Mood stabilizers and metabolic issues

As previously mentioned in this issue of *TreatmentUpdate*, HIV-positive people are at increased risk for issues affecting their mental health and emotional well-being. In cases of severe mental health issues, a class of drugs called antipsychotics is sometimes used. Healthcare providers and some patients have found that these drugs are useful for the following conditions:

- schizophrenia
- mania
- bipolar disease
- treatment-resistant depression

The second generation of this class of antipsychotics (SGA) is associated with a reduction in certain side effects that were seen with the first generation of these medicines:

- muscle spasms
- twitchiness
- restlessness
- involuntary movements

However, SGAs can also have side effects, particularly metabolic issues such as these:

- elevated blood sugar
- unintentional weight gain, particularly belly fat
- elevated levels of fatty substances (lipids) in the blood
- increased blood pressure

Together these issues make up what is called the metabolic syndrome and can increase the risk for cardiovascular disease.

Research suggests that the reasons for weight gain and other metabolic issues in people with serious mental health conditions are likely complex and related to an intersection of factors such as the following:

- behavioural – smoking tobacco, poor eating habits, insufficient exercise
- additional medical issues (called comorbidities) prior to the diagnosis of serious mental health issues
- an underlying predisposition to develop the metabolic syndrome among some people with schizophrenia and bipolar disorder

Researchers in Modena, Italy, and in San Diego, California, have collaborated on a study of the impact of SGA on the health of HIV-positive people, particularly among people who use potent combination anti-HIV therapy (commonly called ART or HAART). They have found that exposure to SGA is probably linked to an increase in elements of the metabolic syndrome. We caution readers that this does not mean SGA should be abandoned. Rather, the international team of researchers has released helpful recommendations about the use of SGA when caring for HIV-positive people. These recommendations appear later in this report.

**Study details**

Researchers recruited 2,229 HIV-positive people for the study and divided them into two groups as follows:

- taking SGA – 258 people
- not taking SGA – 1,971 people
Participants had the following average profile upon entering the study:

- age – 45 years
- gender – 80% men, 20% women
- duration of HIV infection – 7 years
- current CD4+ cell count – 435 cells/mm$^3$
- current viral load – 50 copies/ml

**Results**

On average, participants had been taking antipsychotics for 15 months. Here are the drugs that were used:

- aripiprazole (Abilify)
- clozapine (Clozaril)
- paliperidone (Invega)
- quetiapine (Seroquel)
- risperidone (Risperdal)
- olanzapine (Zyprexa)

Researchers found that, in general, exposure to SGA was associated with certain elements of the metabolic syndrome, such as the following:

- increased levels of fatty substances in the blood (triglycerides)
- increased weight
- increased blood pressure
- new cases of type 2 diabetes

These results have also been found in studies of SGA in HIV-negative people.

There are several possible reasons for the occurrence of these side effects in the present study:

- Both SGA and some anti-HIV meds could have interfered with the hormone insulin. This hormone is used to help regulate blood sugar. Excess sugar is turned into fat and leads to weight gain.
- Both SGA and some anti-HIV meds could have interfered with the growth and development of fat cells, causing fat cells to concentrate and grow in the belly.

**Researcher recommendations**

The study team, which included psychologists, psychiatrists and neurologists, made the following recommendations:

- When prescribing or using SGA, healthcare providers and patients should note that many factors contribute to metabolic side effects.
- Non-drug therapies that can be considered for SGA-related side effects can include the following: “individual or group psycho-education, self-monitoring, cognitive behavioural therapy, nutritional intervention, supervised exercise programs and/or nutritionist and dietician counselling.”
- If a change to drug therapy must be made, the researchers advise doctors to consider switching therapy to an SGA less likely to cause an increase in appetite or weight. They added that doctors might also consider changing their patients’ ART regimen. However, the researchers warn that any changes to existing SGA “should be weighed against potential worsening of psychopathology” and, in the case of ART, new side effects and/or the potential development of HIV that is resistant to therapy.
- Additional therapies, such as cholesterol-lowering medicines, may be deployed to deal with metabolic side effects of SGA.
- The drug metformin (Glucophage) works by making the body more sensitive to the effect of the hormone insulin. Along with exercise and diet, metformin can help people to normalize blood sugar levels. The researchers suggested that doctors consider the use of metformin to help reduce SGA-related side effects.

**Looking ahead**

Another important outcome of the present research on SGA is that the scientists involved have realized that long-
term prospective studies are needed to assess the impact of SGA as well as interventions (exercise, nutritional advice, drugs such as metformin) to reduce the side effects of these antipsychotics and improve the health of people who use them.

—Sean R. Hosein

REFERENCES:


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