An Individualized Approach to Treatment-Resistant Bipolar Disorder: A Case Series

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Context: Treatment-resistant bipolar disorder (TRBD) is an increasingly prevalent, debilitating condition with substandard treatment outcomes. Polypharmacy has become the mainstay among practitioners though long-term efficacy of this method has not been adequately tested.

Objective: Determine retrospectively if individualized, integrative treatment strategies applied while withdrawing pharmaceuticals were beneficial and safe among a TRBD clinic population.

Design: A chart review was performed for six adult patients, treated in a private psychiatric practice. Data were collected regarding psychiatric diagnosis, hospitalizations, medications, side effects, substance abuse, and applied treatments.

Results: Using individualized, integrative psychiatric treatment methods, the majority of medications were eliminated. Long-term remission was attained in all cases, defined as clinical stability with no discernable symptoms of bipolar disorder for at least one year.

Conclusions: Applying an integrative treatment approach, and eliminating most medications, provided lasting resolution of symptoms and side effects in a selected sample of TRBD outpatients. These data may provide the basis for future randomized, controlled trials.

Key words: holistic medicine, integrative medicine, bipolar disorder

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INTRODUCTION

Bipolar disorder (BD) is among the top 10 leading causes of disability globally for men and women, affecting an estimated 4.4–5.9% of the United States population and 1.4% worldwide.[1–4] A clear delineation of what constitutes successful resolution of BD has not yet been established, however, reduction in symptoms is the prevalent theme. The definition of remission, or resolution, frequently fluctuates among practitioners and researchers due to personal, professional, marketing, and political interests. Because of this discrepancy in terminology, the treatment outcomes measured in each trial are often arbitrarily established and vary between studies. While one study defines a successful outcome as a 50% reduction in symptoms, another considers it to be less than two depressive or manic episodes in an eight-week period.[5,6] There have been no studies to date defining long-term remission or recovery as being symptom free for the duration of the study, and no contemporary studies examining whether patients can be medication free after several months of illness.

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When remission of BD is not achieved, an individual's condition is considered treatment resistant (TR). Though TRBD is an increasingly prevalent condition, there is astonishingly little research regarding its treatment and definition.[5] The definition and classification of TRBD has not formally been established, however, it is commonly accepted that treatment resistance occurs when symptoms persist beyond six weeks of treatment, despite implementation of at least two phases of drug therapy.[7] The prevalence of TRBD is not known, but estimated to be nearly half of all diagnosed BD patients based on long-term, prospective, pragmatic studies.[8,9] A recent review of TRBD found that "our typical treatments are woefully inadequate for sustaining euthymic mood over a long period of time."[10]

The current conventional treatment model for BD consists primarily of pharmaceuticals, including lithium, anticonvulsants, antipsychotics, antidepressants, benzodiazepines, mood stabilizers, and combinations of these classes.[11,12] Polypharmacy has evolved as the main treatment modality among psychiatrists and the medical community as a result of poor outcomes with single medications. Even with polypharmacy, BD symptoms and remission rates often remain unchanged.[13] Though few multi-drug combinations have been tested in short-term studies and less so in long-term studies, they have emerged as a dominant way of managing BD.[14,15] The effectiveness of bipolar therapies varies dramatically between patients and requires continuous, closely monitored maintenance. The percentage of patients who do not respond to,

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or relapse during, at least one year of active treatment, regardless of compliance, is not known.

In addition, polypharmacy risks a number of serious side effects. Common side effects from mood stabilizers and antipsychotics include weight gain, diabetes, metabolic syndrome, sedation, insomnia, headache, impaired sexual function, muscle rigidity, parkinsonism and tremors, akathisia, prolonged QTc interval, tardive dyskinesia, and frequent urination.[16,17] Such side effects have led to particularly high participant drop-out rates in clinical trials, demonstrating the substantial impact these medications may have on quality of life.[18,19] Given the frequent lack of effectiveness and often unfavorable side effect profile of medical management, new approaches to the treatment of BD are needed that would allow the reduction or discontinuation of pharmacotherapy.

Integrative medicine refers to a treatment approach that addresses the whole person, including the mind, body and spirit, using evidence-based conventional and non-conventional therapies, through a partnership between the patient and physician. These methods are highly individualized and focus on promoting health and wellness. Integrative treatment of BD is not well studied, however, and the few reports that have been published focus on specific supplements prescribed in addition to traditional pharmaceutical medications.[20] Commonly applied integrative therapies for BD include nutritional programs, herbs and supplements, exercise, detoxification, mind–body therapies, and acupuncture.[21–25] Clinically, many of these therapies are used in combination with one another, not as stand-alone treatments. To our knowledge, there are currently no publications that examine the effect of an integrative psychiatry approach in the absence of pharmaceuticals within a TRBD population.

METHODS

The six cases presented in this series were derived from an adult TRBD population under the care of a board certified psychiatrist, M.G., applying an integrative psychiatry approach. The individual cases within this practice were selected among patients who successfully completed treatment and subsequently became predominantly medication free under his care. Data was compiled from each chart to include patient demographics, psychiatric diagnoses, co-morbid conditions, age when psychiatric care was initiated, reason(s) for seeking holistic care, medication history, side effects experienced, hospitalizations pre-holistic and post-holistic care, suicide attempts, history of substance abuse, holistic treatments applied, weeks of titration, and weeks of holistic treatment to date.

Integrative treatment consisted of three phases: preparation, medication titration, and medication free maintenance. In the first phase, the possible etiologies for BD such as psychological trauma, toxicity, vitamin and mineral deficiencies, allergies, food sensitivities, and chronic infections were explored. Lifestyle changes, supplementation, detoxification, and resolution of emotional traumas were implemented. During the second phase, pharmaceutical medications were gradually tapered according to each patient's sensitivity and presentation of withdrawal symptoms. Up to 5–10% reduction of one medication at a time was performed, every 7–60 days. Primarily non-pharmacological approaches were used while medications were substituted with various herbs, vitamins, minerals, and homeopathic remedies. After a closely monitored gradual titration and tapering of medications, all pharmaceutical medications were discontinued, if feasible. Phase three was focused on maintaining long-term emotional and physical stability. Acute needs were addressed as necessary, while supplements, acupuncture, counseling, and support continued to be implemented longterm.

Several working assumptions were made in the process of establishing a successful treatment protocol used among a TRBD population. (1) The first assumption was that BD is a very complex, non-specific condition with multiple etiologies. (2) Second, there is currently no clear evidence that particular medications are able to create long-term stability, with a notable improvement of symptoms without side effects. Contrary to that, it has been observed that some blockbuster medications can cause long-term mood instability. (3) Additionally, patients who failed to respond to three or more adequate medication trials were highly unlikely to respond to another trial. There is no scientific evidence that more medications will improve patient outcome. Therefore, medications themselves may be an obstacle to recovery. Getting patients off of medications was the only rational option left to return them to the state of well-being.

An effective treatment strategy needed to be comprehensive and address multiple biological, psychological, and spiritual needs. This necessitated that treatment be strictly individualized. The use of naturally derived herbs, vitamins, minerals, and lifestyle changes can be a valuable asset as reported in pediatric mood disorders.[26,27] These agents have largely been ignored, however, in the treatment of adult TRBD patients. Though naturally derived supplements have not been well studied and do carry some risk of side effects, they are thought to have fewer, and less serious, adverse reactions when compared with conventional medications, with the main concerns being supplement–drug interactions, gastrointestinal (GI) upset, and precipitation of mania.[27–29]

Medication discontinuation was performed following the addition of naturally derived supplements. All psychotropic medications create a state of biological dependence. Even the smallest reduction in medication dose can create withdrawal symptoms. These withdrawal or discontinuation symptoms are often difficult to distinguish from the original disorder. Therefore, medication reduction was prolonged and adjusted individually.[30,31]

A number of supplements and therapies were implemented with the goal of discontinuing medications. Emotional psychotherapy usually consisted of supportive psychotherapy and writing or drawing assignments. energetic modalities included treatments like applied psycho-neurobiology,[32] the emotional freedoms technique (EFT), and eye movement desensitization and reprocessing (EMDR). applied psycho-neurobiology[32] is a method combining systemic family constellation (SFC),[33] EFT,[34,35] and EMDR,[36,37] guided by kinesiological testing. EFT is a method in which patients mentally focus on traumatic events while tapping specific acupuncture points. EMDR is a well-researched method involving the imitation of eye movements while holding