The Period Prevalence of Catamenial Epilepsy at Prasat Neurological Institute, Bangkok

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Abstract

The study was performed to assess the period prevalence of catamenial epilepsy in Thai female epileptic patients. Such a condition is defined as seizures related to menstruation which occur for at least 2 consecutive months within 1 patient during 4 days prior to and/or 6 days after the onset of menstruation. Patients with regular menstruation aged between 15-50 years attending the Out-Patient Department of Prasat Neurological Institute in Bangkok from 1 November, 1995 to 31 January, 1996 were recruited. Patients and/or their relatives were interviewed directly or by telephone using a questionnaire concerning menstrual history, seizures related to menstruation and they were requested to record these data for 2 further consecutive months. In cases where the interview could not be directly performed, a mailed questionnaire was used instead. All information was considered together with information reviewed from the OPD cards. Forty-six from 467 epileptic patients were considered to have catamenial epilepsy. The period prevalence thus was 98.5 in 1,000 women at risk and the mode of frequency of seizure occurrence was 2 days before menstruation. Generalized seizure was found more common in these patients than partial seizure. In particular, general tonic-clonic seizure and complex partial seizure were the most common for each type, respectively. About 70 per cent of the patients used more than 1 anti-convulsant drugs to control their seizures. Some have received other drug supplements to relieve seizure exacerbation but only mild improvement was observed. No change in body weights measured in 2 or 1 day before menstruation, on the first menstrual day and in 1 day after menstruation was demonstrated in all patients. The results suggest that catamenial epilepsy is one of the clinically significant problems of seizure control in Thai female epileptic patients and multi-factors may be involved in this condition.

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Epileptic seizure is a neurological disorder that usually disturbs patients' way of living. In some women, seizures have occurred more frequently than usual around their menstrual period despite good compliance on anticonvulsant therapy. Catamenial epilepsy is the term used to denote such a condition. Most reports refer this condition to a increase in seizure frequency around the menstrual period; either just before or during the first few days of the period[1]. A wide range of criteria and methods for determination and assessment have been used in various studies. Accordingly, the incidence varies from 10 to 100 per cent of women at risk as reported in Table 1, whereas no reports on prevalence are availabel[1-3].

In Thailand, female epileptic patients also suffer from catamenial epilepsy but neither incidence nor prevalence has been documented. This study was, therefore, designed to assess the period prevalence of such a condition in Thai female epileptic patients. The results obtained from this study would indicate the magnitude and pattern of the problem which would provide valuable information for further management and study.

PATIENTS AND METHOD

Criteria for catamenial epilepsy

Patients would be determined to have catamenial epilepsy if they have exacerbation of seizures in relation to menstruation which occurs within 4 days prior to and/or 6 days after onset of menstruation and this exacerbation occurred consecutively for at least 2 months[3].

Patient recruitment and information gathering

Female epileptic patients with regular menstruation, aged between 15-50 years attending the out-patient department of Prasat Neurological Institute from 1 November, 1995 to 31 January, 1996 were recruited. All patients and/or their relatives were interviewed by the investigators using a questionnaire asking about menstrual history, history of seizures and medication, history of seizures related to menstruation and past medical history including self-medication. After the interview, the patients were requested to record the period of menstruation, seizure frequency (number of seizures in each day) for a further 2 consecutive months on the seizure record card provided. Moreover, all patients were asked to record their body weights 2 days before menstruation; the first day of menstruation and the first day after their menstrual period. After the record was finished, the card was mailed back to the investigator. Telephone interview or mailed questionnaire including seizure record card was provided by the investigators for patients who did not keep their appointment. The questions in the mailed questionnaire were modified to be more simple, only details of menstrual history and history of seizures related to menstruation were concerned. We excluded the history of medication used for seizure control since patients may not know the names of the medication. This mailing was repeated 30 days later if no response was received the first time. All information in the patients' OPD cards was concurrently reviewed whether diagnosis of seizure exacerbation or history of medication supplement i.e. anticonvulsants or acetazolamide around the menstrual period was specified. This would indicate potential catamenial epilepsy. In cases with a mailed questionnaire, if no reply was received after two mailings, only information from the OPD card was retrieved for consideration.

Prevalence of catamenial epilepsy

Period prevalence (P) was calculated using the following equation :

$$P = \frac{n}{N}$$

where : n = number of female epileptic patients who were considered to have catamenial epilepsy.

N = total number of recruited female epileptic patients during the study period

The period prevalence was reported as number per 1,000 women at risk.

RESULTS

Fig. 1 shows the numbers of patients recruited and their categories according to the methods of information gathering. Sixty-one cases were considered to have seizures related to menstruation. Among these, 46 patients were concluded to have catamenial epilepsy therefore, period prevalence was 98.5 per 1,000 women at risk.

The occurrence of catamenial seizures during the whole period from 41 patients is illustrated in Fig. 2. In another 5 patients, although catamenial seizures occurred within a 10-day interval defined in the criteria certain dates of seizure occurrence could not be clearly specified. Most patients tended to have seizure exacerbation a few

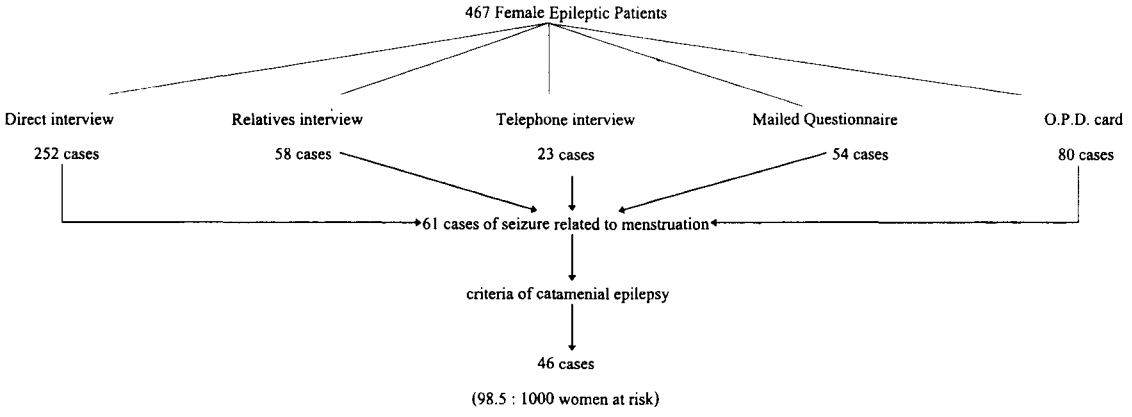

Fig. 1. Numbers of patients recruited and their categories.

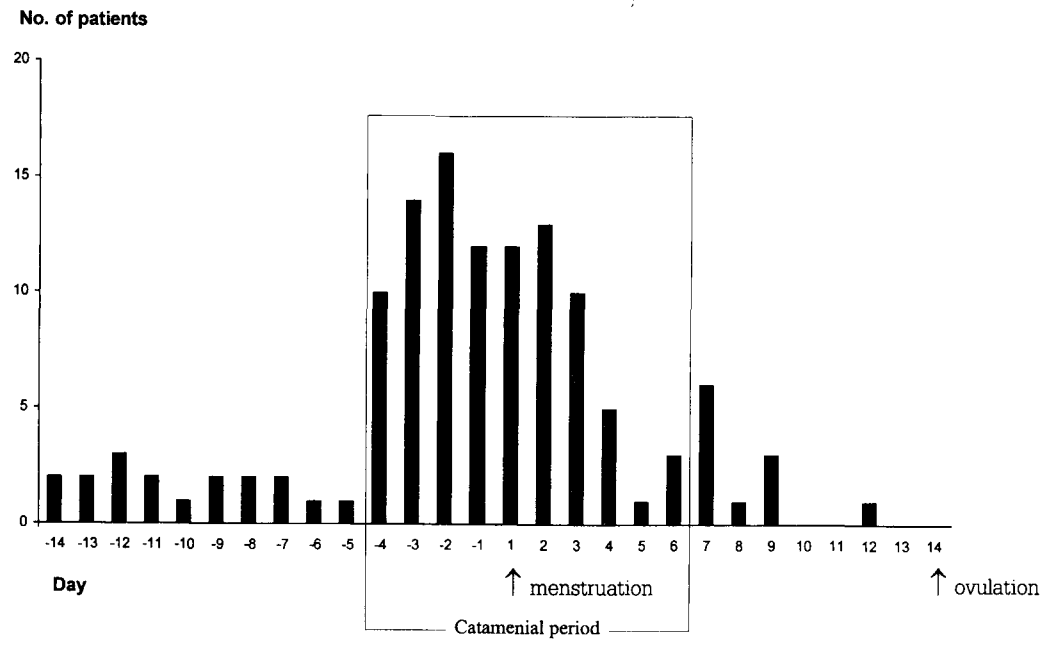

Fig. 2. Occurrence of catamenial seizure
Day 1 represents the first day of menstrual period, day 14 is the expected ovulatory day while day - 1 to - 14 represent premenstrual period.

Table 1. Incidence of catamenial epilepsy.

Author	n	Age (yr)	Seizure type	No. with catamenial epilepsy	%
Gowers, 1885	82	-	-	32	39
Gordon, 1909	23	-	-	21	91
Toulouse and Marchand, 1913	10	-	Essential	4	40
Rebattu et al., 1922	100	-	-	35	35
Healey, 1928	73	-	-	45	62
Dickerson, 1941	269	10-49	-	27	10
Thiy et al., 1954	58	-	-	37	64
Almquist, 1955	84	18-63	Generalized tonic-clonic	17	20
Ansell and Clark, 1956	42	-	-	26	62
Laidlaw, 1956	50	-	Generalized tonic-clonic	36	72
Bandler et al., 1957	22	-	-	7	32
Logothetis et al., 1959	10	16-45	-	10	100
Lennow and Lennox, 1960	686	-	-	333	49
Bunter and Rosciszewska, 1975	11	-	-	11	100
Backstrom, 1976	7	13-45	Generalized tonic-clonic, Complex partial	7	100
Rosciszewska et al., 1986	64	-	-	37	58
Atkinson Morley's Hospital	69	-	-	6	9
Duncan et al., 1993	40	16-45	Generalized tonic-clonic, Partial	5	12.5

Modified from Crawford, 1991[1], Newmark and Penny, 1980[2] and Duncan et al., 1993[3]
n = Total number of female patients in each report
- = no data

days prior to and during the first few days of menstruation. The mode of frequency was 2 days prior to menstruation.

Type of seizures in catamenial epileptic patients is shown in Table 2. Generalized seizure was found more common than partial seizure (65.2% and 34.8%, respectively). The most common type of generalized seizure was general tonic-clonic seizure whereas complex partial seizure was the most common for partial seizure. Anticonvulsants used in these catamenial epileptic patients are shown in Table 3. The most common regimen used was a two-drug combination (56.4%).

Only 10 from 46 patients have received drug supplement to control their catamenial seizures as seen in Table 4. Mild improvement was observed from those regimens but most patients were not improved.

Concerning the alteration of body weights, no change in body weights measured 2 or 1 day before menstruation, on the first menstrual day and

Table 2. Type of seizure in catamenial epileptic patients.

Type of seizures*	No of female with catamenial epilepsy	%
Partial seizure	**16**	**34.8**
Complex partial	14	30.4
Simple partial seizure develop into 2nd generalized seizure	2	4.4
Generalized seizure	**30**	**65.2**
Atonic seizure	3	6.5
Absence seizure	1	2.2
General tonic-clonic seizure	23	50
Grand mal seizure turn	3	6.5
Complex partial seizure		
Unspecified	**0**	**0**
Total	**46**	**100**

* Based in ILAE 1981 (International League Against Epilepsy)

Table 3. Anticonvulsant drugs used in catamenial epileptic patients.

Medications	No. of female with catamenial epilepsy	%
1. One anticonvulsant :	**13**	**28.3**
PHT	4	8.7
PB	5	10.9
CBZ	3	6.5
CZP	1	2.2
2. Combination of two anticonvulsants:	**26**	**56.4**
PHT+PB	18	39.1
PHT+CBZ	2	4.3
PHT+CZP	1	2.2
PB+CBZ	2	4.3
PB+VPA	2	4.3
CBZ+CZP	1	2.2
3. Combination of three anticonvulsants:	**4**	**8.7**
PHT+PB+CBZ	1	2.2
PHT+PB+CZP	1	2.2
PB+CBZ+VPA	1	2.2
PHT+CBZ+CZP	1	2.2
4. Combination of four anticonvulsants:	**3**	**6.6**
PHT+PB+CBZ+CZP	1	2.2
PHT+PB+VPA+CZP	1	2.2
PHT+CBZ+VPA+CZP	1	2.2
Total	**46**	

PHT = Phenytoin
CZP = Clonazepam
CBZ = Carbamazepine
VPA = Valproic acid
PB = Phenobarbital

1 day after menstruation was demonstrated in all patients in our study.

DISCUSSION

The existence of catamenial epilepsy in the present study was assessed as period prevalence instead of incidence as in other studies. This was considered to be a more convenient method since all existing cases could be evaluated. In addition to information gathered from the designed questionnaire and the seizure record card, we also considered physicians' judgment and medication history recorded in the OPD cards to help confirm reliability of the data before making a final conclusion. Concerning our patient recruitment and methodology, only 46 cases were included in our criteria for catamenial epilepsy. For the others, 15 patients, evidence for consideration was inconclusive. This was because the certain date of seizure occurrence around menstruation was not in the defined period. Furthermore, their seizure record cards were not sent back, thus, only information recorded in the OPD cards which was not complete in some cases was gathered for consideration. The period prevalence of 98.5 per 1,000 women at risk found in our study cannot be compared directly to the incidence reported in Table 1 owing to the differences in characteristics of measurements, criteria and methods for determination. The very wide range of incidence reported previously, up to 100 per cent of women at risk, (Table 1) might be the result of differences in the defined criteria and methods for determination of such a condition in each study. Moreover, some studies were particularly performed on a small

Table 4. Drug supplement in catamenial epileptic patients.

Drug supplement	Duration	No. of patients who received drug supplement	Outcome	
			Improved	Not improved
1. Acetazolamide (250 mg) 1 tablet OD	5 days before menstruation	6	2	4
	5 days during menstruation	2	-	2
2. Clonazepam (2 mg) 1 tablet hs	During menstruation	1	-	1
3. Acetazolamide (250 mg) 1 tablet OD and phenobarbital gr. 1/2 1 tablet OD	During menstruation	1	1	-

number of patients which might not represent the female population with epilepsy[1]. Unfortunately, we could not find any report about a prevalence study to directly compare with our result. However, the period prevalence obtained from our study suggests that such seizures can contribute a significant problem in clinical practice. More studies in various centers concerning the significance and magnitude of this problem are recommended. Furthermore, more cycles of menstruation may be followed in order to assure the relation between seizure occurrence and menstruation[4].

The mode of seizure occurrence days observed in our study agreed with previous reports[1-3,5] and it was found that seizure attacks could occur more than one time within a day in some cases. This proposes that aggressive treatment should be considered during this particular period. Interestingly, less frequent seizures were evident near the expected ovulatory period even though some catamenial epileptic patients still suffered more or less from seizure exacerbation during some other times of the cycle.

Concerning seizure type, we found that generalized seizure was more common than partial seizure which is different from some previous reports, which mentioned that catamenial epilepsy was usually found in women with complex partial seizures due to relative resistance to anticonvulsant therapy[1,2]. Nevertheless, the others did not support these observations. From our findings, general tonic-clonic seizure was the most common type in generalized seizure while complex partial seizure was the most common in the partial seizure group. Additionally, we noticed that no catamenial epileptic patients were found with 2 types of seizures, simple partial and tonic seizure. This may be because these 2 groups are more easily controlled. However, both general tonic-clonic and complex partial seizure are also the common seizure types found in Thai female epileptic patients. Thus, the relation between seizure type and catamenial epilepsy might be inconclusive, at this time. Further study on this relationship is recommended in order to provide more concern for effective treatment.

About 70 per cent of catamenial epileptic patients need more than 1 drugs to control their seizures. The two-drug combination, phenytoin combined with phenobarbital, was the most commonly used combination (39.1%). This implies that such seizures are particularly difficult to control. Certain etiology of such a condition, however, remains unclear. Various potential causes have been proposed including premenstrual psychic disturbances, emotional instability[1,2], water retention[6], estrogenic but not progestogenic hormone [7-9] or fluctuation of anticonvulsants especially phenytoin levels[10-12]. In the present study, those factors were not inspected except water retention which may influence the volume of distribution of anticonvulsants and consequently their blood levels. Nevertheless, this factor was just indirectly monitored by body weight measurement around the menstrual period and no change was observed. Therefore, potential water retention may not influence the occurrence of catamenial seizure observed in the study. This seems to be supported by the study of Ansell and Clarke[6]. Relative estrogen and progesterone concentrations have been well accepted to have an important role in catamenial seizures. A rapid fall in progesterone level premenstrually usually results in an increase of seizure attacks[7-9], whereas, high progesterone concentration is suggested to have a protective effect. This finding is supported by many reports about the satisfactory outcome of progesterone replacement in catamenial seizure control[7-9, 13-15]. Therefore, it could be suspected that the absence of seizures around ovulation found in our study may be in part due to this hormonal effect. Such evidence suggests that multifactors may be involved in catamenial epilepsy. Efficient control, thus, may need various kinds of drug supplement. Anticonvulsant supplement, hormonal replacement, some add-on drugs e.g. clobazam or diuretic supplement during premenstrual period is the suggested treatment[6,16-19] In our institute we choice to use clonazepam, phenobarbital or acetazolamide, as inhibitors of carbonic anhydrase in the brain, as drug supplements. Unfortunately, these drugs were effective in only 30 per cent of cases as show in Table 4. Further studies searching for those etiologies either the assessment of anticonvulsant or hormonal blood level during the period may provide better understanding and more successful control of such seizures in those sexually-active women.

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การศึกษาความชุกของโรคลมชักที่สัมพันธ์กับการมีระดู ณ สถาบันประสาทวิทยา กรุงเทพมหานคร

สมชาย โตวณะบุตร, พ.บ., วว. ประสาทวิทยา, สุวัฒนา จุฬาวัฒนทล, ปร.ด.**, จุฑามณี สุทธิสีสังข์, ปร.ด.***, อุษณีย์ วนรรฆมณี, วท.ม.*****

การศึกษาความชุกของโรคลมชัก, ที่สัมพันธ์กับการมีระดูในผู้ป่วยโรคลมชักหญิงไทย, โดยให้คำจำกัดความว่าเป็นการชักที่สัมพันธ์กับการมีระดูติดต่อกันอย่างน้อย 2 เดือน และเกิดขึ้นในช่วง 4 วันก่อนมีระดูจนถึง 6 วันหลังเริ่มมีระดู. ผู้ป่วยหญิงที่ร่วมในการศึกษาเป็นผู้ป่วยนอกของสถาบันประสาทวิทยา ที่มารับการรักษาระหว่างวันที่ 1 พฤศจิกายน พ.ศ. 2538 ถึงวันที่ 30 มกราคม พ.ศ. 2539 ผู้ป่วยต้องมีระดูสม่ำเสมอ อายุระหว่าง 15–50 ปี, เก็บข้อมูลโดยการสัมภาษณ์ผู้ป่วยและ/หรือญาติผู้ป่วยโดยตรงหรือทางโทรศัพท์, โดยใช้แบบสอบถามเกี่ยวกับประวัติการมีระดู, การชัก, โดยเฉพาะการชักที่สัมพันธ์กับการมีระดู, และให้ผู้ป่วยบันทึกความถี่ของการเกิดการชัก, และระยะเวลาของการมีระดู, เป็นเวลาติดต่อกันอีก 2 เดือนหลังการสัมภาษณ์. หากไม่สามารถสัมภาษณ์ผู้ป่วยและ/หรือญาติผู้ป่วยโดยตรงจะทำการการสอบถามทางไปรษณีย์, ข้อมูลทั้งหมดจะนำมาพิจารณาร่วมกับข้อมูลจากเวชระเบียนผู้ป่วยนอก.

ผลการศึกษา, พบผู้ป่วยโรคลมชักที่สัมพันธ์กับการมีระดู 46 ราย, จากผู้ป่วยหญิงที่สำรวจทั้งสิ้น 467 ราย, คิดเป็นความชุก 98.5 : 1,000 ของผู้ป่วยหญิงโรคลมชักที่มีความเสี่ยง, และการชักเกิดบ่อยที่สุด 2 วันก่อนมีระดู, การชักแบบเกร็งกระตุกทั้งตัวจะพบบ่อยกว่าการชักแบบเฉพาะที่, โดยเฉพาะที่ชักแบบทำอะไรไม่รู้ตัว (Complex partial seizure). ประมาณร้อยละ 70 ของผู้ป่วยต้องใช้ยากันชักมากกว่า 1 ชนิดในการควบคุมอาการ, บางรายยังได้รับยาอื่นเสริมเพื่อบรรเทาอาการชักด้วย, แต่พบว่าได้ผลเพียงเล็กน้อยเท่านั้น. ไม่พบการเปลี่ยนแปลงน้ำหนักตัวของผู้ป่วยซึ่งชั่งในช่วง 2 วันก่อนมีระดู, วันแรกที่มีระดู, และวันแรกหลังหมดระดู, ผลการศึกษาชี้ให้เห็นว่า, โรคลมชักที่สัมพันธ์กับการมีระดูจัดเป็นปัญหาหนึ่งที่มีความสำคัญทางคลินิก, ในการควบคุมอาการชักของผู้ป่วยหญิงโรคลมชัก, และอาจมีสาเหตุมาจากหลายปัจจัยร่วมกัน.

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