Management of Libyan Patients with Catamenial Epilepsy


Abstract:
This study was conducted to assess in Libyan females the incidence of catamenial epilepsy. This form of epilepsy is defined as the increase in seizure frequency in relation to the menstrual cycle. We also evaluated retrospectively the pattern of seizures, and the drug management of these patients using acetazolamide as an add-on drug or by increasing the dose of the usual antiepileptic drug (AED). The preliminary results have demonstrated that the incidence of catamenial epilepsy among Libyan females studied was 8.83%. The period prevalence for the exacerbation of the seizures was during the perimenstrual phase and during the entire second half of the cycle (60.19%). Catamenial seizures were more common (79.61%) among women with complex partial type of seizure. Acetazolamide was effective in improving the conditions of patients with catamenial epilepsy. In 88.89% the number of seizures was reduced by more than 50%, and the combination was as effective as using multiple drug therapy based on combination of more than one AED (89.39%).

Introduction:
The term catamenial epilepsy refers to the increased seizure frequency in women at the time of menstruation. The incidence of catamenial epilepsy varies from 10% to 78%, partly because of the lack of a universally adapted definition. Catamenial seizures are common among women with focal or generalized epilepsies. The exact cause of the exacerbation of epileptic seizures around the time of menses is not well understood, but it may be related to hormonal fluctuations, mainly estrogen and progesterone. Clinical studies aimed to identify the cause(s) of catamenial epilepsy have shown increased seizure frequency during phases of the menstrual cycle characterized by a high ratio of estrogen to progesterone. This supports the hypothesis that estrogen exerts a proconvulsant influence, whereas progesterone is anticonvulsant. Herzog et al. provided evidence for the existence of at least three distinct patterns of seizure exacerbation in relation to the menstrual cycle. The first and most common pattern involves epileptic exacerbation during the perimenstrual phase (days 24-28), which may be related to reduction in progesterone levels associated with menstruation. The second pattern involves seizure exacerbation during the preovulatory phase (days 10-14) in normal cycles, and it may be related to the increase of estrogen that precedes ovulation. The third pattern of seizure exacerbation occurs in women with inadequate luteal phase (anovulatory cycles) and involves the entire second half (days 10-28) of the cycles. Several approaches have been proposed for the treatment of catamenial epilepsy including: antiepileptic drug supplementation immediately before the time of exacerbation or use of acetazolamide. Other strategies included treating patients with natural or synthetic progesterone, especially in cases of inadequate luteal phase.
This study was aimed to evaluate in Libyan patients at fertile age, the prevalence, the patterns and pharmacological management of catamenial seizures.

Materials and Methods:
The files of epileptic female patients with catamenial epilepsy attending the National Epilepsy Center Outpatient Clinic in Tripoli for treatment and follow-up during the period from January 2000 to December 2002 were selected for this study. The criteria for selection of the patients are: a) Women were in the menacme age (14-30 years) b) Regular attendance to the clinical follow-ups c) Refractory to antiepileptic drug treatment despite compliance d) Increased seizure frequency at or near the time of menstruation

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The assessment included: the prevalence of catamenial epilepsy in these patients, the type of seizure, the patterns of exacerbation of epileptic seizures and the effectiveness of either increasing the antiepileptic drug (AED) doses or the addition of acetazolamide (250 mg/day) to their usual AED dose.

Results:
One hundred and three from 1167 (8.82 %) epileptic women in the period of study were considered to have catamenial epilepsy. These patients showed different patterns of seizures: 60.19% (62 out of 103 patients had experienced an exacerbation of their epileptic seizures during the perimenstrual phase and during the entire second half of the cycle, while 39.81% (41 patients out of 103) had exacerbation of seizures during the preovulatory phase (Figure 1). Complex partial seizure was found more common in these patients 79.61% (82 out of 103) and generalized tonic-clonic seizure was the type of epilepsy diagnosed in 18.45% (19 out of 103). Only two patients (1.94%) had absence seizures (Figure 2).

About 65% of the patients (66/103) used more than one anticonvulsant drugs to control their seizures and in these patients, seizures were controlled in 59 out of 66 (89.39%). Acetazolamide was added to the usual dose of anticonvulsants in 18 out of 103 patients in whom 16 patients (88.89%) had their seizures controlled. The seizures were controlled in all 17 patients with increased dose of anticonvulsant drug. Only two out of 103 patients went out of treatment (Figure 2).

Discussion:
Our results have demonstrated that the incidence of catamenial epilepsy in Libyan females (8.83%) was close to that reported by Duncan et al.\(^1\) (12.5%) and by Towanabut et al.\(^10\) (9.85%). However, this value remains lower than that reported by Herzog et al.\(^11\) (39.1%) and by Reddy\(^1\) (70%).

The small number of patients involved in the study its retrospective nature might have contributed to this small value as there may be many patients missed to be diagnosed as having catamenial epilepsy, because of the lack diaries where they can report the incidence of the seizure in relation to the menstrual cycle.

The pattern of exacerbation of epileptic seizure in our study have demonstrated that about 2/3 of the patients (60.19%) had an increased seizures in the perimenstrual phase and during the entire second half of the cycle. This group of patients includes those with an abnormal (anovulatory) cycles and probably inadequate luteal phase syndrome, which might contribute to elevation in estrogen levels and low progesterone levels.

This can only be confirmed by measuring the levels of these hormones and also levels of antiepileptics to differentiate between those with anovulatory cycles and other patients whose exacerbation may be related to a decline in anticonvulsant medication levels due to increased metabolism\(^12,13\) or decreased patients compliance.

In this study Complex partial seizure was found more common (79.61%) than generalized seizure (18.45%). Towanabut et al.\(^10\) reported a different incidence in Thai patients i.e. higher rate of catamenial epilepsy in patients with generalized seizures compared with partial seizures.

Concerning the management of catamenial patients using different regimens, we conclude that the intermittent use of acetazolamide as an add-on drug was as effective as using multiple drug therapy in controlling the seizures 88.89% vs. 89.39%. This approach has the advantage that acetazolamide is safer and patients will avoid increasing the dose of anticonvulsants which might increase toxic reactions.

Conclusions and Recommendations:
We conclude from this study, despite the small number of the sample and the lack of an exact definition of catamenial epilepsy, that acetazolamide is effective in controlling the seizures in Libyan patients when used in a dose of 250 mg/day. Its efficacy was comparable to that of using multiple AEDs. However, we recommend the following:
1. The study will be extended to involve a large group of patients to whom a seizure calendar will be provided and patients will be asked to carefully record the seizure frequency in relation to the menstrual cycle.
2. In those patients with exacerbation of seizures during the second half of the cycle, an assessment of hormone levels is essential to determine the anovulatory cycles (low progesterone levels) and those patients will be good candidates for hormonal therapy based on synthetic progesterone.
Fig 1. Patterns of exacerbation of epileptic seizures in women with catamenial epilepsy

Fig 2. The outcome of treatment of catamenial epilepsy using different regimens

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