
**Treatment of Morbidly Obese Psychotic Patients
With Molindone: Three Case Reports**

To the Editor: The problem of increased obesity in the US population is magnified among patients with major psychiatric disorders, whose rates of obesity are multiples of the general population's.¹ Many psychotropic medications, particularly some second-generation antipsychotics, are associated with weight gain. However, molindone is a first-generation antipsychotic of the dihydroindolone class with a package insert² stating that changes in weight are in the direction of normal or ideal weight and that excessive weight gain has not occurred. In fact, it has been shown to lead to weight loss.³

While this property would seem to recommend its use in light of present-day concerns about obesity and the metabolic syndrome, molindone has not been well studied⁴ and has a very small market share.⁵ We have found that more recently trained psychiatrists are completely unfamiliar with the drug, while those trained before the development of second-generation antipsychotics have vague memories of its being questionably effective. In a move toward reintroducing this drug into our practice, we treated 3 adult patients with both morbid obesity and a psychotic disorder with molindone. All experienced both an improvement in mental status and weight loss. We present the 3 cases here.

Case 1. Mr A is a 51-year-old man with a history of *DSM-IV* paranoid schizophrenia, alcohol abuse, obesity, and hypertension who was admitted to our hospital in November 2008. Presenting problems were grandiose and persecutory delusions, auditory hallucinations, tangential thought processes, and irritability. Mr A's Brief Psychiatric Rating Scale (BPRS)⁶ score on admission was 43. His weight on admission was 326.9 lb, and his body mass index

(BMI) was 41.1 kg/m². He had been discharged from another facility 2 weeks earlier on treatment with risperidone, but had not taken it.

Treatment was started with molindone, and the dose was gradually increased to 100 mg bid. During the course of dose titration, Mr A developed mild parkinsonism. The addition of benztropine 1 mg bid was successful in controlling this side effect. One month after hospitalization, the patient had shown marked improvement, with resolution of all psychotic signs and symptoms; his BPRS score was 19. His weight had decreased to 306.5 lb and BMI to 38.5 kg/m². In addition to molindone and benztropine, the patient was also taking labetalol 400 mg bid and hydrochlorothiazide 25 mg/losartan 100 mg daily.

Case 2. Ms B is a 51-year-old woman with a history of DSM-IV undifferentiated schizophrenia, obesity, and hypertension who was admitted to our hospital in September 2008. Presenting problems were auditory hallucinations, disorganized thought processes, and restlessness. Ms B's BPRS score on admission was 38. Her weight on admission was 350.1 lb, and her BMI was 53.6 kg/m². She had been off psychotropic medication treatment for 2 to 3 months prior to admission.

After a poor response to haloperidol, molindone treatment was started, and the dose was increased to 50 mg in the morning and 125 mg at night. Ms B developed tremors of the upper extremity that were controlled with benztropine 2 mg bid. Five weeks after admission, the patient was discharged with a BPRS score of 27. Her weight had decreased to 343.9 lb and BMI to 52.1 kg/m². In addition to molindone and benztropine, she was also taking hydrochlorothiazide 25 mg daily and trazodone 100 mg at night for insomnia.

Case 3. Ms C is a 50-year-old woman with a history of DSM-IV recurrent major depressive disorder with psychosis, DSM-IV panic disorder with agoraphobia, obesity, hypercholesterolemia, and hypertension who was admitted to our hospital in November 2008. Presenting problems were severely depressed and anxious mood, insomnia, panic attacks, auditory hallucinations, and paranoia. Ms C's BPRS score on admission was 37. Her weight on admission was 321.0 lb, and her BMI was 42.5 kg/m². The patient had been taking escitalopram, lithium carbonate, and clonazepam as an outpatient, but these had not been sufficiently helpful.

After these medications were tapered, Ms C was started on treatment with fluoxetine, lorazepam, and molindone. There was moderate improvement in her mood and complete resolution of the psychosis. Two weeks after hospitalization, she was discharged with a BPRS score of 31. Her weight had decreased to 313.7 lb and BMI to 41.6 kg/m². Discharge medications were molindone 75 mg daily, fluoxetine 20 mg daily, lorazepam 2 mg bid, ramipril 5 mg daily, simvastatin 20 mg at bedtime, trazodone 200 mg at bedtime, and enteric-coated aspirin 81 mg daily.

Molindone's effectiveness as an antipsychotic and propensity for weight loss is not new information. We believe that the value in presenting these cases is to reinforce these points, as, at present, the prevalence of obesity in psychiatric patients is high, while the utilization of molindone as an antipsychotic is low.

All of the patients received an 1,800-calorie diet during the hospital stay, but no specific behavioral weight management. The diet may have helped with weight loss, although this has generally not been our experience. Additionally, we report on the weight loss during the hospitalization; we do not know if the loss continued after discharge. Two of the 3 patients developed extrapyramidal side effects. This confirms that molindone is not without potential toxicity. The selection of a therapeutic agent requires a risk-benefit analysis with patient participation. However, using a medication such as molindone that may lead to weight loss

should be an important factor in this analysis for obese patients, since the comorbidities and increased mortality of this condition are well known.

The much-cited recent study by Sikich et al⁷ showing molindone to be of equal efficacy to risperidone and olanzapine in early-onset schizophrenia and schizoaffective disorder may lead to a reassessment of the usefulness of this drug. We hope that these case reports will also lead to psychiatrists' placement of molindone in their antipsychotic armamentarium, particularly for obese patients. It is important to have this option, since many antipsychotics lead to weight gain.

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