

Review Article

Clinical perspectives on the management of common psychiatric disorders in India

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ABSTRACT

Psychiatric disorders are common health problems in patients of all age groups, under-diagnosis and under-treatment of these disorders can result in disability and serious complications. With an objective of creating a comprehensive evidence-based consensus on common mental health disorders and their management in the Indian setting, 10 expert groups meetings involving 98 psychiatrists across India were conducted in the month of May 2020. Clinical insights related to burden, signs and symptoms, diagnosis and management were summarized based on the discussions during these meetings. Experts agreed that depressive disorders and anxiety disorders represent two important psychiatric disorders in India. Selective serotonin reuptake inhibitors (SSRIs) are commonly used for the treatment of depression. Benzodiazepines are effective for the treatment of comorbid anxiety in patients with depression, but their long-term use causes adverse events such as dependence and withdrawal reaction. Obsessive compulsive disorder (OCD), bipolar disorder, substance use especially alcohol withdrawal syndrome, and sleep disorders are other common psychiatric disorders found among Indian patients. Lithium and valproate represent the commonly used and effective pharmacological treatments for bipolar disorder. SSRIs are preferred drugs in the treatment of OCD, whereas benzodiazepines such as chlordiazepoxide and diazepam represent important pharmacological treatment options for alcohol withdrawal. Early identification and timely and effective treatment of psychiatric disorders is important for prevention of complications. Treatment should be individualized based on efficacy, tolerability profile of the medicine, risk of drug interactions, and cost. This consensus may be useful to psychiatrists and general practitioners treating common psychiatric conditions in Indian patients.

Keywords: Alcohol withdrawal syndrome, Anxiety, Bipolar disorder, Depression, Obsessive compulsive disorder

INTRODUCTION

Mental disorders are an important cause of health burden in terms of years lived with disability, and they contribute

significantly to the disability-adjusted life-years especially in low- and middle-income countries. Considering the enormous disease burden of mental disorders, mental health is a part of health policies across the world.¹ According to published literature, prevalence

rates of psychiatric disorders in India range from 9.5 to 370 per 1000 people.² Among industrial employees, the range are even higher at 14.0%-37%.³ According to the recently published results of the Global Burden of Disease study, in the year 2017, a total of 197.3 million people in India had some type of mental disorder. Overall, one in seven Indians are affected by mental health-related disease. Over the years, in India, there has been increase in contribution of the mental disorders to overall disease burden even though differences in disease burden have been observed between different states within India.¹

Depressive disorders and anxiety disorders represent two leading mental health disorders in India. In 2017, a total of 45.7 million and 44.99 million people in India had depression and anxiety disorders, respectively.¹ Substance abuse contributes to 1.16% of all psychiatric consultations in the emergency services.⁴ Among the difference substances, alcohol (21.4%) cannabis (3.0%), and opioids (0.7%) are commonly abused.⁵ Insomnia is another common but neglected disorder. In a cross-sectional Indian study, chronic insomnia was observed in 33% of the adult population.⁶

Substance use i.e., use of licit substances is an important concern in the mental health related issues. The main examples related to substance use include tobacco, alcohol, cannabis and opioids.⁵ In emergency services, alcohol withdrawal is the most common substance use disorder for which patients seek consultation.⁴ Therefore, it is essential for primary care physicians and those involved in emergency care to understand the management of alcohol withdrawal syndrome.

Obsessive compulsive disorder (OCD) is another common disabling mental condition characterized by recurrent and persistent obsession and compulsion resulting in distress to the affected patients. The condition can be seen in children as well as adults. Genetic predisposition is suggested in its pathogenesis. Delayed treatment can lead to poor outcomes of management. Similarly, untreated patients may develop severe functional limitations. Bipolar disorder is also a chronic and functionally challenging mental disorder. It is often misdiagnosed as unipolar depression because of initial presentation in most patients. Misdiagnosis can result in wrong treatment and adverse outcomes.

Comorbidities are commonly reported in patients with psychiatric disorders. A study from India reported that 65% of patients with psychiatric disorders also have comorbidities.³ The common comorbidities in patients with psychiatric disorders include diabetes mellitus, hypothyroidism, and hypertension.⁷

Several factors, including education level, stress level, job satisfaction, family life, and stressful life event are important factors, determine the extent of morbidity in patients with psychiatric disorders.³ Early identification

and timely and effective treatment of psychiatric disorders is important for prevention of complications.

Ten expert groups meetings involving 98 psychiatrists across India were conducted in the month of May 2020 with the main objective of preparing evidence-based consensus on common mental health disorders and their management in the Indian setting. Clinical insights related to burden, signs and symptoms, diagnosis, and management of these disorders were summarized based on the discussions during these meetings. Literature search was performed using key databases including PubMed and Google Scholar to identify relevant articles to support the discussion points. All articles including review papers, systematic reviews, and meta-analyses were used for preparation of this manuscript.

Bipolar disorders

Common chronic psychiatric illness is characterized by alternating episodes of mania or hypomania and depression, or combination of mania and depressive symptoms.^{8,9} Lifetime population prevalence of bipolar disorder is 4%.¹⁰ Bipolar disorder is divided into two subtypes: bipolar I and bipolar II. Patients with bipolar I disorder have at least one episode of mania, whereas patients with bipolar II disorder have depressive and hypomanic episodes.¹¹

The symptoms of disease are recurrent and can be severe. The disease is associated with significant burden on patients, families, and society.¹⁰ Both bipolar I disorder and bipolar II disorder can be potentially disabling.⁸ Patients with mixed episodes i.e., manic phase with depressive symptoms, or mania with bipolar depression may present with challenges of management as they are associated with multiple episodes, severe symptoms, multiple comorbidities, and hence poor outcomes. Presence of mixed episodes is not uncommon in bipolar disorders. About 40% of patients with bipolar disorder have mixed episodes.¹²

The management of bipolar disorder requires accurate diagnosis. Better awareness of the disease symptoms increases chances of early and successful identification of the disease and hence selection of an appropriate treatment option.¹⁰ Several non-pharmacological and pharmacological treatment options are available for the treatment of bipolar disorder. The treatment options can be broadly classified into acute treatment and maintenance therapy.¹⁰ Pharmacological and non-pharmacological interventions, such as psychosocial therapy and electroconvulsive therapy (ECT), are selected based on the specific phase of the disease.⁸

Lithium in bipolar disorder

Despite its availability since more than five decades, lithium still represents an important pharmacological treatment for bipolar disorder. Its antimanic effect is well

established.¹³ There are conflicting results with use of lithium monotherapy in the treatment of acute bipolar depression.¹³ Lithium is one of the most effective long-term treatments for bipolar disorder.⁹ It is also a good option as maintenance treatment considering its long-term stabilizing properties.¹³ The limitations of lithium monotherapy in acute treatment of severe mania are toxicity risk and requirement of blood monitoring.¹³ Common adverse effects with lithium include diarrhea, polyuria, increased thirst, and enuresis.¹⁴ In highly agitated patients, lithium monotherapy may not show adequate response.¹³ About 20%-40% of patients with bipolar disorder do not show adequate response to lithium therapy.¹⁴ Benefit-risk ratio should always be evaluated while selecting lithium in the treatment of bipolar disorder.

Sodium valproate in bipolar disorder

Valproate, an anticonvulsant, is effective in acute mania and is commonly used as maintenance therapy in patients with bipolar disorder.¹⁴ Similar to lithium, valproate is another effective long-term treatment option for bipolar disorder.⁹ Valproate has been studied in comparative trials versus placebo, lithium, or olanzapine and in combination with lithium. A Cochrane review has reported that valproate is associated with lesser drop-out rate for any cause than placebo or lithium. Valproate plus lithium has shown to have more chances of prevention of relapse as compared to valproate monotherapy.¹⁴ The patient profiles for recommending lithium or sodium valproate in bipolar disorder is depicted in (Table 1).

Table 1: Patient profiles for use of lithium and sodium valproate in bipolar disorder.

Lithium	Sodium valproate
Classical euphoric grandiose mania, Few prior episodes of illness, a mania-depression-euthymia course, Patients with family history of bipolar disorder, Patients with family history of lithium response.	Acute manic exacerbations, Euphoric mania, Dysphoric or mixed mania, Patients with rapid cycling bipolar disorder, Multiple prior episodes, Predominant irritable or dysphoric mood and/or comorbid substance abuse, Patients with history of head trauma, Maintenance treatment for bipolar disorder, Patients with bipolar disorder with migraine, Male patients with bipolar disorders, Female patients not in child-bearing potential.

Valproate is also effective in migraine prophylaxis or in patients with bipolar disease having migraine comorbidity. Divalproex sodium has been reported to

have well-established efficacy in bipolar I disorder, manic episode, as well as mixed episode of bipolar disorder. It has a broad spectrum of activity with usefulness in bipolar depression and rapid cycling, psychotic symptoms, and impulsive aggression. According to the results of a meta-analysis, valproate is effective in acute bipolar depression.¹⁵ Literature also suggests that with a significant antimanic effect of valproate, it is also useful in the treatment of rapid cycling.¹⁶ Extended-release formulation and advantage of once-daily administration have the potential to improve compliance and hence treatment outcomes in bipolar disorder. One of the major limitations for use of valproate is risk of teratogenicity. Many pregnancies are unplanned; hence, in addition to the risks associated with disease, potential risks with pharmacotherapy should be considered in women of reproductive age.

Treatment of mixed episodes of bipolar disorder

In a study involving 71 patients with bipolar I disorder (mania-14.7% and mixed phase-85.3%), combination of valproate and lithium was found to be effective in severe mania. Combination resulted in significantly higher improvement in mixed, psychotic, and anxiety symptoms.¹⁷ Most patients with mixed states showed good responses with sodium valproate.¹⁶ In a randomized trial, Bowden et al compared response of valproate and lithium administered for 12 weeks in 268 patients with bipolar I disorder having a manic or mixed episode. Response rates with lithium and valproate were 72.6% and 79.5%, respectively, and there was no difference in median time to response, suggesting their comparable efficacy. Tolerability of the two agents was also similar.¹⁸ In mixed manic episodes, if pharmacotherapy does not provide adequate relief or has contraindications for use, ECT can be an effective treatment.¹²

Management of rapid cycling

Rapid-cycling bipolar disorder is another important challenging presentation as these patients may have poor treatment response and are at a high risk of suicide. Depressive episodes are more prevalent than manic episodes in these patients, and they tend to be more refractory than rapid-cycling episodes. In rapid cycling, use of antidepressants may cause worsening of the condition. Treatment approaches include removing the triggering drug (if present) and using mood stabilizers. Pharmacological agents useful in some patients with rapid cycling include lithium, anticonvulsants (divalproex, lamotrigine, and carbamazepine) and atypical antipsychotics. Non-pharmacological treatment in the form of psychosocial therapy is also useful.

Patients with bipolar disorders may approach primary care physicians or psychiatrists for treatment. Misdiagnosis is common in patients with bipolar depression. Many patients with bipolar disorder are initially diagnosed as having unipolar/major depression.

Most patients with bipolar disorder present with an episode of depression before an episode of mania. Often, it is depression rather than mania that drives people to seek medical treatment. Some patients would have never experienced manic episodes when they seek treatment for depression. Many patients with mania do not have insight into their manic symptoms and failing to recognize the disease. Therefore, primary care physicians should understand that many patients with depression may have bipolar disorder. Patients may spend the majority of time experiencing depression, and this typically is the presenting symptom.

Early diagnosis and treatment result in better outcome.⁹ Traditional antidepressants are not used for the treatment of mixed episodes, as they may worsen mania without resulting in improvement in depressive symptoms.¹² Therefore, primary care physicians should have high index of suspicion for diagnosis and should promptly refer patients to psychiatrists for appropriate pharmacologic therapy.

In addition to the primary symptoms, patients with bipolar disorders may have associated cardiovascular and/or metabolic comorbidities and substance use disorders.^{8,19} Considering their adverse effects on outcomes, these disorders also need attention during treatment. Patients with bipolar disorders and comorbid substance use disorder receive benefit from treatment with valproate. Valproate has also been found to be well tolerated in these patients.²⁰ Better understanding of pathophysiology, biomarkers for prediction of response and risk of adverse events, and personalized or targeted treatment affecting underlying cause remains an unmet need in the management of bipolar disorders.

Depression with comorbid anxiety

Depression is another highly prevalent affective disorder in the general population. It can be seen in adults as well as elderly people. Depression and anxiety share close association. It has been reported that comorbid depression and anxiety are observed in up to one quarter of patients in general practice. Most (~85%) patients with depression also have anxiety. Similarly, about 90% of patients with anxiety disorders also have depression. These epidemiological evidences suggest a close relation between depression and anxiety.²¹ Depression and anxiety can also occur in patients with other chronic medical problems including infertility, congenital heart disease, and irritable bowel syndrome.²²⁻²⁴ Anxiety and depression are common in cardiovascular disease, and they may have adverse effects on cardiovascular parameters. These disorders can have an effect on cardiac disease and contribute to adverse outcomes in these patients. Similarly, people with self-reported anxiety and depression have a 2-fold higher risk for onset of irritable bowel syndrome.²⁴ Depression and anxiety can also be associated with sleep-related problems. General practitioners may miss the diagnosis because of initial

vague and non-specific presentation. Physicians should take a careful history and conduct clinical examination supported with necessary investigations for accurate diagnosis.²¹ After the diagnosis, severity of illness should be measured by using appropriate tools/scales such as Montgomery-Asberg depression rating scale (MADRS), Hamilton anxiety rating scale (HAM-A), and Hamilton depression rating scale (HAM-D).

These scoring systems also help monitor disease progression and treatment response.²¹ Treatment options for depression and anxiety are classified into non-pharmacological and pharmacological therapies. Psychological interventions are important non-pharmacological interventions for the treatment of depression whereas antidepressants, benzodiazepines and antipsychotics (adjuvants) represent important pharmacological treatments for both depression and anxiety.²¹ Cognitive behavioral therapy (CBT), a form of psychological therapy, is a useful non-pharmacological treatment for these patients.^{21,25}

Antidepressants are the cornerstone of depression management, and several antidepressants are available in the market. All these medications have been found to be more effective than placebo in adult patients with major depressive disorder. However, some difference may be seen in the efficacy outcomes of different antidepressants.

Antidepressants may also cause different adverse events, and have tolerability and overall acceptability issues. According to the results of a meta-analysis, escitalopram, fluoxetine, and sertraline are among the more well-tolerated agents.²⁵ In the same meta-analysis, the tricyclic antidepressants amitriptyline and clomipramine were reported to have higher drop-out rates. Among the selective serotonin reuptake inhibitors (SSRIs), duloxetine and fluvoxamine had high drop-out rates. Venlafaxine, reboxetine, and trazodone also have high drop-out rates.²⁵ Tricyclic antidepressants may cause anticholinergic side effects and are also associated with risk of adverse cardiac events. Some antidepressants may be associated with cardiac autonomic dysregulation.²⁶ Considering this, appropriate antidepressant should be selected based on the efficacy, side effect profile, and risk of drug interactions. Currently, SSRIs are being preferred over tricyclic antidepressants due to their tolerability profile.²⁷ Considering its advantages of efficacy, safety, fewer drug-drug interactions, and simple dosing schedule, escitalopram is one of the preferred agents for initial treatment of depression.

Some antidepressants may provide a little improvement in the quality of sleep after short-term treatment of low-dose doxepin and trazodone. Evidence on long-term treatment with antidepressants for insomnia is lacking. Therefore, well-designed clinical trials with antidepressants for the treatment of insomnia are required. Side effect profiles of antidepressants vary considerably. According to the results of a meta-analysis,

fluoxetine is associated with a significantly lower incidence of side effects than tricyclic antidepressants (50.9% versus 60.3%). However, there was no difference between fluoxetine and other SSRIs (59.4% versus 59.3%). The common adverse events associated with fluoxetine can be broadly divided into activating types of adverse events and gastrointestinal adverse effects. Insomnia and anxiety are examples of activating adverse effects.²⁷

Benzodiazepines can also help reduce anxiety and insomnia, but they are not useful in treatment of depression. Moreover, benzodiazepines are associated with adverse effects such as dependence and increase in fall risk among the elderly.²¹ Withdrawal symptoms are another major problem with the use of benzodiazepines, especially when they are used for long periods of time. A meta-analysis favored sertraline over other antidepressants both for efficacy and acceptability.²⁸ Escitalopram is another commonly used, efficacious, and well-tolerated antidepressant. Several studies have documented its efficacy in patients with depression and anxiety.²⁹ In adult patients, escitalopram at 10-20 mg/day doses has been shown to be effective and is well-tolerated as a long-term treatment of depression with anxiety symptoms.³⁰ Weight gain is an important adverse effect of some antidepressants. Use of antidepressants such as amitriptyline, mirtazapine, and paroxetine are associated with increased risk of weight gain. Some antidepressants such as fluoxetine and bupropion can cause weight loss. Therefore, antidepressants should also be selected based on patient characteristics. Cytochrome P450 enzymes play an important role in the metabolism of antidepressant drugs. Polymorphisms in cytochrome P450 enzymes can affect efficacy and side effect profile of some antidepressants.³¹ Escitalopram has a low potential for drug-drug interactions with CYP metabolized drugs. Moreover, it is not extensively bound to plasma proteins.²⁹

Regular treatment with antidepressants is important for prevention of relapse among patients with anxiety disorders. According to the results of a meta-analysis with up to 1-year of follow-up data, discontinuation of treatment was associated with higher rates of relapse among responders when compared with patients continuing treatment.³² Another meta-analysis of randomized controlled trials further suggests a small, but increased, risk for suicidal events with the use of antidepressants in adolescents and young adults. In older adults, antidepressants may provide a protective effect. However, results of pharmacoepidemiologic studies have suggested a protective role of antidepressants in all age groups.³³ Under-treatment of depression and anxiety is common because many (~40%) patients do not seek the help of clinicians. Less than 50% of patients who approach clinicians are given effective treatments for depression or anxiety.²¹ Thus, appropriate treatment is essential in the management of depression and the specific anxiety disorder. Attention should be given to

psychosocial well-being of patients with medical conditions associated with comorbid depression and anxiety. Effective treatment of the underlying medical condition can improve comorbid anxiety and depression.

Obsessive compulsive disorder

Obsessive-compulsive disorder (OCD) is a common neuropsychiatric disorder, with a lifetime prevalence of 2%-3% in the general population.^{34,35} This disorder can be severe and significantly disabling. The onset of disease is usually seen during late adolescence or early years of adulthood.³⁶ Familial and heritable nature of the disease strongly suggests a role of genetics in the pathophysiology of OCD.³⁷ Neurological insults are also known to play a role in the pathogenesis of OCD.³⁸ In the development of OCD, serotonin system plays an important role.^{34,38} Dopamine and glutamate are also known to have a role in pathophysiology of OCD.³⁸

Classification of OCD as a psychiatric disorder has been a debatable issue. Prior to the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 classification, OCD was classified as an anxiety disorder. However, in DSM-5, it received a new category, namely, obsessive-compulsive and related disorders.³⁴ Repetitive acts in persistent OCD are performed by the person in response to the underlying obsession. Some symptoms of OCD are under-diagnosed and hence remain under-treated. OCD is a heterogeneous disorder. This can be explained by the types of obsessions and compulsive activities performed by different people, tics, causes, and response to drugs. Neuroanatomical correlates in the development of OCD include orbitofrontal cortex, anterior cingulate gyrus, and basal ganglia.³⁸

A study reported that period prevalence rate of OCD increases by 60% with an increase in the study period by one year.³⁹ Thus, the diagnosis of OCD is often delayed, and many patients with OCD fail to receive effective treatment.³⁹ Early and effective treatment of OCD is critical in preventing a chronic course and several long-term complications.^{36,40} Patients with OCD may also have difficulties in maintaining interpersonal relations. There are other risks in untreated patients including loss of job/employment, substance abuse, criminality, and risk of traumatic injuries.³⁸

Treatment of OCD comprises of medical and surgical options. Medical treatment consists of pharmacological and non-pharmacological options. Psychotherapy and cognitive behavioral therapy are the forms of non-pharmacological treatment used in OCD.^{36,38} Psychotherapy in the form of exposure and response prevention can be effective in many patients.³⁸ SSRIs are preferred drugs in the treatment of OCD.^{34,38} Many patients with OCD need SSRIs in higher than normal doses and for longer duration as compared to patients with other psychiatric disorders.^{38,40,41} Treatment response time with SSRIs is also longer.⁴⁰ Therefore, patients need

to counselled in order treatment discontinuation without consulting a clinician. If an SSRI is effective in a patient, it can be administered as a long-term treatment to prevent relapse.⁴⁰

Other treatment options that can be used as alternatives to SSRIs are clomipramine and serotonin/norepinephrine reuptake inhibitors.^{38,40} Difficult-to-treat cases may be given additional pharmacotherapy in the form of atypical antipsychotics.^{38,40} Other options for augmentation are pindolol, buspirone, and glutamate-blockers.³⁸ Pharmacotherapy should be considered based on the severity of disease, side effect profile of the medicine, and comorbidities in the patient. D-cycloserine is a promising drug which works in conjunction with CBT.³⁶ In severe cases, combination of psychotherapeutic and psychopharmacological interventions may provide better results as compared to psychotherapeutic interventions alone.⁴² Clinicians should also be aware of drugs that may worsen symptoms in patients with OCD. Examples of such drugs include atypical antipsychotic agents and dopaminergic drugs. ECT and transcranial magnetic stimulation are other options of treatment for patients with OCD.³⁸ Brain stimulation therapy is an attractive add-on treatment in refractory cases. In children with OCD, age-appropriate treatment (both non-pharmacological and pharmacological) should be given. Developmental level should also be considered. Parents should be educated and counselled regarding the course of the disease and their roles in overall management of OCD.

Treatment can significantly improve symptoms of OCD, and some patients can achieve remission. Patients should be carefully monitored for development of other psychiatric symptoms such as depression and suicidal thoughts.^{40,41} Considering the risk of relapse, treatment should be discontinued with care.⁴¹ Neurosurgery can be an option for the treatment of severe and refractory cases of OCD.

Alcohol withdrawal syndrome

Alcohol dependence is a common social problem and one of the important reasons for clinicians or psychiatric consultations in general practice. It has been reported that about 2%-9% of patients visiting family physicians have alcohol dependence.⁴³ In a retrospective study evaluating profiles of substance abusers, alcohol withdrawal was the most common cause contributing to 57.4% of presentations to emergency services in a tertiary care hospital.⁴ Patients with alcohol dependence are at risk of development of alcohol withdrawal syndrome if alcohol consumption is suddenly stopped. Patients with dependence may develop symptoms of alcohol withdrawal after few hours (6-24 hours) after the last intake of alcohol. There are varied and generalized symptoms of withdrawal affecting different systems. Central nervous system-related symptoms in these patients include agitation, hallucinations, insomnia, delirium, and seizures. Gastrointestinal symptoms include

nausea and vomiting. Tachycardia and hypertension are cardiovascular system-related symptoms. Tremors and sweating are other symptoms related to alcohol withdrawal syndrome.⁴³ Patients with alcohol withdrawal syndrome may have abnormal glucose metabolism. Therefore, these patients are at risk for the development of type 2 diabetes mellitus. Duration of alcohol intake and intensity of withdrawal symptoms also contribute to the risk of development of diabetes in patients with alcohol dependence.⁴⁴

The objectives of treatment include providing relief from symptoms and preventing complications. While doing this, patients should be motivated and treated for continued alcohol abstinence. In patients having mild or moderate symptoms, outpatient treatment can be given. Out-patient treatment reduces cost burden on the patient and allows continuation of work and less disturbance to family life.⁴³ The revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar) can be used for assessment of response to therapy.⁴⁵ Hospitalization is required for patients with severe condition or those at risk of developing complications.⁴³ Treatment for alcohol withdrawal syndrome can be pharmacological or non-pharmacological. The components of treatment include supportive, behavioral, nutrition, and drug treatment. Benzodiazepines such as chlordiazepoxide and diazepam represent important pharmacological treatment options. Pharmacological treatment is initiated with symptom onset. Treatment is continued till patients achieve symptomatic relief. Patients should be carefully evaluated and followed till symptomatic relief is achieved.⁴³ Chlordiazepoxide is a long-acting benzodiazepine with an elimination half-life of 24-48 hours.⁴⁶ Treatment with chlordiazepoxide can either be symptom triggered or administered as fixed schedules.

A randomized trial with chlordiazepoxide suggested symptom-triggered treatment with chlordiazepoxide is as safe as fixed-schedule regimen. In the symptom-triggered group, maximum daily dose of 300 mg was used for 10 days for patients with short alcohol withdrawal scale (SAWS) scores of >12 at baseline, and for patients with scores <12, maximum daily doses of 120 mg were used for 10 days. In the fixed-schedule regimen, chlordiazepoxide was given as 200 mg starting dose and reduced daily by 25 mg for patients with SAWS scores >12 at baseline.⁴⁷

In other studies, chlordiazepoxide was used at a dose of 80 mg/day. The dose was tapered with fixed schedule over 8 days of treatment.^{48,49} These chlordiazepoxide regimens were found to be well tolerated, and tapering of doses was fast and smooth, with low rates of withdrawal seizures and delirium.^{48,49} Thus, chlordiazepoxide was found to be an effective anti-anxiety agent with less risk of drug discontinuation reactions. Some patients may develop benzodiazepine-resistant withdrawal. Important predictors of benzodiazepine-resistant withdrawal include history of psychiatric illness, thrombocytopenia, gender,

and baseline severity.⁵⁰ Validated scales such as CIWA-Ar, SAWS, and severity of alcohol dependence questionnaire (SADQ) can be used for assessment of severity and monitoring response to therapy.^{45,47,48} Antiepileptics such as carbamazepine, oxcarbazepine, valproic acid, and gabapentin are associated with less abuse potential. Patients and their families should be involved in the decision of treatment and the overall treatment process for better outcomes.⁴³

CONCLUSION

Psychiatric disorders are an important cause of mental health burden across the world. Depressive disorders and anxiety disorders represent two important psychiatric disorders in India. SSRIs are commonly used medications for the treatment of depression. Benzodiazepines are effective for the treatment of comorbid anxiety in patients with depression. However, their long-term use is associated with several adverse events including dependence and withdrawal reaction. Obsessive compulsive disorder, bipolar disorder, substance use especially alcohol withdrawal syndrome, and sleep disorders are other common psychiatric disorders. Comorbidities are common in patients with psychiatric disorders. Early identification and timely and effective treatment of psychiatric disorders is important for prevention of complications. Treatment should be individualized based on the efficacy, tolerability profile of the medicine, risk of drug interactions, and cost.

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