

short & snappy

-A CLINICAL OVERVIEW

Mitigating Antipsychotic-Induced Weight Gain: Is Metformin the Answer?

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Clinical issue:

- The standardized mortality ratio in schizophrenia is 1.5 times that of the general population. [1] Much of this mortality risk stems from cardiovascular disease. [1,2]
- Antipsychotics are used in the treatment of many mental health disorders. Second-generation antipsychotics in particular are associated with weight gain and other metabolic complications that increase cardiovascular risk, including dyslipidemia, insulin resistance, and diabetes. [1-4]
- Among antipsychotics, clozapine and olanzapine generally have the highest risk of weight gain, while aripiprazole, lurasidone, and ziprasidone have the lowest risk. [1,3]
- **Clinical question:** In patients on second-generation antipsychotics, can metformin prevent and/or treat antipsychotic-induced weight gain and other metabolic complications?

Review of the literature:

- A meta-analysis of 12 RCTs (n=743) found that in patients treated with antipsychotics, metformin treatment resulted in significantly better anthropometric and metabolic parameters than placebo with a mean change in weight of -3.27 kg [95% CI -4.66 to -1.89; p < 0.001]. [1]
 - Metformin appeared to be more effective in preventing weight gain in first episode patients than in chronic patients who already gained weight [-5.94 kg vs. -2.06 kg].
 - Metformin doses ranged from 500-2550 mg/day, with the majority using 1000 mg/day.
- A second meta-analysis of 21 RCTs (n=1547) demonstrated that metformin was significantly superior to placebo in the primary outcome measures of body weight, body mass index, fasting glucose, fasting insulin, triglycerides, and total cholesterol. [4]
- Adverse effects in RCTs did not differ between metformin and placebo-treated participants. Nausea, abdominal pain, and diarrhea can be lessened with a gradual increase in dose. [2]
- Many of the studies included some aspect of lifestyle management. No studies reported data on whether transition to diabetes was reduced in metformin versus placebo groups, or whether metformin provided a mortality benefit in these patients. [2]

Recommended approach:

Metformin may be modestly beneficial for preventing weight gain or promoting weight loss in patients taking antipsychotic medications. [5] Other beneficial strategies include providing patients with advice on diet and lifestyle modifications, and switching to an antipsychotic with less risk of weight gain. [1] For those started on metformin, ongoing monitoring of renal function and adverse effects is required.

References

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