DSEN ABSTRACT

Serotonin Affinity of Anti-Depressant Agents and the Occurrence of Fractures, Falls, and Bone Mineral Density Change in Patients With Depression

Summary

Several differences in terms of risks of adverse effects that may cause falls were noted between classes of antidepressants, though how often they may lead to falls is unclear. These differences may warrant consideration for treatment selection.

Minimal research addressing serotonin affinity and its impact on bone mineral density or fracture risk was located. No consistent patterns of association were observed. More research addressing this issue is needed.

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What is the issue?

- In 2012, 5.4% of Canadians aged 15 years or more had symptoms consistent with a mood disorder, and 4.7% were documented as having a major depressive episode.
- Literature has suggested a potential association between antidepressant use and an increased risk of fractures. One hypothesis for this relationship is the serotonin affinity level of antidepressants. A second is presence of a short-term effect of antidepressants wherein there may be differential risks for side effects which may cause patients to fall more frequently.

What was the aim of the study?

- Does the choice of antidepressant agent increase the risk of falls? Is there a differential risk in fall-related events between individual anti-depressant agents? (i.e.vision problems, hypotension, dizziness, insomnia, fatigue, drowsiness?)
- Does the serotonin affinity level of anti-depressant agents (i.e. SSRIs, TCAs, non-SSRI and TCA agents) impact the risk of fractures?
- Does the serotonin affinity level of anti-depressant agents (i.e. SSRIs, TCAs, non-SSRI and TCA agents) modify the risk of negative changes in bone mineral density?

How was the study conducted?

- Systematic searches were performed to identify two types of evidence in patients with depression: (1) randomized trials reporting on side effects that could place patients at an increased risk of falls: vision problems, dizziness, hypotension, insomnia, fatigue, and drowsiness; (2) observational studies including antidepressant treatments which could be classified into serotonin affinity classes (low, moderate or high based on dissociation constant value) reporting on fractures or change in bone mineral density. All screening and data collection was performed by two reviewers.
- Network meta-analyses of randomized trials were used to explore the relative frequencies of fall-related outcomes. Data from observational studies related to the occurrence of fractures and changes in bone mineral density were summarized and critically appraised with consideration of the serotonin affinity of agents studied.

What did the study find?

- 202 trials and five observational studies were located. Variable amounts of data were available for analyses of each outcome. For most outcomes, all classes of agents showed increased risks of harms compared to placebo. Agents within classes were generally comparable. The reputation of increased risk of TCAs was reflected for several agents in this class for several outcomes. Several SSRIs and non-SSRI/TCA agents were associated with an increased risk of insomnia compared to TCAs, though SSRIs were associated with less drowsiness relative to the other classes.
- Based on limited and heterogeneous observational data, there is not sufficient evidence to confirm a long-term association between the serotonin affinity level of antidepressants and fracture risk or changes in bone mineral density.

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