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Depression and antidepressant medications: Both are linked to increased fracture risk

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Abstract

Our series of meta-analyses showed that depression and antidepressant use are linked independently to an increased risk of fracture. However, in our meta-analysis research we never dismiss the possible of additional contributions of antidepressants to fractures, nor underestimate the role antidepressants play in the risk of fractures. Existing data indicates that the underlying mechanisms of the impact of depression and antidepressant on fracture risk are likely to be different. We agreed with Dr. Donzelli and his colleagues that promotion of physical activity and exercise, as well as effective psychotherapeutic intervention, is important to prevent and treat mild depression. However, determining if pharmacological therapies are needed, and which medication(s) should be prescribed for individual patients, should be done in clinic, on a case-by-case basis. Different adverse effects, varied impact on risk of fracture by antidepressant medication, severity of depression, and effectiveness of non-medication treatments should all be considered in clinical situations, in order to determine if pharmacological therapies are needed and how to treat individual patients.

Keywords

Bone loss; Depression; Antidepressant; Fracture

I thank Dr. Donzelli and his colleagues for their interest in our recent meta-analysis research. I agree that antidepressant use contributes to fracture risk, and is associated with many other adverse effects. The scope of our meta-analysis was to investigate the association between depression, fracture risk, and bone loss [1]. Within that scope, we conducted a compressive meta-analysis and concluded that depression is associated with a significantly increased risk in fracture and bone loss. We also conducted subgroup analyses, and after controlling for antidepressant use found that the association between depression and fracture is significant. However, we did not “dismiss the possible additional contribution of antidepressant to fractures,” or underestimate “antidepressants’ role in risk of fractures.” In fact, our prior meta-analyses, which focused on antidepressant use, demonstrated that either SSRIs [2] or TCA antidepressant [3] use is significantly associated with increased fracture risk.

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Measuring the impact of depression on fracture risk remains a challenge when participants use antidepressants. Also, quantifying the influence of antidepressants on fracture risk is difficult when such an effect is confounded by indication or severity, factors which are concomitant with antidepressant medications. Our meta-analysis demonstrated depression is significantly associated with increased risk of fracture after adjusting for the effect of antidepressant use [1]. In addition, our prior meta-analyses showed that either SSRIs [2] or TCAs [3] exert an increased risk of fracture that is independent of depression. Although the underlying mechanisms of the impact of either depression or antidepressants on fracture risk have not been fully elucidated, their underlying mechanisms are different: our meta-analyses indicated that declining BMD creates a pathway for depression that increases fracture risk [1, 4]; furthermore, one of our meta-analyses strongly suggested that the effect of TCAs increases the propensity for falling rather than causing bone loss [3]. Our additional meta-analysis also indicated that SSRIs may exert an increased risk of fracture independent of BMD reduction [2]. Depression can lead behavioral changes [7, 8] that might also affect BMD and fracture risk. Therefore, both depression and antidepressant medications are associated with increased risk of fracture; however, the mechanisms are likely to be different.

I agree with Dr. Donzelli and his colleagues that “the promotion and prescription of physical activity and exercise, as well as effective psychotherapeutic interventions,” are important to preventing and treating mild depression. On the other hand, clinical decision-making for individual patients should vary case by case. Clinicians should also be aware that different antidepressants have different adverse effects and different impacts on the risk of fracture due to variation in the basic mechanisms. Such impact also varies with the different duration of medications. For example, the increased risk of fracture with a shorter duration of TCA treatment (<6 weeks) is much higher than that with extended treatment (≥ 6 weeks) [3]. Given this information, together with severity of depression, the effectiveness of non-medication treatments, should be considered together in clinic, in order to accurately determine if pharmacological therapies are needed and which medication(s) should be prescribed for individual patients.

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