Improving Monitoring outcomes in patients with Bipolar disorders
According to the World Health Organization (WHO), bipolar disorder is the sixth cause of disability-adjusted life years among all other diseases [2]. Bipolar disorder has been classically described as a cyclical illness, with full blown manic or depressive episodes interspaced with normal (stable/euthymic) periods. In contrast to the traditional view, evidence now suggests that patients experience a more subtle chronic course, characterized by residual symptoms, emotional dysregulation, sleep and circadian rhythm disturbances, cognitive impairment, and increased risk for psychiatric and medical comorbidity in between mood episodes. Maintenance therapies have traditionally focused on mood stabilizers including lithium, valproic acid, carbamazepine, and, recently, lamotrigine. All agents have been shown to be effective relative to placebo in preventing relapses and typically need to be used in combination to control symptoms [3]. Lithium has long been considered the gold standard of therapy. Relative to placebo, lithium use reduces the rates of manic or hypomanic episodes by 64% and depressive episodes by 30%–50% [4].

**Monitoring the outcome of treatment:**

To optimize treatment in patients with bipolar disorder, physicians need to monitor psychiatric and medical outcomes as well as medication adherence. Primary care professionals are accustomed to monitoring medical outcomes, but are less familiar with monitoring psychiatric outcomes and treatment adherence. The focus of monitoring changes during the course of bipolar disorder. In the asymptomatic phase monitoring commonly focuses on medication emergent side effects and treatment acceptability of the patient, both of which affect treatment adherence. In the symptomatic phase focus is given on depressive symptoms as the depressive symptoms are more pervasive than mood elevation symptoms. Several practical tools and strategies are available to assist clinicians in monitoring outcomes of patients with bipolar disorder in primary care practices.

**Psychiatric monitoring:** This includes monitoring not only of the primary psychiatric disorder that is not only of the depressive and manic symptoms, but also of the associated psychiatric co morbidities such as anxiety and substance use disorders. Clinicians should also remain vigilant for psychiatric adverse effects of medications, which may include treatment-induced suicidality and mood elevation. The variables used to assess psychiatric outcomes in patients with bipolar disorder are grouped into 3 basic dimensions: **general subjective (patient-rated quality of life and depression)**, **functioning/disability**, and **manic/psychotic symptoms**. The **general subjective dimension** is correlated with comorbid anxiety and personality disorders and a history of past year hospitalizations. The **functioning/disability** dimension correlated with the number of prior bipolar episodes, poor premorbid adjustment, low income, and disability. The **manic/psychotic symptoms** dimension correlated with treatment non adherence and low agreeableness.

**Tools for psychiatric monitoring:** Self-report instruments are more feasible than clinician-rated scales, given the time constraints that are typical in clinical practice. The 9-item **Patient Health Questionnaire (PHQ-9)**, is particularly useful because it is brief and validated and can be completed by the patient. The Beck Depression Inventory can also be used. The PHQ-9 has been validated for use as a categorical diagnostic screening tool that detects the presence or absence of a major depressive episode. If the PHQ-9 depression screen is positive, then, time permitting, more formal diagnostic tools may be used to confirm the presence of a major depressive episode. The PHQ-9 can also be used as an ordinal monitoring tool for severity of depressive symptoms that can track symptomatic improvement after treatment has begun [5]. The PHQ-9 can also be used to monitor improvement in depressive symptoms in patients with mood disorders. Response (clinically meaningful improvement) is present if the total score decreases by at least 50% from baseline. A score ≤ 5 and no more than mild symptoms indicates remission. A useful tool to assess the presence or absence of mood elevation symptoms is the **Mood Disorder Questionnaire (MDQ)** [6]. The MDQ is a 13-item, self-report assessment that screens for the DSM-IV criteria of manic or hypomanic episodes. To screen positive for mania or hypomania, the patient must have answered “yes” to
at least 7 of the 13 items. The MDQ is validated as a diagnostic screening instrument for detecting a lifetime history of mood elevation episodes, and repeated testing with this instrument can detect treatment-emergent mood elevation episodes. However, the MDQ is not an ordinal metric for severity of mood elevation symptoms.

**Psychiatric Comorbidities to Monitor:** Psychiatric comorbidities are extremely common in patients with bipolar disorder and detection and treatment of these comorbidities are crucial for optimal management [7, 8]. Psychiatric disorders that often co-occur in patients with bipolar disorder include anxiety, substance use, personality, and eating disorders. Patients diagnosed with a mood, substance use, or anxiety disorder should be screened for the other 2 types of disorders in this triad. When clinicians monitor the treatment of a patient with bipolar disorder, they need to know whether concurrent substance use or anxiety disorders are present, whether those disorders are impacting the treatment of the bipolar disorder, and which of these problems constitutes the main or primary condition, and as such, merits particular attention.

**Monitoring Adherence to medication:** Several factors contribute to suboptimal adherence to treatment for bipolar disorder. These factors may relate to the patient, the illness, the particular intervention, or the way the physician administers that intervention. Patient factors include demographic characteristics; for example, being of younger age, male, and unmarried are risk factors for nonadherence [9]. The stage or characteristics of the illness can also contribute to nonadherence to treatment; for example, patients have been found to be less likely to adhere to medication begun following grandiose and manic symptoms than to medication begun following a depressive episode [10]. Having fewer previous episodes or having comorbid personality or substance use disorders increases likelihood of poor adherence to medication. Treatment issues, such as adverse effects, and clinicians' treatment strategies, such as the use of polypharmacy, also may contribute to decreased adherence to medication. A poor therapeutic alliance between the clinician and the patient can adversely affect adherence as well.

**Strategies to Monitor Adherence:**

Monitoring patterns of appointment-keeping can help because patients who keep appointments tend to be adherent to treatments; conversely, those who miss appointments are more likely to be nonadherent. Using patients' self-reports is another strategy. Although these reports have a high likelihood of being true, the sensitivity of the report may be less reliable than other methods. Pill counts, electronic monitoring, laboratory measures of plasma drug concentrations, and pharmacy records are sometimes used to assess adherence to medication in clinical trials. Distinguishing whether the patient does not want to take medication regularly (e.g., due to fear of developing a dependence) or does not have the ability to take it regularly (e.g., due to forgetfulness or disorganization) is helpful. Clinicians can also recommend psychotherapy with a psycho education component to increase understanding of the nature of the illness and the need for preventive treatment. Other strategies to facilitate adherence to medication include discussing a preferred treatment formulation (e.g., orally disintegrating tablets versus injectable formulations) with the patient, reviewing benefits versus limitations of different medications, and assessing the tolerability of possible treatment options collaboratively with the patient. Patient education and frank discussions with patients and their families should be done to improve treatment adherence.
Medical Monitoring: Medical monitoring of patients with bipolar disorder is necessary (1) to assess the safety and tolerability of psychotropic medications and (2) to actively monitor for medical conditions common in this population. Some of the more common side effects of psychotropic medications used in the management of bipolar disorder that arouse concern are sedation and weight gain, but serious side effects for which clinicians have to remain vigilant, such as hepatotoxicity or pancreatitis, also occur on rare occasion. In addition, patients with bipolar disorder are at risk for medical conditions such as metabolic disorders, including excessive weight gain, obesity, and diabetes; endocrine disorders such as thyroid problems; and cardiovascular conditions.

Monitoring Medication Safety and Tolerability Side effects commonly seen in psychiatric patients involve the central nervous system (i.e., sedation, hypersomnia, insomnia, tremor, restlessness, and unsteadiness) and the gastrointestinal system (i.e., nausea, vomiting, diarrhea, constipation, weight gain, and metabolic problems).

Selected Safety and Tolerability Concerns in Psychopharmacologic Treatments for Bipolar Disorder: The antipsychotic agents all have a boxed class warning for increased mortality in elderly patients with dementia-related psychosis and unboxed class warnings or precautions for tardive dyskinesia, neuroleptic malignant syndrome, and leukopenia, neutropenia, and agranulocytosis. Second generation antipsychotics also have an unboxed class warning for hyperglycemia. Any medication with an indication for treating either unipolar or bipolar depression, including standard antidepressants as well as some second-generation antipsychotic agents, has a boxed class warning about the increased risk of suicidality in people aged 24 years or younger (in contrast, such risk is not increased for ages 25 to 65 and is decreased for age greater than 65) [11]. Anticonvulsants, that are commonly prescribed as maintenance agents in bipolar disorders have an unboxed class warning for suicidality. When monitoring patients treated with mood stabilizers, clinicians need to be vigilant for adverse effects such as neurotoxicity, hepatotoxicity, pancreatitis, rash, blood dyscrasias, teratogenicity, and serious rash. Clinicians also need to carefully watch for cardiac problems and pneumonia among elderly patients taking antipsychotic agents.

Common medical disorders comorbid with bipolar disorder: These include overweight and obesity, diabetes mellitus, cardiovascular disease, hypothyroidism, migraine, and pain disorders. Medical conditions that especially need to be followed closely are obesity, diabetes mellitus, and cardiovascular disease because they are so prevalent in this population and may be exacerbated not only by having bipolar disorder, but also by medications used to treat bipolar disorder. The ADA also produced a monitoring protocol for metabolic symptoms in patients taking second-generation antipsychotics [12]. The protocol sets out a minimal monitoring regimen, but more frequent assessments may be warranted depending on clinical status. At the outset of treatment, the protocol recommends that a personal and family history of diabetes should be obtained, and weight, waist circumference, blood pressure, fasting glucose, and lipid profile should be measured. Thereafter, weight should be carefully monitored for the first 3 months. Blood pressure, fasting glucose, and fasting lipids should be checked at 3 months and then annually together with other baseline indices. Cholesterol checks are recommended every 5 years, but, in clinical practice, cholesterol is commonly assessed once a year.

Conclusion: Bipolar illness is a chronic psychiatric illness with interspersed acute episodes of depression and mood elevation. Maintenance therapies used in treating the illness include lithium, valproic acid, carbamazepine, and, recently, lamotrigine. To optimize treatment in patients with bipolar disorder, physicians need to monitor psychiatric and medical outcomes as well as medication adherence. The variables used to assess psychiatric outcomes in patients with bipolar disorder include general subjective, functioning/disability, and manic/psychotic symptoms. Adherence to treatment is monitored by patient patterns of appointment keeping, pill counts, patients’ self reports, electronic monitoring, laboratory
measures of plasma drug concentrations, and pharmacy records. Medical monitoring to treatment is done by assessing the safety and tolerability of psychotropic medications and monitoring the medical conditions common in these population.

References:


