Hypoactive sexual desire disorder caused by antiepileptic drugs

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ABSTRACT

Female sexual dysfunction is common but poorly understood sexual problem in women. Sexual dysfunction in female is multi-factorial in origin and also observed with intake of drug acting on central nervous system. This case report describes a female epileptic patient who developed sexual dysfunction with intake of antiepileptic drugs.

KEY WORDS: Antiepileptic, epilepsy, female sexual dysfunction, hypoactive sexual desire disorder

INTRODUCTION

Female sexual dysfunction (FSD) is highly prevalent but poorly understood clinical entity.[1] FSD is defined as a disorder of sexual desire, orgasm, arousal and sexual pain that results in significant personal distress.[2] A survey estimated prevalence of hypoactive sexual desire disorder (HSDD) 16%, sexual arousal disorder (lubrication) 7%, orgasmic disorder 8%, and dyspareunia 1% when FSD is associated with distress.[3]

Masters and Johnson, in 1966, was the first to describe a normal female sexual response cycle into four phases: Excitement, plateau, orgasm and resolution. While in 1979, Kaplan further divided excitement phase into desire and arousal and removed plateau phase.[2,4] Integration of psychological, neurovascular and hormonal factors is implicated in a normal female sexual response cycle. In a normal sexual response cycle, a sexual arousal result in increases blood flow to the clitoris and labia minora with subsequent engorgement of these organs. This causes protrusion of glans clitoris and eversion and engorgement of a labia minor and further increase in blood flow to vagina and uterus. In response to this, uterus and Bartholin's glands start to secrete, which provide vaginal lubrication.[2]

Initially, the Diagnostic and Statistical Manual of Mental Disorders (DSM-4) classified FSD into four categories: HSDD, female sexual arousal disorder, female orgasm disorder and pain disorder.[5] However, revised version of DSM-5 divided FSD as: Female sexual interest/arousal disorder, female orgasmic disorder, and genito-pelvic pain/penetration disorder.[6] Revised diagnostic criteria (DSM-5) for sexual dysfunction state that the disorder must be experienced 75–100% of the time with an exception of substance or medication-induced disorder, with a minimum duration of 6 months and must cause significant distress.[4,6]

Hypoactive sexual desire disorder, is now merged into female sexual interest/arousal disorder,[6] is a common type of FSD characterized by decrease in sexual desire that results in marked personal distress and/or interpersonal difficulty.[7] In female with HSDD, persistent or recurring absence of sexual fantasies and thoughts along with lack of responsiveness to sexual activity results in sexual dissatisfaction with adverse effect on quality of life.[2,4,7]

Sexual dysfunction in female is multi-factorial in origin involving anatomical, physiological, medical, psychological and social factors.[8] FSD develops commonly with pelvic surgeries, ageing, and in a postpartum period. However, medications such as antihypertensive agents, chemotherapeutic agents, antiandrogens, and drug acting on central nervous systems are also possible mediators for sexual dysfunction.[2] Studies conducted in male epileptic patients have

well documented results of association between antiepileptic drugs (AEDs) and sexual dysfunction.[9-11] However, very little is known about association between AEDs and FSD. This case report describes a female epileptic patient who developed HSDD with AEDs.

CASE REPORT

A 30-year-old married female patient came to a psychiatric outpatient department with old history of seizure disorder since 9 years. Earlier patient was on antiepileptic treatment (oxcarbazepine 150 mg twice a day and clobazam 5 mg at night) for 1-year but had poor and erratic compliance to medications. Patient was started on oral oxcarbazepine 300 mg and etizolam 0.25 mg both twice a day with clobazam 10 mg at night. After treatment for 2 months, the patient reported decreased interest in sexual desire; absent sexual thoughts along with reduce arousal and satisfaction in sexual activity. She also complained of decreased in lubrication during intercourse. The couple had satisfactory sexual activity earlier before the start of regular AEDs therapy. Her menstrual history and gynecological examination were normal. Her regular blood investigations were normal. Mental status examination revealed no active psychopathology. She had three children of which oldest daughter died 6 months after birth. Now the patient is a mother of two sons aged 7 years and 2 years. Patient denied history of any other medical illness, psychiatric illness or history of pelvic surgery.

She was diagnosed as a case of antiepileptic induced FSD, HSDD type, based on current complaints of diminished sexual desire after commencing regular AEDs therapy and after ruling out other possible etiological factors for FSD like depression or medical illness. As per revised diagnostic criteria (DSM-5) of female sexual interest/arousal disorder (previously HSDD) our patient exhibited three criteria: (1) Decreased sexual interest (2) absent sexual thoughts (3) reduce arousal, and satisfaction in sexual activity.

DISCUSSION

Sexual dysfunctions are commonly reported in epileptic patients in both male and female.[10,12] The estimated prevalence of sexual dysfunctions in epileptic patient ranges from 38% to 71%.[10] The pathogenesis of sexual dysfunction in epileptic is probably multi-factorial in origin.[12] Epilepsy itself is a well-documented cause of sexual disorders due to seizure induced alteration in concentration of sex steroid hormones.[12,13] Sexual dysfunction is also recorded due to depression associated with seizures. A feeling of poor self-esteem or fear of seizure precipitation with sexual activity lead to sexual unattractiveness.[13] Epileptic patients are more prone to develop anxiety disorders due to common involvement of nural regions (Amygdala and Hippocampus).[14] Anxiety and associated fear is also evident as one of the reason for FSD.[2] Moreover, AEDs are also identified as a significant cause of sexual dysfunction due to their effect on hormone and neuroendocrine system.[10]

Use of AEDs is the cornerstone for the management of epileptic seizures. AEDs not only reduce seizure-related risks but improve quality of life of epileptic patients. Approximately, 70% women respond well to monotherapy while remaining 30% requires a combination of two or more AEDs.[15] Mostly all AEDs have several pharmacologic targets and hence contribute to efficacy as well as side effects.[16] Thus, AEDs therapy carries a significant risk due to potential side effects, and sexual dysfunction is noted as one of them.[10,11,16]

Antiepileptic drugs contribute to sexual dysfunction either by direct cortical effect or by alteration in concentration of sex hormones.[13] AEDs especially with enzyme-inducing drugs when get metabolized in the liver increases the activity of the hepatic microsomal enzyme system (cytochrome P450). This in turn increases metabolism of sex steroid hormones and enhances production of sex hormone binding globulin (SHBG). Increase in sex hormone protein binding reduces the level of active sex hormone in blood circulation. Normal sexual function requires normal sex hormone level. However, a decrease in amount of free and biologically active sex hormones results in a reduced sexual drive in a patient on AEDs therapy.[10,13] Urso *et al*. when analyzed the data of 61 male epileptic on AEDs therapy found 36.7% developed sexual dysfunction of which 19.7% had sexual drive dysfunction.[10] A study by Herzog *et al*. compared sexual function, sex hormonal levels and gonadal efficiency in male epileptic patients on various AEDs drugs. Patients on enzyme-inducing AEDs therapy reported high SHBG and low sexual function score as compared to epileptic on lamotrigine therapy and compared to the control men.[11]

A revised diagnostic criteria (DSM 5) of female sexual interest/arousal disorder (HSDD) needs presence of three out of six diagnostic criteria. They are absent or decreased in sex related activities like sexual interest, erotic thoughts or fantasies, initiation of sexual activity or responsiveness to partner's attempts to initiate it, excitement and pleasure, response to sexual clues and genital, and nongenital sensations during sexual activity.[6] Of these six, our patient presented with three criteria of decreased sexual interest, absent sexual thoughts and reduce excitement and pleasure in sexual activity. In spite of history of chronic epilepsy (since 9 years), our patient had satisfactory sexual behavior in initial years. Patient reported symptoms of sexual dysfunction only after initiation of regular AEDs. Hence, though epilepsy is a well-established cause for sexual dysfunction, this may not

be the reason for a low sexual drive in our case. Literature mentioned depression as a cause of sexual dysfunction in epileptic patients. However, in our case, patient had normal mental status examination and no history of psychiatric illness. Our patient is on oxcarbazepine, an AED that induces liver enzymes, since a last 1-year. All these point favors as AEDs as a possible cause for low sexual desire in current case.

Hormone replacement therapy (HRT), reduction in a dose of AEDs and psychological interventions would be different choices for management of HSDD in our case. However, because of concern on AEDs drugs interactions with hormonal supplements, HRT may not be effective in our case. Second, epileptic seizures demand to continue AEDs at current doses to reduce seizure-related risks. Moreover, many AEDs are useful in management of anxiety disorders leading to sexual dysfunction. This is due to suppressive effect of AEDs on outburst of neuronal circuit having a key role in initiation of both anxiety and epileptic seizures.[14] In such scenario, psychological intervention is a better alternative to improve sex life of our patient. Individual and couple-based psychosexual therapy along with additional counseling of the partner is intended to achieve optimal outcomes.[7] Couple should be made aware of the role of foreplay and nonsexual intimacy to improve the desire and sex life.

CONCLUSION

Female on AEDs therapy can experience symptoms of sexual dysfunction due to alteration in concentration of sex steroid hormones. For persistent problem and need to continue AEDs it is necessary to reassess and reconsider the available treatment. Second, psychological interventions and awareness of the role of foreplay and nonsexual intimacy can help to improve the desire and sex life of a couple.

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