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Sexual Dysfunction in Bipolar Patients using Lithium

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Abstract

Background: Bipolar Disorder (BD) is a psychopathological condition affecting 1-2% of the population. The best mood stabilizer for its treatment is lithium carbonate. One of its common side effects is Sexual Dysfunction (SD). Studies that specifically assessed this SD suggest a ratio of 25 to 50%.

Objectives: To determine the frequency of SD in patients with BD using lithium, distinguishing this phenomenon between genders.

Methods: This is an association and cross-sectional study whose target population were bipolar patients. Were recruited part of the 105 patients in euthymia at a specialized ambulatory. Internationally validated questionnaires were applied: Hamilton, Young, Arizona Sexual Experience Scales and Male and Female Sexual Quotient. Lithium serum levels and time of euthymia were accessed by the outpatient database.

Results: The SD frequency was 40%, with higher rates among women (71.4%).

Discussion/Conclusion: The higher frequency at women could be explained by the influence of the psychosocial and emotional factors. Is raised the discussion of the peculiarities in the management of lithium in the occurrence of SD and of its active investigation considering the impact in quality of life and therapeutic adherence.There is no association between SD and lithium level, euthymia time, treatment adherence, use of other psychotropics, and climacteric.

Keywords: Sexual dysfunction; Bipolar disorder; Lithium carbonate; Psychotropic drugs; Lithium

Introduction

Bipolar disorder is a chronic and recurrent disorder that affectsboth genders at any age. It has mood alterationscharacterized by two poles varyingbetween mania and depression. It is a frequent medical condition affecting 1 a 2% of world population. Psychotropic drugs could be used for treatment and reduces incapacity and mortality,notable among them lithium,aneffective mood stabilizer for depression or mania episodes, maintenance treatment, decreasing the frequency and severity of new episodes and mitigating the suicide risk. Although have been use in large scale, its mechanism is still unknown, working by intracellular signalization and by genetic transcription by enzymatic inhibition, such as monophosphatase inositol and glicogênio-sintetase-kinase-3-ß (GSK-3-ß) [1-4].

Data relating the use of lithium and the onset of sexual dysfunction are limited [5], differently from other psychotropic drugs - including antipsychotic, antidepressant [6,7] and benzodiazepine medications [8]. However, from preclinical studies, it is known that lithium significantly reduces testosterone levels and spermatogenesis in rats [9], as well as it has an ability to impair the relaxation mediated by nitric oxide of the cavernous body [10]. Regarding the clinical studies, those who describe the prevalence of various adverse effects of lithium report a rate of sexual dysfunction of approximately 5% [11,12] while studies that specifically seek this data suggest a relationship of 25 to 50% [2,13-17].

Currently, the literature defines sexual dysfunction as a clinical syndrome characterized by complaints of sexual dissatisfaction resulting from partial or total blockage of the physiological response evidenced by desire, arousal and/or orgasm [18]. By evidencing sexuality as an indicator of quality of life, the World Health Organization (WHO) establishes sexual dysfunction as a public health issue to be researched and continuously discussed by health professionals in order to repair the limitations reported by them when faced with such theme [18].

Among the most frequent sexual complaints of lithium patients, studies have reported decreasing sexual desire and quality of orgasm in both men and women, obtaining and maintaining erection in men, and decreasing vaginal lubrication in women [16] and not showed a direct association with litemia [15].

Despite the conclusions presented in these studies, some of them presented important biases, such as the use of invalidated instruments for the evaluation of adverse sexual effects [13,15,17] and therapeutic adherence [16], in addition to disregarding the concomitant use of other psychotropic drugs [14] and the distinction between genres. A lack of reliable data is therefore feasible.

The aim of the study was to determine the frequency of SD in patients with BD using lithium, distinguishing this phenomenon between genders. In addition, to explain the epidemiological profile of these patients and to seek the association between lithium serum

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Table 1: Epidemiological profile: age, economy class, time of euthymia and lithium serum level.

Variable	Mean	Median	Standard deviation
Age (19-68 years)	42,43	40,50	12,846
CCEB (10-35 points)	21,60	21,50	5,525
Time of euthymia (1-37 months)	8,37	5,00	9,026
Lithium serum level (0,93-1,12mEq/L)	0,74	0,795	0,304

Table 2: Frequencies of variables: gender, use of other drugs, participation in psycho education group and adherence to treatment.

Variable		Number of patients	Frequencies (%)
Gender	Male	16	53,3
	Female	14	46,7
Use of other drugs	Antidepressants	3	10,0
	Typical antipsychotic	5	16,7
	Atypical antipsychotic	16	53,3
	Benzodiazepine	13	43,3
	Others	9	30,0
Participation in psycho education group	Participate	11	36,7
	Do not participate	19	63,3
Adherence to treatment	Adhere	20	66,7
	Do not adhere	10	33,3

levels, time of euthymia, degree of adherence to treatment and use of other psychotropic drugs with the frequency of sexual dysfunction.

Methods

This is an association and cross-sectional study [19] whose target population were bipolar patients. The non-probabilistic sampling was composed by 105 patients previously diagnosed with BD, recruited for convenience in follow-up at a specialized ambulatory. In this study were included: all euthymic patients at the time of evaluation, using lithium, and with active sexual life. Were exclusion criteria: (i) change in lithium dose by the month prior to the interview and (ii) irregular use of lithium, once the drug takes at least 21 days for ideal therapeutic effect [20]; (iii) be under age 18, due to ethical issues; (iv) last sexual intercourse over more than 01 year ago, respecting the validation of the scales used for SD [21-24]; (v) presence of another psychiatric diagnosis, and (vi) presence of organic mental disorder or significant cognitive difficulty.

Recruited patients accepted voluntarily to participate in the research, signing the informed consent form, approved by the ethics committee of the institution where the research was carried out, and undertook to answer the questionnaires in a reliable manner.

The researchers were calibrated for two months by simulator videos, role play with residents and trained with patients with other disorders other than BD. The instruments used were the following internationally validated questionnaires: (I) to determine patient euthymia: Hamilton Depression Scale [25] and a Young Mania Scale [26]; (II) to detect the presence of SD: Arizona Sexual Experience Scale (ASEX) [22] and Male and Female Sexual Quotient: QS-M [23] and QS-F [24]; (III) to evaluate the treatment: Morisky and Green [27]; and (iv) to stratify the socioeconomic situation: Brazil's Economic Comparison Criteria (CCEB) [28]. The lithium serum level and the time of euthymia were accessed by the outpatient database. The instruments of sexual evaluation could be answered by the patients themselves or filled out by the researchers, which was the option determined by all patients as the most comfortable one.

Data collection lasted 5 months and the results were tabulated, analyzed and processed using the Statistical Package for Social Sciences (SPSS) software version 16.0. Calculations of mean, median and standard deviation were made to define the socio-economic profile, lithium level and the time of euthymia of the patients. The frequency of SD was calculated, as well as gender, use of other medications, adherence to treatment and participation in a psychoeducation group. To establish an association between the variables, chi-maximal and Fisher tests were performed, considering the associations which the value of p was <0.05.

Results

Of the 105 patients recruited initially, 59 patients did not meet the inclusion criteria: 12 patients were non-euthymic and 47 did not use lithium. 4 follow-up losses were identified. Were excluded (12 patients): 01 for change in lithium dose by the month prior to the interview; 03 for irregular use of lithium; 01 were under age 18; 01 for last sexual intercourse over more than 01 year ago, 05 had another psychiatric diagnosis (02 schizoaffective and 03 with personality disorder) and 01 patient with mild mental retardation.

The sample consisted of 30 patients, 16 men and 14 women. Table 1 shows the epidemiological profile of the evaluated group: mean age of 42.43 years; 21.6 points in the CCEB (economy class C1); 8.37 months of euthymia; and 0.74mEq / L of lithium serum level. Table 2 shows the frequencies of other variables collected, such as the gender of the patients; the concomitant use of other drugs, especially psychotropic drugs; participation in psychoeducation group; and adherence to treatment.

Considering the frequency of SD by gender, it was more frequently in women than men, regardless of the sexual scale applied (ASEX: 50% women and 0% men, QS: 64% women and 12.5% men). Considering global frequency, the results showed 70.4% in females and 12.5% in males. By chi-square analysis, this fact is statistically significant (Table 3), regardless of the scale used (ASEX or QS).

The presence of sexual dysfunction in female patients was analyzed using the climacteric phase as a variable, but there was no statistically significant difference (Table 4).

The relationship between the gender of the interviewer and the

Table 3: Statistical analysis of Sexual Dysfunction by gender using chi-square.

Sexual scales	Sexual Dysfunction	Female	Male	TotaVl	*p*
ASEX	**YES**	7	0	7	0,002
	NO	7	16	23	
Total		14	16	30	
QS	**YES**	9	2	11	0,005
	NO	5	14	19	
Total		14	16	30	

Table 4: Statistical analysis of female Sexual Dysfunction and climacteric phase.

Sexual scales	Sexual Dysfunction	Menacme	Climateric	Total	*p*
ASEX	YES	4	3	7	0,704
	NO	4	3	7	
Total		8	6	14	
QS	YES	5	4	9	0,657
	NO	3	2	5	
Total		8	6	14	

Table 5: Statistical analysis of Sexual Dysfunction and others variables.

	ASEX (*p*)	QS (*p*)
Use of Anticonvulsants	0,515	0,646
Use of Antidepressants	0,564	0,239
Use of Antipsychotic	0,671	0,245
Use of Benzodiazepine	0,340	0,579
Adherence to treatment	0,571	0,452
Time of euthymia	0,668	0,316
Lithium serum level	0,557	0,261

gender of the interviewee was evaluated in the application of the questionnaires, without statistical significance. ASEX questionnaire, p = 0.345 and for QS, p = 0.341.

It was analyzed the aspects of the treatment of these patients with the presence of sexual dysfunction. No significant results were found (Table 5).

About the adherence to medication treatment, no association was significant: lithium serum level (p = 0.274), time of euthymia (p = 0.651), gender (p = 0.450), and participation in a psychoeducation group (p = 0.548).

Discussion

The SD frequency evidenced in this study (23,3% by ASEX and 36,6% by QS) is in accordance with literature data (25 to 50%) [2,13-17]. There is no scientific evidence found about the SD caused by the use of lithium in each gender. However, this study demonstrates a fairly significant distinction between genders. Female frequency: 71, 4% (50% by ASEX and 64% by QS-F) against 12, 5% in male (0% by ASEX e 12, 5% by QS-M). This is consistent with the literature regarding the higher prevalence and intensity of SD in women in general population [29]. However, there are few explanations for this difference. Female sexual disorders receive less attention in the investigation of the psychological, physiological and therapeutic aspects [30]. Among the physiological changes that have impact in the loss of sexual interest, we can name: the reduction of genital blood flow with less vaginal lubrication, dryness and fragility of the vaginal mucosa causing intercourse pain, reduction of vaginal contractions to intercourse and orgasm [31]. Was sought the association between climacteric state and SD found in women because hypoandrogenism and drop in testosterone levels at this stage are responsible for decreased libido [31], but there was no statistical significance (Table 4).

The influence of psychosocial factors in women SD was questioned, since any of the phases of the sexual response (desire, excitement, orgasm and resolution) can be influenced by the emotional and physical state of the individual [32]. Female SD can be a reflection of continuous stress or negative emotional states resulting from prohibitions and disapprovals [33], justifying how complex is to establish if the phenomenon has a causal association with adverse drug effects, basic psychiatric pathology, and previous sexual and conjugal difficulties of the patient or a combination of those factors [18].

In view of the low frequency of SD in men, was proposed that them could be less exposed to the adverse effects of lithium by the fact that they present lowest treatment adherence, but there was no statistical significance (p = 0.450). A possible bias of prevarication related to the gender of the interviewer was considered, due to the constraint of the male patients before the woman interviewer during the application of the questionnaires, however, there was no statistical significance: ASEX, p = 0.345; QS, p = 0.341.

In this study, treatment adherence (66.7%) was superior to what is found in the literature (28.5%) [34], what is not explained by the association between gender (p = 0.450), time of euthymia (p = 0.651), lithium serum level (p = 0.274), and the participation of patients in the psychoeducation group (p = 0.548). Itsuggested that this finding could be associated with family support [35], an aspect widely reported by the patients during the interviews, besides the research take places at a specialized outpatient clinic, where patients have individualized psychoeducation, as well as faster return and research participation.

In disagreement with the literature, that shows us high frequency of SD in patients using antidepressants (59.1%) [36], in the present study, only 03 patients used this type of medication, of which only 01 had SD. Thus, the analysis did not allow a significant result (Table 5), which can be justified by type 2 probabilistic error.

Also discordant in the literature, the association of benzodiazepines and lithium causing SD was not significant (Table 5). Other studies show an association of 49% [15].

Due to its study design, this research generated hypotheses, without being possible to test them; defining without high certainty if the results found had a causal or no causal relationship [37].

Besides, our data collection was limited because the exposure and outcome were analyzed at the same time. It is emphasized the difficulty in working with questionnaires, due to the elimination of the information bias, since we are subject to the subjectivity of the volunteer; even though we work with internationally validated questionnaires and calibrated interviewers, which reduces calibration bias [37].

Conclusion

The SD frequency of the study (40%) was consistent with literature data (25 a 50%), and with non-association with lithium serum levels. The females SD was significant (71, 4%), but without association with climacteric, time of euthymia, adherence to treatment and use of others psycho tropics. Further studies are suggested only with bipolar women, with and without lithium use to identify the frequency of SD independently to the use of lithium and other study with

bipolar woman and healthy woman to evaluate the involvement of psychosocial and cultural factors. Due to the high frequency found, the discussion of the peculiarities in the management of lithium in the occurrence of SD and of its active investigation considering the quality of life and therapeutic adherence is reinforced.

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