



Female sexual function mediates the effects of medication adherence on quality of life in people with epilepsy



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ABSTRACT

Purpose: The purpose of this study was to understand the mediating effects of female sexual functioning in the association between medication adherence and quality of life (QoL) in Iranian women with epilepsy (WWE).

Methods: Women's sexual functioning was measured using Female Sexual Function Index; QoL using Quality of Life in Epilepsy; epilepsy severity using Liverpool Seizure Severity Scale; subjective medication adherence using Medication Adherence Report Scale; and objective medication adherence using serum level for antiepileptic drugs in 567 WWE. Medication adherence was measured at baseline, while women's sexual functioning, QoL, and epilepsy severity were measured at the 6-month follow-up. Structural equation modeling and regression models were conducted to examine the mediating role of women's sexual functioning.

Results: The mediating effects of sexual functioning in the relationship between medication adherence (including subjective and objective measures) and QoL were supported in the total score of Female Sexual Function Index (coefficient = 0.415, SE = 0.117, $p < 0.001$ for subjective medication adherence; coefficient = 1.980, SE = 0.446, $p < 0.001$ for objective medication adherence). Seizure severity was significantly associated with QoL but only when objective medication adherence was measured (coefficient = -0.094 , SE = 0.036, $p = 0.009$).

Conclusion: Our results extended the importance of medication adherence from symptom reduction to the beneficial effects of women's sexual functioning and QoL. Health care providers should be aware of these additional benefits of medication adherence and use these arguments to encourage female patients to take their medication, which can eventually increase their sexual satisfaction and overall QoL.

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1. Introduction

Sexuality is an important component of quality of life (QoL) in women and men. This is, for example, reflected in the World Health Organization Quality of Life Questionnaire, where the item "Are you satisfied with your sexual life?" is included in the list of questions [1]. Thus, sexuality has to be considered an integral part in an individual's life [2]. Many chronic disorders and conditions have been shown to have detrimental effects on a person's well-being by negatively impacting sexual QoL (sQoL) [3,4]. This is also true for people with epilepsy (PWE). According to a review conducted in 2005, about 20% to 30% of women with epilepsy (WWE) report some form of sexual

dysfunction, including decreased libido or problems with arousal and infrequent orgasms [5]. Women with epilepsy have further been shown to have an earlier onset of menopause [6] which consequently may affect their sexual life due to the influence of menopause-associated changes in sex hormones [7]. Other factors observed to influence sexual functioning in WWE include anxiety, stigmatization, epileptic activity in cortex, and certain antiepileptic drugs (AEDs) [5,8].

Although AEDs may increase a woman's risk for sexual problems due to a range of previously reported drug-related side-effects such as changes in sex hormones [5,9], it is equally possible that the treatment benefits of AEDs may outweigh these negative consequences for a number of reasons. First, AEDs can improve disease symptoms which in turn can lead to a reduction of anxiety and can soften the stigma sufferers often report to be associated with the condition [10]. By decreasing anxiety and minimizing the stigma, women's sexuality may indirectly benefit, especially given the fact that anxiety has repeatedly been reported to be an important risk factor in the development of sexual problems [11]. Second, although some AEDs have been shown to lower certain reproductive hormones [10], this is not the case for all

Abbreviations: QoL, Quality of life; AEDs, Antiepileptic drugs; FSFI, Female Sexual Function Index; QOLIE-31, The Quality of Life in Epilepsy; LSSE, Liverpool Seizure Severity Scale; MARS, Medication Adherence Report Scale; DWLS, Diagonally weighted least squares; PWE, People with epilepsy; WWE, Women with epilepsy.

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AEDs. Lossius et al. [9], studied the change of free testosterone levels in seizure-free women with epilepsy and taking a range of AEDs, and found that valproate in contrast to carbamazepine, did not significantly change free testosterone levels. Similarly, a study conducted by Stephen and colleagues [12] where PWE were randomly assigned to either a group taking valproate or lamotrigine, showed no changes in total testosterone after 6 and 12 months of treatment in either group. Yet another study of 141 PWE (of which 66 were women) demonstrated that lamotrigine even improved sexual function in WWE after changing their AEDs [13]. Overall, it seems that some AEDs can improve epilepsy symptoms without necessarily exerting a negative impact on sexual functioning.

Research has also shown medication adherence to be closely linked to QoL in PWE [14]. People with epilepsy have a high rate of comorbidities (e.g., attention-deficit hyperactivity disorder symptoms and mood disorders) and other somatic and psychological symptoms which substantially and negatively influence their QoL [15,16]. Fortunately, most of the seizure symptoms and negative consequences of the comorbid conditions can be overcome by means of the prescribed AEDs [17]. In this regard, several studies have provided evidence for a positive association between higher level of medication adherence and better QoL in PWE [18–20]. It is, therefore, legitimate to conclude that medication adherence plays an important role for QoL in WWE.

Despite strong evidence for a link between sexuality and QoL [21], between medication adherence and sexuality [13], and between medication adherence and QoL [14,18–20], no studies simultaneously examine the three factors (sexuality, QoL, and medication adherence). Further exploration and identification of mediators of QoL can provide health care providers with additional insights on how to improve female QoL and offer strong reasons to counsel WWE to adhere to prescribed medication to increase their QoL.

Therefore, the aim of the study was to examine the mediating effects of female sexual functioning in the relationship between medication adherence and QoL in an Iranian sample of WWE. Sexual functioning was measured across 6 individual domains and assessment of medication adherence included both a subjective and objective measure.

2. Methods

2.1. Sample, recruitment, and study procedure

This longitudinal study was carried out across four neurologic clinics in Qazvin and Tehran between October 2015 and June 2016; and targeted a sample of WWE. The study was approved by the Ethics Committee of Qazvin University of Medical Sciences prior to participant recruitment and all participants provided informed consent before entering the study. Inclusion criteria were: being an 18 + -year-old female, being in a stable sexual relationship with a male partner for at least the past 6 months, and having been diagnosed with epilepsy according to the International League Against Epilepsy criteria [22]. Patients with other chronic diseases including diabetes mellitus, cardiovascular diseases, hypertension, rheumatic diseases, kidney disease, severe mental and psychiatric disorders, substance abuse or pregnancy, were excluded from the study because of the likely interference with their sexual functioning.

Every patient interested in participating and providing informed consent was screened for eligibility by two trained physicians. Afterward, two trained research assistants informed the potential participants about the study aims, and those willing to participate were asked to sign an informed consent. The study measures were provided for the patients with assistance in a quiet and private clinic room after the patient visited the physician. A small portion of the patients (13%) did not receive formal education, which means that we recruited both literate and illiterate participants. For the illiterate patients, a trained research assistant read all questions including the response scale for them without any further guidance. Identified eligible patients completed a

baseline assessment consisting of a questionnaire asking about socio-demographic information (including age, educational attainment, and monthly income) and self-reported medication adherence. Moreover, blood samples were collected on the same day as an objective measure of AED adherence. Six months later, the patients were re-contacted by telephone and asked to attend the clinic to complete a set of questionnaires assessing sexual functioning, QoL, and seizure severity. Of the 703 patients identified as meeting the eligibility criteria, 19% ($n = 136$) did not agree to participate in the study, resulting in a final sample of $n = 567$. The dropout rate after 6 months was 3.3% ($n = 18$).

2.2. Instruments

2.2.1. Female Sexual Function Index

The Female Sexual Function Index (FSFI) is regarded as the gold-standard for the assessment of women's sexual functioning [23]. It includes 19 items which tap into the following six domains: sexual desire (2 items), arousal (4 items), lubrication (4 items), orgasm (3 items), satisfaction (3 items), and pain (3 items). Except for four items (2 in the desire and satisfaction domains each) with scores that range between 1 and 5, all other items have a score ranging from 0 and 5, with a higher item score indicating better sexual functioning. Subdomain scores can be computed by adding up the relevant items and multiplying it by a predefined subscale weight. The known-group validity of the FSFI has been supported based on its capability to detect significant differences between women with sexual arousal disorder and women without such problems. A translated and validated Persian version of the FSFI exists which – similar to the original English version – has shown satisfactory internal consistencies ($\alpha = 0.72$ to 0.90) and high test–retest reliability (intraclass correlation coefficient = 0.73 to 0.86) [24].

2.2.2. Quality of life in epilepsy

The Quality of Life in Epilepsy (QOLIE-31) instrument includes 31 items, of which one item is a visual analogue scale and the other 30 items are ordinal scales. Questions are responded to on a 6-point Likert-type scale. The QOLIE-31 captures seven domains: seizure worry (5 items), cognitive function (6 items), energy/fatigue (4 items), emotional well-being (5 items), social function (5 items), medication effects (3 items), and overall QoL (2 items). Based on the developer's instruction, each domain score can be converted into a 0–100 scale, with a higher score representing better level of QoL [25]. In addition, an overall questionnaire score can be computed by summing up the average scores of the seven domains. Like the original English version, the psychometric properties of the translated Persian version were satisfactory with high test–retest reliability ($r = 0.68$) and good internal consistency ($\alpha = 0.90$) [25,26].

2.2.3. Liverpool Seizure Severity Scale

The Liverpool Seizure Severity Scale (LSSS) includes 20 items rated on a 4-point Likert-type scale with higher scores indicating more severe seizures. The known-group validity of the LSSS can be rated as satisfactory as it differentiates well between people with severe seizure symptoms and those with minor seizure symptoms [27]. The LSSS has been translated into Persian with excellent internal consistency ($\alpha = 0.90$), test–retest reliability (intraclass correlation coefficient = 0.96), and criterion-related validity ($r = -0.43$ with the total QOLIE-31 score) [28].

2.2.4. Medication Adherence Report Scale

The Medication Adherence Report Scale (MARS) is used for the assessment of subjective medication adherence and includes five items rated on a 5-point Likert-type scale, scoring from *never* (1) to *always* (5). Adding up all items yields a total score with a score equal or greater than 20 suggesting high level of medication adherence [29]. The concurrent validity of the MARS has been supported by means of correlational

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