

Bipolar Disorder: Balancing Mood for a Stable Life

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The emphasis of the treatment of bipolar disorder is on effective management of the long-term course of the illness, which can involve treatment of emergent symptoms. Treatment methods include pharmacological and psychological techniques. A variety of medications are used to treat bipolar disorder; most people with bipolar disorder require combinations of medications.

Principles

The primary treatment for bipolar disorder consists of medications called mood stabilizers, which are used to prevent or control episodes of mania or depression. Proven mood stabilizers include lithium, and anticonvulsants such as Valproic acid (Depakote), carbamazepine (Tegretol), and lamotrigine (Lamictal). The atypical antipsychotics are all FDA approved for acute treatment of mania; these include quetiapine (Seroquel), olanzapine (Zyprexa), and risperidone (Risperdal). Generally speaking, mood stabilizers are more effective at treating or preventing manic episodes; however, some medications (i.e. lamotrigine, quetiapine) have been shown to be effective for the treatment of bipolar depression. In particular, lamotrigine is often the first-line treatment for bipolar II, where depression, rather than mania, tends to be the dominant symptom. Antidepressants are often prescribed to treat depressive symptoms, however the role of antidepressants remains controversial because antidepressants have been known to induce mania, and some researchers believe that they can worsen the course of the disease (see below). Medications are not the only available treatment for bipolar disorder; other treatments include omega 3 fatty acids, therapy such as psychotherapy and cognitive behavioral therapy, and exercise. Stress, alcohol abuse, and drug abuse can all cause bipolar disorder to worsen, and so effective treatment may require management of stress and moderation or elimination of alcohol and drug use. The goal of treatment is not to cure the disorder but rather to control the symptoms and the course of the disorder. Generally speaking, maintenance treatment of bipolar disorder continues long after symptoms have been brought under control.

Drugs used for bipolar disorder sometimes have significant side effects, which vary from drug to drug. Lithium may be associated with gastrointestinal upset (e.g. nausea, diarrhea), memory problems, weight gain and other side effects. Higher doses equal more side effects, but lower doses (within the therapeutic window) have little to no side effects. Anticonvulsant medications commonly cause sedation, weight gain, electrolyte disturbances, or other side effects. If one cannot tolerate one of the anticonvulsants, it's advisable to try another anticonvulsant. Two or more anticonvulsants in combination can often result in a lower effective dose of each and lower side effects. The side effect profile of the atypical antipsychotics vary widely between agents. Generally speaking, the most common side effects of the atypicals are sedation and metabolic disturbances (i.e. weight gain, dyslipidemia, hyperglycemia). Atypical antipsychotics may also cause extrapyramidal side effects and restlessness. Atypical antipsychotics also carry a risk of causing tardive dyskinesia; however, the risk with the newer atypical agents is much less than the risk associated with older antipsychotics (e.g. haloperidol). The risk of TD is thought to be proportionate

to the duration of neuroleptic/antipsychotic use (roughly 5% per year in non-elderly patients treated with older antipsychotics). Patients and physicians need to be careful to watch for symptoms of this side effect carefully so that an antipsychotic can be reduced in dosage, or changed to another medication, before the condition progresses. The physician should, of course, be consulted about any change in dosage.

A recent large-scale study found that severe depression in patients with bipolar disorder responds no better to a combination of antidepressant medications and mood stabilizers than it does to mood stabilizers alone. Furthermore, this federally funded study found that antidepressant use does not hasten the emergence of manic symptoms in patients with bipolar disorder.

Medications work differently in each person, and it takes considerable time to determine in any particular case whether a given drug is effective at all, since bipolar disorder is by nature episodic, and patients may experience remissions whether or not they receive treatment. For this reason, neither patients nor their doctors should expect immediate relief, although psychosis with mania can respond quickly to anti psychotics, and bipolar depression can be alleviated quickly with electroconvulsive therapy (ECT). Many doctors emphasize that patients should not expect full stabilization for at least 3-4 weeks (some antidepressants, for example, take 4-6 weeks to take effect), and should not give up on a medication prematurely, nor should they discontinue medication with the disappearance of symptoms as the depression may return.

Compliance with medications can be a major problem. Some people, as they become manic, may lose the awareness of having an illness, and they therefore discontinue medications. Patients also often quit taking medication when symptoms disappear, erroneously thinking themselves "cured", and some people enjoy the effects of unmedicated hypomania. Other reasons cited by individuals for discontinuing medication are side effects, expense, and the stigma of having a psychiatric disorder. In a relatively small number of cases stipulated by law (varying by locality but typically, according to the law, only when a patient poses a threat to himself or others), patients who do not agree with their psychiatric diagnosis and treatment can legally be required to have treatment without their consent. Throughout North America and the United Kingdom, involuntary treatment or detention laws exist for severe cases of bipolar disorder and other mental illnesses where there is a potential for harm to oneself or others.

Mood Stabilizers

Lithium salts

The use of lithium salts as a treatment of bipolar disorder was first discovered by Dr. John Cade, an Australian psychiatrist who published a paper on the use of lithium in 1949.

Lithium salts had long been used as a first-line treatment for bipolar disorder. In ancient times,

doctors would send their mentally ill patients to drink from "alkali springs" as a treatment. They did not know it, but they were really prescribing lithium, which was present in high concentration in the waters. The therapeutic effect of lithium salts appears to be entirely due to the lithium ion, Li⁺.

The two lithium salts used for bipolar therapy are lithium carbonate (mostly) and lithium citrate (sometimes). Approved for the treatment of acute mania in 1970 by the Food and Drug Administration (FDA), lithium has been an effective mood-stabilizing medication for many people with bipolar disorder. Lithium is also noted for reducing the risk of suicide. Although lithium is among the most effective mood stabilizers, persons taking it may experience side effects similar to the effects of ingesting too much table salt, such as high blood pressure, water retention, and constipation. Regular blood testing is required when taking lithium to determine the correct lithium levels since the therapeutic dose is close to the toxic dose.

The mechanism of lithium salt treatment is believed to work as follows: some symptoms of bipolar disorder appear to be caused by the enzyme inositol monophosphatase (IMPase), an enzyme that splits inositol monophosphate into free inositol and phosphate. It is involved in signal transduction and is believed to create an imbalance in neurotransmitters in bipolar patients. The lithium ion is believed to produce a mood stabilizing effect by inhibiting IMPase by substituting for one of two magnesium ions in IMPase's active site, slowing down this enzyme.

Lithium orotate is used as an alternative treatment to lithium carbonate by some individuals with bipolar disorder, mainly because it is available without a doctor's prescription. It is sometimes sold as "organic lithium" by nutritionists, as well as under a wide variety of brand names. There seems to be little evidence for its use in clinical treatment in preference to lithium carbonate. Individuals with bipolar disorder have complained that it is much weaker than lithium carbonate and, therefore, less effective.

Lithium has problems with its side effects, including hand trembling and intolerance of hot weather. Bzotropine is sometimes used to control the trembling, but itself causes sedation. Lithium has a very narrow window of effectiveness. Below that level it has no effect, and above it is toxic. For that reason blood must be sampled frequently to determine if the proper blood level is currently present.

Anticonvulsants

Anticonvulsant medications, particularly valproate and carbamazepine, are often used instead of, or along with, lithium. Valproate (Depakote, Epival) was FDA approved for the treatment of acute mania in 1995, and is now considered by some doctors to be the first line of therapy for bipolar disorder. A similar medication, valproic acid (Depakene) is also used. For some, it is preferable to lithium because its side effect profile seems to be less severe, compliance with the medication is

better, and fewer breakthrough manic episodes occur. However, valproate is not as effective as lithium in preventing or managing depressive episodes, so patients taking valproate may also need an antidepressant as an adjunct medicinal therapy.

New research suggests that different combinations of lithium and anticonvulsants may be helpful. Anticonvulsants are also used in combination with antipsychotics. Newer anticonvulsant medications, including lamotrigine and oxcarbazepine, are also effective as mood stabilizers in bipolar disorder. Lamotrigine is particularly promising, as it alleviates bipolar depression and prevents recurrence at higher rates. Lamotrigine is also well tolerated by many patients. ,

Zonisamide (trade name Zonegran), another anticonvulsant, also may show promise in treating bipolar depression according to Frederick K. Goodwin M.D. on a recent Medscape webcast titled "The Accurate Diagnosis and Long-Term Treatment of Bipolar Depression" to view the webcast [click here](#). (free reg required).

Topiramate has not done well in clinical trials; it seems to help a few patients very much but most not at all. It appears to be useful in some treatment resistant cases and for anxiety issues when clonazepam cannot be prescribed. Gabapentin has failed to distinguish itself from placebo as a mood stabilizer.

According to studies conducted in Finland in patients with epilepsy, valproate may increase testosterone levels in teenage girls and produce polycystic ovary syndrome in women who began taking the medication before age 20. Increased testosterone can lead to polycystic ovary syndrome with irregular or absent menses, obesity, and abnormal growth of hair. Therefore, young female patients taking valproate should be monitored carefully by a physician. However, the therapeutic dose for a patient taking valproate for epilepsy is much higher than the therapeutic dose of valproate for an individual with bipolar disorder.

Other anticonvulsants effective in some cases and being studied closer include phenytoin, levetiracetam, pregabalin and valnoctamide.

Atypical antipsychotic drugs

The newer atypical antipsychotic drugs such as risperidone, quetiapine, and olanzapine are often used in acutely manic patients, because these medications have a rapid onset of psychomotor inhibition, which may be lifesaving in the case of a violent or psychotic patient. Parenteral and orally disintegrating (in particular, Zydys wafers) forms are favoured in emergency room settings. These drugs can also be used as adjunctives to lithium or anticonvulsants in refractory bipolar disorder and in prevention of mania recurrence. They also have fewer side effects, and are often used in place of lithium, in combination with an antidepressant, an anticonvulsant, or both.

In light of recent evidence, olanzapine (Zyprexa) has been FDA approved as an effective monotherapy for the maintenance of bipolar disorder. A head-to-head randomized control trial in 2005 has also shown olanzapine monotherapy to be just as effective and safe as lithium in prophylaxis. Eli Lilly and Company also offers Symbyax, a combination of olanzapine and fluoxetine.

In addition, quetiapine (Seroquel and Seroquel XR) has been approved for the treatment of bipolar mania, bipolar depression, and for long-term maintenance treatment of bipolar disorder when used in conjunction with lithium or divalproex.

Ziprasidone (Geodon) and aripiprazole (Abilify) also show promise according to Gary Sachs M.D. of Harvard's Massachusetts General Hospital Bipolar Clinic and Research Program. (View the webcast above at the Bipolar Clinic and Research Program link).

The atypical antipsychotics have some potential for causing weight gain and diabetes, and in larger doses over long periods may sometimes create tardive dyskinesia, though with much lesser probability than with the typical antipsychotics, such as Thorazine, Stelazine, or Haloperidol (Haldol.)

New treatments

Modafinil (Provigil) and Pramipexole (Mirapex) show promise in treating the cognitive deterioration related to bipolar depression. In addition Riluzole, an ALS treatment, has been shown to be effective treatment. The breast cancer medicine tamoxifen has shown quick response to manic phases.

Antidepressants

Depression is one of the major symptoms of bipolar disorder (indeed, in bipolar II it is frequently the dominant symptom) and so antidepressants are often used to treat the disorder. Antidepressants are typically administered along with a mood stabilizer rather than as the primary treatment for bipolar disorder. Antidepressants include serotonin reuptake inhibitors (SSRIs) such as Prozac and Paxil, the serotonin-norepinephrine reuptake inhibitor Effexor, and the dopamine reuptake inhibitor Wellbutrin. Older antidepressants include the monoamine oxidase inhibitors (MAOIs). The herbal supplement Saint John's Wort has also been shown to be an effective antidepressant in a number of clinical studies, although the precise mechanism of action remains unclear.

However, some doctors and researchers argue that antidepressants should be used with caution, if at all, in treating bipolar disorder. Fredrick K. Goodwin M.D.(1), coauthor of Manic Depressive

Illness with Kay Redfield Jamison PhD and the NIMH's Robert M. Post gleaned evidence by comparing the life charts of individuals with BP I and BP II who were medicated with certain mood stabilizers only versus any combination of those mood stabilizers plus certain antidepressants. The life chart trends indicated that use of certain antidepressants (over months to years) caused a long-term worsening of the illness over the life course compared to certain mood stabilizers alone in both bipolar I and bipolar II disorders. Specifically, they observed increased cycle frequency, increased mood episode severity, the emergence of mixed states and more treatment-resistant (difficult to treat) bipolar disorder.. Some studies have also found that antidepressants pose a risk of inducing hypomania or mania , sometimes in individuals with no prior history of mania. Saint John's Wort, although a naturally occurring compound, is thought to function in a fashion similar to man-made antidepressants, and so unsurprisingly, there are reports that suggest that it can also induce mania . For these reasons, some psychiatrists are hesitant to prescribe antidepressants for the treatment bipolar disorder unless mood stabilizers have failed to have an effect, however, others feel that antidepressants still have an important role to play in treatment of bipolar disorder.

Psychotherapy and Cognitive Behavioral Therapy

Certain types of psychotherapy, used in combination with medication, may provide some benefit in the treatment of bipolar disorders. Psychoeducation has been shown to be effective in improving patients' compliance with their lithium treatment. Several studies of family therapy report it can improve family communication, social functioning and lithium compliance, though it appears to be effective mainly on females. Evidence for the efficacy of other psychotherapies is absent or weak, often not being performed under randomized and controlled conditions. Well-designed studies have found interpersonal and social rhythm therapy to be ineffective.

Although medication and psychotherapy cannot cure the illness, therapy can often be valuable in helping to address the effects of disruptive manic or depressive episodes that have hurt a patient's career, relationships or self-esteem. Therapy is available not only from psychiatrists but from social workers, psychologists and other licensed counselors.

Lifestyle Changes

Understanding One's Symptoms

Understanding the symptoms, when they occur and ways to control them using appropriate medications and psychotherapy has given many people diagnosed with bipolar disorder a chance at a better life. Technically this is called prodrome detection and this is partly what is meant by becoming an expert on one's illness.

Stress reduction

Forms of stress may include having too much to do, too much complexity and conflicting demands among others. There are also stresses that come from the absence of elements such as human contact, a sense of achievement, constructive creative outlets, and occasions or circumstances that will naturally elicit positive emotions. Stress reduction will involve reducing things that cause anxiety and increasing those that generate happiness. It is not enough to just reduce the anxiety.

Co-morbid substance use disorder

Co-occurring substance misuse disorders, which are extremely common in bipolar patients can cause a significant worsening of bipolar symptomatology and can cause the emergence of affective symptoms. The treatment options and recommendations for substance use disorders is wide but may include certain pharmacological and nonpharmacological treatment options.

Other Treatments

Omega-3 fatty acids

Omega-3 fatty acids may also be used as a treatment for bipolar disorder, particularly as a supplement to medication. An initial clinical trial by Stoll et al. produced positive results. However, since 1999 attempts to confirm this finding of beneficial effects of omega-3 fatty acids in several larger double-blind clinical trials have produced inconclusive results. It was hypothesized that the therapeutic ingredient in omega-3 fatty acid preparations is eicosapentaenoic acid (EPA) and that supplements should be high in this compound to be beneficial. Omega-3 fatty acids may be found in fish, fish oils, algae, and to a lesser degree in other foods such as flaxseed, flaxseed oil and walnuts. Although the benefits of Omega-3 fatty acids remain debated, they are readily available at drugstores and supermarkets, relatively inexpensive, and have no known side effects.

Exercise

Exercise has also been shown to have antidepressant effects. Its major advantages are that it appears to provide lasting improvement in mood, has no side effects, and is free.

Electroconvulsive therapy

Electroconvulsive therapy (ECT) is sometimes used to treat severe bipolar depression in cases where other treatments have failed and is 60 to 70 percent effective. Although it has proved to be a highly effective treatment, doctors are reluctant to use it except as a treatment of last resort because of the side-effects and possible temporary memory loss complications of ECT, particularly

when repeated treatments ("maintenance ECT") are needed.

Ketogenic diet

A ketogenic diet similar to the diet used for pediatric epilepsy was thought to have mood stabilizing and antidepressant effects. Stanford University Medical School attempted a study using a ketogenic diet protocol on bipolar patients. However due to the lack of ability to attract subjects the trial was never started. Studies have shown it to have anti-depressant properties in rats.

Cannabinoids

While some reports indicate that cannabis can lessen the severity of mania and depression symptoms, others indicate cannabis can trigger mania and has been noted to have "a detrimental and potentially causative role in the development of psychosis." However, a recent study noted neurocognitive functioning improved in bipolar patients who used cannabis. The study added that further research was needed.

THC can relieve depressive phases through its euphoriant action, while the tranquilizing effects of CBD can alleviate manic phases. CBD, another active constituent of cannabis, has proven anti-psychotic effects.

One recent online survey questioned the notion that marijuana smoking increases a user's risk for depression. The authors of the study show that marijuana users reported fewer somatic symptoms and daily users reported less depressed mood and more positive effect than non-users. These self-report data suggest that adults apparently do not increase their risk for depression by using marijuana. Many find that the calming sedation associated with the use of cannabis helps to alleviate depression.

Current medical marijuana pharmaceuticals (such as dronabinol, marketed as Marinol) exist in the U.S. while Sativex, a whole-plant cannabis extract, is currently being marketed in Canada, the UK and Spain. Sativex is used for various illnesses, such as MS, cancer, and depression. Individuals who want to access pharmaceutical cannabis, however, may not be able to receive it due to drug laws against marijuana. Although illegal in many places around the world, cannabis remains easy to grow and purchase. See legal issues of cannabis for more information.

A study listed on clinicaltrials.gov states that the University of British Columbia is conducting a study for bipolar using Cannabinoids.