologic classification was symptomatic for 51 cases (68%), cryptogenic for 18 (24%), and idiopathic in six children (8%). Although there were more males (N=44) than females (N=31), the incidence rates were similar. There was a marked variability in annual and five-year incidence rates. ***Conclusions:*** Although the clinical characteristics of our patients were similar to other reported IS populations, the instability in IS incidence rates indicates a need for caution in interpreting smaller IS epidemiologic studies.

RÉSUMÉ: Épidémiologie des spasmes infantiles. ***Objectif:*** Le but de cette étude était d'estimer l'incidence des spasmes infantiles (SI) dans la population et de valider notre impression clinique que l'incidence des spasmes infantiles a diminué récemment dans deux provinces Canadiennes, la Nouvelle-Écosse et l'Île du Prince-Édouard. ***Méthodes:*** Des cohortes de naissance de 1978 à 1998, identifiées au moyen de dossiers médicaux hospitaliers, de rapports d'ÉEG et de bases de données informatisées de cliniques médicales, ont été suivies pendant deux ans quant à l'apparition de SI. Les taux d'incidence ont été calculés au moyen de dénominateurs tirés des taux annuels de naissances vivantes de Statistique Canada. ***Résultats:*** Les critères d'inclusion des SI étaient présents chez 75 patients. L'incidence globale des SI était de 30.7/100,000 naissances vivantes (IC à 95%, 24.3 à 38.8). La classification étiologique suivante a été utilisée: SI symptomatiques chez 51 cas (68%), cryptogéniques chez 18 (24%), et idiopathiques chez six (8%). Bien qu'il y avait plus de garçons (N = 44) que de filles (N = 31), les taux d'incidence étaient semblables. Il existait une grande variabilité dans les taux d'incidence annuelle et sur cinq ans. ***Conclusions:*** Bien que les caractéristiques cliniques de nos patients étaient semblables à celles des autres populations au sujet desquelles des données ont été rapportées, l'instabilité dans les taux d'incidence des SI indique qu'on doit interpréter les petites études épidémiologiques sur les SI avec prudence.

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There is little recent epidemiologic data available on infantile spasms (IS). Published incidence rates have ranged from 22-45/100,000 live births,[1-6] with apparent stability from 1960-1992.[7] It was our clinical impression that incidence rates have declined more recently. The aim of this study was to estimate population based incidence rates and to provide demographic and clinical data on cases diagnosed with IS in our catchment area between 1979 and 1998.

As the only tertiary care pediatric hospital within a provincially based health care system, our population was ideal for this epidemiologic study.

Methods

The IWK Health Centre is the only tertiary care pediatric hospital serving the Canadian Provinces of Nova Scotia, Prince Edward Island and New Brunswick. All residents of both provinces have universal and complete access to health care, including medical and hospital treatment. The department of Health Records at our institution identified children with a discharge diagnosis of IS (ICD9 code 345.6) between January 1, 1979 and December 31, 1998. As all pediatric EEG records for the regions of mainland Nova Scotia (NS) and Prince Edward Island (PEI) are interpreted in our hospital, the EEG records were audited for cases of hypsarrhythmia and modified hypsarrhythmia for the same birth cohorts. An audit of a

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diagnostic database maintained by the pediatric neurologists was also performed to confirm that all incident cases had been identified, including any who might have been treated as outpatients. Records were reviewed and children were included only if they were resident within either mainland Nova Scotia or Prince Edward Island at the time of treatment initiation for IS, as this is the region which is served exclusively by our EEG department.

The diagnosis of IS was made, according to established criteria,[1,8] through a chart review by two pediatric neurologists. Infantile spasms were defined as sudden bilateral salaam-like contractions of the muscles of the neck, trunk and sometimes extremities, associated with hypsarrhythmia on EEG.[1] If consensus was not reached, the third pediatric neurologist served as arbitrator. Cases were classified as symptomatic, cryptogenic or idiopathic according to previous criteria.[9] Computed tomography scan reports were reviewed.

Disease incidence rates were calculated using denominators derived from Statistics Canada's reported annual live births from 1978-1997,[10-13] with estimated 95% confidence intervals. Differences in rates by sex, etiologic subgroup and by year were examined by chi square analysis, with expected values from the live birth data.

Data processing and analysis were performed using Epi Info version 6.04b.[14]

Results

We identified 111 patients with a discharge diagnosis of IS (ICD9 code 345.6) from 1978-1998. All patients had been seen by one of the pediatric neurologists and all had been treated as inpatients in our hospital. Fifty-three charts were excluded; 46 cases were resident outside mainland Nova Scotia and Prince Edward Island, five had normal EEGs and two patients had myoclonic seizures, not IS. Review of the EEG records identified an additional 17 patients with IS, who had been admitted to hospital but were not captured by health records department coding. Thus there were a total of 75 patients. The physicians' database only identified cases previously identified by the hospital and EEG records. Statistics Canada Vital Statistics data identified the combined annual number of live births for mainland Nova Scotia and Prince Edward Island as 11,927 (1978) – 9,945 (1997).[10-13] Data for 1998 were not available at the time of this study, but were estimated based on the available data.

The overall annual incidence rate of IS was 30.7/100,000 live births (95% CI: 24.3, 38.8). Annual incidence rates showed significant variation and ranged from 8.5/100,000 to 59.1/100,000 live births during the study period (Figure). There were more males (N=44) than females (N=31), but the difference in respective incidence rates was not statistically significant.

The etiology was symptomatic for 51 cases (68%), cryptogenic in 18 (24%) and idiopathic in six children (8%). Initial treatment was with ACTH for 46 (62%) patients, vigabatrin for nine (12%), valproate for two (3%), nitrazepam for six (8%) and other anticonvulsant treatment for 11 (15%).

The median age at hospital admission was seven months (25th percentile: 5 months 75th percentile: 10 months) and the median duration of IS prior to diagnosis was one month (25th percentile: 0 months, 75th percentile: 4 months). When corrected for date of IS onset, there was no significant seasonal or temporal clustering of incident cases.

The annual incidence rate for the period 1978-1991 was 35.8/100,000 live births but fell to 19.6/100,000 live births from 1992-1998 (x^2, p=0.035). When the incidence rates for the symptomatic and cryptogenic groups together were examined for the time periods of 1978-1991 compared to 1992-1998 there was an even more remarkable decline from 34.0/100,000 to 15.7/100,000 (x^2, p=0.012).

Discussion

Our region has been previously shown to provide an excellent cohort for the epidemiological study of childhood epilepsy.[15] The universality of health care access and the concentration of all tertiary care pediatric neurology within a single institution provide a unique model for such studies. We believe that it is likely that all patients with IS in the region were identified through our case finding methods. This study contains a large cohort, representing children with IS from our geographic region over a 21-year period.

Our population does not appear unique, as the clinical features were identical to previously reported groups.[1-4,6,16] The higher incidence in males was consistent throughout the study period and was similar to previous studies.[3,4,6] In addition, our numerator for incidence estimates (N=75 children) was larger than in four of six previous studies.[1-5,7]

Our 21-year study period has demonstrated instability in annual incidence rates with the annualized plot of IS indicating significant yearly variability. The five-year instantaneous rate showed a trend toward decreased incidence rates in the early 1990s, compared to stable incidence rates reported in Finland from 1960-1992.[7] Our annual incidence was 15.7/100,000 live births during the 1992-1998 period compared to 34.0/100,000 live births during 1978-1991. The variation in incidence rates, however, makes us reluctant to conclude that this change is significant. Minor fluctuations in the annual incidence rates of a relatively rare condition, such as IS, might have a dramatic impact.

This study raises methodological concerns about smaller IS epidemiologic studies. A large population based study over a long period of observation is necessary to avoid drawing erroneous conclusions from yearly fluctuations. Confirmation of a decline in incidence rates of IS would require a significant population base. With a baseline incidence of IS at 30/100,000 live births, a decline of 33% to 20/100,000 live births would require approximately 200 cases from a population of approximately 800,000 live births (α=0.05, β=0.2, 1:1 ratio of group sizes). Although our incidence rates are similar to published estimates,[3-5,6,17] the instability of rate over time demands caution in interpreting smaller studies.

In a recent study, Cortez et al[18] reported a seasonal variation in IS onset, with highest frequencies occurring in the fall and winter months. We did not observe seasonal or monthly clustering of IS incidence, despite similarities in latitude and climate.

We have implemented a multi-source surveillance system to ensure accurate case ascertainment. Only patients residing in

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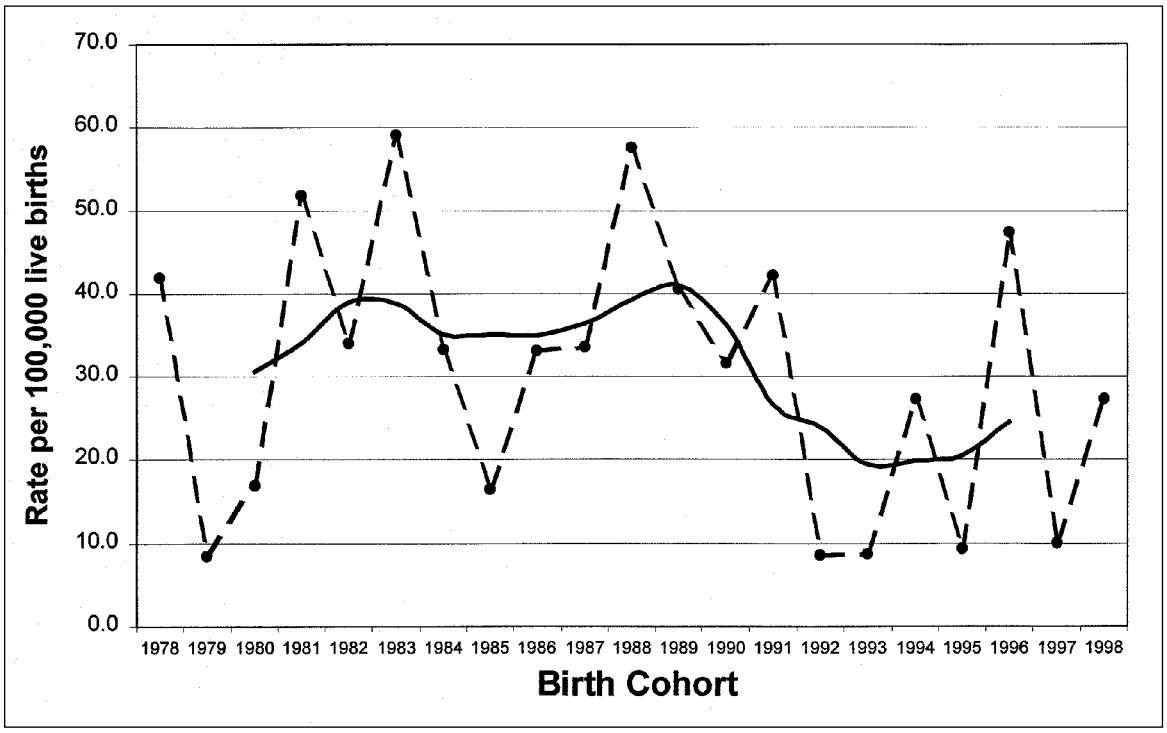

Figure: *Infantile Spasms Rates 1978-1998. Annual and five year rolling average*

provinces consistently served by our tertiary care center and EEG department were included (mainland NS and PEI). We did not include birth cohorts prior to 1978, as the earlier ICD coding system for IS was less specific. The earliest birth cohort included was 1978 with the premise that virtually all IS presents in the first two years of life. The addition of an audit of all EEG records and of our physician outpatient database provided increased certainty to our identification of IS cases.

It is our experience that IS presents with sufficient severity and concern that it is brought to medical attention and referred to a pediatric neurologist. During our study period, it has been standard practice for all cases of IS to be admitted for investigation and treatment. Although there has been a change in treatment practices over the past seven years to initial treatment with vigabatrin, this has not altered our practice of admitting all children with IS to hospital. We believe that we continue to see all IS cases in the region.

Our 20-year data have shown a decrease in the incidence rates of IS over the past six years. The average annual incidence fell to 17.3/100,000 live births during 1993-1998, compared to 33.1/100,000 during 1979-1992 and published estimates of 22-45/100,000.[3-5,7,17] In a similar study, Riikonen[%] observed stable incidence rates in Finland from 1960-1992. Our incidence rates were also stable up to 1992, with the decline beginning in 1993, remarkably in the symptomatic and cryptogenic groups.

The reason for the decline in incidence is unclear. Although there has been a change in treatment practices over the past six years to initial therapy with vigabatrin, this has not altered our practice of admitting all children with IS to hospital for therapy initiation. It is therefore unlikely to explain an erroneous impression of falling incidence.

Another potential source of under-ascertainment is migration in and out of the study area. The authors were not aware of any out-migration for IS treatment from mainland NS and PEI within the 21 year period. There was one patient diagnosed in Nova Scotia while visiting from outside the study area. This patient was not included in our incidence estimates. Migration out of the study area prior to IS diagnosis could result in an underestimate of IS incidence. Such patients would return to NS for further care and would be recorded in the pediatric neurologists' database. Although we cannot definitively exclude out-migration, it is unlikely to have had a significant impact on incidence estimates.

Our cohort is relatively large, is representative of our population and was gathered over a long period. It is impossible, however, to determine if the suggested trend towards a more recent fall in incidence, is real or is due to the rarity of IS and the variability of annual incidence. Multi-center studies, with a large numerator, will be necessary to establish true incidence rates and trends for children with IS.

References

1. Trevathan E, Murphy CC, Yeargin-Allsopp M. The descriptive epidemiology of infantile spasms among Atlanta children. Epilepsia 1999;40:748-751.
2. Rantala H, Putkonen T. Occurrence, outcome, and prognostic factors of infantile spasms and Lennox-Gastaut syndrome. Epilepsia 1999;40:286-289.

3. Sidenvall R, Eeg-Olofsson O. Epidemiology of infantile spasms in Sweden. Epilepsia 1995;36:572-574.
4. Ludvigsson P, Olafsson E, Siguroardottir S, Hauser WA. Epidemiologic features of infantile spasms in Iceland. Epilepsia 1994;35:802-805.
5. Riikonen R, Donner M. Incidence and aetiology of infantile spasms from 1960 to 1976; a population study in Finland. Dev Med Child Neurol 1979;21:333-343.
6. Cowen LD, Hudson LS. The epidemiology and natural history of infantile spasms. J Child Neurol 1991;6:355-364.
7. Riikonen R. Decreasing perinatal mortality: unchanged infantile spasm morbidity. Dev Med Child Neurol 1995;37:232-238.
8. Yeargin-Allsopp M, Murphy CC, Oakley GP, et al. A multiple-source method for studying the prevalence of developmental disabilities in children: the Metropolitan Atlanta Developmental Disabilities Study. [published erratum appears in Pediatrics 1992;90:1001] Pediatrics 1992;89:624-630
9. Chugani HT. Infantile spasms. Curr Opin Neurol 1995;8:139-144.
10. Statistics Canada. Health reports: Births 1989. Suppl 14; 1991;3(1).
11. Statistics Canada- Health Statistics Division. Births and Deaths 1995. Catalogue no:84-210-XPB.
12. Statistics Canada. Vital Statistics by Local Area, 1996. April 1999.
13. E-STAT [database online]. Statistics Canada;1998.
14. Dean AG, Dean JA, Coulombier D, et al. Epi Info, version 6.04b: A word processing, database, and statistics program for epidemiology on microcomputers. Centers for Disease Control and Prevention, Atlanta, Georgia, USA, 1997.
15. Camfield C, Camfield P, Smith B, Gordon K, Dooley J. Biologic factors as predictors of social outcome of epilepsy in intellectually normal children: a population-based study. J Pediatrics 1993;122:869-873.
16. Granstrom ML, Gaily E, Liukkonen E. Treatment of infantile spasms: results of a population-based study with vigabatrin as the first drug for spasms. Epilepsia 1999;40:950-957.
17. Hauser WA, Annegers JF, Gomez M. Incidence of West syndrome in Rochester, Minnesota [Abstract]. Epilepsia 1991;32(suppl 3);83.
18. Cortez MA, McIntyre Burnham W, Hwang PA. Infantile spasms: Seasonal onset differences and zeitgebers. Pediatr Neurol 1997;16:220-224.