CASE SERIES

# Medication-free Alternatives for Long-term Maintenance of Bipolar Disorder: A Case Series

## 用无药替代方式来进行躁郁症的长期护理：病例报告系列

## Alternativas sin medicamentos para el mantenimiento del trastorno bipolar a largo plazo: serie de informes de casos

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### ABSTRACT

Psychopharmacological treatment has been the mainstay in long-term maintenance of bipolar disorder (BD) patients for the last 60 years. Conventionally accepted treatment options are primarily based on expert opinion rather than on well-executed, independently funded research. Investigation of maintaining patients without medications using treatment alternatives has been neglected. This clinical case series examines the outcomes of 7 BD patients who experienced a poor response or significant side effects with conventional treatment modalities. Patients were gradually and safely withdrawn from all medications. Treatment strategies were based on an individualized holistic approach using herbs, nutritional supplements, vitamins, amino acids, acupuncture, dietary recommendations, and behavioral modifications. Multiple treatment modalities were combined addressing the etiological causes for BD symptoms. Upon withdrawal from psychotropic medications, patients were free of medication-induced side effects and obtained psychiatric stability for at least 10 months. Further research is needed to investigate the long-term outcomes of BD treatment modalities based on well-defined successful outcome criteria, such as reduction in symptoms, improvement in quality of life, overall health outcomes, and cost effectiveness.

### 摘要

在过去六十年里，对于躁郁症（BD）患者的长期护理，其主要办法一直是使用精神性药物来治疗。通常被接受的治疗方案主要是基于专家意见，而不是基于执行良好、资金独立的研究。使用无药的替代方法来对患者进行护理，这方面的研究被忽略。此临床病例系列对7名采用通常治疗模式出现效果差或严重副作用的患者进行了研究。患者逐步安全地停止服用所有药物。治疗策略基于个性化全面方法，可使用草药、营养补品、维他命、氨基酸、针灸、饮食建议和行为纠正等方法。结合多种治疗形式来解决躁郁症症状的病因。在停用精神药物后，患者不再出现药物引起的副作用，精神稳定性保持了至少10个月。需要进一步的研究来调查躁郁症治疗方式的长期后果，调查基准是定义完好的成功结果标准，例如症状消退、生活质量提高、总体健康情况以及成本效益。

### SINOPSIS

El tratamiento psicofarmacológico ha sido el pilar fundamental en el mantenimiento a largo plazo de los pacientes con trastorno bipolar durante los últimos 60 años. Las opciones terapéuticas aceptadas convencionalmente se basan principalmente en la opinión de los expertos y no en investigaciones bien realizadas y financiadas de forma independiente. La investigación del mantenimiento de pacientes sin medicamentos usando tratamientos alternativos no ha recibido mucha atención. Esta serie de casos clínicos examina los resultados de 7 pacientes con trastorno bipolar que experimentaron una respuesta escasa o efectos secundarios significativos con modalidades de tratamiento convencionales. A los pacientes se les retiró toda la medicación de forma gradual y segura. Las estrategias terapéuticas se basaron en un enfoque individual holístico, utilizando productos de herboristería, suplementos nutricionales, vitaminas, aminoácidos, acupuntura, recomendaciones dietéticas y modificaciones del comportamiento. Se combinaron múltiples modalidades terapéuticas para abordar las causas etiológicas de los síntomas de trastorno bipolar. Tras la retirada de la medicación psicotrópica, los pacientes no tenían efectos secundarios inducidos por los fármacos y habían conseguido estabilidad psiquiátrica durante al menos 10 meses. Es necesaria más investigación para averiguar los resultados a largo plazo de las modalidades terapéuticas del trastorno bipolar basados en criterios de resultados positivos bien definidos, tales como la reducción de los síntomas, la mejora de la calidad de vida, los resultados generales de salud, y la rentabilidad.



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## INTRODUCTION

Bipolar disorder (BD) is a debilitating disease characterized as a long-term illness requiring diligent, continuous monitoring and maintenance.[1] Once remission from an acute episode is established, long-term maintenance therapy (LTM) is initiated. Current treatment guidelines recommended by the American Psychiatric Association (APA) for the maintenance of BD are comprised of lithium, divalproex sodium, lamotrigine, carbamazepine, antipsychotics, electro-

convulsive therapy (ECT), and psychosocial interventions.[1] In most cases, it is recommended that treatment for this condition continue indefinitely. ECT has been systematically studied only in acute phases,[2-4] and the evidence of long-term effectiveness is lacking.

Many clinicians use combinations of psychotropic medications when monotherapy is determined to be ineffective. The effectiveness of antipsychotic medications and drug combinations in LTM studies has not been established yet has become one of the main strategies for clinicians.[1,5,6] This strategy may be inferred from the rapid rise in atypical antipsychotic medication sales and increased use of polypharmacy.[7-10] It is estimated that nearly half of all BD patients who undergo pharmacological therapy still experience a relapse, accentuating the paucity of effective treatments for this highly diverse, complex illness.[11,12]

Several studies, and APA guidelines, advise against removing medications in the remission (maintenance phase) of BD,[1,13] suggesting that doing so would significantly increase the risk of relapse, suicide, and morbidity. Trials indicating that manic or depressive episodes occur upon the withdrawal of BD medications are often designed to remove medications in an abrupt manner, without allowing prolonged tapering from the medication.[14] Further studies have shown that a prolonged, gradual removal of lithium and other psychotropic medications greatly reduced the risk of relapse, suicide, and morbidity.[14-17] Additional studies indicate that long-term outcomes of BD patients are unchanged, irrespective of whether a patient discontinues lithium or maintains use.[14-16]

The notion of needing life-long medication maintenance was cultivated, in part, by two aspects of previous study designs. The first design issue was an overly rapid or abrupt elimination of medications.[18] Another commonly employed design enhances the sample by eliminating participants who relapse in an arbitrarily chosen elimination period, making selected participants less likely to relapse during the study period.[15,19,20] This idea is further supported by a naturalistic study conducted by Peselow et al.[21] This long-term study excluded 75% of nearly 1200 BD patients screened as a consequence of relapse in the prior 6 months on lithium monotherapy. Of those 305 patients selected, only 56 remained in the final year of follow-up. Only 2.8% (n=34) of the roughly 1200 participants treated were free of an affective episode for the entire 5-year period. This study demonstrates heuristic bias.[22,23]

In addition, the conventional approach to long-term maintenance of BD is accompanied by a number of serious side effects. The most commonly experienced side-effects from mood stabilizers and antipsychotics are weight gain, diabetes, metabolic syndrome, sedation, insomnia, headache, impaired sexual function, muscle rigidity, Parkinsonism, akathisia, prolonged QTc interval, tardive dyskinesia, hand tremor, and frequent urination.[11,24] Many long-term BD medication trials report disproportionately high rates of participant dropouts due to side effects, demonstrating the substantial impact psychotropic medications may have on the quality of life of many patients.[25,26]

Innovative approaches are needed for BD patients to reduce the impact of medication side effects and improve overall quality of life long-term. Few studies using supplementation and nutrition in addition to existing medications have been conducted in BD patients.[27-35] Here we describe a series of 7 patients diagnosed with bipolar disorder, type 1 (BD-1), implementing a holistic treatment approach without the use of pharmaceuticals. The treatment consisted of a combination of healing modalities selected based on patients' distinct individual features. The goal of this innovative approach was to eliminate treatment-related side effects and restore health and wellbeing. Individual outcomes from treatment are discussed.

## METHODS

The 7 cases examined in this series were selected from the private psychiatric practice of a board-certified psychiatrist (MG) and examined retrospectively. Patients were selected among those who (1) had a reliable diagnosis of BD-I, (2) continued with treatment for at least 1 year, (3) were able to adhere to treatment options, and (4) were motivated to pursue a medication-free alternative.

Data were collected from each chart regarding demographics, age at BD diagnosis, other psychiatric diagnoses, onset of psychiatric treatment, number of weeks on psychotropic medications, number of weeks of holistic treatment, conventional medications used, holistic treatments used, total number of hospitalizations, neuropsychological side effects reported, reasons for choosing holistic therapy, weeks of medication titration during holistic treatment, and substance abuse history. The Clinical Global Impression Score for Improvement (CGI-I) was recorded for all cases at the time of data collection. The CGI for Symptoms (CGI-S) at the start of holistic therapy was determined retrospectively according to detailed chart notes. The CGI is a validated instrument that allows clinicians to rate the overall mental health status of patients based on all of the information available to them. The 7-point severity scale on the CGI-S ranges from 1(normal, not at all ill) to 7 (among the most severely ill patients). The improvement scale (CGI-I) is similar and ranges from 1 (very much improved since the initiation of treatment) to 7 (very much worse since the initiation of treatment).[36]

### Patient Population

Patients who presented to the clinic were diagnosed by previous psychiatrists in either inpatient or outpatient settings as suffering with BD-I, and the diagnosis was confirmed during the initial interview with MG. Some patients had additional DSM-IV comorbidities. Patients 3-7 were considered to be

resistant to treatment based upon inadequate responses to prior trials of conventional medications or poorly tolerated side-effects. Patients indicated a preference for individualized care and a desire to discontinue medications. All patients were receiving several psychiatric medications prior to treatment in our clinic. Informed consent to be included in the series was obtained from all patients.

## Treatment Strategies

### *Overview*

Treatment was comprehensive, addressing multiple biological, psychological, and spiritual needs. The best results were attained when patient care was addressed from several angles simultaneously toward one goal: restoring patient health and well-being. Psychotropic medications were gradually eliminated with the support of various treatment strategies, consisting of herbs, minerals, vitamins, acupuncture, homeopathy, diet modification, exercise, and regulation of sleep cycles, as well as the management of gastrointestinal (GI) and endocrine issues with supplements or neural therapy. Guided imagery, energetic/spiritual therapies and psychotherapy were used as needed, as described below in more detail. These interventions were initiated at the beginning of therapy and continuous progress was monitored throughout therapy. Initially patients were followed 2 to 3 times per month by a psychiatrist (MG) or an acupuncturist/naturopath on staff. After a period of stabilization which usually lasted 2 to 6 months, the frequency of visits decreased to once every 1 to 3 months.

### *Lifestyle*

Modifications were made to the sleep-wake cycle, diet, and exercise. Patients were advised to fall asleep by 10:30 PM; avoid external stimulation like TV, computer work, arguments, or exercise for at least 1 hour before sleep; and have nothing to eat for 3 hours prior to sleep. Natural sleeping aids (eg, a combination of ashwagandha, L-theanine, phosphatidylserine, magnolia, and epimedium [Cortisol Manager, Integrative Therapeutics, Green Bay, Wisconsin]; lemon balm; passion flower; valerian root extract; and a mixture of ignatia, acidum phosphoricum, sepia, kalium bromatum, and zincum valerianicum [Nervoheel, Heel, Baden-Baden, Germany]) were employed if needed. Dietary changes included the elimination of all processed food, gluten, cow's milk, sugar, and corn products. All patients were encouraged to choose organic, nonprocessed food. We frequently suggested the Specific Carbohydrate Diet[37,38] for patients who were willing to comply. The addition of digestive enzymes (eg, Bio-Gest, Thorne Research, Sandpoint, Idaho) and probiotics (eg, HMF Forte, Genestra, Richmond Hill, Ontario, Canada) were given as needed. Aerobic exercises of the patient's choice were recommended for 30 to 60 minutes, 3 to 5 times per week, in all cases.

### *Psychotherapy*

Psychospiritual interventions aimed to address past emotional traumas, eliminate substance abuse, and build resilience (eg, by learning to be thankful for what we have in life, finding life lessons in adverse events). The main treatment modalities included supportive psychotherapy, systemic family constellation (SFC),[39] the emotional freedom technique (EFT),[40,41] and eye movement desensitization and reprocessing (EMDR).[42,43] SFC is an approach for resolving past traumas originating from traumatic family events. 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 traumatic events in mind. Applied psychoneurobiology[44] is a method combining SFC, EFT, and EMDR, guided by kinesiological testing. The majority of treatments, with exception of acupuncture, were provided by the main author (MG).

Self-regulation was taught through mindfulness and meditation. Patients were usually guided in meditation during outpatient psychiatry appointments with MG. Sessions were recorded, or audiotapes and books were recommended.[45] Basic qigong or yoga exercises were introduced, with referrals to neighborhood studios.

### *Medication Titration*

Initiating a slow medication titration was crucial to successful LTM. The main principles of medication titration follow. (1) Reduce medications very slowly, often one medication at a time, continuously monitoring for any significant withdrawal reactions. Reduce no more than 5% to 10% of the dose at one time or even less if there is a significant withdrawal reaction. (2) Start reduction with recently added, therapeutically less important agents, or medications with overlapping mechanisms of action. (3) Substitute high-potency medications with low potency-ones to facilitate dosage reduction (ie, substituting diazepam [a low-potency benzodiazepine] for alprazolam [a high-potency benzodiazepine] and subsequently tapering diazepam). Liquid forms of medications can facilitate titration, as with risperidone. Regularly available oral suspensions or customized formulations made by compounding pharmacies may be used.

Supplementation with vitamins, minerals, amino acids, fatty acids, and herbs was utilized to control emerging symptoms and prevent relapse. Their use was individually adjusted according to each patient's emerging symptoms in the collaborative therapeutic process. Each supplement applied in this series was given as directed by the manufacturer on the product label or adjusted individually. The quality of and recommendations for supplements can vary immensely between manufacturers, so in this series, the names of some proprietary blends are indicated. Supplements used for treatment of the most common symptoms are

described in more detail below. Occasionally, when symptoms were severe, prescription medications were used for several days to 2 to 3 weeks.

### *Anxiety Treatment*

Free amino acids (Total Amino Solution, Genesa, Brentwood, California) were used in the majority of patients. Other supplements used were magnesium and potassium (Magnesium-Potassium Taurate, Cardiovascular Research Ltd, Concord, California), Montmorency tart cherry (Keep Calm, TRB Health, Shadow Hills, California), extract of lavender (Aroma 23, UNDA-Seroyal, Pittsburgh, Pennsylvania), *Avena sativa* (Avena Sativa Herbal Liquid No.9, Somaplex), and a combination of herbal extracts including *Xanthium sibiricum* (Wind Pearls, Classical Pearls, Portland, Oregon). Herbs included valerian root, holy basil, lemon balm, linden flower, and gotu kola. Amino acids such as L-taurine, L-theanine, and L-tryptophan were often helpful for anxiety, depression, and insomnia with no apparent adverse events. Homeopathic remedies (Nervousness-Anxiety, Newton Homeopathic, Conyers, Georgia; Rescue Remedy, Bach Flower, Oxon, United Kingdom) were applied as needed.

### *Insomnia Treatment*

Herbs used to treat insomnia were chamomile, holy basil, linden flower, passionflower, and valerian root. Blends prescribed were a combination of ashwagandha, L-theanine, phosphatidylserine, magnolia, and epimedium (Cortisol Manager, Integrative Therapeutics); valerian root, passion flower, L-theanine, hops flower, wild lettuce leaf, and lemon balm (End Fatigue Revitalize Sleep, Integrative Therapeutics); nardostachytis root and rhizome, zizyphus, albizzia bark, hops flower, and L-theanine (Nardova, White Tiger), polygonum multiflorum stem, *Aconitum carmichaelii*, Ziziphus jujube seed, *Wolfiporia cocos sclerotium*, *Angelica sinensis root*, *Ligusticum sinensis root*, *Anemarrhena asphodeloides* rhizome, *Glehnia littoralis* root, *Zingiber officinale* rhizome, *Amomum villosum* fruit, *Sophora flavescens* root, and *Glycyrrhiza glabra* root (Peace Pearls, Classical Pearls, Portland, Oregon), melatonin (1-3 mg); and the amino acid glycine, either as a capsule or a powder (Glysom, Ajinomoto, Fort Lee, New Jersey). Homeopathics used for insomnia were combinations of *Avena sativa*, *Passiflora incamata*, zincum valerianicum, and coffea (Neurexan, Heel, Baden-Baden, Germany) and white chestnut, star of Bethlehem, clematis, cherry plum, impatiens, and rock rose (Rescue Sleep, Bach Flower).

### *Manic and Hypomanic Symptoms*

The key supplements given for an acute mood change or for emerging hypomanic or manic symptoms contained L-isoleucine, L-leucine, and L-valine (Branched Chain Amino Acid Formula [BCAA], JoMar, Campbell, California); choline bitartrate (Douglas Labs, Pittsburgh, Pennsylvania); and lithium orotate (Complementary Prescriptions, Carson City, Nevada). A multivitamin and herbal supplement blend (EMPowerPlus, Truehope, Raymond, Alberta, Canada) was used during medication titration and for relapse prevention. N-acetyl cysteine was also utilized for relapse prevention.

### *Depression*

The amino acid L-tyrosine served as a short-term intervention when patients' moods declined. Free amino acids (Total Amino Solutions, Genesa, Brentwood, California) and a combination of vitamin C, vitamin $B_6$, folate, vitamin $B_{12}$, selenium, magnesium, zinc, taurine, 5-hydroxytryptophan, and L-theanine (Travacor, NeuroScience, Osceola, Wisconsin) were used for anxiety symptoms. Ashwagandha, gotu kola, *Rhodiola rosea*, ginseng, SAMe, and St John's wort were used to elevate depressed mood.

Gastrointestinal balancing focused on improving GI functioning with digestive enzymes (Bio-Gest) or changing to a gluten- and milk-free diet. Hormone balancing was focused on improving thyroid function by using thyroid extracts (Nature Throid, RLC Labs, Cave Creek, Arizona), vitamins, and minerals like selenium, zinc, and iodine and promoting a normal menstrual cycle by using a homeopathic protocol (UNDA, Seroyal). Improving GI and hormonal functioning was essential to balance patients' mood swings.

Other methods applied within this patient population are less well known by the psychiatric community. For example, neural therapy is a widely used method in Germany and South America consisting of injections of procaine to specific areas of the body, which is purported to assist in restoring function of the autonomic nervous system.[46,47]

## RESULTS

The 7 cases presented in this series were previously diagnosed with BD-I, had a history of psychotic symptoms, and underwent at least 1 previous hospitalization (Table 1). Five cases had multiple psychiatric comorbidities; major depressive and anxiety disorders were the most common. The primary reasons indicated for seeking holistic treatment were the side effects experienced from medication. The most common emotional side effects reported prior to holistic therapy were psychological dullness, absence of emotions, and chronic mood instability. Most patients also had complaints of significant weight gain, GI issues (eg, constipation), and endocrine issues (eg, hypothyroidism, menstrual problems, lack of libido).

Patients 1 and 2 had recently been diagnosed with BD and enrolled into holistic treatment after psychiatric hospitalizations. Patients 3 through 7 had been managed with multiple psychotropic medications for 16 to 41 years and experienced multiple relapses and side effects during the courses of their treatment. Psychotropic medications were the mainstay maintenance treatment prior to holistic care in all cases.

**Table 1** Baseline Patient Characteristics

| Patient no. | Age (y)/ gender | Age of BD diagnosis | Psychiatric diagnoses | Hospitalizations | Medications in lifetime | Reasons for seeking holistic treatment |
|---|---|---|---|---|---|---|
| 1 | 17/M | 17 | BD-I | 1 | Clonazepam, divalproex sodium, risperidone | Severe side effects, desire to be medication-free |
| 2 | 23/F | 23 | BD-I, anxiety disorder NOS, major depressive disorder | 2 | Aripiprazole, clonazepam, paroxetine, quetiapine | Side effects, desire to be medication-free, seeking holistic lifestyle |
| 3 | 41/F | 25 | BD-I | 6 | Divalproex sodium, quetiapine, multiple antipsychotics, antidepressants, and mood stabilizers (poor recollection) | Side effects, seeking holistic lifestyle, poor effectiveness |
| 4 | 46/F | 28 | BD-I, bulimia, generalized anxiety disorder | 1 | Alprazolam, bupropion, buspirone, clonazepam, divalproex sodium, fluoxetine, gabapentin, haloperidol, lamotrigine, lithium, lorazepam, mirtazapine, nefazodone, olanzapine, quetiapine, sertraline, trazodone, ziprasidone | Side effects |
| 5 | 48/M | 20 | BD-I, generalized anxiety disorder | 3 | Lithium, quetiapine, trifluoperazine | Severe side effects |
| 6 | 52/F | 17 | BD-I, ADHD, generalized anxiety disorder, major depressive disorder | 3 | Aripiprazole, atomoxetine, bupropion, divalproex sodium, duloxetine, fluoxetine, haloperidol, lithium, mirtazapine, olanzapine, paroxetine, perphenazine, risperidone, sertraline, trazodone, venlafaxine | Side effects, poor effectiveness |
| 7 | 61/F | 19 | BD-I, cyclothymia | 1 | Carbamazepine, divalproex sodium, haloperidol, lithium, quetiapine, risperidone | Side effects |

Abbreviations: ADHD, attention deficit hyperactivity disorder; BD-1, bipolar disorder type 1.

All patients were tapered off of psychotropic medications and subsequently monitored while remaining in remission, free of medication. The average time required to eliminate medications was 43 weeks, with the longest being 105 weeks and the shortest 11 weeks. In spite of prolonged medication elimination, some patients experienced mild mood instability due to withdrawal effects, including increased anxiety, depression, irritability, impulsivity, and suicidal ideation. To offset these effects, the most common treatments used were lithium orotate, choline bitartrate, and branched chain amino acids for symptoms of hypomania; L-tyrosine for symptoms of depression; free amino acids (Total Amino Solution, Genesa) for symptoms of anxiety; and a multivitamin and herbal supplement blend (EMPowerPlus, Truehope)[32,35] during the maintenance period.

As illustrated in Table 2, herbs, vitamins, amino acids, omega-3 oils, sleep cycle regulation, and diet modifications were the predominant courses of treatment applied. Other treatments used were acupuncture, applied psychoneurobiology, guided imagery, and exercise.

At the time data were recorded from charts, the average time under holistic care was 110 weeks (range 42-352 wk; Table 3). Patients were under care for 10 months to 3 years after weaning completely from medications, with the exception of patient 7, who has been receiving care from MG for over 6 years. CGI-S scores improved from an average of 5 upon admission to holistic care to 1-2 at the last recorded visit. There were no hospitalizations or psychotic episodes in any patients during this period. To support long-term stability, patients were advised to continue taking the prescribed herbs, minerals, and vitamins in addition to adherence to dietary and lifestyle modifications. Patient 7 chose to retire, as she is currently over 70 years of age. The rest of the patients were able to return to school or resume otherwise productive lifestyles. As their symptoms were stable, their need for supplements decreased significantly. Patients 1 and 2 are no longer in need of care. Patients 4, 5, and 6 are seen 2 to 4 times per year. Patients 3 and 7 have psychological issues and vulnerabilities that are addressed by sesssions every 3 to 6 weeks.

## DISCUSSION

This case series demonstrates that the clinical application of individualized, holistic treatment methods was effective during the maintenance phase of BD. The slow withdrawal of pharmaceutical medications, supported by adjunct supplements, acupuncture, dietary changes, and behavioral modifications, did not induce a clinically significant manic or depressive episode in any of the cases. All patients were free of manic and depressive symptoms during the psychotropic medication–free period. Multiple side effects present prior to admission to holistic treat-

**Table 2** Treatments Applied

| Patient no. | Biological | Behavioral | Other |
|---|---|---|---|
| 1 | Amino acids, herbs, minerals, omega-3 oils, vitamins | Diet, sleep-wake cycle | None |
| 2 | Amino acids, herbs, minerals, omega-3 oils, vitamins | Diet, sleep wake cycle | Guided imagery, homeopathy |
| 3 | Amino acids, herbs, minerals, omega-3 oils, vitamins | Diet, exercise, meditation, sleep-wake cycle | Acupuncture, homeopathy, psychotherapy |
| 4 | Amino acids, herbs, minerals, omega-3 oils, vitamins | Diet | Acupuncture, guided imagery, homeopathy, psychotherapy |
| 5 | Herbs, minerals, omega-3 oils, vitamins | Anger management, diet, sleep-wake cycle | Acupuncture, Alcoholics Anonymous, homeopathy |
| 6 | Herbs, minerals, vitamins | Gluten-free diet, sleep-wake cycle | None |
| 7 | Herbs, omega-3 oils, supplements | Diet, sleep wake cycle | Acupuncture, guided imagery, psychotherapy |

**Table 3** Treatment Outcomes

| Patient no. | Medication titration (wk) | Holistic treatment (wk) | Medications prescribed prior to titration | Medications after titration | CGI-S at admission for holistic therapy (retrospective) | CGI -S Symptoms at last visit | CGI- I Improvement at last visit |
|---|---|---|---|---|---|---|---|
| 1 | 25 | 56 | Divalproex sodium, risperidone | None | 5 | 1 | 1 |
| 2 | 11 | 54 | Clonazepam, quetiapine | None | 5 | 1 | 1 |
| 3 | 25 | 42 | Divalproex sodium | None | 5 | 1 | 1 |
| 4 | 105 | 152 | Lamotrigine, quetiapine | None | 4 | 1 | 1 |
| 5 | 11 | 43 | Lithium | None | 5 | 1 | 1 |
| 6 | 64 | 82 | Bupropion, divalproex sodium | None | 5 | 2 | 2 |
| 7 | 62 | 352 | Clonazepam, divalproex sodium, lithium, risperidone, trihexyphenidyl | None | 5 | 1 | 1 |

Abbreviations: CGI-I, Clinical Global Impression Score for Improvement; CGI-S, Clinical Global Impression Score for Symptoms.

ment were eliminated during treatment.

Medication-free maintenance is an overlooked, but viable, alternative to conventional BD treatment. The holistic treatment method is an innovative approach in psychiatry that offers patient-specific treatment, allowing flexibility with the integration of multiple modalities in a synergistic manner. There are few, if any, side effects reported among patients treated with this approach, offering long-term, sustainable psychiatric stability.

Current paradigms in psychiatry can roughly be divided into 3 categories: (1) Western/contemporary, (2) integrative, and (3) holistic/traditional. The Western approach is primarily concerned with assigning patients to a specific diagnostic category and treating them with agents thought to be efficacious for that diagnostic category based on statistical significance in clinical trials. Diagnostic classifications, however, are descriptive, inaccurate, lacking in scientific support, and subject to frequent change.[48-51] Most psychopharmacological treatments are nonspecific, short-term, expensive, and have substantial side effects.[52] Furthermore, the cost of psychiatric treatments has become an overwhelming burden.[53] Integrative treatment strategies are similar to contemporary methods but advocate substituting medications with supplements or other approaches. Integrative strategies often utilize multiple laboratory tests to apply particular supplements to particular conditions. Both strategies strive to reduce identified disease-specific symptoms. In contrast, the purely holistic approach has limited interest in assigning patients to a particular medical diagnostic category or amelioration of disease symptoms but rather aims to restore patients to overall health and wellbeing. It is guided by a strictly individualized diagnostic approach. In that respect, the holistic approach shares more in common with traditional acupuncture and Ayurveda strategies. In our series, we utilized a combination of integrative and purely holistic methods.

There are number of studies and case reports in which particular supplements were reported to be helpful for some symptoms of BD. In recent literature, most reports concerned the effectiveness of a multivitamin and herbal supplement blend (EMPowerplus)[54] and were funded by the manufacturer. This supple-

ment has indeed been helpful in the maintenance and medication titration phases, but has a number of unpredictable side effects. While other studies reported positive results with such supplements as branched chain amino acids,[35,55] choline bitartrate,[56] and lithium orotate,[57] their effectiveness remains unclear.[58]

We did not find studies utilizing an amalgam of treatment strategies in a synergistic manner that were specific to individual patients' conditions at particular stages of their treatment. In our experience, applying treatment strategies drawn from diverse fields of healing are more conducive to returning patients to health.

This case series has a number of obvious limitations regarding the sample studied. Patients were selected from those who succeeded in treatment, and the size of the sample is quite small. In addition, the sample was chosen from an active outpatient psychiatric practice, where no standardized medical questionnaires were used, as would be done in an academic center. The severity of a patient's condition was recorded only using CGI scales.

The present methods also have a number of limitations with respect to their application to a general psychiatric practice. Few psychiatrists are familiar with integrative approaches (eg, the use of herbs, supplements, homeopathy, acupuncture, or neural therapy) or transpersonal psychology (eg, systemic family constellation or energy psychology). Our education has become quite limited, as it is more financially advantageous to provide patients with shortcuts of medication management, a strategy reimbursed well by the insurance industry. It may require considerable effort to change this paradigm. Our wish would be for doctors to receive education regarding acupuncture, positive psychology, and the use of herbs and supplements, similar to the paradigms of German Biological Medicine and naturopathic medicine. On the other hand, naturopathic doctors do not receive any training in psychiatry, even though they would be well suited to provide most of the treatments used in the present report. Furthermore, the proposed treatment strategy is not for every patient. It usually relies on self-pay and the motivation to take supplements and follow recommendations that lie outside of the commonly accepted beliefs that constitute a "normal" treatment strategy.

As a profession, psychiatry needs to develop clear criteria of what constitutes a successful treatment outcome and what should be considered a failure. The measure of success should be set sufficiently high to clearly separate success from failure. Definitions of success should include not only symptom reduction, but also an overall improvement in quality of life, health, and economic burdens of treatment. Future case reports, case series, and controlled studies are needed to determine if psychotropic, medication-free maintenance treatment significantly contributes to a decrease in BD symptoms, elimination of side effects, improvement in quality of life, and decreased financial burden. Future studies should be more pragmatic, avoiding arbitrary exclusion criteria and precipitous medication withdrawal. They should be inclusive of what is observed in day-to-day practice settings, including those patients who are considered resistant to treatment or have common medical and substance abuse issues.

BD is considered a life-long condition, but the majority of research on this illness has been performed in short-term pharmaceutical randomized controlled trials (RCTs). Studies examining long-term treatment of BD need to be done with a focus on slowly removing psychotropic medications and maintenance with supplements in lieu of medications. Although RCTs are often regarded as the gold standard, this design does not allow for applications of individualized treatment or multiple treatment strategies. To account for the complex nature of this illness, pragmatic clinical studies need to be designed and implemented to assess the effectiveness of a complex, flexible approach to complex patients based on individual patient needs. Comparative effectiveness studies between current treatment models and integrative treatment approaches, using herbs, supplements, psychotherapy, acupuncture, lifestyle modifications and other emerging treatment modalities also should be conducted.

In summary, an integrative approach to BD in these 7 patients, using slow, careful, supervised medication reduction, supported with the use of supplements, lifestyle modifications, and other modalities, led to moderate to long-term symptom stability and a viable medication-free alternative.

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