Rapid Weight Gain During Mirtazapine Treatment

To the Editor: Mirtazapine is a novel antidepressant with a mechanism that enhances serotonergic and noradrenergic neurotransmission by blocking presynaptic alpha-2 adrenergic receptors and postsynaptic serotonin 5HT₂ and 5HT₃ receptors.¹ The most frequently reported side effects of mirtazapine are transient sedation and weight gain associated with an increased appetite, due to its effects on $5HT_{2C}$ and histaminergic (H₁) receptors. Also, the drug can be effective in the treatment of anorexia nervosa and in cancer patients with nausea symptoms.^{2,3} In addition, diabetic ketoacidosis secondary to mirtazapine-induced weight gain has been reported.⁴ Herein, we report the case of a patient with major depressive disorder who rapidly gained 6.5 kg after administration of 30 mg of mirtazapine in 1 week.

Case Report

A 19-year-old Taiwanese man was admitted for psychiatric inpatient treatment because of major depressive disorder. The patient had presented the characteristic symptoms of depressed mood, loss of interest, anorexia, insomnia, and feelings of worthlessness in the preceding 2 months. He had been healthy in the past, without systemic disease such as metabolic disease. Initial laboratory studies revealed random blood glucose, 73 mg/dl (reference range: 70–105 mg/dl), and the thyroid function examination results were all within the normal range. He weighed 80.5 kg and scored 28 on the 17-item Hamilton Depression Rating Scale (Ham-D) on the first hospital day. Initially, he was treated with paroxetine, 20 mg/day, and zolpidem, 10 mg/night, for 14 days. His symptoms of depressed mood, anorexia, and marked insomnia were little improved. Also, he lost 4 kgs in 14 days. After this, treatment with paroxetine was discontinued, and mirtazapine, 30 mg, was prescribed at night. The patient's mood improved, but he also experienced intermittent headaches, increased appetite, and weight gain—6.5 kgs in 1 week. His Ham-D total score improved to 7 in that same week of mirtazapine therapy.

Discussion

Drug-induced weight gain is a serious problem with most psychotropic drugs, and it may be associated with health risks such as metabolic syndrome, cardiovascular disease, and type 2 diabetes. Weight gain associated with mirtazapine treatment has been reported and may be accounted for by its effects on $5HT_{2C}$ and H_1 receptors. The patient's rapid weight gain of 6.5 kg in 1 week of mirtazapine therapy is much faster

than has been reported in the literature. Meanwhile, a significant improvement in the Ham-D total score was noted during this period. The possible mechanism of the initial weight gain associated with mirtazapine could be a direct effect due to the antihistaminic (H_1) effects or early antidepressant action to improve appetite. In the future, it would be of interest to undertake a study of potential differential effects of mirtazapine versus other antidepressants, such as selective serotonin reuptake inhibitors, in the relationships of weight gain and Ham-D total score.

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