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Researchers conduct comprehensive review of treatments for depression in cancer patients

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Depression is common in cancer, up to half of all patients facing the disease experience depressive symptoms, ranging from mild to severe. When depression co-exists with cancer, patients may be at an increased risk of death from cancer and from suicide.

Antidepressants are commonly prescribed, but the evidence on their efficacy is mixed. The role of antidepressants in treating cancer-related depression has not been rigorously studied. To identify best practice for the treatment of depression in cancer, Dartmouth researchers completed a systematic review and meta-analysis of existing research. The paper was published in *General Hospital Psychiatry* in June.

The review identified two classes of antidepressants that reduce symptoms of depression:

- An alpha-2-adrenergic receptor antagonist: Mianserin
- Two selective serotonin reuptake inhibitors: fluoxetine (Prozac) and paroxetine (Paxil)

Available evidence suggests that paroxetine and fluoxetine can improve depressive symptoms but may be less well-tolerated.

Miaserin also showed a higher depression response rate compared to placebo, whereas paroxetine and fluoxetine did not. The response rates

were low suggesting only modest changes in depressive symptoms.

"All the evidence for alpha-2-andrenergic receptors was based on a single agent, Mianserin," said Natalie Riblet, MD, MPH, lead author of the study, Department of Psychiatry, Geisel School of Medicine. "Unfortunately, the most promising agent, Mianserin, is not available in the US. Given that Mirtazapine is a close pharmacological cousin of Mianserin, there may be clinical benefit to further exploring the role of Mirtazapine in the management of cancer-related depression."

In terms of side effect profiles, Mianserin appeared slightly more tolerable compared to placebo; paroxetine had slightly higher but nonsignificant dropout rate due to side effects compared to placebo; fluoxetine had a significantly higher dropout than placebo, though this finding became non-significant after removing a study outlier.

"Adverse drug interactions are possible between chemotherapy agents and antidepressants," said Riblet. "Specifically tamoxifen, a common chemotherapy agent, may interact with certain antidepressants to increase risk of serious side effects."

The different classes of antidepressants work on different neurotransmitters. The study reported that the alpha-2-andrenergic receptor antagonists show particular promise in cancer patients possibly due to their pharmacological profile, which increases norepinephrine and serotonin. Alpha-2-andrenergic receptor antagonists are less likely to cause common serotonin-related side effects such as headache, agitation, jitteriness, or sexual dysfunction, but may contribute to sedation.

The review included nine randomized trials conducted between 1985 and 2011 with 4,700 eligible records from 1,169 patients from various countries. Overall 83 percent of subjects were female with a mean age of 54 years.

"There is a scarcity of evidence to address the role of antidepressants in cancer-related depression," said Riblet. "Our findings suggest there is a need for high-quality randomized clinical trials that explore the role of antidepressants in treating cancer-related depression."

Provided by The Geisel School of Medicine at Dartmouth