In his lecture, Dr Dratcu focused on the issue of obesity and associated medical conditions, such as metabolic syndrome and diabetes, and considered the implications within the context of treating patients with psychiatric disorders.

Obesity is the worst pandemic of the 21st century in terms of public health, economic and social consequences. In the USA, for example, the number of people that could be considered obese has doubled since the 1980s. But the pandemic is not only affecting affluent countries: in recent years, the greatest increases in the number of obese people are found in emerging economies such as India, Mexico and China.1-3

The rising number of obese people has major implications for society at large, not least because of the increased demand – and pressure – it imposes on health services. Given the central role it plays in the pathogenesis of cardiovascular disease, diabetes and many other serious illnesses, obesity is associated with significant morbidity and mortality. For example, the number of people worldwide with diabetes more than doubled from 153 million in 1980 to 347 million in 2008.4

The causes of this pandemic are multifactorial and complex, but one problem is that humans may in fact be predisposed to obesity. Accumulating fat would have been an advantage to our prehistoric ancestors when food was scarce, every calorie was precious, farming and agriculture were a distant prospect and people were always on the move. This may explain why humans have 10 times more fat cells in relation to body mass than most other animal species. In this age of relative abundance, however, sedentary lifestyles combined with diets high in saturated fat and refined sugar may have turned an inherited survival mechanism into the trigger of a major health crisis.

Metabolic syndrome and mental illness
Sufferers of mental illness may be particularly exposed to metabolic syndrome. Baseline data from Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) showed that the overall prevalence of metabolic syndrome among patients with schizophrenia entered for the trial was 40 per cent (51 per cent among females and 36 per cent among males).5 First, severe mental illness has itself been linked to higher rates of obesity, type 2 diabetes and other metabolic abnormalities.6 Indeed, many authors...
have long argued that diabetes is an integral part of psychotic illness. Second, the lifestyles and habits that many people with severe mental illness tend to adopt – including smoking and substance abuse, unhealthy diets, poor medical care and lack of physical exercise – are likely to aggravate further the risk of obesity and its complications. It often passes unnoticed, for example, that cannabis abuse, a common occurrence in people with schizophrenia, may itself be implicated in weight gain by stimulating cannabinoid receptors that modulate appetite. Finally, some drugs used to treat psychiatric disorders, although effective for this purpose, may add to the problem.

For all psychiatric patients, practical advice to make some modest lifestyle changes, including smoking cessation and discontinuing illicit substance use, improvements in diet and engaging in physical exercise regularly, can undeniably help improve overall general health. Regular screening for and treatment of high blood pressure and cholesterol levels, along with avoiding polypharmacy where possible, will also contribute to a better health status.

Dr Dratcu said that clinicians should also bear in mind factors relating to obesity and related health complications when prescribing psychotropic drugs for patients with psychiatric problems, such as bipolar disorder. Choice of antipsychotic to treat bipolar mania can also play an important part in managing a patient’s overall health profile, in addition to the primary goal of reducing the symptoms of the disorder itself. This applies in particular to patients who are already overweight or who have experienced significant weight gain following previous treatment with antipsychotic drugs.

Antipsychotics traditionally fall into two broad categories – conventional and atypical. The move from conventional to atypical antipsychotics in our prescribing practices has involved a risk/benefit trade off in relation to side-effect profiles. While conventional antipsychotics are typically associated with higher rates of extrapyramidal symptoms (EPS) and tardive dyskinesia, some atypical antipsychotics are associated with side-effects such as weight gain and diabetes, which in turn are linked to the metabolic syndrome.

### Asenapine

Asenapine is a novel atypical antipsychotic with high ratio of serotonin 5HT 2A to dopamine D 2 receptor affinity (5HT 2A: D 2 ratio 19:1), which has been shown to be effective in treating the symptoms of acute manic episodes associated with bipolar I disorder. Pharmacologically, asenapine could be said to be somewhere between olanzapine and risperidone (see Table 1). Asenapine’s efficacy on bipolar I symptoms, as measured by the Young Mania Rating Scale (YMRS), is similar to olanzapine’s (see Figure 1), but it differs from olanzapine in its side-effect profile: while metabolic syndrome is more often seen with olanzapine than with asenapine (asenapine 3 per cent vs olanzapine 9 per cent at 40 weeks), EPS are more frequently seen with asenapine than with olanzapine (asenapine 7.2-10.3 per cent vs olanzapine 2.9-3.1 per cent in studies up to nine weeks; asenapine 35.4 per cent vs olanzapine 19 per cent in studies up to 40 weeks). Other adverse effects commonly seen in patients taking asenapine include somnolence, dizziness and weight gain (asenapine 6.0-7.2 per cent vs olanzapine 12.9-19.0 per cent from baseline in studies up to nine weeks).

Asenapine has to be given sublingually because of high first-pass liver metabolism and no drink should be taken for 10 minutes after putting a tablet under the tongue. It has a rapid onset of action and twice daily dosing achieves steady state plasma levels after two days. As with most antipsychotics (one exception being amisulpride), asenapine’s metabolism is via the cytochrome P450 system in the liver, predominantly CYP1A2, which is accelerated by cigarette smoke (although one study showed that asenapine levels are not affected by smoking). The drug’s metabolites are inactive.

Dr Dratcu concluded that asenapine is a useful addition to the repertoire of drugs licensed to treat bipolar I disorder. In his view, it is a useful alternative to treat patients who otherwise would be prescribed olanzapine or another atypical antipsychotic, and for patients in need of antipsychotic treatment who are at risk of, or who have developed, weight gain, diabetes or metabolic syndrome.

### References


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**Table 1. Properties of asenapine**

- a novel, effective and generally well-tolerated atypical antipsychotic
- effective and useful in bipolar I disorder
- rapid onset of action and sustained therapeutic effect
- lower potential for weight gain or metabolic syndrome than olanzapine
- original mode of administration (sublingual)
Extrapyramidal symptoms with SSRIs

We would like to remind clinicians about the possibility of their patients developing extrapyramidal symptoms (EPS) while taking SSRIs.

A 16-year-old boy was seen in our clinic with his parents. He was under the care of Child and Adolescent Mental Health Services for several years. He had diagnoses of attention deficit-hyperactivity disorder (ADHD), autistic spectrum disorder (ASD) and moderate learning disability. A community learning disability nurse arranged the appointment as she was concerned about his fidgetiness, restlessness and not settling at school.

For the past four years the patient has been treated using generic short-acting methylphenidate 20mg twice daily plus melatonin 6mg at night for sleep difficulties. In addition, ten months previously, fluoxetine had been initiated and increased to 10mg once daily, due to his high level of anxiety and low mood.

The patient stated that for the past few months he has been feeling irritable, agitated and had an internal urge to move. In the clinic setting, he was observed to be fidgety with restless legs. On examination, he had some stiffness in his limbs. Our impression was that he was experiencing akathisia, an EPS that can be associated with the use of fluoxetine.

Fluoxetine was stopped. Over the next four to six weeks there was a significant improvement in the patient’s mood and presentation. He was lot happier in himself and he had settled better at school. Restlessness, fidgetiness and agitation were not observed after six weeks.

EPS are more commonly associated with antipsychotic medication and are an uncommon side-effects of SSRIs. However, concomitant use of antipsychotics or the presence of other risk factors increase patients’ vulnerability to EPS. The most common EPS associated with the use of SSRIs seems to be akathisia, followed by dystonia andparkinsonism. Fluoxetine is the SSRI most associated with EPS in adults. There have also been reports of EPS in adolescents treated with fluoxetine. Cases have been reported of young people with ASD treated with fluoxetine developing EPS. The symptoms are reversible with dose reduction or discontinuation, or by the addition of another agent, such as an anticholinergic agent, beta-blocker or benzodiazepine.

References


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