The Psychopharmacology Algorithm Project at the Harvard South Shore Program at www.psychopharm.mobi

2020 Bipolar Depression Algorithm

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BACKGROUND

The psychopharmacology algorithm project at the Harvard South Shore Program published algorithms for bipolar depression in 1999 and 2010. Developments over the past 10 years suggest another update is needed.

METHODS

The 2010 algorithm* and associated references were re-evaluated. A literature search was conducted on PubMed including review articles and recent studies to see what changes in the recommendations were justified. Exceptions to the main algorithm for special patient populations, such as patients with mixed states, ADHD, PTSD, substance use disorders, anxiety disorders, and women of childbearing potential and pregnant women, and those with common medical co-morbidities were considered.

RESULTS

ECT is still the 1st line option for patients in need of urgent treatment. Five medications are recommended for early usage in acute bipolar depression, singly or in combinations when monotherapy fails, the order to be determined by considerations such as side effect vulnerability and patient preference. The five are lamotrigine, lurasidone, lithium, quetiapine, and cariprazine. After trials of these, possible options include antidepressants (bupropion and SSRIs are preferred) or valproate (very small evidence-base). In bipolar II depression, the support for antidepressants is a little stronger but depression with mixed features and rapid cycling would usually lead to further postponement of antidepressants. Olanzapine + fluoxetine, though FDA-approved for bipolar depression, is not considered until beyond this point, due to metabolic side effects. The algorithm concludes with a table of other possible treatments that have some evidence.

CONCLUSIONS

This revision incorporates the latest FDA-approved treatments (lurasidone and cariprazine) and important new studies and organizes the evidence systematically.

Wang D, Osser DN. The Psychopharmacology Algorithm Project at the Harvard South Shore Program: An update on bipolar depression. Bipolar Disorders 2019 DOI: 10.1111/bdi.12860 epub ahead of print.

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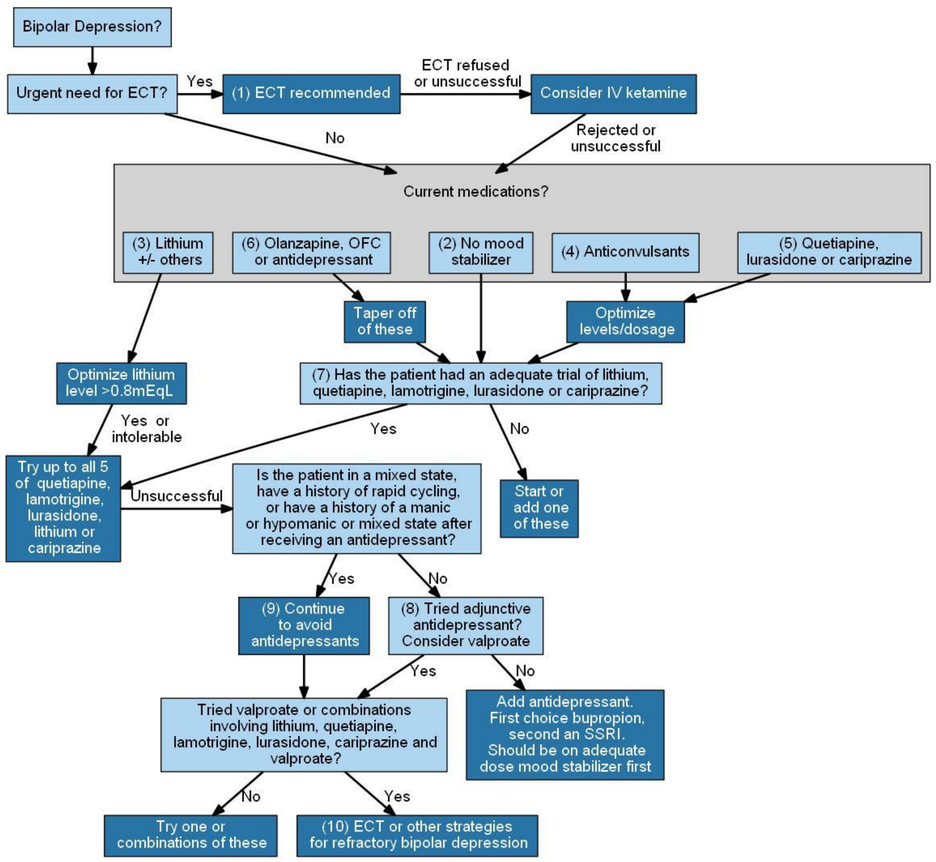

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COMORBID CONDITIONS	RECOMMENDATIONS
Posttraumatic Stress Disorder	Common symptoms require differentiation (irritability, insomnia, decreased concentration). PTSD related insomnia and anxiety could be treated with **prazosin** instead of antidepressants. **Quetiapine** could be reasonable (weight gain). **Lamotrigine** has efficacy in BP depression and PTSD.
Attention Deficit/ Hyperactivity Disorder	Given the high prevalence of this comorbidity, patients should be on a **mood stabilizer** before adding any stimulant to address ADHD symptoms or excessive day time fatigue. Patients should be informed of the apparent high risk of mood destabilization if not on a mood stabilizer (7 fold). **Psychotherapeutic** approaches should be preferred if possible.
Treatment of women of child bearing potential and women who become pregnant during treatment	**Avoid valproate** in any woman with the potential to become pregnant: should the patient become pregnant it may already be too late to remove it before harm is done. **Carbamazepine is almost as harmful and should be avoided.** **Lithium** preferred over valproate and carbamazepine. The **atypical antipsychotics** with efficacy in BD are first choice. Though data are very limited in pregnancy, **lamotrigine** may be considered. A recent review of published cases concluded that **electroconvulsive therapy may be a last resort treatment**, contrary to previous impressions. But, if steps are taken to decrease potential risks taking into account both mother and fetus, it can be used for severe depression, catatonia, medication resistant illness, extremely high suicide risk, psychotic agitation, severe physical decline due to malnutrition or dehydration or other life threatening conditions. Procedure should be administered in hospital emergency setting or delivery room involving skilled team of psychiatrist, gynecologist/obstetrician, and anesthesiologist. Prescribe as few drugs as possible – ideally, one. When pregnancy occurs during treatment, it is usually best to continue the previous therapy to avoid exposure to multiple agents. Exception: if on valproate or carbamazepine (probably switch). **Adjust doses** as pregnancy progresses. Blood volume expands 30% in third trimester. Plasma level monitoring is helpful. Consider the risk of relapse or withdrawal while switching medications or changing doses. Anticholinergic drugs should not be prescribed to pregnant women except for acute, short-term need. Depot antipsychotics should not be routinely used in pregnancy: infants may show extrapyramidal symptoms for several months. Close follow up in post-partum and aggressive medication adjustment is recommended post-delivery.
Cardiac disease or presence of QTc-prolonging drugs	If risk of QTc prolongation is a significant concern, **quetiapine would be relatively undesirable**. Consider **lurasidone**. Review the patient's medications for other QTc-prolonging agents and monitor for risk factors for Torsade's such as bradycardia and electrolyte abnormalities.