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An interdisciplinary intervention for detection of sexual dysfunction associated with antidepressants: A pilot study

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Abstract

Introduction: Treatment-emergent sexual dysfunction (TESD) is a commonly reported side effect of antidepressant medications in clinical trials. Limited literature exists exploring the role of routine use of the Arizona Sexual Experience Scale (ASEX) in identification of TESD in clinical practice. Therefore, we completed a retrospective study with the primary goal of capturing the rates of sexual dysfunction associated with antidepressant use among adult patients at an outpatient encounter with a psychiatric clinical pharmacist between June 2020 and March 2022.

Methods: Rates of identification of sexual dysfunction were compared pre-ASEX survey (June 2020 to June 2021) to post-ASEX survey (July 2021 to March 2022).

Results: There was a significant increase in the identification of sexual dysfunction following implementation of the ASEX scale (10% in the pre-ASEX group versus 59% meeting sexual dysfunction criteria with the ASEX scale). Approximately 70% of patients in the post-ASEX group shared they would not have reported symptoms unless directly asked.

Discussion: In conclusion, a validated survey (ASEX) in an ambulatory psychiatry clinic improves identification of sexual dysfunction associated with antidepressants. Use of interdisciplinary care teams in the setting of medication follow-up can assist with identifying tolerability concerns between visits with patients' prescribing clinicians.

Keywords: antidepressants, treatment emergent sexual dysfunction, pharmacist, outpatient psychiatry

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Introduction

Treatment-emergent sexual dysfunction (TESD) is a commonly reported side effect of almost every antidepressant medication, but understanding the prevalence of patients experiencing antidepressant-induced TESD is complicated due to apparent differential risk within and among medication

classes.[1–5] Additionally, reports of TESD range from 15% to 20% when considering patients spontaneously reporting this side effect compared with 14% to 73% once patients are specifically asked about sexual side effects associated with antidepressants.[1–5]

Given that it seems likely many patients with TESD are missed when relying on unsolicited reporting, it is crucial to ask patients about this potential medication side effect. The Arizona Sexual Experience Scale (ASEX) is a validated, 5-item scale assessing sexual function over the past week that has been studied for self-identified females and males and can be either self or clinician rated.[1,6,7] The ASEX scale's domains assess sex drive, arousal, erection in natally assigned males and vaginal moistness in natally assigned females, ability to reach orgasm, and orgasm satisfaction.[6] The scale has excellent internal consistency, scale reliability, and strong test-retest reliability in addition to having been utilized to assess rates of TESD in antidepressant clinical trials.[7]

Background

The ambulatory psychiatry clinic at our institution consists of psychiatrists, nurse practitioners, psychologists, physician assistants, social work clinicians, medical and pharmacy residents and students, and a psychiatric clinical pharmacist. The ambulatory psychiatric pharmacy service is referral-based and consists primarily of over-the-phone follow-up on medication changes between prescriber visits focusing on tolerability and efficacy assessments. One psychiatric clinical pharmacist is dedicated to the ambulatory psychiatric service 4 half-days per week. There is not a collaborative practice agreement in place allowing for pharmacist prescribing in this setting, so recommendations for medication changes are sent to the prescriber.

Prior to July 2021, there was no standardized method for addressing sexual dysfunction caused by antidepressants in the adult ambulatory psychiatry clinics. Based on the available literature, this suggested that our care teams were potentially missing patients who could be experiencing antidepressant-induced sexual dysfunction. Therefore, in July 2021, the ASEX scale was added to the adult psychiatry pharmacy services follow-up calls to identify and improve follow-up regarding antidepressant-associated sexual dysfunction. Additional questions were added related to patient perceptions on the relationship between medication changes and sexual function, and if patients would have reported symptoms of sexual dysfunction without being prompted after the assessment was complete. The authors hypothesized that addition of the ASEX scale would increase identification of TESD in the clinic.

Methods

This was an institutional review board–exempt, retrospective, quality improvement study involving adult patients using any antidepressant with an ambulatory psychiatry pharmacy services medication phone outreach encounter. Data on the post-ASEX survey group was collected via chart review from July 2021 through March 2022. Presurvey data was collected via chart review from June 2020 through June 2021. Patients in the presurvey cohort were randomly collected from encounters within the time frame listed to equal the number of postsurvey patients. Inclusion criteria consisted of adults $\geq$18 years old with an ambulatory psychiatry pharmacy follow-up encounter. Exclusion criteria consisted of encounters with patients not prescribed antidepressants at the time of the encounter. Exclusion criteria for the postsurvey cohort also included ASEX scale not completed during a pharmacist follow-up encounter. The following elements were collected via chart review: baseline demographics, diagnoses, concomitant disease states and risk factors that could contribute to sexual dysfunction (eg, alcohol use disorder and obesity, concomitant medications that could contribute to sexual dysfunction such as benzodiazepines and beta-blockers), if history of sexual dysfunction due to medication was previously documented, antidepressant medication class, and medication intervention recommended by the pharmacy team and if those recommendations were accepted.

The primary outcome was to compare incidence of sexual dysfunction identified during a clinical psychiatric pharmacist follow-up encounter as noted before and after implementation of the ASEX scale. For the presurvey group, this was measured by reported incidence by patient to pharmacist or pharmacy resident during selected phone encounters. Reported incidence was defined by any reported symptom of sexual dysfunction. For the postsurvey group, this was measured by an ASEX score of greater than or equal to 19, any single item with a score of 5 or greater, or any 3 items with a score of 4 or higher. The maximum possible ASEX score is 30. Secondary outcomes included patient's self-reported likelihood of reporting sexual dysfunction without being prompted and any recommended medication intervention by the pharmacy team and if it was accepted. History of sexual dysfunction was determined by searching key phrases in the patient's electronic medical record, such as sexual dysfunction, libido, erection, impotence, arousal, and orgasm. Psychiatric diagnoses were gathered from the patient's psychiatry encounter that prompted referral to ambulatory psychiatry pharmacy services. Concomitant medications and medical diagnoses were determined by problem list and medication list at the time of the pharmacist phone encounter.

TABLE 1: Demographics

Demographics	Presurvey (n = 39)	Postsurvey (n = 39)	*P* value
	Mean (SD)		
Age, years	39 ± 16.1	39 ± 13.9	.91
Weight, kilograms	86 ± 28.0	91 ± 30.2	.41
BMI	30 ± 9.9	32 ± 9.1	.28
	Count (%)		
Female	22 (56)	27 (44)	.48
Race			
White	30 (76.9)	32 (82.1)	.77
Hispanic	4 (10.3)	0	.11
Black	2 (5.1)	6 (15.4)	.26
Asian	1 (2.6)	0	1.00
More than one	2 (5.1)	1 (2.6)	1.00
Diagnosis			
Depression	35 (89.7)	22 (56.4)	.0018
Anxiety	32 (82.1)	31 (79.5)	1.00
Bipolar Disorder	1 (2.6)	5 (12.8)	.20
PTSD	2 (5.1)	1 (2.6)	1.00
Concomitant Disease States			
T2DM	3 (7.7)	1 (2.6)	.61
CV Disease	10 (25.6)	4 (10.3)	.13
HLD	7 (17.9)	6 (15.4)	1.00
Alcohol Use Disorder	2 (5.1)	1 (2.6)	1.00
CKD	2 (5.1)	0	.49
Obesity	3 (7.7)	6 (15.4)	.48
History of Spontaneously Reported Sexual Dysfunction	15 (38.5)	18 (46.2)	.64
Reported to			
Primary Care	3 (7.7)	6 (15.4)	.48
Psychiatrist	11 (28.2)	10 (25.6)	1.00
Pharmacist	1 (2.6)	0	1.00
Concomitant Medications			
Benzodiazepines	5 (12.8)	9 (23.1)	.37
Beta-Blockers	3 (7.7)	2 (5.1)	1.00
ACEi	2 (5.1)	1 (2.6)	1.00
CCBs	3 (7.7)	3 (7.7)	1.00
Thiazides	3 (7.7)	2 (5.1)	1.00
Alpha-Blockers	3 (7.7)	2 (5.1)	1.00
Amphetamines	7 (17.9)	5 (12.8)	.75
Cannabis	4 (10.3)	0	.11
Opiates	3 (7.7)	1 (2.6)	.61
History of Tobacco Use	8 (20.5)	4 (10.3)	.34
Antidepressant			
SSRI	20 (51.3)	23 (59.0)	.64
SNRI	5 (12.8)	5 (12.8)	1.00
Bupropion	5 (12.8)	4 (10.3)	1.00
TCA	3 (7.7)	0	.24
Other	4 (10.3)	7 (17.9)	.51

ACEi = angiotensin-converting enzyme inhibitor; BMI = body mass index; CCB = calcium channel blocker; CKD = chronic kidney disease; CV = cardiovascular; HLD = hyperlipidemia; PTSD = posttraumatic stress disorder; SD = standard deviation; SNRI = serotonin and norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor; T2DM = type 2 diabetes mellitus; TCA = tricyclic antidepressant.

All analyses were conducted using IBM SPSS version 28.0.1.0. Baseline demographics were analyzed using unpaired *t* test for continuous variables and Fisher exact test for categorical variables. A Fisher exact test was used to assess the primary outcome. Descriptive statistics were used for all secondary outcomes. Continuous variables are presented as means with standard deviation, and categorical variables are presented as percentages.

Results

Baseline Demographics

From July 2021 to March 2022, 39 patient encounters were determined eligible for inclusion into the post-ASEX implementation group. From July 2020 through June 2021, 300 patient encounters were identified, and 39 patients meeting inclusion criteria were randomly chosen for assessment to equal the amount in the postsurvey group. Baseline demographics were similar across both groups except for a statistically significantly higher rate of a diagnosis of depression in the presurvey group (Table 1).

Primary Outcome

A statistically significant difference in the rate of identified sexual dysfunction was observed as 59% of patients meeting criteria in the postsurvey group (n = 23; $P \leq .001$; Table 2) compared with 10.3% (n = 4; $P \leq .001$; Table 2) in the presurvey group.

Secondary Outcomes

Secondary outcomes were assessed using descriptive statistics. Highlights include that more than 70% of patients in the postsurvey group note that they would not have discussed sexual function with the pharmacist if not directly asked. The most common pharmacist intervention was referring patient to psychiatrist followed by patient education, and pharmacist medication recommendations included addition of medication (buspirone) and alternative medication recommended (mirtazapine). Patient education included an in-depth discussion of TESD risk with the individual patient's medication and possible next steps in response to patient questions. Additionally, most patients qualified for the definition of sexual dysfunction by scoring an ASEX score of $\geq$19 (38.5%), followed by a score of $\geq$4 in any 3 items (12.8%), and last a score of $\geq$5 in a single item (7.7%) (Table 2).

Discussion

The study's primary goal was to assess the rates of identified sexual dysfunction associated with antidepressants pre– and post–sexual dysfunction questionnaire administered by psychiatric clinical pharmacists. We hypothesized that rates of sexual dysfunction identified would be higher in the postsurvey group compared with the presurvey group. Prior to implementation of this survey, there was no standardized way pharmacists (or other providers) in the ambulatory psychiatry services identified sexual dysfunction.

Additionally, in the postsurvey cohort, sexual dysfunction was reported without use of the ASEX scale to primary care providers (15.4%) and psychiatrists (25.6%) at lower rates as compared with pharmacist encounters utilizing the ASEX scale (59%). The difference in the rate of identification of sexual dysfunction among the postsurvey group demonstrates that a standardized survey increases identification of sexual dysfunction and is likely of value to improve detection rates. In a similar study, Liu et al[8] utilized psychiatrist-prompted and patient-administered ASEX scales in patients within a psychiatric outpatient center who were treated with at least 1 antidepressant for 8 to 12 weeks. Sexual dysfunction was reported in 61.9% of patients, which is similar to our pharmacist-led ASEX scale identification of 59%. As compared with our study, the investigation led by Liu had a larger sample size (N = 273), the aim was to investigate factors associated with sexual dysfunction, and the investigators did not detail what interventions occurred in response to the identification of TESD. Taken together, our study and that of Liu et al demonstrates there are multiple successful methods of administering the ASEX survey.

However, utilizing psychiatric clinical pharmacist encounters to assess changes in sexual health associated with medications is reasonable and naturally fits within the expectation that pharmacists can support patient care and the interdisciplinary team by assessing medication tolerability, efficacy, and monitoring. At the time of this manuscript, only 1 article was identified that used clinical pharmacists for the identification of drug-induced sexual dysfunction in the psychiatry setting. Shakya et al[9] found in their pilot study using clinical pharmacist screening for sexual dysfunction with the ASEX scale that overall prevalence of drug-induced sexual dysfunction was 16% in the inpatient and outpatient psychiatric department over 3 months with no comparison prior to implementation of ASEX scale. The lower rate of sexual dysfunction in the Shakya et al study may be due to differences in cultural values and norms, and perhaps other demographic differences (more females). Our study was able to identify the rate of sexual dysfunction both preimplementation and postimplementation of the ASEX scale overseen by a Board-Certified Psychiatric Pharmacist in an outpatient clinic setting. Additionally, our study was able to follow up with patients closely after a psychiatric medication change, whereas the Shakya et al pilot study retrospectively interviewed patients without regard to time of medication initiation. Our study adds to the Shakya et al study that implementation of an intervention by a clinical pharmacist to actively identify drug-induced sexual dysfunction can increase identification of TESD.

Once sexual dysfunction is identified, treatment is difficult due to lack of robust research investigating potential interventions. Some strategies used empirically in practice include waiting for spontaneous remission, dose reduction of medication, adjunct medication such as phosphodiesterase-5 inhibitors for cases of erectile dysfunction, withdrawal from antidepressant for 24 to 48 hours prior to sexual relations, switching to or adding

TABLE 2: Primary and secondary outcomes

	Presurvey (n = 39)	Postsurvey (n = 39)	*P* value
	Count (%)		
Primary Outcome			
Sexual Dysfunction Identified	4 (10.3)	23 (59.0)	<.001
Secondary Outcomes			
ASEX Category			
≥19	NA	15 (38.5)	
≥5 (Single Item)	NA	3 (7.7)	
≥4 (Any 3)	NA	5 (12.8)	
Total ASEX Score		18 ± 5.8	
Would Report AE Without Being Prompted (yes)		11 (28.2)	
Intervention			
Education		5 (12.8)	
Route to psychiatrist		11 (28.2)	
Add medication		1 (2.6)	
Alternative medication		1 (2.6)	
Medication Intervention Acceptance			
Yes		1	
No		1	
Repeat ASEX scale done		1	

AE = adverse effect; ASEX = Arizona Sexual Experience Scale.

another antidepressant with less incidence of sexual dysfunction (often bupropion), or nonpharmacologic measures such as psychoeducation.[1,2] Regarding the secondary outcomes of reported medication interventions recommended by the pharmacy team, few interventions were noted. Watching and waiting for resolution of symptoms without intervention was often favored by patients when education was provided because there is some chance (~5% to 10%) that, with more time, sexual dysfunction symptoms may resolve before further medication adjustment is required.[2,10,11] In our clinical setting, most patients have had many medication trials prior to intake, and addressing sexual dysfunction through medication adjustment or change at the time of the pharmacy phone call was often not preferred. Although we did not record reasons why this approach was often utilized with a standardized question, many patients shared that sexual dysfunction was not their primary concern, but education on treatment options were provided in case patients were interested in pursuing them at a future date.

With respect to specific medication interventions made during follow up calls, addition of buspirone was recommended on 1 occasion and added at the next psychiatry encounter. Recommendation of mirtazapine as an alternative antidepressant medication was not accepted; however, an alternative selective serotonin reuptake inhibitor was initiated following the pharmacist phone encounter. Other than notifying the prescriber, the next most frequent intervention was education. Patient education opened an opportunity for patients to recognize that their symptoms were possible side effects of their medication and to provide an environment to openly discuss them. Following our patients longitudinally could benefit general understanding of best treatment approaches for TESD.

Strengths to the study included use of a validated questionnaire. The ASEX was shown to have internal consistency and scale reliability as well as accurately identifying patients with TESD.[5] This study is also the first to describe the pharmacist role and impact in identifying TESD due to antidepressants in an ambulatory psychiatry clinic.

Limitations to the study included potential selection bias as only patients who agreed to take the survey were administered the survey. Other reasons the ASEX scale may not have been completed for eligible patients includes time constraints or that the patient did not find the scale applicable to their life circumstances (ie, not sexually active). Additionally, there were differences in baseline demographics of presurvey and postsurvey patients with the most notable being the presurvey group having a higher incidence of noted diagnosis of depression compared to the postsurvey group (n = 35 versus n = 22; $P \leq .001$; Table 2). This could represent a potential confounding factor, but it is unlikely that it would have changed the observation that the ASEX scale implementation was associated with higher reported rates of sexual dysfunction because sexual dysfunction is commonly associated with depression even prior to medication initiation.[12,13] Finally, this was a small, single-center study completed in an ambulatory psychiatry clinic with an embedded psychiatric clinical pharmacist

who was able to administer the ASEX survey within medication follow-up encounters. This may not be reproducible at other sites if the infrastructure does not exist.

In the future, determining reasons why patients deferred the survey can help characterize the patient population that may be missing from assessment. Regarding time constraints on the encounter, transitioning the ASEX scale to a pre-encounter electronic survey could eliminate this concern. Additional considerations for future studies are analyzing more closely data from gender nonconforming or transgender patients and patients with other risk factors, such as trauma, to identify how to adapt this scale to a more diverse patient population. Future directions should also include further assessment into strategies on how to better intervene on symptoms of sexual dysfunction. In our setting, many patients did not want to address the reported sexual dysfunction at the time of the phone call. Understanding what factors contribute to this decision (for example, patient comfort discussing the topic further, severity of symptoms, or extent of treatment resistance) would also be valuable for future clinical and research endeavors.

Conclusions

Use of a validated survey, such as ASEX, improves identification of sexual dysfunction side effects associated with antidepressants in routine clinical care. In our clinic, pharmacists were able to both improve identification of TESD and increase patient awareness of sexual dysfunction associated with antidepressant use, contributing to team-based care of patients with mental illness.

References

1. Montejo AL, Priento N, de Alarcón R, Casado-Espada N, de la Iglesia J, Montejo L. Management strategies for antidepressant-related sexual dysfunction: a clinical approach. J Clin Med. 2019; 8(10):1640. DOI: 10.3390/jcm8101640
2. Winter J, Curtis K, Hu B, Clayton AH. Sexual dysfunction with major depressive disorder and antidepressant treatments: impact, assessment, and management. Expert Opin Drug Saf. 2022; 21(7):913-30. DOI: 10.1080/14740338.2022.2049753
3. Serretti A, Chiesa A. Treatment-emergent sexual dysfunction related to antidepressants: a meta-analysis. J Clin Psychopharmacol. 2009; 29(3):259-66. DOI: 10.1097/JCP.0b013e3181a5233f
4. AlBreiki M, AlMaqbali M, AlRisi K, AlSinawi H, Al Balushi M, Al Zakwani W. Prevalence of antidepressant-induced sexual dysfunction among psychiatric outpatients attending a tertiary care hospital. Neurosciences (Riyadh). 2020;25(3):55-60. DOI: 10.17712/nsj.2020.3.20200047
5. Higgins A, Nash M, Lynch A. Antidepressant-associated sexual dysfunction: impact, effects, and treatment. Drug Healthc Patient Saf. 2010;2:141-50. DOI: 10.2147/DHPS.S7634
6. McGahuey C, Gelenberg A, Laukes C, Moreno FA, Delgado PL, McKnight KM, et al. The Arizona Sexual Experience Scale (ASEX): reliability and validity. J Sex Marital Ther. 2011;26(1):25-40. DOI: 10.1080/009262300278623
7. Elnazer H, Baldwin D. Structured review of the use of the Arizona sexual experiences scale in clinical settings. Hum Psychopharmacol Clin Exp. 2020;35(3):2730. DOI: 10.1002/hup.2730
8. Liu X, Feng Z, Galling B, Qi N, Zhu XQ, Xiao L, Wang G. Gender specific sexual dysfunction in patients with depression. Front Psychiatry. 2023;14:1194228. DOI: 10.3389/fpsyt.2023.1194228
9. Shakya B, Babu T, Shafi M, Tejasri V, Sebastian J, Manohar S, et al. A pilot study on identification and management of drug induced sexual dysfunction: A collaborative approach by clinical pharmacist and psychiatrist. Int J Pharm Pharm Sci. 2019;12(2):32-7. DOI: 10.22159/ijpps.2020v12i2.34334
10. Labbate LA, Croft HA, Oleshansky MA. Antidepressant-related erectile dysfunction: management via avoidance, switching antidepressants, antidotes, and adaptation. J Clin Psychiatry. 2003; 64(suppl 10):11-9. PMID: 1297181112971811
11. Iosifescu DV, Jones A, O'Gorman C, Streicher C, Feliz S, Fava M, et al. Efficacy and safety of AXS-05 (dextromethorphan-bupropion) in patients with major depressive disorder: a phase 3 randomized clinical trial (GEMINI). J Clin Psychiatry. 2022;83(4):21m14345. DOI: 10.4088/JCP.21m14345
12. Thakurta RG, Singh OP, Bhattacharya A, Mallick AK, Ray P, Sen S, et al. Nature of sexual dysfunctions in major depressive disorder and its impact on quality of life. Indian J Psychol Med. 2012; 34(4):365-70. DOI: 10.4103/0253-7176.108222
13. Jiang F, Liu Z, Wu X, Tan A, Qin X, Su RC, et al. Prevalence of sexual dysfunction and its association with psychological symptoms in drug-naive major depressive disorder patients in West China. Front Psychiatry. 2023;14:1291988. DOI: 10.3389/fpsyt.2023.1291988