Bipolar disorder in women: Indications for preconception and prenatal maintenance pharmacotherapy

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INTRODUCTION

For bipolar patients who plan to or do become pregnant, maintenance pharmacotherapy is often indicated to delay or prevent mood episodes [1,2]. Onset of bipolar disorder in women typically occurs during childbearing years [3], and most patients are thus at risk for recurrences during pregnancy [1].

This topic reviews indications for preconception and prenatal maintenance pharmacotherapy in female bipolar patients. Preconception and prenatal maintenance treatment, the teratogenic and postnatal risks of medications used for bipolar disorder, and contraception and preconception counseling for female bipolar patients are discussed separately.

- (See "Bipolar disorder in women: Preconception and prenatal maintenance pharmacotherapy".)
- (See "Teratogenicity, pregnancy complications, and postnatal risks of antipsychotics, benzodiazepines, lithium, and electroconvulsive therapy".)
- (See "Bipolar disorder in women: Contraception and preconception assessment and counseling".)

DEFINITION OF BIPOLAR DISORDER

Bipolar disorder is a mood disorder that is characterized by episodes of mania (table 1), hypomania (table 2), and major depression (table 3) [4]. The subtypes of bipolar disorder include bipolar I and bipolar II. Patients with bipolar I disorder experience manic episodes, and nearly always experience major depressive and hypomanic episodes. Bipolar II disorder is marked by at least one hypomanic episode, at least one major depressive episode, and the absence of manic episodes. Additional information about the clinical features and diagnosis of bipolar disorder is discussed separately. (See "Bipolar disorder in adults: Clinical features" and "Bipolar disorder in adults: Assessment and diagnosis", section on 'Diagnosis'.)

FACTORS INVOLVED IN THE DECISION TO USE MAINTENANCE PHARMACOTHERAPY

The decision to use preconception and prenatal maintenance pharmacotherapy involves many factors, including the [1,5-14]:

- Patient's lifetime course of illness:
  - Number of mood episodes
  - History of episodes that included psychotic features (delusions and hallucinations) and/or suicide attempts
  - Comorbid psychopathology (eg, anxiety or substance use disorders) and general medical illnesses
  - Occupational and interpersonal functioning
  - Duration of euthymia during pharmacotherapy
  - Time to relapse following discontinuation of pharmacotherapy
  - Time to recovery following resumption of pharmacotherapy
  - Efficacy of specific medications during gravid and nongravid periods
- General risk of mood episodes during pregnancy (see "Bipolar disorder in women: Contraception and preconception assessment and counseling", section on 'Risk of maternal mood episodes')
- Reproductive safety data for medications, including (see "Teratogenicity, pregnancy complications, and postnatal risks of antipsychotics, benzodiazepines, lithium, and

electroconvulsive therapy"):

- Miscarriage
- Major and minor structural malformations
- Fetal growth restriction
- Neonatal toxicity and withdrawal
- Adverse postnatal developmental effects upon behavior, cognition, and emotional regulation

- Potential consequences of maternal mood episodes during pregnancy:
  - Suicidal behavior
  - Impulsive, risky behavior
  - Substance abuse
  - Malnutrition
  - Poor adherence with prenatal care
  - Low birth weight
  - Adverse postnatal developmental effects
  - Diminished mother-infant bonding
  - Disrupted family functioning
- Patient's preferences and values regarding:
  - Recurrent mood episodes compared with teratogenicity. As an example, one patient may be more concerned about remaining asymptomatic and working to support herself and other children, while another patient with more financial resources may place more value upon avoiding fetal toxicity.
  - The possibility of terminating a pregnancy if there is evidence of a malformation.
- Support and monitoring that is available

INDICATIONS

Preconception and prenatal maintenance treatment are often indicated for female bipolar patients, based upon the high risk of recurrent mood episodes in prospective observational studies, particularly in patients who discontinued pharmacotherapy [2,15]. However, for patients with a mild lifetime course of illness, it is reasonable to try to forego medications during pregnancy [1,16]. The risk of recurrent mood episodes is discussed separately. (See "Bipolar disorder in women: Contraception and preconception assessment and counseling", section on 'Risk of maternal mood episodes'.)

Mild lifetime course of illness — A mild lifetime course of illness is characterized by [1,17]:

- Persistent euthymia (eg, ≥2 years) between mood episodes
- Mood episodes that resolve completely within weeks of initiating treatment
- No history of suicide attempts or psychotic features (delusions or hallucinations)

For female bipolar patients with a mild lifetime course of illness who are planning a pregnancy, we suggest maintenance pharmacotherapy during conception and pregnancy to prevent mood episodes, based upon prospective observational studies that found untreated pregnant patients were at increased risk of recurrent mood episodes [2,15], as well as our clinical experience and that of several authorities [1,16-18]. However, patients with good social support may reasonably attempt to forego pharmacotherapy during the first trimester (when the risk of malformations is greatest), during the third trimester to avoid postnatal effects of drugs, or during the entire pregnancy to minimize any drug-related effects [1,16].

For bipolar patients who decline maintenance pharmacotherapy during the first trimester and remain euthymic, we suggest restarting pharmacotherapy during the second trimester, when organogenesis is essentially completed. A reasonable alternative is for patients to wait until they develop prodromal symptoms before resuming pharmacotherapy; however, subsyndromal symptoms are associated with an increased risk of full-blown relapses [19].

For female bipolar patients who are receiving maintenance pharmacotherapy and decide to stop it in anticipation of a pregnancy, we suggest that clinicians:

- Taper and discontinue pharmacotherapy over a period of two to four weeks. The risk of recurrence may be greater if medications are stopped more abruptly [1,2,20]. (See "Bipolar disorder in women: Contraception and preconception assessment and counseling", section on 'Relapse after discontinuing pharmacotherapy'.)

- Taper the medications by the same amount for each dose decrease; as an example, lithium 1200 mg per day is decreased by 300 mg per day, every five to seven days.

- Monitor patients every one to four weeks, depending upon the number and severity of mood symptoms [21].

- Observe patients during a short medication-free trial (eg, two to three months) before patients attempt to conceive, to gauge whether patients will remain euthymic during pregnancy without medications [16,18].

- Educate patients about methods to increase their likelihood of conception (eg, home ovulation detection kits and intercourse every other day during the week ovulation is expected), to minimize the time off of medications [21].

If bipolar symptoms recur during the medication taper, the medication is generally titrated back up to the full dose used initially to maintain euthymia. If a full-blown mood episode develops despite resuming the initial medication dose and does not improve within four to eight weeks, we suggest switching treatment. The treatment of bipolar mood episodes in patients is discussed separately. (See "Bipolar mania and hypomania in adults: Choosing pharmacotherapy" and "Bipolar major depression in adults: Choosing treatment".)

For bipolar patients who are medication free during the entire pregnancy, we suggest restarting maintenance pharmacotherapy after delivery to prevent postpartum mood episodes, based upon the high risk of recurrent postpartum mood episodes [1,21]. (See "Bipolar disorder in postpartum women: Treatment", section on 'Euthymic patients'.)

Moderate to severe lifetime course of illness — A moderate to severe course of illness is exemplified by one or more of the following [1,17]:

- Frequent mood episodes (eg, ≥1 episode every two years) despite adequate maintenance treatment
- Mood episodes resistant to treatment (eg, require months to years to resolve completely)
- History of suicide attempts or psychotic features (delusions and hallucinations)

For female bipolar patients with a moderate to severe lifetime course of illness who are planning a pregnancy, we suggest preconception and prenatal maintenance pharmacotherapy to prevent mood episodes, based upon prospective observational studies that found untreated pregnant patients were at increased risk of recurrent mood episodes [2,15], as well as our clinical experience and that of several authorities [1,16-18,21,22].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Bipolar disorder".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, “The Basics” and “Beyond the Basics.” The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on “patient info” and the keyword(s) of interest.)

- Basics topics (See "Patient education: Bipolar disorder (The Basics)" and "Patient education: Coping with high drug prices (The Basics)".)
- Beyond the Basics topics (See "Patient education: Bipolar disorder (Beyond the Basics)" and "Patient education: Coping with high prescription drug prices in the United States (Beyond the Basics)".)

These educational materials can be used as part of psychoeducational psychotherapy. (See "Bipolar disorder in adults: Psychoeducation and other adjunctive maintenance psychotherapies", section on 'Group psychoeducation'.)

The National Institute of Mental Health also has educational material explaining the symptoms, course of illness, and treatment of bipolar disorder in a booklet entitled "Bipolar Disorder," which is available online at the website or through a toll-free number, 866-615-6464. The web site also provides references, summaries of study results in language intended for the lay public, and information about clinical trials currently recruiting patients.

More comprehensive information is provided in many books written for patients and family members, including The Bipolar Disorder Survival Guide: What You and Your Family Need to

Know, written by David J. Miklowitz, PhD (published by The Guilford Press, 2002); An Unquiet Mind: A Memoir of Moods and Madness, written by Kay Jamison, PhD (published by Random House, 1995); and Treatment of Bipolar Illness: A Casebook for Clinicians and Patients, by RM Post, MD, and GS Leverich, LCSW (published by Norton Press, 2008).

The Depression and Bipolar Support Alliance (available at the website or 800-826-3632) is a national organization that educates members about bipolar disorder and how to cope with it. Other functions include increasing public awareness of the illness and advocating for more research and services. The organization is administered and maintained by patients and family members, and has local chapters.

The National Alliance on Mental Illness (available at the website or 800-950-6264) is a similarly structured organization devoted to education, support, and advocacy for patients with any mental illness. Bipolar disorder is one of their priorities.

SUMMARY

- Bipolar disorder is a mood disorder that is characterized by episodes of mania (table 1), hypomania (table 2), and major depression (table 3). (See 'Definition of bipolar disorder' above and "Bipolar disorder in adults: Assessment and diagnosis", section on 'Diagnosis'.)

- The decision to use maintenance pharmacotherapy for female bipolar patients planning a pregnancy involves many factors, including the following (see 'Factors involved in the decision to use maintenance pharmacotherapy' above):

  - Patient's lifetime course of illness
  - General risk of maternal mood episodes during pregnancy
  - Reproductive safety of medications
  - Potential consequences of maternal mood episodes during pregnancy
  - Patient's preferences and values
  - Support and monitoring that is available

- Bipolar disorder is a highly recurrent illness, particularly in pregnant patients who forego pharmacotherapy. For patients who are planning a pregnancy, maintenance pharmacotherapy is generally indicated. However, for patients with a mild lifetime course of illness, it is reasonable to try to avoid medications during pregnancy. (See 'Indications' above.)

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