

Evidence Based Practice Critically Appraised Topic

Bipolar Disorder & Antidepressants

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Clinical Scenario

A 51 year old female presents to the clinic for evaluation and medication management. Patient is currently on numerous antidepressants for different reasons, with 2 of the antidepressants being used for a diagnosis of depression. Patient describes periods of 'down in the dumps' and other times being able to be 'like the energizer bunny'. Patient's previous records indicated a diagnosis of rule out bipolar disorder. The nurse practitioner confirmed a diagnosis of bipolar disorder, and plans to change the medication management approach to accommodate the bipolar disorder.

Clinical Question

In patients with bipolar disorder, do antidepressants alone compared to a combination of antidepressants and mood stabilizers decrease the frequency of manic/depressive episodes?

Articles

Koszewska, I. & Rybakowski, J. K. (2009). Antidepressant-induced mood conversions in bipolar disorder: A retrospective study of tricyclic versus non-tricyclic antidepressants drugs.

Neuropsychobiology, 59, 12-16. DOI: 10.1159/000202824

Licht, R. W., Gijssman, J., Nolen, W. A., & Angst, J. (2008). Are antidepressants safe in the treatment of bipolar depression? A critical evaluation of their potential risk to induce

switch into mania or cycle acceleration. *Acta Psychiatrica Scandinavica*, 118, 337-346.

DOI: 10.1111/j.1600-0447.2008.01237.x

Summary and Appraisal of Key Evidence**Study 1**

Koszewska & Rybakowski (2009) conducted a retrospective data analysis from clinical records of the Affective Disorder Unit of the Institute of Psychiatry and Neurology for the period of 1972-1996 providing a Level IV level of evidence. The purpose of the study was to analyze "antidepressant induced mood conversions occurring in bipolar inpatients treated" with antidepressants (ADs) during the stated time frame. A total number of 333 bipolar patients were treated with antidepressants. There were 118 patients that experienced mood conversion while on antidepressants. This group had two analyses done: "(1) comparison of depressive episodes treated with ADs with and without mood conversions, and (2) comparison of the frequency of mood conversions induced by particular ADs, especially TCAs versus non-TCAs." This analysis of clinical records was performed because contemporary standards were not affecting treatment strategies.

Limitations of this study include a short duration, only bipolar inpatients were used, and the study wasn't based on randomized trials, but instead, was retrospective. Also, only a small

number of participants were taking non-TCAs and mood stabilizers. Strengths of the study include a large number of participants analyzed, and the performed observation of the study was naturalistic, which mimicked clinical practice.

Study 2

Licht et al. (2008) performed a critical review of published randomized-controlled trials (RCTs) providing a Level I, Grade A level of evidence. The purpose of this study was to determine if bipolar patients have a switch of depression to hypomania/mania with use of antidepressants, or if the switch is caused by the natural history of the bipolar disorder. To examine the RCTs the Bradford-Hill criteria was used; “specificity of the potential causative agent, strength of effect, consistency in findings, dose-response relation, temporal relation with exposure to agent preceding effect and biological plausibility.”

Limitations of this study include limited availability of studies conducted, methodological limitations of the reviewed studies, and there wasn't data to guide providers to continue or discontinue an antidepressant between hypomania/manic states. There needs to be more RCTs to determine if antidepressants are successful in the treatment of bipolar depression. There is an assumption by experts and guidelines that state that antidepressants cause a switch in bipolar patients. Based on the current literature review, no clinical recommendations can be made at this time. The only way to determine the risk of antidepressants in patients with bipolar is to conduct RCTs where there is a placebo-controlled monotherapy group. RCTs are not usually powered for adverse events.

Results

The results of these studies suggest that antidepressants cause bipolar patients to experience bouts of hypomania/mania with the use of antidepressants alone. The study performed by Koszewska & Rybakowski (2009) stated that the switch from depression to mania occurred more frequently in patients using TCA's. This study also concluded by stating that the most susceptible period for a switch is during the initiation of antidepressants. Licht et al. (2008) concluded that when antidepressants are combined with a mood stabilizer for acute bipolar depression, there seems to not be a switch to hypomania or mania. Antidepressants cannot be suggested as monotherapy for patients with bipolar disorder. It is advisable for providers to stop an antidepressant when the bipolar patient develops mania or mixed states.

Clinical Bottom Line

According to these two studies, the use of antidepressants, especially the use of TCAs, as monotherapy for bipolar patients leans toward a switch from depression to hypomania/mania. When antidepressants are used in combination with mood stabilizers, a switch in bipolar patients' mood does not seem to occur as frequently. The natural history of the disorder should be kept in mind when caring for bipolar patients. There were several limitations to the studies such as short duration, limited availability of RCT studies conducted, and the first study was a retrospective analysis. To determine the absolute effect of antidepressants on bipolar patients', a RCT would need to be conducted using antidepressant monotherapy.

Implications for Practice

Based on the above studies, I would recommend the use of antidepressants and mood stabilizers as a combination treatment in bipolar patients. I would not recommend antidepressants as monotherapy for patients with bipolar disorder.

References

- Koszewska, I. & Rybakowski, J. K. (2009). Antidepressant-induced mood conversions in bipolar disorder: A retrospective study of tricyclic versus non-tricyclic antidepressants drugs. *Neuropsychobiology*, *59*, 12-16. DOI: 10.1159/000202824
- Licht, R. W., Gijsman, J., Nolen, W. A., & Angst, J. (2008). Are antidepressants safe in the treatment of bipolar depression? A critical evaluation of their potential risk to induce switch into mania or cycle acceleration. *Acta Psychiatrica Scandinavica*, *118*, 337-346. DOI: 10.1111/j.1600-0447.2008.01237.x