Alcohol and Substance Use in BD Patients

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It is common knowledge among clinicians that BD and substance use disorders (SUD) often co-occur in the same patient. However a number of methodological problems and limitations made research difficult on this specific topic. Additionally, clinicians are often unwilling to invest the time and effort needed to elicit the key features of the personal and psychiatric history which will reveal the presence of a SUD and elucidate its relationship with the development of BD and its role in the shaping of the patient's clinical picture.

Both for research as well as for clinical practice, a core issue is the direction of cause and effect in the relationship between BD and SUD. BD has a higher prevalence of SUD than that observed in any other mental disorder, and patients with both disorders have a more severe course of BD and worse outcome. They usually manifest an earlier age at onset, more frequent episodes, and more comorbid conditions. They more often face problems with the law and exhibit higher suicidality (Swann 2010). Some patients manifest BD first and SUD follows, while in others the sequence is the opposite. Obtaining a detailed chronology of the clinical history of the patient as well as a careful family history will be essential for the correct assessment and diagnosis.

9.1 Epidemiology

The data from the Epidemiological Catchment Area (ECA) suggest that drug abuse is present in 13 % of BD-I and in 9 % of BD-II patients and drug dependence is present in 28 and 12 % respectively. These rates suggest that BD-II patients had similar SUD rates in comparison to unipolar depressive patients but BD-I had double rates. All patient groups had much higher frequency of SUD (three to seven times) in comparison to the general population (Regier et al. 1990).

The most recent literature supports the high prevalence of alcohol and substance abuse comorbidity in BD, and this seems more pronounced in BD-I males which are

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single, with low education and with interepisodic cyclothymia and hyperthymia (Azorin et al. 2013; Lagerberg et al. 2010b). However, there are some data which relate SUD more with BD-II than with BD-I (Mazza et al. 2009). This high prevalence includes also the bipolar spectrum and extends to include the use of social drugs such as tobacco and coffee (Maremmani et al. 2011). The comorbidity is especially high in teenagers and young adults, and in these age groups, it often represents self-treatment of mood instability. It has been reported that the lifetime prevalence of any SUD among adolescents with BD was 16 % (Goldstein et al. 2008b). SUD usually arises during the early course of BD, even before the first mood episode. The peak hazard is between 14 and 20 years of age, and it constitutes a risk factor or alternatively a prognostic sign for the development of BD with psychotic features (Hazard Ratio HR = 3) (Duffy et al. 2012).

In adults, the lifetime prevalence of SUDs is at least 40 % in BD-I patients, with alcohol and cannabis being those most often abused, followed by cocaine and opioids (Cerullo and Strakowski 2007; Lagerberg et al. 2010a). In comparison to the general population, BD is associated with a significant age-adjusted risk for any substance use disorder (HR = 8.68) including alcohol abuse (HR = 7.66), drug abuse (HR = 18.5) and dependence (HR = 12.1) and cigarette smoking (HR = 12.3), and this relationship is independent of a comorbid attention deficit/hyperactivity disorder, multiple anxiety, and conduct disorder (Wilens et al. 2008).

SUD is higher among patients with BD-I, followed by BD-II, and unipolar depression (Moreno et al. 2012). In terms of specific substance use, it seems that BD patients have higher rates of alcohol consumption and cannabis use, while schizophrenia patients more often use stimulants and other substances except alcohol (Ringen et al. 2008).

9.1.1 Epidemiology of Alcohol Use Disorder

BD and alcohol use disorder represent a significant comorbid population (Farren et al. 2012; Bernadt and Murray 1986). From all mental patients, BD patients might be at a particularly higher risk to develop alcoholism during lifetime, especially during periods of acute mania (Helzer and Pryzbeck 1988).

In clinical samples, alcohol use disorder is reported to affect more than one-third and up to 75 % of BD patients. However, the reports vary significantly by geographical location, gender (with males having double rates in comparison to females) and specific clinical characteristics of the study sample (Di Florio et al. 2013; Lai et al. 2012; Farren et al. 2012; Freed 1969; Morrison 1974; Estroff et al. 1985). This specific comorbidity is reported to be higher for BD-I males which are single and with interepisodic cyclothymia and hyperthymia (Azorin et al. 2013). The data of the ECA suggest that alcohol abuse is present in 15 % of BD-I and in 18 % of BD-II patients and alcohol dependence in 31 and 21 %, respectively. These rates are two to three times higher than those observed in unipolar depressive patients and four times higher in comparison to the general population (Regier et al. 1990).

9.1.2 Epidemiology of Cannabis Use Disorder

The cannabis use disorder rate is reported to be 5.7 % in patients with BD (Lai and Sitharthan 2012) but probably this is not higher in comparison to the rate observed in the general population. Other studies report much higher rates (15–65 %) especially during acute mania (Goodwin and Jamison 2007), but they were presented as posters or chapters in books and thus the methodology is of unknown quality.

9.1.3 Epidemiology of Gambling

The large Canadian Community Health Survey on Mental Health and Well-Being (CCHS 1.2), which included 36,984 individuals (aged 15 years or older), reported that the weighted prevalence of problem gambling was significantly higher for BD patients in comparison to the general population (6.3 % vs. 2.0 %; $p<0.001$) with an odds ratio (OR) equal to 2.3 even after controlling for potential confounders. Being male, single and with low education were factors that were increasing the risk. The risk was also increased in the presence of alcohol and illicit drug dependence and decreased with moderate to active physical activity level (McIntyre et al. 2007b). This strong relationship of problematic gambling to mood disorders and BD in particular is observed even after adjustment for medical conditions, health-related quality of life and recent stressful life events (Chou and Afifi 2011). In clinical samples the prevalence might be even higher. One study reported a rate of 12.5 % of problem gambling in BD and a similar rate in unipolar depression with males having more than double rates in comparison to females in the BD group (19.5 % vs. 7.8 %). Mood disorder appeared before gambling in the majority of patients (71 %) and was associated with a comorbid anxiety disorder and lower quality of life (Kennedy et al. 2010).

9.1.4 Epidemiology of Methadone

One study in BD-I and BD-II patients or patients with cyclothymia both HIV-infected and HIV-noninfected reported that 6.4 % were receiving methadone maintenance therapy (Applebaum et al. 2010).

9.1.5 Epidemiology of Cocaine

In a clinical sample of BD patients, 3.4 % were found to suffer from cocaine abuse and 6.7 % from cocaine dependence (Chengappa et al. 2000). The literature suggests that cocaine use is mostly related with periods of acute mania (Estroff et al. 1985; Weiss and Mirin 1986; Weiss et al. 1986).

9.1.6 Epidemiology of Opioids

It has been reported that 5.4 % of opiate users were suffering from BD (Kosten and Rounsaville 1986; Rounsaville et al. 1986), while up to 5–25 % of BD patients might suffer from heroin abuse especially during periods of acute mania (Estroff et al. 1985; Miller et al. 1989).

9.1.7 Epidemiology of Smoking

A study which covered the period 1999–2011 reported that 44 % of BD patients in comparison to 64 % of patients with schizophrenia and to 19 % of controls were smoking. It also reported that these rates were relatively stable without any detectable time trends. These authors reported that in psychiatric patients smoking was correlated with less education, a history of substance abuse, longer illness duration and Caucasian race, but not with psychiatric symptom severity (Dickerson et al. 2013). Somewhat lower rates were reported by another study which however utilized a different research approach and studied 80 adolescents between 13 and 22 years of age with co-occurring BD-I and cannabis abuse or dependence who reported ever trying a cigarette. These authors reported that 49 % of these participants were current heavy smokers and 70 % of these met DSM-IV-TR lifetime criteria for nicotine dependence (Heffner et al. 2013). A similar prevalence for smoking (45.5 %) has been reported concerning the time of first hospitalization. Also, it has been reported that cigarette smokers were significantly more likely in comparison to non-smokers to report recent use of marijuana (55.7 % vs. 18.1 %) and alcohol (67.2 % vs. 25.4 %) (Heffner et al. 2008).

A similar prevalence of smoking (53.9 %) was reported in BD-I patients from Israel and this rate that was 2.36 times higher in comparison to that of the general population in Israel (22.8 %) (Kreinin et al. 2012). This higher risk is comparable to that reported in the US population (2.4 times) and might correlate with specific genes (COMT, SLC6A3 and SLC6A4) (McEachin et al. 2010).

Overall, the epidemiological data suggest that in comparison to the general population, half of BD patients are current smokers in comparison to approximately one-fifth of the general population (2.5 higher percentage), one-third regularly use alcohol and more than 6 % marijuana and methadone and manifest problematic gambling behaviours (three times higher in comparison to general population).

9.2 Etiopathogenesis of SUD in BD

9.2.1 General Causative Factors and Mechanisms

The high comorbidity of alcohol and substance use disorders with mood disorders cannot be explained as merely the chance occurrence of two prevalent disorders (Farren et al. 2012). Although the classical interpretation for the increased prevalence of SUD in mood disorders is that of self-treatment, this might not be the sole valid

approach concerning BD. In the case of this specific disorder, it might also concern the augmentation or the triggering of desired or pleasurable states (e.g. use of stimulants to trigger hypomania or mania) (Bizzarri et al. 2007). Alcohol is usually used for both reasons, both because it exerts a disinhibiting effect but also because it possesses sedative and anxiolytic properties (McDonald and Meyer 2011) and thus alcohol use is related in a differential way to different phases of BD (Meyer et al. 2012).

The research on the causative relationship of BD with SUDs is limited in contrast to the significant amount of data which exist concerning schizophrenia. Recent research suggests that a subgroup of BD patients might develop a relatively milder form of the disorder only after extended exposure to alcohol or substance abuse (Cerullo and Strakowski 2007; Winokur et al. 1995; Feinman and Dunner 1996) and at a relatively later age at onset (Goldstein and Levitt 2006a, b).

The reverse, that is, how many BD patients develop alcohol and SUD secondary to an underlying bipolar diathesis, remains to be determined. Adolescents with BD are more likely than SUD patients without a mood disorder to report that they had started using the specific substance for its mood-altering effects. After the development of the SUD, there was no difference between mood disorder and non-mood disorder SUD patients concerning the reason why they continue using the substance (Lorberg et al. 2010). Early-onset and especially adolescent-onset BD especially in males was reported to predict the development of SUD but this was not the case concerning BD type or family history of BD (Kenneson et al. 2013; Feinman and Dunner 1996).

9.2.2 Neurobiology

The evidence suggests that intermittent stressors, mood episodes and bouts of cocaine use not only show sensitization to themselves but cross-sensitization to the others, and thus a vicious cycle is set to action (Post and Kalivas 2013). In addition, specific vulnerabilities seem to exist. There are some data suggesting that specific genes (COMT, SLC6A3 and SLC6A4) might predispose to the development both of BD and SUD; however the evidence is rare and sparse (McEachin et al. 2010). One study reported that patients with both BD and alcohol use disorders have smaller grey matter volume in the left medial frontal and the right anterior cingulate gyri in comparison to BD patients without alcohol use which had grey matter volumes similar to healthy controls. However it is unclear what is the cause and what is the effect (Nery et al. 2011). In line with this, in young persons with emerging BD who drink at risky levels, there is evidence suggesting there are reduced levels of glutathione which is the main brain antioxidant factor, in the anterior cingulate cortex (Chitty et al. 2013).

9.2.2.1 Endophenotypes

There are family data suggesting that BD and SUD do not share familial risk factors, since they correlate with different family histories. BD patients have mainly psychiatric family history, while SUD patients mainly have a family history of alcohol abuse (Sbrana et al. 2007). However there are data suggesting a more complex

relationship with relatives of patients with BD being at a higher risk to develop SUD no matter whether SUD is present in BD patients themselves (Wilens et al. 2007). Also, SUD in parents predicts BD in the offspring (Duffy et al. 2012).

9.3 Clinical Issues

A major clinical problem is the fact that many patients with active SUD living in the community present with a pattern of mood instability which does not fit into contemporary classification systems (Goldberg et al. 2008). The task to identify and diagnose a SUD in BD patients, and especially in adolescents, might prove to be very difficult since repeated and targeted interviews might be necessary to elicit relevant, accurate and reliable information (Black et al. 2012).

It is important to recognize both the specific SUD as well as BD so that competent treatment is provided to both. Unfortunately in most programmes which aim SUD, the diagnosis of BD is often neglected even when properly put. Since BD is a treatable mental disorder, missing the opportunity to properly treat it is unacceptable, and this concerns also the whole bipolar spectrum (Maremmani et al. 2008), which appears particularly likely to invite self-medication.

There are several reports which link specific clinical features of BD with the presence of SUD. In many cases, substance use and abuse is associated with mood states (Baethge et al. 2008). It has been reported that during an acute depressive episode, SUD patients were using more often non-prescribed anxiolytic hypnotics, while during a hypomanic episode, they were using cocaine and amphetamines. During a full-blown acute manic episode, they were using more frequently cannabis and cocaine amphetamines, while during mixed episodes, the pattern of use included alcohol, cocaine amphetamines and cannabinoids. According to these data, the use of stimulants is more prevalent during the 'up' rather than the 'down' phase of the illness (Maremmani et al. 2012). It is possible that SUD alters the clinical presentation of BD and induces a kind of 'mixed' states (Winokur et al. 1969; Himmelhoch et al. 1976) and it might also increase the risk of switching during treatment with antidepressants (Goldberg and Whiteside 2002). According to one study, current psychomotor agitation and lifetime BD each were associated with increased prevalence of lifetime nicotine, alcohol and drug dependence (Leventhal and Zimmerman 2010). Concerning the bipolar type, the literature is inconclusive with some authors suggesting that SUD is related more with BD-I (Azorin et al. 2013; Lagerberg et al. 2010b), while others suggest it is related more with BD-II (Mazza et al. 2009). In patients with both BD and SUD, often there is also a comorbid personality disorder and the impairment is more severe (Mazza et al. 2009; Merikangas et al. 2008). An important psychological characteristic linking BD with SUD seems to be increased trait impulsivity (Powers et al. 2013).

BD preceded by substance misuse may represent a clinically milder subtype of bipolar illness. This subtype would be less 'primary' and might be more early targeted by primary prevention with programmes focused on substance misuse (Pacchiarotti et al. 2009). Overall, it seems that patients with a manic predominant

polarity have a better prognosis concerning their substance use (Gonzalez-Pinto et al. 2010). However, even if remitted, substance use is related to a poorer acute treatment response, longer time to remission and more time with subthreshold symptoms, more often depressive. There is also a relationship of rapid cycling with SUD but the direction of causality is unknown (Schneck et al. 2004). This poor outcome does not seem to correlate with sporadic subsequent substance abuse during follow-up (Gaudiano et al. 2008). It is reflected also in the rates of hospitalization. It is reported that practically all BD patients with substance abuse will be rehospitalized within a year in comparison to only one-fifth of the rest. This is especially true for polysubstance abuse in combination with separation from their spouse or partner. For those patients who were not separated, only half will be rehospitalized, and in comparison only one in ten patients without substance abuse and without being separated from spouse or partner would be rehospitalized within a year (Hoblyn et al. 2009). In contrast to these, there are some studies which report that the overall long-term outcome of BD is not necessarily worse in SUD patients (Mandelli et al. 2012; Lagerberg et al. 2010a).

A significant issue is that the presence of SUD is also related to higher medical comorbidity (Magalhaes et al. 2012) with the exception of obesity, since BD patients with SUD had a lower rate of overweight/obesity when compared with non-substance-dependent bipolar patients (39 % vs. 54 %, $p<0.01$) (McIntyre et al. 2007a). It is important to note that one of the most important medical comorbidities is HIV infection which is related with greater drug use severity (Meade et al. 2008). Another important fact is that SUD among bipolar adolescents is associated with a higher risk for suicide attempts and teenage pregnancy and abortion (Goldstein et al. 2008b; Goldstein and Levitt 2008).

As a result, the prevalence of comorbid SUD was reported to be higher among unipolar and BD deaths than that among all other deaths, and this was mainly because of suicide and other unnatural death in both men and women. Consequently, SUD is associated with a reduced mean age at death in comparison to the general population (11.7–33.8 years). In general, these effects were much stronger for drug use disorders than for alcohol use disorders (Yoon et al. 2011).

9.3.1 Clinical Issues Related to Alcohol Use

Overall, the literature suggests that the presence of mood symptoms is related to alcohol abuse and dependence. One consistent finding in BD patients is that alcohol use and abuse preceded or coincided with depression (Baethge et al. 2008; Reich et al. 1974), but it has also been reported that it increases only during periods of mania (Winokur et al. 1969). In the general population, the presence of hypomanic symptoms increases the likelihood of alcohol abuse and dependence (Do and Mezuk 2013). Some authors suggest that problems with alcohol in BD patients exist irrespective of phase of the illness (Hensel et al. 1979; Dunner et al. 1979; Bernadt and Murray 1986). There are some inconsistent data suggesting that BD disorder has a later onset when comorbid with alcohol abuse. This implies that alcohol probably

does not trigger BD but instead it is used as a self-healing method (Lagerberg et al. 2011). However, on the contrary, another study suggested that alcohol use is related to an earlier age at onset (Cardoso et al. 2008).

From a reverse angle, the risk to develop hypomania was specifically related to an unstable drinking pattern and binge drinking, but not higher consumption or alcohol abuse in general (Meyer and Wolkenstein 2010). Generally, bipolar alcoholics might have a better outcome concerning their alcohol problem in comparison to unipolar depressives (Farren et al. 2013).

Alcohol abuse and dependence are associated with a number of sociodemographic factors, including male gender and lower education. They are also related to a number of clinical characteristics, including the presence of psychotic features during the first episode, depressive symptoms, generalized anxiety and worse overall functioning (Mitchell et al. 2007; Cardoso et al. 2008). In this frame it is important for the clinician to have in mind that the number of days of alcohol use as well as any increase in this number are strong predictors of the emergence of a depressive episode in the subsequent month (Jaffee et al. 2009).

Increased impulsivity might mediate some severe manifestations of this comorbidity (Nery et al. 2013) including the remarkably high rates of suicide attempt observed in patients with comorbid BD and alcohol use. This increased suicidality might also be caused at least in part because of the greater overall burden of the disease which is experienced by these patients (Cardoso et al. 2008).

A specific clinical feature of comorbid alcohol abuse and dependence concerns the worse neurocognitive function both in BD-I and BD-II patients (Chang et al. 2012). These patients might have severe impairment on tests of executive functioning, verbal and visual memory as well as performance IQ (Levy et al. 2008). Patients without concomitant alcohol abuse show a much better recovery of their neurocognitive function when in remission (Levy et al. 2012).

In spite of the worse overall clinical picture related with alcohol abuse and dependence in BD patients, the literature does not suggest that these patients suffer from prolonged mood episodes of any type in comparison to the rest of patients. Concerning whether high levels of alcohol intake increase the risk of a mood recurrence, increase the rates of rapid-cycling and worsen the overall course of BD, the data are contradictory and inconclusive (Rakofsky and Dunlop 2013; van Zaane et al. 2010).

9.3.2 Clinical Issues Related to Cannabis Use

Cannabis abuse is reported to be significantly and independently associated with earlier onset of BD probably in a dose-dependent way (Lev-Ran et al. 2013; Lagerberg et al. 2011, 2013; De Hert et al. 2011; Aas et al. 2013). This implies that cannabis might trigger BD in vulnerable individuals (Lagerberg et al. 2011). The literature suggests that very often cannabis use selectively and strongly preceded and coincided with mania/hypomania (Baethge et al. 2008), and it was reported to correlate with a greater number of mood episodes of any type, a more severe course of BD

(Lev-Ran et al. 2013) and with prolonged mood episodes (Strakowski et al. 2007). BD patients who suffer from a concomitant cannabis abuse are similar to patients with schizophrenia in terms of worse outcome (De Hert et al. 2011).

Cannabis use was also related with lifetime history of at least one suicide attempt (Aas et al. 2013) and a trend for rapid cycling (Aas et al. 2013; Strakowski et al. 2007).

9.3.3 Clinical Issues Related to Cocaine Use

It has been reported that BD patients with concomitant cocaine use manifest higher rates of post-traumatic stress disorder and antisocial personality traits and are more likely to present with a mixed episode. They were also more likely to suffer from BD-I instead of BD-II (Mitchell et al. 2007). It is interesting that greater cocaine use severity was an independent predictor of total HIV risk, risk-taking sexual behaviour and an increased risk of sex trading (Meade et al. 2008, 2011).

9.3.4 Clinical Issues Related to Opioid Use

The literature on opioid use in BD patients is rather limited and does not suggest any difference between those patients that use opioids and the rest in terms of any of the examined clinical and course indices (Shabani et al. 2010).

9.3.5 Clinical Issues Related to Nicotine Use and Smoking

According to a recent study, in most BD patients with lifetime nicotine dependence, BD appears first and smoking follows. In these patients the onset of BD occurred at an earlier age and was characterized by a higher number of manic episodes. In the minority of BD patients where nicotine dependence preceded the onset of BD, the age at onset of both BD and smoking was earlier and there was an increased coexistence of alcohol use disorder (Martinez-Ortega et al. 2013). On the other hand, it seems that in BD patients, smoking is related more with the concomitant use and abuse of other substances, rather than with the clinical characteristics of BD (Kreinin et al. 2012; Heffner et al. 2008), and it is specifically related with earlier age at onset of regular marijuana and alcohol use (Heffner et al. 2008).

In comparison to non-smokers, current smokers with BD showed greater episode severity (Baek et al. 2013), higher rate of history of conduct disorder (Goldstein et al. 2008a; Wilens et al. 2009), more frequent concomitant alcohol and drug use (Goldstein et al. 2008a; Baek et al. 2013) and poorer functional levels (Baek et al. 2013). Previous smokers displayed intermediate characteristics between current smokers and non-smokers. Current smoking status but not lifetime smoking history was related to a higher suicide risk but the data for lifetime history are controversial (Baek et al. 2013; Goldstein et al. 2008a).

There seems to be a dose–response relationship between smoking and worse overall clinical picture and long-term outcome in BD patients (Goldstein et al. 2008a). Probably the dose–response relationship and the complex pattern of smoking and nicotine use and dependence are responsible of a number of studies which report no relationship between the clinical characteristics of BD and smoking (Heffner et al. 2008; Kreinin et al. 2012).

9.3.6 Substance Use and Neurocognitive Disorder

There are only limited data concerning the neurocognitive deficit specifically in BD patients with concomitant SUD. BD patients with a history of alcohol abuse or dependence obtained lower scores in the interference task of the Stroop test compared to patients with BD alone. Both patient groups showed a poorer performance in some verbal memory and executive function measures than healthy controls. In those BD patients with history of alcohol misuse, greater difficulties of inhibitory control were found, and this could be attributed to higher impulsivity (Sanchez-Moreno et al. 2009). A rather consistent finding suggests that the history of alcohol abuse is not associated with the current neurocognitive deficit in BD patients (Sanchez-Moreno et al. 2009; van der Werf-Eldering et al. 2010).

It is interesting that one study reported a better than expected neurocognitive function in BD patients with concomitant cannabis use, which is in sharp contrast to the findings reported concerning patients with schizophrenia (Ringen et al. 2010).

9.3.7 Comorbidity

In comparison to controls, patients with BD and comorbid SUD seem to have an over fourfold increase in the relative risk for HCV and this increased risk can be attributed to both conditions (Matthews et al. 2008).

9.3.8 Disability

When SUD is present, the overall disability of BD patients is reported to be similar to that of patients with schizophrenia. Also, in the BD plus SUD group, a number of features, including suicide attempts, poor compliance, longer hospitalizations, shorter periods of remission and criminal activity, were also more frequently observed. It seems that the presence of SUD has a greater impact than the main diagnosis (schizophrenia vs. BD) in the prediction of worse social adjustment and poorer outcome (Jaworski et al. 2011).

9.3.9 Suicidality

It has been reported that SUD was associated with suicide attempts especially in BD patients (Harris and Barraclough 1997). This effect seems to be present in BD-I but not BD-II, and this was mostly explained by higher impulsivity, hostility and

aggression scores and earlier age at BD onset (Elizabeth Sublette et al. 2009). A more recent study suggested that specifically comorbid alcohol use puts the BD patient at a greater risk for a suicide attempt (OR = 2.25; 95 % CI, 1.61–3.14). In contrast, nicotine dependence and drug use disorders did not seem to increase the risk for suicidal behaviour. The data concerning the interaction between alcohol use and other SUDs in the emergence of an additional risk among BD patients are controversial (Oquendo et al. 2010; Elizabeth Sublette et al. 2009).

9.4 Legal Issues

Legal problems are consistently found to be more frequent in patients with both BD and SUD in comparison to BD alone (Goldstein et al. 2008b; Goldstein and Levitt 2008; McCabe et al. 2013). The odds of having a comorbid SUD diagnosis for arrested female BD patients was more than 38 times higher in comparison to community female BD patients (McDermott et al. 2007).

Women were more likely to have been arrested for violent and substance use charges, while men were more likely to have been arrested for theft and miscellaneous charges (McDermott et al. 2007). Apart from criminal activities, patients with BD and SUD are more likely to be involved in a variety of activities with potential legal implications, including teenage pregnancy and abortion (Goldstein et al. 2008b; Goldstein and Levitt 2008).

9.5 Treatment

Three open-label medication trials provide limited evidence that quetiapine, aripiprazole, and lamotrigine may be effective in treating affective and SUD symptoms in BD patients with cocaine dependence. Also, aripiprazole might be helpful in patients with alcohol use disorders (Cerullo and Strakowski 2007). There are two placebo controlled trials to date which suggest that valproate given as an adjunct to lithium in BD patients with co-occurring alcohol dependence improves both mood and alcohol use symptoms and that lithium treatment in BD adolescents improves mood and SUD symptoms (Cerullo and Strakowski 2007). It is important to note that there are data suggesting that substance use might increase the risk of switching during treatment with antidepressants (Goldberg and Whiteside 2002).

Overall the data are insufficient to support an informed design of pharmaceutical treatment strategy in BD patients with SUD. Some data are available for alcohol, cannabis and cocaine SUD comorbid with BD but the literature is poor concerning heroin, amphetamine, methamphetamine and polysubstance SUD comorbid with BD (Beaulieu et al. 2012).

Psychotherapeutically, it is important to investigate and recognize the patterns and reasons of substance use as well as the motivation for treatment. The reasons are usually idiosyncratic to the patient and evolve through personal experience (Healey et al. 2009). Further well-designed studies are needed in order to properly assess the potential usefulness of psychotherapeutic interventions in a specific and targeted manner in the treatment of specific SUDs comorbid with BD (Beaulieu et al. 2012).

The observed positive associations between GAD, later treatment with a mood stabilizer, and early childhood trauma and history of SUDs suggest that adequate treatment of comorbid anxiety, early treatment with a mood stabilizer and prevention of childhood trauma may reduce the risk for the development of SUDs in patients with BD (Gao et al. 2010a).

However the literature suggests not only that half of the patients might not receive correct treatment (Gao et al. 2010b) but also that the risk of long treatment delays is increased in patients with excessive substance use, and this puts the patients in vicious cycles and worsens the outcome (Lagerberg et al. 2010b).

An important implication of the comorbid SUDs in BD patients is the frequent manifestation of poor medication adherence and the presence of negative attitudes concerning medication management (Keck et al. 1997) which often leads to poorer outcome (Calabrese and Delucchi 1990). Helping patients with BD achieve remission from SUD may lead to a more successful course of BD treatment (Teter et al. 2011; Manwani et al. 2007).

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