Juvenile myoclonic epilepsy: Sporadic and familial cases. Do they differ?

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Abstract

Introduction: Genetic factors are the only identified cause of juvenile myoclonic epilepsy but some of the cases do not have affected first degree relatives.

In this study we wanted to know whether subjects with sporadic and familial JME differ in terms of clinical characteristics and response to treatments. Differences would support the hypothesis of a different etiology for sporadic cases.

Methods: We analyzed 70 patients with JME, diagnosed on clinical and EEG criteria. All patients and their first degree relatives were interviewed.

Patients with first degree relatives affected with epileptic seizures were regarded as familial and the others were regarded as sporadic.

Results: 34.3% of the patients had familial epilepsy. The types of the seizures, age at the onset of the seizures, response to treatment and side effects of the drugs did not differ between familial and sporadic cases.

Conclusions: No difference was found between familial and sporadic JME patients. This doesn't support the hypothesis that sporadic and familial JME cases have separate etiologies.

Keywords: **Juvenile, Myoclonic Epilepsy, Sporadio Familial.**

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Introduction

Juvenile myoclonic epilepsy is a common from of idiopathic generalized epilepsy, having on overall prevalence of 5-10%.[1] It is the most common form of idiopathic generalized epilepsies especially in women. Age of onset is usually between 12-18 years, but may be seen after the age of 20[2].The characteristic feature is myoclonic jerks of the shoulders and arms that usually occur after awakening.

Generalized tonic-clonic seizures develops in 90% of the cases and approximately one third have absence seizures.[3]

Genetic factors are one of the identified causes of JME, although some of the cases appear sporadic, with no family history.[4]

In familial cases a gene locus has been mapped to the short arm of chromosome 6[5,6] and another one on chromosome 15.[7]

The same locus on chromosome 6 may be responsible for other forms of epilepsy.

This study was conducted to determine if there were differences in demographic data, clinical characteristics, precipitating factors and response to treatment in familial versus sporadic cases of JME.

Methods

70 patients (48F, 22M) with JME were studied. Subjects were identified from patients who referred to epilepsy clinic in Sina Hospital (A teaching hospital of Tehran University of Medical Sciences) from June 2002 to December 2004. Patients were included based in the following criteria:

History of myoclonic jerks with or without generalized tonic–clonic convulsions or absence seizures between 8-25 years old, at least one EEG with fast spike- slow waves or polyspike and slow wave complexes that is accompanied by normal background activity, normal neurologic exam and intelligence.

Patients with mental retardation, history of severe head trauma, pregnancy during the study, structural brain lesions revealed by MRI, were excluded from the study.

New patients were treated with valporic acid and they were monitored for drug response and side effects. After final titration all the patients were followed for one year.

Following data collection, statistical analysis performed by SPSS software (version 11.5). Student T-Test and chi square were used for univariate and logistic regression for multivariate parameters.

Results

70 patients met the selection criteria. 24 patients (34.3%) had family history of JME in their one or more than one first degree relatives (group I), and 46 patients (65.7%) were without family history (group II). The mean age of the patients was 23.4 in group I, and 23.8 years in group II (P=0.40). 75% of the patients were male in group I and

65.2% were male in group II (P=0.42). History of absence seizures was present in 41% of the familial and 26% of the sporadic cases. The age of onset of absences was 10.1 in group I and 10.3 years in group II (P=0.355).

The mean age for starting myoclonic jerks was 14.83 in familial and 14.54 in sporadic groups (P=0.80).

These myoclonic jerks were predominantly in shoulders and upper extremities. There was no significant difference regarding myoclonic jerks in these two groups (P=0.67). The mean age of onset of generalized tonic-clonic seizures was 17.36 years in group I and 16.74 in group II (P=0.58). The provocative factors for myoclonic jerks or generalized tonic-clonic seizures are listed in table 1.

Table 1. Aggravating factors in patients with familial and sporadic JME.

Aggravating factors	Total %	Familial %	Sporadic %	P-value
Sleep deprivation	72.9	70.8	73.92	0.78
Stress	52.9	54.2	52.2	0.87
Fatigue	32.9	25	36.9	0.31
Hanger	21.1	25	28.3	0.77
Light	11.4	8.3	13	0.7
Alcohol	2.9	0	4.3	1
Menstruation	No:48	18	30	1
Drug withdrawal	31.4	37.5	28.3	0.12

The mean daily dosage of valporic acid was 800mg/day in both groups (Range 400-1500 mg)

Serum valporate level was 74.08 in group I and 78.39 mg/ml in group II (P=0.29) (Table 2).

Table 2. Mean daily dose of valporic acid and serum levels in familial and sporadic cases of JME.

Variables	All the patients	Familial JME	Sporadic JME	P-value
Mean daily dose of valporic acid mg/kg	12.6	13.06	12.37	>0.05
Mean daily dose of valporic acid mg/day	800	800	800	0.95
Mean serum level of valporic acid μg/ml	76.91	74.08	78.33	0.29
History of absence	31.4%	41.7%	26.1%	0.183

The response of myoclonic jerks, absences and generalized tonic-clonic seizures were almost equal in both groups. Familial and sporadic cases were also compared regarding side effects of valporic acid therapy; there was no significant difference in adverse reactions to the drug. (Table 3).

Table 3. Side effects of valporic acid in familial and sporadic JME.

Side effects	Total %	Familial %	Sporadic %	P- value
Weight gain	27.1	20.8	3.4	0.39
Hair loss	18.6	20.8	17.1	0.75
Tremor	17.1	20.8	15.2	0.73
Acne	10	8.3	10.9	1
Nausea	8.6	4.2	10.9	1
Drowsiness	1.4	-	72	1
Menstrual irregularities	14.6	11.1	16.1	1

Patients in both groups were also comparable in mean age, gender and age of onset of seizures.

Discussion

Our data showed no difference between sporadic JME, defined as absence of first degree relatives affected with epileptic seizures and familial JME, in clinical features and response to treatment. Based on previous studies and the prevalence of JME our sample size could be 50 patients but we continued the study and 70 patients were selected, therefore our sample size provided enough power to test for a major difference between sporadic and familial JME. The absences of demonstrable clinical difference between these two groups do not support the hypothesis that they have different etiologies.

These findings are not surprising as sporadic cases are expected in disorders with complex inheritance. The proportion of affected first-degree relatives is much lower than that in conditions with simple mendelian inheritance additionally the potential role of reduced penetrance, the possibility of new mutations and the question of post fertilization genetic changes could all result in the observation of sporadic cases.[8]

Another point of interest is that statistical analysis showed no significant difference between familial and sporadic cases regarding response to valporic acid and its side effects.

These findings also do not support the hypothesis that they have separate etiologies. In conclusion we suggest that sporadic cases maybe included in molecular genetic studies of JME where appropriate to the experimental design. Perhaps additional studies with thorough genetic evaluation could be more informative.

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مقایسه موارد تک گیر و ارثی صرع میوکلونیک نوجوانی

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چکیده

زمینه و هدف: تا امروز وراثت تنها عامل شناخته شده در ایجاد صرع میوکلونیک نوجوانی می باشد اما بسیاری از بیماران سابقه چنین حملاتی را در خانواده خود ندارند . این مطالعه به بررسی و مقایسه موارد تک گیر و ارثی صرع میوکلونیک نوجوانی می پردازد.

روش بررسی: هفتاد بیمار مبتلا که تشخیص این نوع صرع بر اساس معیارهای بالینی و نوار مغزی تایید شده بود مورد مطالعه قرار گرفتند . بیمارانی که سابقه تشنج در بستگان درجه اول آنان وجود داشت بعنوان موارد فامیلی و بقیه بیماران به عنوان موارد تک گیر تقسیم بندی گردیدند .

یافته‌ها: درصد بیماران سابقه خانوادگی مثبت داشتند . در این بیماران از نظر سن شروع بیماری، نوع تشنج، پاسخ به درمان و ایجاد عوارض ناشی از دارو تفاوت معنی داری با موارد تک گیر مشاهده نگردید.

نتیجه گیری: نتایج این مطالعه بیانگر این نکته میباشد که موارد تک گیر و ارثی صرع میوکلونیک نوجوانی به احتمال قوی منشأ و اتیولوژی متفاوتی نداشته و درمان هر دو گروه باید به صورت یکسان انجام گردد.

واژگان کلیدی: نوجوانی، صرع میوکلونیک، تک گیر، ارثی