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Review

SUBSTANCE ABUSE COMORBIDITY IN BIPOLAR AFFECTIVE DISORDER

P.N.SURESH KUMAR,
M.D, D.P.M,D.N.B.(Psych.),
S.S.RAJU,M.D.

Abstract

The co-occurrence of bipolar disorder and substance abuse has been little studied. The authors reviewed the literature in order to clarify the current state of knowledge of this subject and to identify possible areas of future research.

Introduction

The term comorbidity is defined as any distinct additional clinical entity that has existed or that may occur during the clinical course of a patient who has the index disease under study (Feinstein, 1970). Studies of comobidity in psychiatry is difficult because of the lack of clearly defined etiology and the limitation in establishing a distinct psychiatric diagnosis. However, it is because of these limitations that studies of co- occurrence in psychiatry are important. Psychiatric symptoms that share many signs and symptoms and that occur together may simply reflect the variable presentation of same psychopathology or may share a common pathophysiological mechanism. For example, syndromes like panic disorder, major depression and obsessive compulsive disorder may have many of the symptoms in common and respond to similar treatment suggesting a common underlying pathophysiological mechanism (Hudson et al, 1990). Alternatively a syndrome or illness may represent a risk factor for another. For example. alcohol abuse may lead to likelihood of developing depression (Schuckit, 1986).

Despite the important link between mania and depression in bipolar disorder, relatively few studies of comorbidity have been reported and this literature has not been recently reviewed.

Community sample.

Unlike other psychiatric comorbidities it has been well established that alcohol and drug abuse are significantly more common in bipolar disorders than the general population. The National institute of Mental Health Epidemiological Catchment Area (ECA) study (Regier et al, 1990) estimated the US lifetime prevalence rate of any substance abuse mental disorder at 22.5%, 13.5% for alcohol abuse/dependence and 6.1% for other drug abuse/dependence. In the same study, mood disorder (major depression, bipolar affective disorder) had an overall prevalence of 8.3%, the odds ratio of having any substance abuse disorder if a person has a mood disorder was 2.6%. Bipolar affective disorder was associated with the highest risk of any axis-1 disorder for coexistence with alcohol or drug abuse. The bipolar 1 group was found to have a prevalence rate of 60.7% with an odds ratio of 7.9 for any substance abuse or dependence diagnosis. Alcohol and drug dependence, the more severe form of the disorder when compared with alcohol or drug abuse is twice likely to be found in bipolar patients as in unipolar patients. Helzer and Pryzbeck (1988) in an earlier analysis of the same data found that patients with mania had an odds ratio of 6.2 for co-occurrence in alcoholism which was higher than any other axis-diagnosis.

Substance abuse in bipolar patients

This perspective comes from the investigation of substance abuse in samples of patients being treated for bipolar affective disorders. Reich and coworkers (1974) in a retrospective study of bipolar patients found that 31% had a history of excessive drinking and the excessive use predominated during the manic phase of illness. El-Gubaly (1975) reported 21% prevalence of drug or alcohol abuse among 110 hospitalised bipolar patients. Estroff and colleagues (1985) studied 36 patients who met the D.S.M. III-R criteria for bipolar affective disorders. 58% of those presenting with mania and 50% with mixed or atypical features had history of substance abuse. Hasim and colleagues (1985) reported alcohol and drug abuse in 835 patients with affective symptoms. Although they did not divide patients diagnostically into unipolar or bipolar groups, they found that overall 25% abused substances at a diagnostically significant level during the current episode. Keller and co-workers (1986) found that out of the 155 patients presenting with bipolar disorders, 5% of pure manics, 8% of pure depressives and 13% of those with mixed or cycling disorder met the criteria

for alcohol abuse. Miller and colleagues (1989) in their study of 60 bipolar patients reported that 25% abused one or more drugs, 18% alcohol, 8% abused cannabis and 5% abused opiates.

Brody and co-workers (1991) found that 30% of patients hospitalised with bipolar disorders (6 of 20) met current criteria for alcohol or drug abuse. Fogarty et al (1994) in a prospective study on 3258 randomly selected household residents of Edmonton, found that comorbidity of alcohol abuse was 45% and substance abuse was 34% in those with lifetime prevalence of manic episode. Sonne et al (1994)conducted a study to explore the onset, course and features of bipolar affective disorder complicated by substance abuse. 44 patients presenting with a diagnosis of bipolar affective disorders were interviewed using structured clinical interview Schedule for D.S.M. III-R. The prevalence of past/current substance abuse was 68%. Russel (1994) in a study assessing the comorbidity of axis- I disorders in a group of patients with alcohol or drug abuse/dependence found that 36% of manics have life time prevalence of drug abuse/dependence. Strakowski et al in a series of studies (1992, 1993, 1994, Compr. Psych.- in press) have observed alcohol abuse/ dependence to be common even at the time of the first episode, affecting up to 39% of patients. In a recent study conducted by Sureshkumar and Raju (1996) on 100 hospitalised bipolar patients in Central Institute of Psychiatry, Ranchi, using Structured Clinical Interview Schedule for DSM III-R, the prevalence of past or current alcohol/drug abuse or dependence was 68%. Out of 100 patients 38.7% were abusing/ dependent on alcohol, 26.7% were abusing/dependent on cannabis, 10% were abusing nicotine, 4% were abusing sedative hypnotics and 3% were abusing multiple drugs (more than three).

Overall the rate of drug abuse/dependence appears to be elevated in bipolar patients ranging in records from 8 to 60% (Black et al, 1988; Wolf, 1988; Calabrese, 1990; Regier,1990 & Mueser, 1992). Lehman (1994) in a study assessing the prevalence and patterns of dual diagnosis among psychiatric inpatients found that out of 109 patients having an independent mental disorder with psychoactive substance use disorders, 27.5% had bipolar disorders.

Bipolar disorder in substance abuse treatment seeking population

The percentage of patents with bipolar disorder in substance abuse treatment-seeking population exceeds all studies reported to date. In a study by Hesselbrack and collages (1985) on hospitalised alcoholics, manic was found to have occurred in 2% of the population. Ross and co-workers (1988) found that 1.9% of 501 patients with alcohol and drug abuse disorders whom they interviewed met lifetime diagnosis of bipolar

affective disorder.Lydiard and coworkers (1987) found that 4.7% of alcoholic patients they interviewed met the criteria of bipolar affective disorders set forth in DSM III-R. Mirin and coworkers (1988) reported in 160 treatment seeking substance abuse patients that 3.3% of opiate abusers, 22.2% of stimulant abusers and 6.1% of depressant abusers met DSM III-R criteria for bipolar spectrum disorder (bipolar I and II and cyclothymia). In a more recent report by this group (1991), compiled data on 350 hospitalised drug dependent patients treated over 10 years had a 4% prevalence of bipolar disorder and cyclothymia. Bipolar disorder was more frequent in stimulant abusers (17.5) than in opiate (5.4) or sedative-hypnotic (6.8) abusers.

Several recent studies focusing on psychopathology in cocaine abuse have reported similar results. Gawin and Kleber (1986) found that a significant percentage (20%) of cocaine abusers seeking treatment had affective disorders in the bipolar spectrum. In a study by Weiss et al (1988) on 149 patients hospitalised for cocaine abuse between 1982 and 1986, there were more affective disorders and cyclothymia in cocaine abusers than in other drug abusers. Nunes and colleagues (1989) found that in a group of 30 treatment seeking cocaine abusers, 30% met the lifetime diagnostic criteria for bipolar spectrum disorder. More recently, Rounsaville and colleagues (1991), in their study of 298 cocaine abusing patients reported that 20% met current criteria for bipolar disorders. Most reports of cocaine use in cyclothymia and bipolar disorder indicate that patients use cocaine to intensify and strengthen euphoric moods than to self medicate depressive episodes(Weiss et al, 1988). Although the prevalence rates may somewhat depend on the diagnostic criteria and methodology used, all studies suggest that a substantial number of cocaine abusers have bipolar spectrum disorders.

Genetic studies

Because bipolar disorder and substance abuse frequently co-occur, a common genetic predisposition or link has been suspected. In a true relationship there would be an increased prevalence of the first disorder in the relatives of patients with the second disorder. At present, data concerning genetic link between bipolar affective disorder and substance abuse are inconclusive.

Goodwin and colleagues (1973) have observed a higher rate of mood disorder in adopted away sons of alcoholics. The same group (1973) found an increased risk of depressive disorders in daughters of alcoholics only if they were reared by an alcoholic parent. Schukit (1985) has reported an increased risk of mood disorders in first

degree relatives of primary alcoholics. Mirin and co-workers (1991) found that the rate of mood disorders was consistently higher in female relatives than in male relatives of primary drug abuse patients. These findings are consistent with studies showing independent transmission of mood disorder and alcoholism (Cloninger et al; 1979, Merikingas, 1985).

The other side of the question concerns an increase in substance abuse disorders in the relatives of patients with mood disorder. Winokur and colleagues (1967,1971) have found an increase in alcoholism in relatives of patients with mood disorders, particularly if the mood disorder has an early on set. James and Chapman(1975) observed no increase in alcoholism in families of patients with bipolar affective disorder. While the relationship between these disorders is clearly complex and it appears that they may aggregate in different families, there is little evidence for a genetic linkage. It is possible that there is some genetic associations between these disorders or that these disorders are genetically linked in some families, but not in others. Clearly more work in this important area is needed.

Diagnostic difficulties

There is much difficulty in diagnosing bipolar affective disorder in the face of substance abuse, particularly with chronic use; which can mimic any psychiatric disorder. This is particularly true in the case of stimulant abuse in which intoxication can mimic mania or hypomania where as withdrawal can mimic depressive episode . Hence psychiatric disorders can be diagnosed only If, it occurs before the onset of substance abuse or during the remission from substance abuse. The difference in percentages reported from various studies may reflect different times of diagnostic interviews after abstinence. Another important point is the addition of bipolar spectrum disorders including cyclothymia in recent studies in the diagnostic system which will obviously increase the percentage of patients with mood disorder. If more subtle mood disorders contribute to substance abuse, recognition and treatment of the former is important.

Theoretical Implications

The theoretical perspective on this area comes from "behavioral sensitization model" or kindling which postulates that bipolar affective disorder is a kindled phenomenon because the course of illness is characterised by acceleration with successive shortened periods of remission between episodes (Post et al, 1984). Acute cocaine intoxication and alcohol withdrawal both appear to produce kindling in this population. Brown and colleagues (1986) found that alcoholics with more episodes of alcohol withdrawal were more likely to suffer

seizures during alcohol withdrawal which suggest progressive changes in nervous system as a result of repeated administration and withdrawal of alcohol. With increasing dose and duration of use cocaine produces symptoms resembling mood disorders ranging from mild hypomania to severe dysphoria with psychotic features (Post et al, 1989). Interestingly this progression resembles bipolar affective disorders. Cocaine potentially kindles neurons (Post & Weiss, 1988) and it has been postulated that this progression of symptomatology induced by cocaine may represent cocaine induced kindling of psychopathology.

It is interesting to speculate that when persons with underlying bipolar diathesis abuse substances associated with kindling, this abuse may produce or worsen the affective illness. Several studuies indicate that persons with bipolar affective disorders with comorbid substance abuse require more hospitalisation and do less well with treatments (Reich et al, 1974; Keller et al, 1986; Brody et al. 1995; Sureshkumar & Raju, 1996). Although there are conflicting data, these studies indicate that perhaps, substance abuse may worsen the course of bipolar affective disorder, An alternative explanation is that substance abusers may suffer from a worse form of bipolar disorder that makes them difficult to treat and more likely to abuse substances in an attempt to self medicate dysphoric mood or to enhance euphoric mood states.

Impact of substance abuse comorbidity on course of bipolar disorder

The role that comorbid substance abuse/dependence plays in the expression, severity and course of psychiatric disorders has attracted increasing attention and has become a point of interest in clinical research and practice. Although numerous studies have estimated the association between bipolar affective disorders and the risk of substance abuse, to date there is little information on the impact of substance abuse on the severity and outcome of coexisting bipolar disorders.

Reich et al (1974) found that excessive use of alcohol distinguishes manic patients with history of hospitalisation from those without. Himmelhoch et al (1976) in an investigation of the incidence and significance of mixed affective state found that mixed state correlate well with sedative abuse and poor psychopharmacological response. However it was not correlating with the severity of illness or mood circularity. Cohen et al (1988) have also shown similar findings as Himmelhoch et al that mixed state correlates with sedative abuse and poor treatment response Black et al (1988) compared complicated manics (with substance abuse) with uncomplicated manics and found that more uncomplicated manics(68.4%)

were recovered at discharge compared to complicated manics (45.6). Further analysis suggested that the influence of comorbidity was more important for women than men. Tohen et al (1990) in a four year follow -up study to investigate the outcome after an episode of mania. found a history of alcohol abuse as a predictor of poor outcome. Strakowski et al (1993) in a study to asses the prevalence and effects of comorbid psychiatric and medical comorbidity found that patients with affective psychosis were significantly more likely than non affective psychosis to have comorbid substance abuse diagnosis and they had poor intial outcome compared to those with medical morbidity.

Sonne et al (1994) studied the on set. course and features of bipolar affective disorder complicated by substance abuse, and found that individuals with bipolar affective disorder and comorbid substance abuse have more hospitalisation, higher incidence of dysphoric mania, earlier onset of mood problems and more comorbid axis I disorders. Sureshkumar and Raju (1996) compared the short term outcome of manic patients with comorbid substance abuse and without comorbidity. Three months follow-up showed that manics with comorbid substance abuse were more symptomatic, more likely to be unmarried , dysphoric and with irritable mood states than pure manics and had an earlier on set of mood disorders and longer duration of illness. From these studies it is clear that substance abuse is associated with pure outcome in bipolar disorders Additionally the presence of bipolar II diagnosis has been associated with a short term remission from comorbid alcoholism in contrast to bipolar I and schizoaffective disorders (Hasin et al, 1989).

Conclusion

Substance abuse is a commonly occurring comorbidity with bipolar affective disorder. The ECA data, and evidence from patient samples seeking treatment for substance abuse disorders as well as bipolar affective disorder confirms this finding. Follow-up studies show that patients with bipolar affective disorders complicated by substance abuse have poor prognosis both in terms of affective disorder and substance abuse. Considering these finding, it is unfortunate that there are very few controlled data addressing either the clinical aspects or the specific treatment efforts of this population. There is some theoretical rationale for the use of anticonvulsants (antikindling agents) in this population, but controlled studies are very few (Brody et al, 1995). In particular, a comparison of mood stabilising agent (such as lithium, valproate or carbamazepine) with antikindling effect would be of theoretical and practical interest. It is hoped that future studies will focus on this important and difficult to treat popula-

tion.

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Dr. P.N. Sureshkumar

Central institute of Psychiatry,
Ranchi - 834 007. BIHAR