What is Seroquel and should you take it for insomnia?

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The evidence so far suggests off-label prescribing for insomnia places users at unnecessary risk of harm. Credit: Flavio Ronco/Flickr, CC BY-NC-ND

Quetiapine, sold under the brand name Seroquel, is a short-acting antipsychotic drug. It's used to treat schizophrenia, bipolar I disorder and as an add-on treatment for major depression and generalised anxiety disorder in people who haven't responded to other therapies. The recommended dose range for these conditions is 200-800mg a day.

Off-label prescribing is when a drug is prescribed for uses outside those for which it has been licensed. It's relatively common in psychiatry and may help patients who haven't responded to standard treatments. But due to the lack of evidence for the safety and efficacy of off-label uses, there is a potential for harm.

Doctors prescribe quetiapine off-label for various conditions, including anxiety, autism, post-traumatic stress disorder, substance abuse and obsessive compulsive disorder. It is also increasingly prescribed off-label for insomnia, usually at lower doses of 100mg or less a day.

But the evidence so far suggests the risks of prescribing quetiapine off-label outweigh any benefits.

Rise in use

Since quetiapine came onto the market in 1997, prescription rates have skyrocketed, especially in the United States, where it became the fifth-biggest-selling pharmaceutical in 2010.

Prescriptions for quetiapine also increased significantly in Australia between 2000 and 2011.

Patients switching from another antipsychotic to quetiapine cannot account for these changes; the rise is most likely due to off-label prescribing.

In fact, drug company AstraZeneca paid US$520 million in 2010 to resolve allegations the company illegally marketed Seroquel for uses not approved by the US Food and Drug Administration (FDA).

Antipsychotic drugs

All antipsychotic drugs – both first generation, which were developed in the 1950s, and second generation, developed since the 1950s – exert their effect mainly by blocking dopamine transmission in various parts of the brain. They block dopamine D2 receptors, which alleviates symptoms of psychosis such as hallucinations, delusions and thought disorder.

Other receptors may also be blocked. However, these blockages may cause serious side effects.

Quetiapine is a second-generation antipsychotic drug that also blocks histamine H1 and serotonin type 2A receptors. This is thought to account for its sedative properties, which is why it's used off-label for insomnia.

Antipsychotic drugs, especially first-generation antipsychotics such as haloperidol, fluphenazine and trifluoperazine, can be associated with some serious side effects, such as the neurological disorder tardive dyskinesia. This involves involuntary movements of the face, tongue and mouth and, less commonly, the limbs, head, neck and trunk. In some cases, tardive dyskinesia may be irreversible.

All antipsychotic drugs can also cause neuroleptic malignant syndrome, a neurological disorder which can progress rapidly over 24 to 72 hours. Neuroleptic malignant syndrome can cause instability, altered consciousness, muscle rigidity and even death. The incidence is greatest in young men.

Both first- and second-generation antipsychotics have been reported to contribute to heart arrhythmia, where the electrical impluses co-ordinating your heartbeats malfunction. In a recent large cohort study, researchers reported that antipsychotic drugs, including quetiapine, almost doubled the risk of sudden death from a heart attack.

Quetiapine has fewer side effects than first-generation antipsychotics. But recent research and clinical trials have reported considerable risk of metabolic side effects. These include weight gain, elevation of cholesterol and triglycerides, and diabetes, even when prescribed at recommended doses.

Quetiapine as a sleeping drug

Studies on the use of quetiapine for sedation have produced conflicting results.

A very small randomised placebo-controlled study, funded by AstraZeneca (manufacturer of quetiapine) and involving 14 healthy subjects, reported that, compared to placebo, both 25mg and 100mg quetiapine administered at night increased the sleep quality and the amount of sleep.

Another independent study conducted in Thailand did not support these findings. Researchers tested the drug in a randomised two-week controlled trial (where one group received the drug and another received a placebo). They found 25mg quetiapine at night for primary insomnia did not improve sleep.

Quetiapine can cause significant weight gain, even when used in small to moderate doses for sleep. It has also been associated with increased blood glucose (sugar) and dyslipidaemia (an imbalance of fats circulating in the blood). These increase the risk of developing type 2 diabetes and heart disease.

In a retrospective study in the United Kingdom, 43 psychiatric patients aged 19 to 65 years were prescribed low-dose quetiapine for insomnia, usually 100mg at bedtime. Over the 11-month study period, their weight increased by an average of 2.22kg.

Despite the safety concerns associated with using quetiapine as an antipsychotic, the risks may be acceptable when treating patients with serious mental illness, given there are few alternatives.

But the evidence so far suggests prescribing quetiapine off-label for people who have problems sleeping places them at unnecessary risk of harm.

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