Metformin for Weight Loss and Control in Patients With Mood Disorder

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Two-thirds of patients in long-term treatment with a second-generation antipsychotic (SGA) experience weight gain.[1] Weight gain might be due to receptor blockade to H_1 receptors (as with tricyclic antidepressants) and to 5-HT_{2C} receptors, impaired metabolic regulation, down-regulation of appetite suppression, and less physical activity due to sedation.[2] Metformin promotes the decrease of glucose absorption, suppression of gluconeogenesis in liver, stimulation of glucose uptake in skeletal muscle, and augmentation of insulin activity. There is growing evidence that metformin might prevent or alleviate metabolic side effects of SGAs, but data so far are based on patients with schizophrenia or schizoaffective disorder.[3–6]

We present data on 11 consecutive patients with bipolar disorder (n = 7) and major depressive disorder (n = 4) (*ICD-10* criteria) treated with metformin to prevent or treat weight gain as a side effect of psychopharmacologic treatment. Data were gathered from July 2012 to November 2013. To our knowledge, this is the first dataset used to observe the effect of metformin on weight gain induced by psychopharmacologic treatment in patients with mood disorders.

Case series. Patients seen at the Outpatient Clinic at Mental Health Centre North Zealand, Hillerød, Denmark, were treated with metformin. All patients were white, and all but 1 were female. Mean age was 40 years, and mean duration of illness was 33 months.

For 2 patients, treatment was preventive, as the patients had resistance to SGA treatment because of fear of weight gain (and previous experience of SGA-induced weight gain). For the remaining patients, metformin therapy was given because of weight gain induced by SGAs, SGAs combined with antidepressants, and antidepressants. Mean duration of treatment with an SGA or antidepressant prior to metformin treatment was 15 months. Quetiapine was the most frequent drug treatment (73% of patients). Mean weight and mean body mass index (BMI) (kg/m^2) at baseline were 97.3 kg and 33.3, respectively. See Table 1 for details.

Metformin doses were 1,000–2,000 mg daily (mean = 1.7). Mean duration of metformin treatment was 6.8 months (range, 2–14). Mean weight change was –2.4 kg, and mean reduction in BMI was 0.8. Two patients gained weight, and 1 remained with stable weight. The most pronounced weight loss was 8.2 kg. Weight loss occurred in patients with bipolar disorder and in patients with major depressive disorder.

About a third of patients (36%) informed that they felt satiated with less food and experienced less craving for sugar-rich food with metformin treatment. Two patients (18%) reported better compliance to SGA treatment as a consequence of metformin treatment. Treatment was well tolerated, and patients were, in general, satisfied with the intervention.

In this series of consecutive patients with a mood disorder, treatment with metformin was helpful to make patients accept effective mood-stabilizing treatment with an SGA in spite of previous weight gain with SGAs. Metformin was also helpful in promoting weight loss among patients with weight gain induced by SGAs, antidepressants, and SGAs combined with antidepressants.

Metformin might be a useful adjunctive treatment for weight gain induced by SGAs and perhaps antidepressants among patients with a mood disorder. Prospective, controlled data are warranted to establish its safety and efficiency in this patient group.

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Drug names: aripiprazole (Abilify), citalopram (Celexa and others), duloxetine (Cymbalta and others), lamotrigine (Lamictal and others), lithium (Lithobid and others), metformin (Fortamet, Glucophage, and others), pregabalin (Lyrica and others), quetiapine (Seroquel and others), risperidone (Risperdal and others).

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Table 1 follows this Case Series.

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Table 1. Clinical Characteristics and Metformin's Effect on Weight

Patient No.	*ICD-10* Diagnosis	Duration of Illness, mo	Psychopharmacology (daily doses)	Weight, kg	Baseline BMI (kg/m^2)	Metformin Daily Dose, mg	Indication	Follow-Up, mo	Weight Difference, kg	Percent Weight Difference	Change BMI (kg/m^2)
1	Bipolar I disorder	36	Quetiapine 200 mg	66.2	24.9	2,000	Preventive	2	−3.2	−4.8	−1.20
2	Bipolar I disorder	48	Quetiapine 200 mg, duloxetine 60 mg, lamotrigine 350 mg	101.2	35.9	2,000	Preventive	13	−4.0	−4.0	−1.42
3	Bipolar II disorder	24	Sustained-release quetiapine 300 mg, lamotrigine 200 mg	97.2	32.9	2,000	Weight gain, SGA	14	−8.2	−8.4	−2.77
4	Bipolar II disorder	36	Risperidone 1 mg, lithium 600 mg, pregabalin 150 mg	70.3	24.3	1,000	Weight gain, SGA	13	−3.3	−4.7	−1.14
5	Bipolar II disorder	24	Quetiapine 200 mg; lithium 1,200 mg; lamotrigine 400 mg; citalopram 20 mg	119.0	37.6	2,000	Weight gain, SGA	7	−1.4	−1.2	−0.44
6	Bipolar I disorder	36	Quetiapine 200 mg, aripiprazole 10 mg	78.0	29.0	1,000	Weight gain, SGA	2	−8.0	−10.3	−2.97
7	Bipolar disorder NOS	24	Sustained-release quetiapine 400 mg, lithium carbonate 750 mg, lamotrigine 200 mg	97.4	36.7	2,000	Weight gain, SGA	5	1.2	1.2	0.49
8	MDD, psychotic	12	Quetiapine 600 mg	94.3	32.6	1,500	Weight gain, SGA	6	12.7	13.5	4.39
9	MDD	24	Amitriptyline 125 mg, lithium citrate 18 mmol, quetiapine 100 mg	109.0	32.9	2,000	Weight gain, SGA, antidepressant (lithium?)	7	−6.0	−5.5	−1.81
10	MDD	72	Duloxetine 180 mg (slow metabolizer), agomelatine 25 mg	102.1	35.7	2,000	Weight gain, antidepressant	3	0	0.0	−0.04
11	MDD	24	Amitriptyline 150 mg	135.8	43.3	1,000	Weight gain, antidepressant	3	−6.1	−4.49	−1.95
All patients, mean (SD)		33 (15)		97.3 (19.6)	33.3 (5.3)	1,682		6.8 (4.3)	−2.4 (5.6)	−2.6 (6)	−0.8 (1.9)

Abbreviations: BMI = body mass index, MDD = major depressive disorder, NOS = not otherwise specified, SGA = second-generation antipsychotic.

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