Published in final edited form as:
J Affect Disord. 2009 May ; 115(1-2): 262–268. doi:10.1016/j.jad.2008.09.012.

Treatment of depressed bipolar patients with alcohol use disorders: plenty of room for improvement

Enrique Baca-Garcia[1,2], **Leo Sher**[1], **M. Mercedes Perez-Rodriguez**[3], **Ainsley K Burke**[1], **Gregory M. Sullivan**[1], **Michael F Grunebaum**[1], **Barbara H Stanley**[1], **J John Mann**[1], and **Maria A. Oquendo**[1]

[1]Molecular Imaging and Neuropathology Division, NYS Psychiatric Institute and Columbia University, New York, USA

[2]Department of Psychiatry, Fundacion Jimenez Diaz University Hospital, Autonoma University of Madrid, Spain

[3]Department of Psychiatry, Ramon y Cajal Hospital, Madrid, Spain

Abstract

Background—We aimed to examine the adequacy of antidepressant treatment and compliance with treatment in bipolar patients with and without alcohol use disorders (AUD). We hypothesize that the adequacy of antidepressant treatment and the compliance with treatment for those with AUD are lower than for those without AUD.

Methods—Subjects were 97 patients with current bipolar major depressive episode, 39 (40.2%) with lifetime history of AUD and 58 (59.8%) without AUD. Adequacy of antidepressant medication treatment in the 3 previous months was assessed using the Antidepressant Treatment History Form. Compliance rates were estimated.

Results—Rates of inadequate treatment were high in all patients. Bipolar patients with AUD (74.3%) showed higher rates of inadequate antidepressant treatment than those without AUD (67.3%). The proportion of intensive treatment was higher in bipolars without AUD (15.5%) than in those with AUD (2.6%). Median compliance was similar in bipolars with and without AUD.

Limitations—We lack serum medication levels to assess the compliance. We do not have data to address the possibility that the presence of AUD adversely affected prescribing practices.

Conclusions—Bipolars with AUD had lower rates of adequate treatment than those without AUD, but the two groups were not different in terms of self-reported treatment adherence. The finding that bipolar patients with or without comorbid AUD did not receive adequate treatment is of considerable clinical relevance. It raises the question as to whether inadequate treatment of depression contributes to the high rates of morbidity, and attempted and completed suicides in bipolar patient populations.

Keywords

Bipolar disorder; Alcoholism; Patient compliance; Antidepressants

Corresponding author: Enrique Baca-Garcia. Department of Neurosciences, Columbia University Medical Center, 1051 Riverside Drive. Suite 2719 / Unit 42, New York, NY 10032. Phone: (+1) 212-543-6234; Fax number: (+1) 212-543-6017; ebacgar2@yahoo.es.

Introduction

Several clinical and epidemiological studies have noted a high prevalence of alcohol abuse and dependence (alcohol use disorders, AUD) among patients with bipolar disorder (Krishnan, 2005;Regier et al., 1990). Moreover, this association is stronger than with other drug use disorders (Goldstein et al., 2006;Regier et al., 1990).

AUD has a deleterious effect on the course of bipolar disorder and is associated with poor outcomes (Goldstein and Levitt, 2006). However, the temporal relationship between AUD and worsening bipolar symptomatology has not been clearly established and remains an open question (Fleck et al., 2006). In addition, bipolar-AUD comorbidity is influenced by gender and age (Frye et al., 2003;Krishnan, 2005).

Bipolar disorder is often inadequately treated (Arvilommi et al., 2007;Sajatovic et al., 2006a) and bipolar patients show high rates of treatment nonadherence (Baldessarini et al., 2008). Moreover, treatment may be negatively influenced by AUD (Ries, 2006). One of the putative effects of AUD is the reduction of compliance with treatment (Baldessarini et al., 2008). Baldessarini et al., (2008) assessed compliance with pharmacological treatment, but no studies have assessed adequacy of antidepressant treatment in bipolar patients with comorbid AUD. The primary objective of this study is to examine the adequacy of and compliance with pharmacological treatment in bipolar patients with and without comorbid AUD. We hypothesize that the adequacy of antidepressant treatment and compliance with treatment for those with AUD is lower than for those without AUD.

Methods

Participants were recruited through advertising and referrals and participated in mood disorders research in a university hospital. The investigation was carried out in accordance with the Declaration of Helsinki, the study design was reviewed by the Institutional Review Board, and informed consent of the participants was obtained.

Subjects were 97 patients diagnosed with current bipolar major depressive episode using the Structured Clinical Interview (SCID) for the DSM-III-R or DSM-IV. Severity of depression was evaluated using the 17-item version of the Hamilton Rating Scale for Depression (HRSD17) (Hamilton, 1960;Hamilton, 1967). The Young Mania Rating Scale was used to evaluate manic symptoms (Young et al., 1978). Lifetime aggression and hostility were assessed using the Brown-Goodwin Scale (Brown et al., 1979) and the Buss-Durkee Hostility Inventory (BUSS et al., 1957), respectively. A lifetime history of all suicide attempts was recorded on the Columbia Suicide History Form (Oquendo et al., 1999). Medical lethality of the most lethal suicide attempt was rated using the total score in Beck Lethality Rating Scale (Beck et al., 1975). Thirty nine (40.2%) patients had a lifetime history of alcohol abuse or dependence according to SCID (comorbid AUD group) while 58 (59.8%) had never suffered from alcohol abuse or dependence (no AUD group). 27 patients in the AUD group (69.2%) were diagnosed with alcohol dependence (current dependence: n=4, 14.8%; partial remission n=6, 22.2%; full remission n=17, 63.0%, according to SCID criteria), and 12 (30.8%) with alcohol abuse (current abuse: n=4, 33.3%; full remission n=8, 66.7%, according to SCID criteria).

Medication treatment received in the 3 months prior to study entry (as prescribed by the patients' psychiatrists) was assessed using the Antidepressant Treatment History Form (Sackeim et al., 1990). Length of treatment was determined by the MD in charge of the patient's management. The treatments analyzed included not only antidepressants, but also all other types of medication used for treating bipolar major depressive episodes. Adequacy of antidepressant treatment was assessed using a computer algorithm for calculating the adequacy of antidepressant treatment in unipolar and bipolar Depression (Oquendo et al., 2003) based on

the Antidepressant Treatment History Form (ATHF) (Sackeim et al., 1990). The ATHF assigns a score from 0 to 5, scaled for each type of treatment (Oquendo et al. 2003), and takes into account dose, duration of treatment, and patient compliance with the treatment. A rating of 0 indicates that no psychopharmacologic treatment was prescribed. A rating of 1 or 2 indicates inadequate treatment. Treatment receives a rating of 1 if the medication dose is less than 50% of an adequate dose and a rating of 3 or greater indicates not only adequacy, but increasing strength of antidepressant prescription. We collapsed the scores into inadequate (1 and 2) and adequate treatment (3, 4, 5) for statistical analysis.

Compliance was calculated by dividing the self-reported total dose of medication taken (in milligrams) by the total dose of medication prescribed (in milligrams) and multiplying it by 100 (Oquendo et al., 2003). We considered the median compliance of the different treatments as a measure of global compliance.

Antidepressant treatment adequacy and compliance were compared in bipolar patients with AUD versus bipolar patients without AUD using Fisher exact tests for categorical data and t-tests for continuous data as appropriate.

Results

A sample description is provided in Table 1. Six (15.4%) of the subjects with comorbid AUD were in partial remission of the alcohol abuse or dependence, and 25 (63.1%) were in full remission of the alcohol abuse or dependence. The types of medications prescribed in the AUD and the non-AUD groups are described in Table 2. There were no significant differences in the types of medications prescribed between the AUD and the non-AUD groups.

AUD were significantly more prevalent in male bipolar patients (16/27, 59.3%) than in female bipolar patients (23/70, 32.9%) (Fisher exact test p=0.022), as has been previously reported (Frye et al., 2003). There were no significant differences between the group of bipolar patients with comorbid AUD and the group of bipolar patients without AUD in the scores on any of the scales, with one exception: bipolar patients with comorbid AUD had significantly higher scores in the Brown-Goodwin aggression scale (mean, m=23.5, Standard Deviation, SD=6.9) than bipolar patients without AUD (m=18.9, SD=5.0) (t=3.7; d.f.=87; p<0.001). This is consistent with the putative link between alcohol use disorders and aggressive behavior that we and others have previously reported (Conner et al., 2004;Grunebaum et al., 2006;Sher et al., 2005).

The adequacy of the antidepressant treatments received by the subjects is presented in Table 2. Bipolar patients with comorbid AUD (74.3%) showed a higher proportion of inadequate antidepressant treatment (ATHF ratings of 1 and 2) than bipolar patients without AUD (67.3%) (χ^2=9.3; degrees of freedom [d.f.]=3; p=0.025). In addition, the proportion of intensive antidepressant treatment (ATHF ratings of 4 and 5) was much higher in bipolar patients without AUD (15.5%) than in bipolar patients with comorbid AUD (2.6%). Compliance rates (%) for each pharmacological treatment are shown in Table 2. The self-reported median compliance with all treatments was not significantly different in bipolar patients with (m=90.7, SD=14.0) and without comorbid AUD (m=90.6, SD=20.2) (t<0.1, d.f.=85, p=0.978) (Table 4).

Discussion

The main finding of this study is that bipolar patients with comorbid AUD had significantly lower rates of adequate antidepressant treatment than bipolar patients without AUD, but the two groups were not different in terms of self-reported treatment adherence. Both groups had high rates of inadequate antidepressant treatment. This suggests that inadequate antidepressant treatment in bipolar patients with comorbid AUD may be related to physician rather than patient

behavior. It is possible that the presence of AUD adversely affected prescribing practices. Alcoholism is highly stigmatized and both current alcoholics and alcoholics in remission may be treated differently compared to non-alcoholics (Aviram, 2006; Peluso & Blay, 2008; Ritson, 1999). Alternatively, or in addition, the lower rates of adequate antidepressant treatment among bipolar patients with comorbid AUD may be related to the fact that bipolar patients with comorbid AUD had significantly higher aggression levels than bipolar patients without AUD.

Another issue is the fact that some psychiatrists are against antidepressant prescription for bipolar patients. However, two recent studies reported that antidepressant use was not associated with a higher rate of treatment-emergent affective switch (Sachs et al., 2007) or increased rates of mania-related office visits (Fu et al., 2007) in bipolar patients. However, the results regarding the benefit of adjunctive antidepressant treatment were inconclusive. Sachs et al. (2007) reported that the use of adjunctive antidepressant medication, as compared with the use of mood stabilizers, was not associated with increased efficacy. In contrast, Fu et al. (2007) observed that the use of second-generation antidepressant was associated with a decreased number of depression-related visits in bipolar patients.

It is difficult to compare our results regarding treatment adequacy with those of other studies because of the diversity of definitions of treatment adequacy. (Arvilommi et al., 2007) found that lifetime substance use disorders were not among the factors most strongly associated with inadequate treatment in patients with bipolar disorder. They reported rates of treatment adequacy ranging between 100% in patients diagnosed with bipolar disorder with a manic index episode and 43.3% among rapid cyclers. In that sample, depressed bipolar patients had a higher rate (49%) of adequate treatment than in our sample. However, the definition of treatment adequacy utilized in that study did not take into account relevant variables such as dosage or treatment duration, which may explain the higher rates of treatment adequacy in their report. Rates of adherence in our study are higher than those reported in other studies.The reported rates of non-adherence with mood-stabilizers range between 18% and 52% (Scott et al., 2002) and around 50% of bipolar patients have been reported to be nonadherent with medications (Fleck et al., 2005;Sajatovic et al., 2006b). The relatively high rates of adherence in the group of bipolar patients with AUD is particularly surprising given that aggressive behavior has been associated with lower treatment compliance in psychiatric patients in general (Janssen et al., 2006).

The effect of alcohol abuse or dependence on treatment adherence in bipolar patients has been specifically explored in only one study which reports a significant association between alcohol dependence and nonadherence (Baldessarini et al., 2008). Several studies have reported increased treatment nonadherence in bipolar patients with comorbid substance use disorders compared to bipolar patients without substance use disorders (Aagaard et al., 1990;Gonzalez-Pinto et al., 2006;Sajatovic et al., 2006a;Sajatovic et al., 2006b). However, the available data provide inconsistent results, with some studies showing increased rates of noncompliance in patients with comorbid substance use disorders (Aagaard and Vestergaard, 1990;Gonzalez-Pinto et al., 2006;Sajatovic et al., 2006a;Sajatovic et al., 2006b), while others show little effect of substance use disorders on compliance (Arvilommi et al., 2007). Warner et al. (1994) observed that alcohol use to the point of intoxication, but not heavy substance use, was associated with medication noncompliance. These discordant results may be partially explained by the different definitions of compliance that are used and the inclusion of individuals with current or past substance use. Sajatovic et al. (2006a) observed that current substance use disorders were associated with treatment nonadherence in bipolar patients, but past substance use disorders were not. Of course, the high compliance rate in some of these studies may be explained by the fact that all patients consented to participate in a research program, possibly representing a highly motivated sample. Maybe this explains the high rate of compliance in our sample, which is also a research sample.

The main limitation of this study and most previous studies is the lack of serum medication levels to assess the compliance. We only have data as retrospectively reported by the patients themselves which may introduce recall bias. Self-report may not be a reliable way to detect non-adherence in bipolar patients with AUD. However, self-report is the standard procedure to assess compliance in the majority of studies that have analyzed compliance in bipolar patients (Fleck et al., 2005; Sajatovic et al., 2006a). We do not have data to address the possibility that the presence of AUD adversely affected prescribing practices. In fact, it is unclear whether the physicians were aware of the AUD diagnosis. Nonetheless, the finding that bipolar patients with or without comorbid AUD did not receive adequate treatment is of considerable clinical importance. Indeed, it raises the question as to whether inadequate treatment of depression contributes to the high rates of morbidity, and attempted and completed suicides in bipolar patient populations.

Reference List

Aagaard J, Vestergaard P. Predictors of outcome in prophylactic lithium treatment: a 2-year prospective study. J Affect Disord 1990;18(4):259–266. [PubMed: 2140378]

Arvilommi P, Suominen KS, Mantere OK, Leppamaki S, Valtonen H, Isometsa ET. Adequacy of treatment received by diagnosed and undiagnosed patients with bipolar I and II disorders. J Clin Psychiatry 2007;68(1):102–110. [PubMed: 17284137]

Beck AT, Beck R, Kovacs M. Classification of suicidal behaviors: I. Quantifying intent and medical lethality. Am J Psychiatry 1975;132(3):285–287. [PubMed: 1115273]

Brown GL, Goodwin FK, Ballenger JC, Goyer PF, Major LF. Aggression in humans correlates with cerebrospinal fluid amine metabolites. Psychiatry Res 1979;1(2):131–139. [PubMed: 95232]

Buss AH, Durkee A. An inventory for assessing different kinds of hostility. J Consult Psychol 1957;21 (4):343–349. [PubMed: 13463189]

Conner KR, Duberstein PR. Predisposing and precipitating factors for suicide among alcoholics: empirical review and conceptual integration. Alcohol Clin Exp Res 2004;28:6S–17S. [PubMed: 15166632]

Fleck DE, Arndt S, DelBello MP, Strakowski SM. Concurrent tracking of alcohol use and bipolar disorder symptoms. Bipolar Disord 2006;8(4):338–344. [PubMed: 16879134]

Fleck DE, Keck PE Jr, Corey KB, Strakowski SM. Factors associated with medication adherence in African American and white patients with bipolar disorder. J Clin Psychiatry 2005;66(5):646–652. [PubMed: 15889954]

Frye MA, Altshuler LL, McElroy SL, Suppes T, Keck PE, Denicoff K, Nolen WA, Kupka R, Leverich GS, Pollio C, Grunze H, Walden J, Post RM. Gender differences in prevalence, risk, and clinical correlates of alcoholism comorbidity in bipolar disorder. Am J Psychiatry 2003;160(5):883–889. [PubMed: 12727691]

Fu AZ, Liu GG, Christensen DB, Hansen RA. Effect of second-generation antidepressants on mania- and depression-related visits in adults with bipolar disorder: a retrospective study. Value Health 2007;10 (2):128–136. [PubMed: 17391421]

Goldstein BI, Levitt AJ. Factors associated with temporal priority in comorbid bipolar I disorder and alcohol use disorders: Results from the national epidemiologic survey on alcohol and related conditions. J Clin Psychiatry 2006;67(4):643–649. [PubMed: 16669730]

Gonzalez-Pinto A, Mosquera F, Alonso M, Lopez P, Ramirez F, Vieta E, Baldessarini RJ. Suicidal risk in bipolar I disorder patients and adherence to long-term lithium treatment. Bipolar Disord 2006;8(5 Pt 2):618–624. [PubMed: 17042834]

Grunebaum MF, Galfalvy HC, Nichols CM, Caldeira NA, Sher L, Dervic K, Burke AK, Mann JJ, Oquendo MA. Aggression and substance abuse in bipolar disorder. Bipolar Disord 2006;8(5 Pt 1): 496–502. [PubMed: 17042888]

Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960;23:56–62. [PubMed: 14399272]

Hamilton M. Development of a rating scale for primary depressive illness. Br J Soc Clin Psychol 1967;6 (4):278–296. [PubMed: 6080235]

Janssen B, Gaebel W, Haerter M, Komaharadi F, Lindel B, Weinmann S. Evaluation of factors influencing medication compliance in inpatient treatment of psychotic disorders. Psychopharmacology (Berl) 2006;187(2):229–236. [PubMed: 16710714]

Krishnan KR. Psychiatric and medical comorbidities of bipolar disorder. Psychosom Med 2005;67(1): 1–8. [PubMed: 15673617]

Linehan MM, Goodstein JL, Nielsen SL, Chiles JA. Reasons for staying alive when you are thinking of killing yourself: The reasons for living inventory. J Consult Clin Psychol 1983;51:276–286. [PubMed: 6841772]

Oquendo MA, Baca-Garcia E, Kartachov A, Khait V, Campbell CE, Richards M, Sackeim HA, Prudic J, Mann JJ. A computer algorithm for calculating the adequacy of antidepressant treatment in unipolar and bipolar depression. J Clin Psychiatry 2003;64(7):825–833. [PubMed: 12934985]

Oquendo MA, Malone KM, Ellis SP, Sackeim HA, Mann JJ. Inadequacy of antidepressant treatment for patients with major depression who are at risk for suicidal behavior. Am J Psychiatry 1999;156(2): 190–194. [PubMed: 9989553]

Regier DA, Farmer ME, Rae DS, Locke BZ, Keith SJ, Judd LL, Goodwin FK. Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. JAMA 1990;264(19):2511–2518. [PubMed: 2232018]

Ries RK. Co-occurring Alcohol Use and Mental Disorders. J Clin Psychopharmacol 2006;26:S30–S36.

Sachs GS, Nierenberg AA, Calabrese JR, Marangell LB, Wisniewski SR, Gyulai L, Friedman ES, Bowden CL, Fossey MD, Ostacher MJ, Ketter TA, Patel J, Hauser P, Rapport D, Martinez JM, Allen MH, Miklowitz DJ, Otto MW, Dennehy EB, Thase ME. Effectiveness of adjunctive antidepressant treatment for bipolar depression. N Engl J Med 2007;356(17):1711–1722. [PubMed: 17392295]

Sackeim HA, Prudic J, Devanand DP, Decina P, Kerr B, Malitz S. The impact of medication resistance and continuation pharmacotherapy on relapse following response to electroconvulsive therapy in major depression. J Clin Psychopharmacol 1990;10(2):96–104. [PubMed: 2341598]

Sajatovic M, Bauer MS, Kilbourne AM, Vertrees JE, Williford W. Self-reported medication treatment adherence among veterans with bipolar disorder. Psychiatr Serv 2006a;57(1):56–62. [PubMed: 16399963]

Sajatovic M, Valenstein M, Blow FC, Ganoczy D, Ignacio RV. Treatment adherence with antipsychotic medications in bipolar disorder. Bipolar Disord 2006b;8(3):232–241. [PubMed: 16696824]

Scott J, Pope M. Nonadherence with mood stabilizers: prevalence and predictors. J Clin Psychiatry 2002;63(5):384–390. [PubMed: 12019661]

Sher L, Oquendo MA, Galfalvy HC, Grunebaum MF, Burke AK, Zalsman G, Mann JJ. The relationship of aggression to suicidal behavior in depressed patients with a history of alcoholism. Addict Behav 2005;30(6):1144–1153. [PubMed: 15925124]

Warner R, Taylor D, Wright J, Sloat A, Springett G, Arnold S, Weinberg H. Substance use among the mentally ill: prevalence, reasons for use, and effects on illness. Am J Orthopsychiatry 1994;64(1): 30–39. [PubMed: 8147425]

Young RC, Biggs JT, Ziegler VE, Meyer DA. A rating scale for mania: reliability, validity and sensitivity. Br J Psychiatry 1978;133:429–435. [PubMed: 728692]

J Affect Disord. Author manuscript; available in PMC 2009 November 1.

Table 1

Sociodemographic and clinical characteristics of the sample.

	Bipolar subjects with AUD* (n=39)		Bipolar subjects without AUD* (n=58)		Statistic test
	n	%	n	%	
Gender					
Male	16	41.0	11	19.0	Fisher exact test p=0.022
Female	23	59.0	47	81.0	
Marital status					
Single (not presently living with a partner for 6 or more months)	23	59.0	21	36.2	χ^2=5.5; d.f.=4; p=0.237
Married (or sustained conjugal situation for 6 or more months)	9	23.1	19	32.8	
Separated (if legally married, or apart from common law spouse with chance of returning)	1	2.6	4	6.9	
Divorced (or left common law spouse for good)	6	15.4	13	22.4	
Widowed	0	0.0	1	1.7	
Race					
Asian	0	0.0	2	3.6	χ^2=2.0; d.f.=3; p=0.563
Black or African American	3	8.3	7	12.7	
White	31	86.1	42	76.4	
More than one race	2	5.6	4	7.3	
	Mean	SD	Mean	SD	
Age	36.3	11.4	36.8	9.9	t=-0.2; d.f. =95; p=0.833
Hamilton Depression Rating scale 17 (Hamilton, 1960, 1967)	18.6	5.5	19.5	6.0	t=-0.7; d.f.=95; p=0.463
Lethality of most lethal suicide attempt (Beck Lethality Rating Scale total score) (Beck et al., 1975)	3.6	1.5	3.7	1.8	t=-0.2; d.f.=71; p=0.831
Total number of suicide attempts	2.5	2.1	2.2	2.4	t=0.6; d.f.=94; p=0.554
Young Mania Rating Scale (Young et al., 1978)	8.6	10.5	4.3	6.5	t=1.8; d.f.=53; p=0.070
Aggression history (Brown-Goodwin Scale) (Brown et al., 1979)	23.5	6.9	18.9	5.0	t=3.7; d.f.=87; p<0.001
Buss-Durkee Hostility Inventory total score (Buss and Durkee 1957)	42.4	12.2	39.0	11.9	t=1.3; d.f.=82; p=0.208
Reasons for Living Inventory (RFL) total score (Linehan et al. 1983)	143.4	43.3	156.1	49.2	t=-1.2; d.f.=75; p=0.247

* AUD=Alcohol Use Disorders

Table 2

Pharmacological treatment in bipolar subjects with and without AUD, compliance rates for each type of pharmacological treatment (according to Oquendo et al., 2003) and treatment adequacy rating.

	Bipolar subjects with AUD*		**Bipolar subjects without AUD***		**t-test**	**Power****	**Mean Detectable Difference**
	Mean (n)	**SD**	**Mean (n)**	**SD**		**%**	
Number of medications	3.2 (36)	1.7	3.4 (51)	2.0	t-0.4 d.f.=85 p=0.705	95	1.0
Median compliance	90.7 (36)	14.0	90.6 (51)	20.2	t<0.1 d.f.=85 p=0.978	95	14.4
Compliance Norepinephrine Agonists	88.8 (8)	21.0	81.8 (11)	34.0	t=0.5 d.f.=17 p=0.618	37	23.5
Compliance Serotonin Agonists	90.4 (23)	15.5	89.2 (32)	22.8	t=0.2 d.f.=53 p=0.826	82	16.1
Compliance Combined Norepinephrine & Serotonin Agonists	88.0 (10)	21.5	97.1 (14)	7.3	t=-1.5 d.f.=22 p=0.151	46	11.9
Compliance Mood Stabilizers	92.1 (14)	14.8	88.3 (26)	24.2	t=0.6 d.f.=38 p=0.589	65	17.1
Compliance Neuroleptics	89.4 (16)	16.1	97.5 (16)	6.8	t=-1.9 d.f.=30 p=0.073	59	9.9
Compliance Benzodiazepines	91.1 (18)	12.3	95. 5 (22)	10.6	t=-1.2 d.f.=38 p=0.237	69	9.9
Compliance Stimulants	90.0 (2)	14.1	90.0 (7)	12.9	t<0.1 d.f.=7 p=1.000	14	10.0
Compliance Hynotics	90.0 (6)	16.7	75. 6 (9)	38.4	t=0.9 d.f.=13 p=0.406	29	10.7
Compliance Others	100.0 (1)	-	70.0 (2)	42.4	t=0.6 d.f.=1 p=0.667		
Adequacy*	n	%	N	%			
1	21	53.8	36	62.1	χ^2=9.3; df=3; p=0.025		
2	8	20.5	3	5.2			
3	9	23.1	10	17.2			
4-5	1	2.6	9	15.5			
Total	39	100.0	58	100.0			

*AUD=Alcohol Use Disorders

**Large Effect size (0.8SD)