Original Article

Sexual Function in Thai Males with Epilepsy

Phunikhom K, MD, PhD[1,4], Tiamkao S, MD, MSc[1,4], Pranboon S, MSN[2,4], Tiamkao S, MD[3,4], on behalf of the Integrated Epilepsy Research Group[4]

[1] Department of Pharmacology, Faculty of Medicine, Khon Kaen University Khon Kaen, Thailand
[2] Nursing Division, Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand
[3] Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand
[4] Integrated Epilepsy Research Group, Khon Kaen University, Khon Kaen, Thailand

Background: Sexual dysfunction is more common in patients with physical and mental disorders. The complexity of the epilepsy disease itself is manifested both physical and psychological, and is more likely to cause sexual dysfunction problems.

Objective: To assess the prevalence of sexual dysfunction in patients with epilepsy, factors associated with sexual dysfunction, and partial androgen deficiency in aging males (PADAM).

Materials and Methods: The patients responded to the questionnaire asking about the general information, and took IIEF (The International Index of Erectile Function) and PADAM tests. Another data were derived from medical records of Srinagarind Hospital, Faculty of Medicine, Khon Kaen University.

Results: 64 patients were enrolled in the study. The average age was 40.53 years. The mean onset of epilepsy and the duration of treatment were 25.24 and 12.27 years, respectively. The most common type of seizure was complex partial seizure. Over half of the patients were unable to control seizures with antiepileptic drugs (AEDs). The drugs mostly taken were sodium valproate, phenytoin, and carbamazepine. Evaluation of sexual performance showed that 64.06% had erectile dysfunction, 51.56% had orgasmic dysfunction, 92.19% had sexual desire problem, 83.94% had intercourse dissatisfaction, and 46.87% had overall sexual dissatisfaction. No relationships of sexual dysfunction were found with age at the onset of epilepsy, duration of treatment, type of seizure, frequency of seizures, or AEDs. According to the evaluation on PADAM, it was revealed that 50% had physical and neurological problems and circulatory problems, 60.94% had mental problems, and 15.63% had sexual problems.

Conclusion: The men with epilepsy were more likely to have sexual dysfunction and psychological problems. Therefore, for the holistic patient care, not only outcome of epilepsy treatment but also sexual and psychological evaluations should be conducted to improve the quality of life of the patients.

Keywords: Male with epilepsy, Sexual dysfunction, Erectile dysfunction

J Med Assoc Thai 2019;102(Suppl.3):12-8
Website: http://www.jmatonline.com

Sexual dysfunction (SD) refers to the inability of the male genitalia to achieve or remain an erection sufficient until the end of sexual activity, a lack of sexual desire, and the inability to shed the semen or reach orgasm[1]. This problem is considered a physiological problem. Some men may occasionally have the problem while some find it turns chronically problematic[2]. The problem can be found worldwide. The incidence of sexual dysfunction is found up to 52 percent in males aged 40 to 70 years. It is estimated that 150 million men worldwide have this problem[3] and the number may increase to 225 million by 2025[4]. Meanwhile, by the same range of age, 37 percent of the same problem was found in Thailand[5]. The risk factors that cause this problem include increasing age, smoking, and obesity[6,7]. It is found that 20 percent are caused by mental disorders, especially in the majority of depressed patients[8] and another 80 percent by physical problems such as diabetes, cardiovascular disease, neurological disease, high serum cholesterol. These causes lead to the clog of the tissue around the blood vessels of the penis, making less blood flow to the penis. As a result, the male genitalia does not remain erectile until the end of sexual activity. Based on data collected in the Andropause Clinic at Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, high incidence of sexual dysfunction was found where the risk factors are diabetes and kidney disease. The research team suggested that there should be sexual dysfunction screening for all males with andropause and prompt treatment should be provided to improve the quality of life for them[9].

In men, Androgen hormones are produced from the testis and in relatively higher amount in reproductive age.

Correspondence to:
Tiamkao S.
Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.
Phone: +66-43-348399, **Fax:** +66-43-347542
E-mail: somtia@kku.ac.th

How to cite this article: Phunikhom K, Tiamkao S, Pranboon S, Tiamkao S, on behalf of the Integrated Epilepsy Research Group. Sexual function in Thai males with epilepsy. J Med Assoc Thai 2019;102(Suppl.3):12-8.

It plays important parts in enhancing sexual desire and maintaining adequate sleep-related erections. When getting older, Androgen hormone, in contrast, decreases. This affects the physical and mental changes of men. Doctors call men at this age "andropause". Reduction of hormone causes high serum lipid and blood becomes easily clogged[10,11]. Therefore, men at old age usually become obese, and have the risk of vascular disease (coronary heart disease, stroke, sexual dysfunction). When the sex hormone decreases, men will have erectile dysfunction, less sexual desire, stress, and irritation. They, in addition, get angry easily, sometimes feel hot and then shortly turn to become cold, sweaty, very distracted, and also develop insomnia, less strength and loss of hair. The body structures, such as bones, begin to degenerate. The muscle turns thinner (muscle atrophy). There are risks for diseases such as heart disease, osteoporosis, benign prostatic hyperplasia, difficult urination and excess fat[12]. Andropause men, therefore, are likely to become obese. In addition to the decrease of testosterone levels owing to increasing age, there are also other factors causing men to become andropause earlier than usual, such as hereditary, hard work and less rest, stress, obesity, lack of nutrients such as zinc and minerals, binge drinking and smoking, chronic diseases (such as diabetes, hypertension, kidney failure, etc), excessive exercise, and taking certain medications, especially psychoactive drugs: sertraline, venlafaxine, citalopram, paroxetine, fluoxetine, imipramine, phenelzine, duloxetine, escitalopram, and fluvoxamine, induce SD ranging from 25.8% to 80.3% of patients[13].

Epilepsy is a neurological disease found in around 50 million patients worldwide[14]. In Thailand, despite 1 to 2% of the population have epilepsy; it remains a mysterious disorder shrouded in myths and misunderstanding for most people[15]. According to a recent study, people with epilepsy had sexual dysfunction about five times more than normal people[16] with a prevalence of 50 to 66%, compared to 20 to 22% of normal people[17]. The causes of sexual dysfunction in epilepsy patients vary, including: 1) neuro-endocrinological factors derived from abnormalities of hypothalamic-pituitary-adrenal axis and sex steroid hormones[18], 2) Iatrogenic factors from antiepileptic drugs, particularly the drug with its quality as an enzyme inducer or enzyme inhibitor, such as carbamazepine, phenytoin, phenobarbital[19,20], valproate, levetiracetam[21], 3) psychosocial factors from stress, anxiety and depression[22-24], 4) vasculogenic consideration from the degeneration of the tissue around blood vessels, such as atherosclerotic changes[25-27], 5) combination of these etiologies that is, there are many coexisting causes. Regarding the antiepileptic drugs, it was found that some drugs have hepatic enzyme induction, such as carbamazepine and phenytoin, resulting in increasing metabolism of testosterone. Valproate, an enzyme inhibitor, and other drugs which have high protein binding increase free androgen hormone in the blood level[28]. A study by Han[21] reported that patients receiving sodium valproate and levetiracetam had lower level of luteinizing hormone (LH) and follicle-stimulating hormone than the control group. The patients receiving valproate demonstrated that prolactin and proportion of testosterone/LH were higher, but sperm morphologic abnormality was found and sperm motility rate became worse.

Srinagarind Hospital has been operating Epilepsy Clinic since 2003. In 2015, there were 1,172 patients visited to the clinic, 553 males (47.18%), 619 females (52.82%). Of the 203 interviewed patients, from both male and female, 44.3 percent had a change concerning their sexual relationship after having the onset of epilepsy. The three most common abnormalities in the men with epilepsy were as follows; decreased sexual arousal, decreased sexual desire, and decreased rate of sexual intercourse[15].

Although sexual dysfunction is not a serious problem or life threatening, it makes men lack self-confidence and have low self-esteem, have stress, anxiety, and poor quality of life. It causes problems in married life and can lead to family problems. In particular, in epilepsy patients, the problem is more complex than that of normal people in terms of both the disease and the medication. Therefore, the researcher aimed to find the prevalence and severity of sexual dysfunction and factors or causes associated with the severity of sexual dysfunction. This basic information is beneficial for the holistic development of caring patients with epilepsy.

Objectives

1) To study the prevalence of sexual dysfunction among epilepsy patients at Epilepsy Clinic Srinagarind Hospital, Faculty of Medicine, Khon Kaen University.

2) To evaluate the problem of partial androgen deficiency of the aging male: PADAM in epilepsy patients.

3) To investigate risk factors associated with sexual dysfunction in epilepsy patients.

Materials and Methods

Research design

The prospective study method was applied.

Location

Epilepsy Clinic, Srinagarind Hospital, Faculty of Medicine, Khon Kaen University.

Target population

Patients receiving services at Outpatient Department, Epilepsy Clinic Srinagarind Hospital, Faculty of Medicine, Khon Kaen University.

Population

All patients receiving services who were willingly to respond to the questionnaire at the data collection period at the Outpatient Department, Epilepsy Clinic Srinagarind Hospital, Faculty of Medicine, Khon Kaen University.

The criteria are as follows

Inclusion criteria

Men with epilepsy aged 18 to 60 years old, who received treatment at Epilepsy Clinic and were willing to

participate in the research study during the time of data collection.

Exclusion criteria

The patients incapable of reading or responding to the questionnaire.

Security of confidential data of the volunteers

To keep the volunteers' data confidential, only volunteer's code number in numerical order was written in the questionnaire form. When finished answering, the volunteers dropped the form in the box provided at the clinic room. The code numbers matched the basic information previously given by the volunteers.

Research tools

1) International index erectile function (IIEF) and partial androgen deficiency of the aging male (PADAM) questionnaire translated in Thai version.

2) Patient database from the medical record and electronic information.

Data collection

1) The patients under study answered the questionnaire on IIEF and PADAM.

2) The data of the participants were collected on the type of epilepsy, on set of disease, causes of epilepsy, duration of treatment when the seizure occurs, the type and the dose of antiepileptic drug being taken, all of which are derived from the outpatients' medical records and electronic database.

The time of data collection

After approval by the Ethics Committee for Human Research (HE591085), Khon Kaen University, the questionnaire was administered to the male patients who came to receive the treatment at Epilepsy Clinic, Srinagarind Hospital. The data were collected from epilepsy male patients who are willing to participate at Epilepsy Clinic from June 1 to December 31, 2016.

Statistical analysis

The basic information collected included: age (year), occupation, education, marital status, weight, height, number of children, age at the onset of epilepsy, and duration of treatment.

Data and score from the questionnaire were calculated into means and percentages when presented as an overview and input into Microsoft Excel 2007 as database. Continuous data, the age, were calculated and presented by means and standard error of mean (SE). The categorical data, such as marital status and education, were calculated as enumeration and percentage. The questionnaire score was divided into the severity of sexual dysfunction and clinical symptoms of testosterone deficiency. Then the score was investigated to find its relationship with various factors; types of epilepsy, duration and frequency of seizures, and antiepileptic drugs, with STATA program version 10 of which Khon Kaen University had bought the copyright.

Terms and definitions

Epilepsy patients refers to patients who have been diagnosed with epilepsy by a physician specialized in internal medicine or a neurologist, or a psychiatrist.

Erectile dysfunction refers to men with erectile dysfunction whose score on sexual performance (IIEF questionnaire) is equal to or less than 21 points.

Partial Androgen Deficiency of the Aging Male (PADAM) refers to a man with physical or neurological and circulatory system problem (vasomotor) or mental illness (psychological) or sexual problem. The interpretation of the decease of testosterone in males is that the total score of physical symptoms and neurological and circulatory symptoms is more than or equal to 5 points, or that the total psychological symptom score is more than or equal to 4 points, or that the total sexual problem score is more than or equal to 8 points.

Seizure frequency

1) Very frequent: several times a day or intervals shorter than 7 days per month.

2) Frequent: intervals longer than 7 day to 6 weeks shorter than 30 days per month.

3) Occasional: intervals longer than 30 days per month but shorter than one year.

4) Rare: intervals longer than one year.

Degree of control on antiepileptic drugs (AEDs)

1) Controlled: seizure free for ≥1 year.

2) Partially controlled: occasional seizure.

3) Uncontrolled: frequent or very frequent seizure.

Results

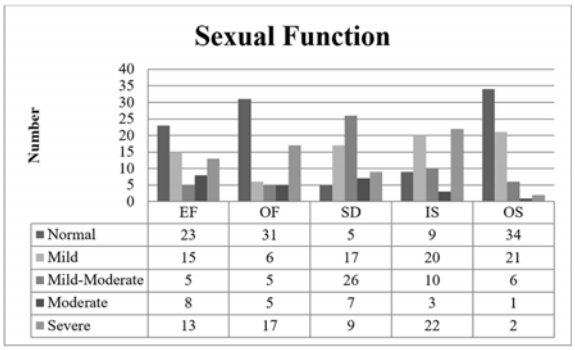
Baseline characteristics

Based on the data collected at Epilepsy Clinic, Srinagarind Hospital, Faculty of Medicine, Khon Kaen University from June 1 to December 2016, there were 404 epileptic patients: 183 males (45.3%), 221 females (54.7%). There were 64 eligible patients who were willing to participate in the study (general data shown in Table 1). The average age of the patients was 40.53 years. Most completed at least a bachelor's degree. Regarding marital status, most patients were married but had no children (51.56%). For the patients having children, most had two children. The average age at the onset of epilepsy was 25.24 years. The average year of treatment was 12.27. The type of seizure mostly found was complex partial seizure (16 people), followed by GTC (15 people). However, there were 29 cases that the doctor identified as epilepsy without specifying the type of epilepsy. More than half of the patients (59.37%) were unable to control the seizure. The retrospective search revealed that 25 (39.06%) patients had a history of undergoing electroencephalography (EEG) and 31 (48.44%) patients had received radiological examination of the brain. The results of the

Table 1. Demographic data of patients with epilepsy (data are present as mean ± SE or number of participant, 95% CI or %)

Variables	Mean ± SE	95% CI or %
Age (years)	40.53±1.66	37.20, 43.86
Weight (kilogram)	68.49±1.58	65.35, 71.65
BMI (kilogram/meter^{-2})	24.35±0.47	23.41, 25.29
Education		
Primary level	4	6.25%
Secondary level	17	26.56%
Diploma level	7	10.94%
Undergraduate level	33	51.56%
Not educated	3	4.69%
Marriage status		
Single	26	40.62%
Married, living together	32	50%
Married, living apart	3	4.69%
Widowed, divorced	3	4.69%
Number of children		
No children	33	51.56%
1 child	6	9.37%
2 children	22	34.37%
3 children	3	4.69%
Age at the onset of epilepsy	25.24±1.93	21.38, 29.09
Duration of treatment (year)	12.27±1.43	9.41, 15.13
Types of seizure		
Generalized tonic clonic (GTC)	15	23.44%
Partial seizure	2	3.12%
Complex partial seizure	16	25%
Myoclonic	1	1.56%
Abdominal epilepsy	1	1.56%
Not identified	29	45.31%
No. of seizure per month	2.64±0.71	1.22, 4.07
Seizure controlled		
Controlled	24	37.5%
Partially controlled	2	3.12%
Uncontrolled	38	59.37%
Electroencephalography (EEG) (n = 25)		
Examined: normal	6	24%
Examined: abnormal	19	76%
CT or MRI brain (n = 31)		
Examined: normal	11	35.48%
Examined: abnormal	20	64.52%

examination of the rest could not be found or they might not have been examined. The abnormalities detected by EEG included epileptic form discharged in different areas of the brain, namely temporal area (8 cases), parietal area (6 cases), parieto-temporal area (4 cases) and fronto-temporal area (1 case). Meanwhile, the radiological examination revealed the abnormalities of brain as follows: ischemic lesions, brain atrophy, temporal sclerosis, lacunar infarction, subarachnoid hemorrhage, and brain abscess. There were 15 patients with other diseases. The most commonly coexisting diseases were diabetes mellitus (4 cases), hyperlipidemia (5 cases), hypertension (5 cases), ischemic stroke (3 cases), valvular heart disease (2 cases). The diseases found in one patient



EF = erectile function; OF = orgasmic function; SD = sexual desire; IS = intercourse satisfaction; OS = overall satisfaction

Figure 1. The number of patients with sexual dysfunction and the severity level.

included delusional, obsessive compulsive disorder, adjustment disorder, alcohol dependence, gout, asthma, colon cancer, liver cancer, cavernous sinus syndrome, and head injury. The antiepileptic drugs mostly taken were sodium valproate (42 cases), phenytoin (25 cases), carbamazepine (12 cases), clonazepam (9 cases), levetiracetam (8 cases), lamotrigine (6 cases), phenobarbital (5 cases), topiramate (4 cases), diazepam (1 case) and gabapentin (1 case). There were 28 patients taking only one type of the antiepileptic drugs, 17 patients taking 2 types, 12 patients taking 3 types, and 1 patient taking 4 types. The rest were able to stop taking drugs.

Sexual function

Evaluation of sexual performance showed that 64.06% of the patients had erectile dysfunction (EF), 51.56% had orgasmic dysfunction (OF), 92.19% had sexual desire problem (SD), 83.94% were dissatisfied with their sexual intercourse (IS), and 46.87% were dissatisfied with their overall sexual performance (OS). The severity of sexual dysfunction in different aspects is illustrated in Figure 1. When we were considering each patient, there was only one person who had no problems at all. There were 18 patients had every problem (EF, OF, SD, IS, and OS), 16 people had 4 problems, 11 people had 3 problems, 13 people had 2 problems, and 5 people had only one problem (data not shown). When the dimensions of sexual dysfunction were examined to find their correlation with the factors, it was found that there were no relationships to age at the onset of epilepsy, duration of treatment, type of seizure, frequency of seizures, or the type of antiepileptic drugs.

Erectile function finding, male with epilepsy had high frequency rate of ED (64.6%), mostly of mild degree (36.58% or 15/41), 31.71% or 13/41 for severe degree (Figure. 1).

Partial androgen deficiency of the aging male (PADAM)

According to the evaluation of partial androgen deficiency in aging men (PADAM, it was found that 50% of

the patients have physical and neurological problems and circulatory problems. There were 60.94% having psychological problem and 15.63% having sexual problem Table 2).

Discussion

The results of the present study showed the prevalence of erectile dysfunction in male with epilepsy at Srinagarind Hospital, Khon Kaen University was higher than normal population[29] and was not different from the previous research study[30,31], but what was different from the previous study report was the factors associated with this problem. It was found that none of the factors was related to sexual dysfunction nor was its severity[16,32]. The most common problem was sexual desire which agreed with the study previously reported in this group of patients[15], followed by intercourse dissatisfaction, which was a related problem. However, although patients had sexual dysfunction, about half of them had overall satisfaction of their sexual performance. Regarding the diagnosis with PADAM, it was found that there were only 10 (15.63%) people having sexual problem. This is likely because there were only three choices in the PADAM questionnaire, compared to 5 choices in IIEF questionnaire which gives more details on severity of the problem. It is noteworthy that the number of people with sexual problems from PADAM assessment is close to IIEF assessment with the highest severity (20.31%).

One-third of our patients had a coexisting disease. As already known literature, a higher probability of sexual function was directly correlated with heart disease, hypertension, diabetes, associated medications, and indexes of anger and depression, and inversely correlated with serum dehydroepiandrosterone, high density lipoprotein cholesterol[6,32].

Differently from the previous studies conducted in this group, type of seizure had a significant correlation with erectile function score. None of the IIEF domains scores were different between the patients with controlled epilepsy and those with uncontrolled epilepsy[33]. In our study we did not find any significant relationship between a particular type of focal or generalized epilepsy and sexual dysfunctions nor analyzing seizure severity or seizure frequency. It could be explained, first of all, considering our small sample. In previous study, GTC was the common type of epilepsy, but in our study found seizure types included generalized tonic-clonic in 23.44% of patients, complex partial in 25%, simple partial in 3.12%, and 45.31% of patients had no identifies of seizure type.In addition, EEG, CT/MRI brain were obtained in 81.2% (our study 39.06%), 78.7% (our study 48.44%) of patients, respectively. The previous report found, etiology of epilepsy was cryptogenic, symptomatic and idiopathic; the commonest were intracranial infection, cerebral vascular disease, cranial trauma and perinatal insult. Our study found same etiology, and other cause was temporal sclerosis. Phenytoin, carbamazepine and valproate were the most frequently used drugs and 25.9% (the present study 29.31%) of patients were taking more than two drugs. 48.3% (59.37%) of patients had active seizures in the past six months[34]. No differently from previous studies, almost of them accepted the necessity of AEDs, and strong concerns about the potential negative effects of AEDs[35].

Table 2. Partial Androgen Deficiency of the Aging Male (PADAM) problem

Testosterone deficiency	Normal n (%)	Abnormal n (%)
Physical and vasomotor	32 (50)	32 (50)
Psychological	25 (39.06)	39 (60.94)
Sexual	54 (84.37)	10 (15.63)

The present study also observed an interesting trend toward better adherence rates with both older and newer AEDs, as observed previously report. Sexual dysfunction associated with newer anti-convulsants is likely to occur through different mechanisms. Some anti-convulsants such as oxcarbazepine and lamotrigine may improve sexual function, but can also rarely be associated with sexual dysfunction[36]. However, we cannot be certain as the present study was not designed to address tolerability of AEDs. Sexual dysfunction is a key AE leading to AED non-adherence[37]. Another interesting finding was that more than half of the present study population were still receiving older-generation AEDs[38]. Seizures in medial temporal lobe structures, through their connectivity to the hypothalamus, alter the secretion of gonadotropins. Levels of circulating bioavailable testosterone are affected by changes in the level of binding proteins, which in turn may be affected by seizure medications. The use of older generation medications that induce the cytochrome P450 system is associated with an increase in sex hormone-binding globulin and lower bioactive testosterone. Sexual dysfunction, including decreased libido and decreased potency, and infertility, is seen commonly in men with epilepsy. However, its relation to sex hormone levels remains unclear. Comorbid depression and anxiety may be important confounding factors. Testosterone and sexual function appear not to be affected by the newer generation (noninducing) anticonvulsants[39].

The most common manifestations of sexual dysfunction in patients with epilepsy are hyposexuality and erectile dysfunction. The cause of this dysfunction is multifactorial and overlapping, and includes changes in the levels of sex hormones, anti-convulsants, the epilepsy itself and psychosocial factors. Traditional anti-convulsants which induce the cytochrome P450 enzyme system have the highest rates of sexual dysfunction, which is primarily mediated by changes in sex hormone levels[36]. Therefore, epilepsy-related ED may have a substantial neurophysiologic component[40]. The management of sexual disorder must include interdisciplinary investigational and therapeutic strategies[41].

Limitation of the study

There were some missing or incomplete information

in the present study, such as electroencephalography, radiological examination, type of seizure, and so on because various medical records at Srinagarind Hospital were being changed from paper to electronic recording, resulting in incomplete data collected from OPD cards. Some cards were not scanned, or some patients brought their brain scan results from other hospitals and kept them back home after showing them to their physicians without scanning them in the computer system.

Sexuality may be a sensitive subject to discuss openly, a questionnaire might give more correct data than an interview, but questionnaires have the disadvantage that misunderstandings in some case.

The present study population was recruited from tertiary epilepsy center. This implies selection of patients with difficult-to-treat epilepsy. Thus, out results may not be representative of the general males with epilepsy population.

Conclusion

The results of the present study indicate that men with epilepsy are more likely to have sexual dysfunction and psychological problems. Therefore, the holistic care of the Epilepsy Clinic, Srinagarind Hospital, Faculty of Medicine Khon Kaen University, in addition to evaluating and treating seizures, should include evaluation on sexual performance and mental status of patients with epilepsy in order to improve the quality of life of the patients.

What is already known on this topic?

Sexual dysfunction (SD) is common with epilepsy. The etiology of SD in patients with epilepsy is multifactorial, involving neurological, endocrine, iatrogenic and psycho-social.

What this study adds?

Information of prevalence, severity, and coexisting factor of SD in Thai male with epilepsy. This basic information is beneficial for the holistic development of caring for males with epilepsy at our clinic.

Acknowledgements

The authors are grateful to the Integrated Epilepsy Research Group, Khon Kaen University, Thailand for the funding support.

Potential conflicts of interest

The authors declare no conflicts of interest.

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