Beyond their well-known role for treating cardiovascular disease, beta adrenergic receptor antagonists—beta blockers—are used for a variety of medical conditions, including coronary artery disease, hypertension, migraines, and tremor. Their usefulness makes them 1 of the most commonly prescribed medication classes. Unfortunately, their increased use comes with increased reports of depression. Being able to sort fact from fiction will help guide your care for patients taking beta blockers who report new or worsening depressive symptoms.

**Does research support a link?**

First reported in the 1960s, beta blocker-induced depression was thought to result from the drugs’ antagonistic effect on norepinephrine at β1 post-synaptic brain receptors. Prompted by case reports of a possible association between beta blockers and depression, 2 prescription database reviews found that patients taking beta blockers were more likely to receive a concurrent antidepressant prescription than patients prescribed other cardiovascular and diabetic medications. However, these reviews had major limitations, such as inadequately defined methods for defining depression and lack of control for potential confounding factors.

Mechanistically, peripheral effects of beta blockers on the heart and kidneys lead to decreased chronotropy and inotropy as well as lower blood pressure. These cardiovascular and hemodynamic changes could cause fatigue, decreased energy, and sexual dysfunction that may be interpreted as symptoms of new-onset depression.

Researchers found that beta-blocker use was not associated with depression in a case-control study examining 4,302 New Jersey Medicaid records. Also, because most patients in this study received propranolol, the authors were unable to confirm a long-held belief that highly lipophilic beta blockers (such as propranolol, 

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**Practice Points**

- Although patients with cardiovascular disease are at increased risk for developing depression, there is no convincing evidence that adding beta blockers will further increase their risk.

- Initiating beta-blocker therapy at the lowest possible dose and slowly titrating the dose over time could minimize adverse effects such as fatigue and sexual side effects.

- If a patient taking beta blockers develops signs of major depression, carefully evaluate and treat symptoms with appropriate psychotherapy, psychotropics, and monitoring.
metoprolol, and timolol) are more likely than hydrophilic beta blockers such as atenolol to produce depression.

A retrospective cohort study analyzed 381 patients from 2 myocardial infarction (MI) trials who had been assessed for depressive symptoms and severity. Researchers matched 254 subjects taking beta blockers during hospitalization for MI with 127 subjects not taking beta blockers. Patients in the study were well balanced on multiple baseline characteristics, including demographics, history of depression, and left ventricular ejection fraction, although those who did not take beta blockers had a significantly higher incidence of chronic obstructive pulmonary disease, digoxin use, and pre-MI beta-blocker use. Researchers assessed depressive symptoms using the Beck Depression Inventory (BDI) at baseline and 3, 6, and 12 months post-MI and identified patients with depression using a Composite International Diagnostic Interview. They found no statistically significant difference in BDI scores between beta-blockers users and nonusers at discharge and at 3, 6, and 12 months post-MI after accounting for potential confounding factors, including:

- contraindications for beta-blocker use (other than history of depression)
- indicators and risk factors for cardiac disease
- baseline depressive symptoms
- benzodiazepine use.

In fact, after controlling for baseline depression, researchers found that beta-blocker users demonstrated significantly lower BDI scores 3 months post-MI than nonusers. Based on these results, the authors concluded that clinicians should not be deterred from prescribing beta blockers because the drugs’ benefit in reducing morbidity and mortality in cardiovascular disease greatly outweighs the risk—if any—of new-onset depression associated with beta-blocker use.

Two additional studies reported no significant difference in the incidence of depression between patients who received beta blockers and those who did not.

### Treatment for psychiatric patients

Evidence supports beta-blocker use in coronary artery disease and congestive heart failure. Although patients with these conditions—

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<th>Study</th>
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<td>Bright et al, 1992&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Case-control study of 4,302 patients with new-onset depression</td>
<td>Beta-blocker use was not associated with depression after controlling for confounding factors, although depressed patients were more likely to receive beta blockers</td>
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<td>van Melle et al, 2006&lt;sup&gt;4&lt;/sup&gt;</td>
<td>A prospective study of post-myocardial infarction patients; 254 taking beta blockers, 127 controls</td>
<td>No significant differences in depressive symptoms or incidence of depressive disorder between beta-blocker users and nonusers</td>
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<td>Gerstman et al, 1996&lt;sup&gt;5&lt;/sup&gt;</td>
<td>New users of propranolol (n=704) other beta blockers (n=587), angiotensin-converting enzyme inhibitors (n=976), calcium channel blockers (n=742), and diuretics (n=773)</td>
<td>Depression occurred no more frequently among beta-blocker users than other subjects</td>
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<tr>
<td>Ko et al, 2002&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Quantitative review of randomized trials that tested beta blockers in myocardial infarction, heart failure, and hypertension</td>
<td>Beta-blocker therapy was not associated with a significant absolute annual increase in risk of depressive symptoms (6 per 1,000 patients; 95% confidence interval, -7 to 19)</td>
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INDICATIONS AND USAGE: resemble neuroleptic malignant syndrome, which includes hyperthermia, muscle rigidity, autonomic instability with labile blood pressure, hyperthermia), neuromuscular aberrations (eg, hyperreflexia, incoordination) and/or Syndrome (NMS)-like reactions have been reported with SNRIs and SSRIs alone, including Pristiq treatment, but Reactions- determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, BRIEF SUMMARY should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in of depression.

controlled maintenance studies in adults with depression that the use of antidepressants can delay the recurrence different indications, with the highest incidence in MDD. The risk differences (drug vs. placebo), however, were ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant Patients with major depressive disorder of depression. In managing an overdose, consider the possibility of multiple drug involvement. The physician should consider contacting a poison control center for additional information on the treatment of any overdose. Telephone

conditions are at increased risk for developing depression, there is little evidence that their risk will be further increased by adding beta blockers (Table, page 51). Although patients taking beta blockers report a higher incidence of fatigue and sexual side effects—which could be interpreted as related to depression—studies do not support an association between these medications and depression. As with any medication, initiate beta-blocker therapy with the lowest possible dose and titrate slowly to minimize side effects. Any patient who develops signs and symptoms of major depression should be thoroughly evaluated and treated with appropriate psychotherapy, psychotropics, and careful monitoring.

References


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