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Commentary Open Access

Weight Gain on Psychotropic Drugs: Has the Obesity Community been Paying Attention?

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Commentary

Weight gain is a well-known side effect of treatment with psychotropic drugs. More than fifty years ago, drugs such as amitriptyline (Elavil) and lithium were known to be associated with substantial increases in weight and despite new generations of psychotropic drugs, this unwelcome side effect has persisted [1-3]. How much weight is gained varies but in general mood stabilizers and antipsychotics drugs cause more substantial weight gain than antidepressants. Two antipsychotics, clozapine (Clozaril) and olanzapine (Zyprexa) are associated with the greatest prevalence of weight gain; up to 31% of patients treated with clozapine and 40% with olanzapine increase their weight during treatment [3]. Some mood stabilizers such as valproate (Depakote) [3] also are associated with a similarly high incidence of weight gain. Mirtazapine (Remeron) and paroxetine (Paxil) are two antidepressants with the greatest weight gain potential among the anti-depressants although except for buproprion (Wellbutrin) weight gain has been reported among all of the other drugs in this category [4].

The amount of weight gained varies depending on dose and duration of treatment. In White, Luthin and Cates 's review of studies looking at weight gain with antipsychotic agents, weight gain with olanzapine was as high as 9.4 kg with an average weight gain of 4.5 kg [3]. Patients gained on average 2.3 kg/month on olanzapine, 1.7 kg/month on clozapine, and 1.8 kg/month on quetiapine according to studies reported by Akhtar et al. [5]. The mood stabilizer, valproic acid also caused substantial weight gain; i.e. 5 kg over a six month treatment period [4]. Treatment with the antidepressant mirtazapine was associated with an average weight gain of 1.74 kg during the acute 4-12 week treatment phase and another 2.59 kg during the maintenance phase. Similar amounts of weight have been gained during treatment with paroxetine [4] but this particular drug has the potential to cause even greater weight gain. In a comparison study of weight gain risk with SSRI therapies, Fava et al. found that patients taking paroxetine gained more than 7% of their baseline weight in about six months [6].

Despite these findings, there is still some dispute over the likelihood that antidepressant therapy will result in elevated weight. A recent study using electronic medical records of patients treated with antidepressants for up to 12 months found little evidence of weight gain [7]. However the absence of this side effect might be explained by the study's finding that two-thirds of the patients were no longer in treatment at the end of twelve months. It is possible that patients withdrew from the study due to unacceptable weight gain or indeed may not have complied with their treatment [7]. Information from the electronic records was not available to address these possibilities.

Individuals whose obesity is associated psychotropic drug treatment have the same co-morbidities as those associated with any excessive BMI, regardless of etiology: dyslipidemias, metabolic syndrome, hypertension, type 2 diabetes and orthopedic stress [3]. The prevalence of these medical risk factors is particularly true of the severely mentally ill [3] who are most likely to be on medications associated with the greatest weight gain. Moreover patients who become obese due to medication associated weight gain find themselves face the same work and social barriers that may confront any obese individual. Covert employment discrimination, social disapproval, subtle and not so subtle remarks about the individual's weight may undo the positive therapeutic effects of the medication .Anecdotal reports from patients indicate that they face the additional burden of not wishing to disclose the cause of their overeating. A patient involved in a weight loss study at McLean Hospital in Belmont Mass [8] described her reluctance to attribute her substantial weight gain to the medication she was taking for bipolar disorder when criticized by family members for being unable to control her eating. Another patient who was a competitive athlete before substantial drug associated weight gain refused to engage in any sports because he feared comments about his now overweight and unfit body.

However it is important to point out that factors related to the mental illness itself rather than the medication also affect weight gain. Fatigue associated with depression can severely limit physical activity, and if prolonged, lead to muscle loss. The resulting decreased caloric utilization might promote weight gain even without appetite changes. Financial limitations due to under- or unemployment negatively impact food choices among the mentally ill as they do among the general population, and social isolation often makes eating the only available recreational diversion.

The options available to prevent continual weight gain are by and large limited to switching patients to alternative medications [3]. However this practice is not always possible due to the risk of withdrawal effects, relapse, drug interaction and altered efficacy of the alternative drug. As a consequence patients may choose to discontinue their psychotropic medication because becoming fat seems a worse alternative than depression or bipolar disorder [9].

Given the prevalence of psychotropic drug use, it is surprising that weight loss strategies specifically directed toward this sub-group of obese individuals have not developed. According to the Medco Health Survey, in 2010 [10], one in five Americans had a prescription written for at least one psychotropic drug. Although some of these drugs are not associated with weight gain, enough are to leave a sizable percent of the population at risk for obesity or if already obese, vulnerable to increased weight gain. But among the multitude of interventions for weight loss, few if any programs are designed for the specific needs of this subgroup. Should they need to lose weight, recommendations

include reduced calorie diets, eliminating calorically - dense foods, portion control, increased physical activity and group support from local weight loss organizations along with the occasional prescription for metformin [3]. In short, the interventions are no different than those given to those whose weight was not gained as a side effect of their medication.

There are several problems with this approach. To begin with, there is now well defined disturbance in the eating patterns of this sub group that may not characterize the overeating of other obese individuals. The weight gain associated with the use of psychotropic drugs is the consequence of an increased appetite for carbohydrate-rich foods, especially those with a high fat content [11,12] and a decrease in satiety. Uncontrolled hunger is not the problem. The problem these individuals experience is the absence of satiety; they don't feel full after eating quantities of food that prior to drug treatment would have satisfied them. This change in their eating behavior may result from blockage by the psychotropic drugs of the serotonergic 5-HT 2c receptors [11-13] that mediate satiety.

The tendency of many current diet regimens is to remove or limit carbohydrate from meals and snacks. This is understandable since carbohydrates are components of foods which have a high fat content (doughnuts, cookies, potato chips, chocolate, ice-cream) and are thus calorically dense. (This unfortunately also eliminates the many fat-free, nutrient- and fiber-rich carbohydrates from the weight loss regimen). However the removal or limitation of carbohydrates from the diet can exacerbate the absence of satiety by preventing serotonin synthesis. This makes dieting especially difficult when the dieter is still taking medications which block serotonin 2c receptors.

The consumption of carbohydrates with the exception of fructose results in the synthesis of serotonin [14]. Protein intake prevents serotonin synthesis; thus consuming carbohydrate along with or after protein has been eaten (as in dessert), will not result in increased serotonin. Chronic intake of high protein/low carbohydrate diets may be counterproductive as the dieter's struggle with the absence of satiety, associated with psychotropic drug treatment, will simply increase.

We conducted a study at the McLean Hospital weight management center to see if increasing pre-meal satiety would help this sub-group of obese patients lose weight. The subjects were being treated with one or more psychotropic drugs, all of which were known to cause weight gain. They were asked to consume a beverage containing sufficient carbohydrate to induce serotonin synthesis sixty minutes prior to lunch and dinner [8]. Total daily calorie intake from meals and the two beverages was 1400 calories for females and 1800 calories for males. Significant weight was lost over 12 weeks by patients following this regimen, despite their concurrent treatment with the drugs that had caused their previous overeating.

Prior to gaining weight on the psychotropic drugs, many of our patients had normal BMIs and followed a healthy lifestyle: They made nutritionally appropriate food choices and engaged in regular physical activity. Overeating was not a problem, and indeed until they gained weight, they had never dieted. Thus many of the weight loss support and behavioral modification programs aimed at the traditionally obese were irrelevant. Problems that many lifetime obese individuals struggle with such as emotional overeating and resistance to exercise were never an issue. Conversely finding themselves in an unfamiliar obese body and dealing with society's attitudes toward the obese was a problem with which many of them struggled. Indeed a few of our patients had become semi-recluses because of embarrassment over their excessive size.

Given the paucity of weight management programs designed to help this sub-group of obese individuals, the obesity community must do more to help. Strategies to prevent weight gain and support weight loss among patients on psychotropic drugs need to be developed and communicated to those who work with the obese so they understand the special needs of this group [1]. The BMIs of this sub group of obese individuals may be the same as those who did not gain weight as a side effect of their medication but this does not mean that interventions to help them lose weight should be the same. It is critical to identify the obesity of these individuals as resulting from the weight gaining side effects of their medication and give them the dietary and social support they need to help them return to their pre-medication weight.

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