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Psychopharmacologic Management of Opioid-Dependent Women during Pregnancy

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Abstract

Illicit drug use during pregnancy presents complex clinical challenges, including reducing drug use and treating psychiatric disorders. Pharmacologic treatment of psychiatric disorders in a pregnant woman requires an evaluation of the balance between potential clinical benefit and the risk of potential neonatal consequences. This study describes psychiatric symptoms in 111 opioid-dependent pregnant women and their prescribed psychotropic medications. Hypomania, generalized anxiety disorder and depression were the most common disorders for which psychiatric symptoms were endorsed. Over half of women studied were prescribed some form of psychoactive medication during pregnancy. Pharmacologic vs. non-pharmacologic treatment approaches in this patient population are discussed.

Background

Opioid use during pregnancy is associated with adverse birth outcomes, which are most likely complications of a multitude of unfortunate life circumstances and the presence of coexisting medical and psychiatric conditions.¹ In a national survey of the prevalence of prenatal drug exposure, it was estimated that 5.5% of pregnant women used illicit drugs at some point in their pregnancy. Annually, 53,400 were estimated to have been exposed to heroin or nonmedically used opioid analgesics.² Arguably, because of the increase in nonmedical prescription opioid abuse, especially among women of childbearing age,^{3,4} this earlier study

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most likely underestimates prenatal exposure to prescription opioids. A more current conservative estimate of opioid analgesic use during pregnancy comes from the National Survey on Drug Use and Health, which indicated that 4.4% of pregnant women aged 15 to 44 (or 109,000 women) used opioid analgesics without appropriate medical oversight in the past year, with 15–17 year old pregnant females having the highest estimate of all age groups reported (15%).⁵

Agonist treatment for opioid dependence is effective in reducing opioid abuse and has been utilized in pregnant women as part of a comprehensive management strategy. Methadone maintenance treatment is the standard of care for opioid dependence in pregnant women but has not been formally approved by the Food and Drug Administration (FDA).⁶ Relative to active heroin addiction, methadone maintenance results in improved prenatal care, increased fetal growth, reduced fetal mortality, reduced foster care placement, and decreased risk of HIV infection, preeclampsia, and neonatal withdrawal.^{7–13} Although comparable studies have not been conducted with pregnant women who are addicted to other opioid analgesics resulting from nonmedical use, support and structure associated with maintenance treatment are expected to be beneficial by bringing stability to an otherwise chaotic lifestyle.

Buprenorphine, a partial μ -agonist has been found to be as equally effective and safe as methadone in the outpatient treatment of opioid dependence in non-pregnant patients.^{14–16} With regard to pregnancy, buprenorphine use is associated with good neonatal outcomes^{17–19} and is being used more frequently for treatment of pregnant opioid-dependent women, though it is also not yet approved by the FDA for this patient population.¹ Both methadone and buprenorphine have been categorized by the FDA as Pregnancy Category C, but there is far more experience with methadone.

Complicating the clinical management of substance use disorders is the co-occurrence of a plethora of psychiatric conditions which may be exacerbated by the psychological and physiological stresses of pregnancy, a period widely considered a time of increased sensitivity to psychiatric disorders.^{20–21} Knowledge of the prevalence of other psychiatric disorders in pregnant women with substance use disorders stems primarily from small studies of clinical samples. In one study, 10.3% of drug-using pregnant women had other psychiatric disorders compared to 1.4% of their non-using counterparts.²² Among a clinical sample of substance-dependent pregnant patients, 73% met criteria for a current co-occurring Axis I disorder with 37% and 36% meeting criteria for a current mood or anxiety disorder, respectively.²³ Comparatively lower prevalence estimates have been reported among pregnant women who do not have a substance use disorder. Prevalence varies by ascertainment source (ie, community-based vs. clinical samples), the instruments used to make psychiatric diagnoses, and the psychiatric diagnosis of interest. For instance, major depression during pregnancy has been observed in 3 to 21% of pregnant women.^{24–28}

In the past, most of our knowledge regarding treatment approaches for psychiatric disorders came from studies of non-pregnant patients. Much recent attention has been focused on the treatment of psychiatric disorders among pregnant women from the general population.^{29,30} To our knowledge, specific issues regarding the treatment of pregnant women with co-occurring substance use disorders (in whom there are distinct pathophysiological and pharmacological concerns) have not been discussed.

There is now consensus that depression is very common among pregnant women in general and should be thoughtfully diagnosed and treated. If left untreated, maternal depression during pregnancy, even without a substance use disorder (SUD), can result in adverse consequences for mother and infant, including increased risk for pre-eclampsia,³¹ low infant birth weight and delivery complications,³² poor maternal weight gain, postpartum depression,³³ maternal

suicide,³⁴ as well as decreased maternal responsiveness and consequent impairment of infant socio-emotional functioning and development.³⁵ In addition, women with antenatal depression are more likely than non-depressed women to use alcohol, cigarettes, and other drugs during pregnancy.³⁶ In a large study using administrative data, Kelly et al.³⁷ demonstrated that psychiatric disorders and SUD are both independently associated with less prenatal care.

Given the degree of overlap between symptoms of substance abuse and other psychiatric disorders in women,³⁸ many clinical challenges exist when a pregnant patient presents for treatment. Most importantly, if psychiatric symptoms abate with adequate management of the drug use disorder (eg, with agonist maintenance treatment), it may not be necessary to treat such disorders independently and to expose the fetus to additional pharmacological agents which have their own levels of risk. Pharmacotherapy of pregnant women is complex because few clinical trials have been conducted to evaluate the safety and efficacy of most medications during pregnancy. Prescription of psychiatric medications, especially, are to be avoided, even when there is “no evidence of risk in humans” (Category C according to the FDA classification) due to poorly defined and understood behavioral teratogenesis.

This paper centers on the issue of clinical management of pregnant women who have opioid dependence. It has two objectives: 1) to estimate the frequency of psychiatric symptoms among a sample of opioid-dependent pregnant women; and, 2) to describe the types of pharmacologic agents prescribed to these women for the treatment of their psychiatric disorders.

Methods

Study Design

This study used cross-sectional data that were collected as part of the Maternal Opioid Treatment: Human Experimental Research (MOTHER) study. The MOTHER study is a double-blind, randomized clinical trial that is currently ongoing at eight clinical sites.* The major goal of the MOTHER project is to evaluate the safety and efficacy of buprenorphine and methadone in pregnant opioid-dependent women and their neonates³⁹ using standardized methods and procedures founded on extensive pilot research in pregnant women and their neonates.^{18,40} All sites received local Institutional Review Board approval, and oversight is conducted by a Data and Safety Monitoring Board. For a more detailed description of site selection, study coordination, subject selection, and protocol details, see Jones et al.³⁹

Subjects

Opioid-dependent pregnant women, between the ages of 18 and 41 years, who planned to deliver at one of the participating site hospitals, were considered for inclusion in the study. All women considered for entry met DSM-IV criteria for current opioid dependence, according to the E module of the Structured Clinical Interview for DSM-IV (SCID I),⁴¹ and provided an opioid-positive urine sample indicating current opioid use or were currently on agonist treatment for opioid dependence. In addition, potential participants were required to have a single fetus pregnancy, with an estimated gestational age (EGA) of 6 to 30 weeks and a normal fetal heartbeat identified by sonogram.

Exclusionary criteria for the study are: (1) a medical condition making participation medically hazardous (eg, HIV, preterm labor, evidence of congenital fetal malformation, abnormal fetal

*The MOTHER clinical sites are: Johns Hopkins University School of Medicine, Baltimore, MD (lead site); Thomas Jefferson University, Philadelphia, PA; Vanderbilt University School of Medicine, Nashville, TN; Wayne State University, Detroit, MI; University of Vermont, Burlington, VT; Alpert School of Medicine at Brown University, Providence, RI; University of Vienna, Vienna, AUSTRIA; University of Toronto, Toronto, CANADA. As of this writing, all sites with the exception of Toronto contributed data from participants for the present analyses.

heartbeat); (2) an acute severe psychiatric condition in need of immediate treatment or which represented an imminent risk to the woman herself or others; (3) a current diagnosis of benzodiazepine or alcohol abuse or dependence according to the E module of the SCID I; (4) regular use of alcohol or benzodiazepines in the past 30 days (as determined by Addiction Severity Index); (5) a positive alcohol breath test or benzodiazepine positive urine during screening; or (6) pending legal action that could prohibit or interfere with participation. We wished to minimize exposure of the women to alcohol consumption or nonmedical benzodiazepine use because such exposure would confound our ability to quantify the major outcome variable of the study, namely the severity of opioid withdrawal in the neonates.

Potential enrollees in the clinical trial undergo a screening process before randomization. As of this writing, 256 potentially eligible women were approached for participation in the study. Of these, 120 (46.9%) consented to participate in the study, and 111 completed the screening assessment for psychiatric disorders. No women have yet to be excluded for having an acute severe psychiatric condition.

Assessment of Substance Use Disorder

The SCID-E⁴¹ was administered during screening by a trained interviewer to assess current and lifetime substance use disorders. Training on the administration of the SCID-E included a didactic review of DSM-IV criteria for Axis I disorders, a standardized review of the SCID instrument, and observation of videotapes purchased from the test makers. In addition, two mock interviews were reviewed by an expert interviewer³⁹ for concordance between expert trainer and interviewer. Finally, trainees were required to pass a knowledge assessment pertaining to DSM-IV criteria for substance abuse and/or dependence. Ongoing review of the trained interviewers' administration of the SCID-E is conducted periodically.³⁹

Screening for the Presence of Psychiatric Disorders

The Mini International Neuropsychiatric Interview (MINI), a short, structured diagnostic interview,⁴² was administered to assess symptoms of DSM-IV Axis I psychiatric disorders. The MINI was designed as a screening instrument, and as such, it yields information that can be used to indicate whether further evaluation for the presence or absence of a psychiatric diagnosis is in order. It has been used in several studies to evaluate the presence of psychiatric conditions in opioid addicts,^{43,44} and other substance users in treatment.^{45,46}

Psychopharmacologic Medications

As part of the clinical trial, information is routinely gathered on concomitant medications that are prescribed to participants during the course of their pregnancy. This information is extracted from the patient record and transferred to the study's Coordinating Center in a standardized fashion on a weekly basis. Complete information on medications that were prescribed was available on 96 of the 111 women enrolled in the study at the time of this writing.

Analysis

Descriptive statistics on the frequency of putative psychiatric disorders and psychotropic medications were generated using SPSS, Version 13.0.

Results

Sample Characteristics

Table 1 presents the sociodemographic characteristics of the participants. At the time of this writing, these participants represent seven of the eight MOTHER clinical sites (The Toronto site had not yet begun participant screening). The mean age of the sample was 27.7 years old;

a majority had never been married, and approximately half (46.8%) had less than a high school degree. The vast majority were White and unemployed.

Psychiatric Diagnosis Screening Results

Table 2 presents the results from the MINI. The first column of percentages denotes the frequency with which each item was endorsed among the sample. The second set of percentages represents the proportion of the sample who met MINI screening criteria for needing further clinical evaluation of the corresponding psychiatric disorder. For example, a little less than a third of women (29.7%) endorsed that they were consistently depressed or down, most of the day, nearly every day, for the past two weeks, and 36.0% had lost interest in things that they previously enjoyed. Continuing with this example, 39.6% met screening criteria for major depressive disorder; namely, having an affirmative response to one or the other of the first two questions. In many cases, multiple symptoms were endorsed, suggestive of the presence of multiple psychiatric conditions.

In this sample, the most common putative psychiatric disorders suggested by subjects' endorsement of screening questions were Hypomania (45.9%), Generalized Anxiety Disorder (43.2%), Major Depressive Disorder and Dysthymia (both 39.6%). Approximately one-quarter of the sample met screening criteria for panic disorder (27.9%) and agoraphobia (26.1%). Less common were Bulimia (9.9%) and Obsessive-Compulsive Disorder (5.4%).

Prescribed Psychoactive Medications

Table 3 provides data on clinically prescribed medications at some point during pregnancy for the subset of 96 participants for whom complete concomitant medication data were available. As can be seen, among the entire sample, 54 participants (56.3%) were prescribed at least one type of medication. The most common class of medication prescribed was anti-anxiety agents (35.4%), followed by SSRIs (24.0%). Less common were mixed neurotransmitter reuptake inhibitors, tricyclics, anti-psychotics, and mood stabilizers. Also presented in Table 3 are the frequencies of prescribed medications within groups of participants with probable psychiatric diagnoses (based on the MINI). From the data available, we cannot determine with certainty if the medication prescribed was for a particular condition, but it is notable that almost three-quarters (71.4%) of participants with a probable diagnosis of major depressive disorder were prescribed some type of medication, with 45.7% prescribed an anti-anxiety agent and about one-third prescribed an SSRI (31.4%). Similarly, 80.0% of women reporting suicidal symptoms were prescribed some type of medication.

Discussion

The current study describes a sample of opioid-dependent pregnant women ($n = 111$) with respect to their psychiatric symptoms as identified by a brief screening instrument, the Mini-International Neuropsychiatric Interview (MINI) and psychoactive medications prescribed in this patient population. Hypomania, Generalized Anxiety Disorder, Major Depressive Disorder, and Dysthymia were the most common disorders for which psychiatric symptoms were endorsed. The fact that almost three-quarters of the women with symptoms suggesting either depression or generalized anxiety were prescribed medications at some point during their pregnancy suggests that there is little reluctance to treat these women with medication. Our data clearly cannot address the appropriateness of the selected psychopharmacological intervention⁴⁷ nor the important assessment of the balance of risk-to-benefit in opioid maintained substance-abusing pregnant women. Namely, the potential risk of pharmacotherapy must be weighed against the risk of untreated maternal psychiatric disorder for the fetus, beneficial effects of opioid agonists on depressive, anxiety, and somatic symptoms, and the availability of non-pharmacological psychosocial treatment approaches that

might offer benefits that persist beyond the treatment period. Nevertheless, this study is unique in that it is the first to report the extent to which opioid-dependent pregnant women are prescribed psychopharmacologic medications.

Several limitations of the study must be acknowledged. The first pertains to an obvious selection bias. Of the 256 women identified, 120 (47%) consented to participate in the study and of these an additional nine women did not complete the screening assessment for psychiatric disorders because of time constraints. Therefore, we cannot state with confidence that the women who provided data for analysis were representative of those who did not consent to participate in terms of manifested psychopathology. The use of the MINI for measurement of psychiatric symptoms is the second limitation of the study. To reduce response burden, the study did not employ extensive measures of psychiatric diagnoses. Rather, the MINI was employed as a screening instrument. Future studies should employ more extensive structured interviews to extend the findings herein. It is possible that the presence of an opiate or other type of substance use disorder exacerbates psychiatric symptoms such that the estimates from this study might overestimate the prevalence of psychiatric disorders. Moreover, it is difficult to disentangle whether psychiatric symptoms reported in our sample are related to significant neurobiological or physiological stresses of pregnancy *per se* or indicative of an underlying psychiatric condition. Ideally, future studies should prospectively measure psychiatric symptoms in the pre-pregnancy period as well as during and through the post-partum period to understand the course of psychiatric symptoms.

Another important limitation is that we did not examine detailed information with respect to the timing of medication during pregnancy, or dose, or whether or not the medication was used consistently. For example, we excluded women who had a diagnosis of benzodiazepine or alcohol abuse or dependence prior to entry into the study, regular alcohol consumption or nonmedical benzodiazepine use in the previous 30 days, or a positive alcohol breath test or benzodiazepine positive urine during the screening period. However, in spite of these selection precautions, some subjects were subsequently prescribed benzodiazepines while participating in the study to manage transient withdrawal and/or anxiety symptoms as shown in Table 3. Because this study is ongoing, future work with larger sample sizes will enable us to conduct more fine-grained analyses including the rationale for choice of benzodiazepines versus antidepressants in this high-risk population. Of note, is the interesting observation that approximately equivalent numbers of patients with putative major depressive disorder were prescribed an anti-anxiety medication (40%) as were prescribed an antidepressant (45.7%). Finally, the current analyses did not examine neonatal outcomes associated with the use of various medications. Subsequent to breaking the blind and examining our primary outcome variables with respect to methadone or buprenorphine exposure, we will have the opportunity to examine the relationship between pharmacologic treatment during pregnancy with antidepressants or anti-anxiety medicines and neonatal outcomes and perhaps the interaction between these agents and opioid agonists.

Given the paucity of literature on the topic of treatment approaches for the management of psychiatric disorders among substance-abusing pregnant women, it is clear that carefully controlled studies are needed to better guide clinical decision-making. Specifically, research is needed to describe the range of treatment approaches for psychiatric disorders in this special population, their relative effectiveness, and how individual characteristics are associated with treatment response. Some symptoms of depression for instance, may be resolved upon adequate treatment of the addiction. Although research data is sparse, it is likely that the presence of psychiatric symptoms during pregnancy would lead to noncompliance with prenatal care and maintenance therapy to reduce drug use.²³ Future prospective studies are needed to explore the degree to which women with co-occurring psychiatric disorders terminate addiction

treatment prematurely, or do not respond to contingency management protocols, for example, to reduce other substance use, such as alcohol, tobacco and cocaine.

As supported by the findings reported here, psychiatric symptoms are widespread and should be treated in the opioid dependent pregnant woman. Although our methods were intended predominantly to screen women who were likely to require further diagnostic assessment for the most common psychiatric diagnoses, the prevalence of *inferred* disorders observed in this sample are consistent with previous reports documenting psychiatric comorbidity in substance-dependent populations. The proportions of women meeting screening criteria for various psychiatric disorders in our study are understandably higher than previous studies of non-addicted pregnant women. Opioid-dependent pregnant women are likely to be experiencing a multitude of stressful life circumstances that serves to exacerbate any underlying psychiatric disorder and increases the likelihood of reporting psychiatric symptoms beyond those related to pregnancy itself.

This study serves as a starting point for thoughtful discussion regarding the balance of risk and benefit in substance-abusing pregnant women. A notable proportion of women who screened positive for psychiatric conditions were not treated with pharmacologic agents. We cannot determine whether upon further evaluation and assessment of the balance of risk and benefit, the clinician made a decision to treat the symptoms with non-pharmacologic interventions or whether the disorder was not severe enough to warrant pharmacotherapy. While pharmacologic agents are available and have been shown to be effective in non-pregnant samples, pregnancy and substance use disorder complicate the clinical picture significantly and change the risk-benefit equation. Given the adverse consequences of untreated mental illness and opioid addiction during pregnancy, the pharmacological treatment of pregnant women is an area of growing research. While older tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) were presumed to be safe in pregnant women^{48–50} and are traditionally the most commonly prescribed medications among pregnant and postpartum patients, clinicians still use this treatment during pregnancy and lactation with caution, as few medications are adequately evaluated for safety and efficacy during pregnancy.⁵¹ Nevertheless, one study reported that as many as 35% of women use psychotropic medications during pregnancy.⁵² Newer studies have shown that there are some teratogenic concerns with SSRIs.^{53,54} Accordingly, it seems appropriate to also consider the demonstrated long-lasting beneficial effects of cognitive behavioral therapy (CBT) in psychiatric disorders,^{55–58} and its potential role in pregnant opioid dependent women.

Another important consideration in the decision to use pharmacologic agents in pregnant women maintained on opioid-substitution therapies is the issue of pharmacologic interaction between methadone and antidepressants.^{59–61} Although many studies have identified interactions between methadone and antidepressants in opioid dependent individuals, these results cannot be generalized to pregnant mothers receiving similar treatment. An unresolved issue is whether methadone *per se* (or other maintenance therapy) is associated with decreases in depressive symptoms in pregnant women. The risk/benefit considerations in psychopharmacotherapy remain in flux as our healthcare system changes so that the physician has less available time to see each patient. Recently conducted clinical trials of new antidepressant medications as they are developed show increasingly greater placebo effects, especially in patients in whom depression is complicated by substance use disorders or is not profound.⁶² Therefore, it remains to be elucidated when medications beyond *adequate* opioid substitution are needed in depressed opioid dependent pregnant women who have access to good behavioral treatment with careful monitoring.

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TABLE 1Characteristics of sample ($n = 111$)

Demographic characteristics	Mean	Sd
Age	27.7	5.8
Estimated gestational age (weeks)	19.1	6.4
	<i>n</i>	<i>%</i>
Marital status		
Never married	75	67.6
Married	17	15.3
Widowed/divorced/separated	19	17.1
Educational level		
Less than 12 years	52	46.8
High school graduate	38	34.2
More than high school	21	18.9
Race/ethnicity		
White	94	84.7
Black/African American	17	15.3
Employment status		
Employed	14	12.7
Unemployed	95	86.4
Disabled	1	0.9
Missing	1	0.9
Other current drug dependence in addition to opioid dependence		
Cocaine	28	25.9
Cannabis	10	9.3

TABLE 2

Frequency of putative psychiatric disorders based on screening items from the mini-international neuropsychiatric interview (MINI) (*n* = 111)

Individual MINI items	<i>n</i> ("yes")	%	Corresponding probable psychiatric diagnosis	<i>n</i>	%
1. Have you been consistently depressed or down, most of the day, nearly every day, for the past two weeks?	33	29.7			
2. In the past two weeks, have you been much less interested in most things or much less able to enjoy the things you used to enjoy most of the time?	40	36.0		44	39.6
3. Have you felt sad, low or depressed most of the time for the last two years?	44	39.6		44	39.6
4. In the past month did you think that you would be better off dead or wish you were dead?	18	16.2		18	16.2
5. Had you ever had a period of time when you were feeling 'up' or 'high' or 'hyper' or so full of energy or full of yourself that you got into trouble, or that other people thought you were not your usual self? (Do not consider times when you were intoxicated on drugs or alcohol.)	26	23.4			
6. Have you ever been persistently irritable, for several days, so that you had arguments or verbal or physical fights, or shouted at people outside your family? Have you or others noticed that you have been more irritable or overreacted, compared to other people, even in situations that you felt were justified?	43	38.7		58	45.9
7. Have you, on more than one occasion, had spells or attacks when you suddenly felt anxious, frightened, uncomfortable or uneasy, even in situations where most people would not feel that way? Did the spells surge to a peak, within 10 minutes of starting?	31	27.9		31	27.9
8. Do you feel anxious or uneasy in places or situations where you might have a panic attack or panic-like symptoms, or where help might not be available or escape might be difficult: like being in a crowd, standing in a line (queue), when you are away from home or alone at home, or when crossing a bridge, traveling in a bus, train, or car?	29	26.1		29	26.1
9. In the past month, were you fearful or embarrassed being watched, being the focus of attention, or fearful of being humiliated. This includes things like speaking in public, eating in public or with others, writing while someone watches, or being in social situations?	24	21.6		24	21.6
10. In the past month, have you been bothered by recurrent thoughts, impulses, or images that were unwanted, distasteful, inappropriate, intrusive, or distressing? (e.g., the idea that you were dirty, contaminating or had germs, or fear of contaminating others, or fear of harming someone even though you didn't want to, or fearing you would act on some impulse, or fear of suspicions that you would be responsible for things going wrong, or obsessions with sexual thoughts, images	13	11.7		6	5.4

Individual MINI items	<i>n</i> ("yes")	%	Corresponding probable psychiatric diagnosis	<i>n</i>	%
or impulses, or hoarding, collecting, or religious obsessions.)					
11. In the past month, did you do something repeatedly without being able to resist doing it, like washing or cleaning excessively, counting or checking things over and over, or repeating, collecting, or arranging things, or other superstitious rituals?	20	18.0			
12. Have you ever experienced or witnessed or had to deal with an extremely traumatic event that included actual or threatened death or serious injury to you or someone else?	55	49.5	Post Traumatic Stress Disorder: "yes" to #12 and #13	20	18.2
13. During the past month, have you experienced the event in a distressing way (such as, dreams, intense recollections, flashbacks or physical reactions)?	22	20.0			
14. In the past three months, did you have eating binges or times when you ate a very large amount of food within a 2-hour period?	11	9.9	Bulimia Nervosa: "yes" to #14	11	9.9
15. Have you worried excessively or been anxious about several things over the past 6 months?	48	43.2	Generalized Anxiety Disorder: "yes" to #15	48	43.2

Medication classes prescribed for participants by probable psychiatric diagnosis based on the MINI

TABLE 3

Probable psychiatric diagnosis based on MINI

Medication class ^J (total number of individuals prescribed)	Major depressive disorder (n=35)			Dysthymia (n=38)			Suicidality (n=15)			Mania (n=41)			Panic disorder (n=35)			Social anxiety disorder (n=18)				
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%		
Anti-anxiety (n=34)	16	45.7	14	36.8	5	33.3	17	41.5	16	45.7	9	50.0	11	31.4	12	36.6	14	40.0	8	44.4
SSRI (n=23)	11	31.4	12	31.6	7	46.7	15	36.6	14	40.0	8	44.4	2	5.7	3	9.3	1	2.9	1	5.6
Mixed Neurotransmitter Reuptake Inhibitors (n=4)	1	2.9	1	2.6	0	0.0	3	7.3	3	8.6	0	0.0	3	8.6	2	6.0	4	11.4	4	11.4
Tricyclics (n=3)	3	8.6	2	5.3	1	6.7	5	12.2	4	11.4	3	16.7	2	5.7	3	9.3	4	11.4	0	0.0
Anti-psychootics (n=7)	2	5.7	3	7.9	1	6.7	3	7.3	4	11.4	0	0.0	2	5.7	3	9.3	4	11.4	0	0.0
Mood Stabilizers (n=5)	2	5.7	3	7.9	1	6.7	3	7.3	4	11.4	0	0.0	2	5.7	3	9.3	4	11.4	0	0.0
Any Medication (n=54)	25	71.4	25	65.8	12	80.0	29	70.7	27	79.3	15	83.3	16	45.7	16	45.7	16	45.7	9	50.0

Probable psychiatric diagnosis based on MINI

Medication Class, cont.	Obsessive-compulsive disorder Post-traumatic stress disorder (n=45)			Eating disorder (n=8)			Generalized anxiety disorder (n=39)			
	n	%	n	%	n	%	n	%	n	%
Anti-anxiety	9	45.0	17	37.8	4	50.0	17	43.6	9	23.1
SSRI	9	45.0	9	20.0	4	50.0	14	35.9	8	20.5
Mixed Neurotransmitter Reuptake Inhibitors	3	15.0	1	2.2	1	12.5	3	7.7	1	2.6
Tricyclics	2	10.0	2	4.4	0	0.0	3	7.7	0	0.0
Anti-psychootics	2	10.0	4	8.9	1	12.5	3	7.7	3	7.7
Mood stabilizers	2	10.0	3	6.7	0	0.0	4	10.3	0	0.0
Any medication	15	75.0	25	55.6	6	75.0	29	74.7	15	38.5

^J Anti-anxiety: buspirone, clonazepam, diazepam, hydroxyzine, lorazepam, lorazepam, midazolam, oxazepam, passedan tropfen (Austria), Zolpidem; Zolpidem; SSRI (Selective Serotonin Reuptake Inhibitors): citalopram, escitalopram oxalate, fluoxetine, paroxetine, sertraline; Mixed Neurotransmitter Reuptake Inhibitors: bupropion; Tricyclic Antidepressants: doxepin; Anti-psychootics: olanzapine, quetiapine fumarate, trazadone Mood Stabilizers: lamotrigine, lithium carbonate.