Original Contributions

Medication Adherence and Subjective Weight Perception in Patients with First-Episode Psychotic Disorder

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Abstract

Introduction: Medication adherence is critical to the management of psychotic disorder. Different factors associated with medication adherence have been investigated in previous studies. However, the association with subjective weight perception, which is related to the weight gain side effect of antipsychotics, has not been thoroughly investigated. Subjective weight perception may not equal objective weight status. This study tests the hypothesis that medication adherence is related to subjective weight perception in a group of patients with first-episode psychotic disorder who have taken antipsychotics for one year. **Methods:** This study recruited 160 participants with one-year histories of first-episode psychotic disorder and measured their actual and perceived weights, amount of weight gain in the past year, body size satisfaction and medication adherence levels. The associations between medication adherence and both the actual and perceived weight status were analyzed controlling for other confounding factors including insight, drug attitude, illness severity and other medication side effects. **Results:** Stepwise multiple regression analysis found that the participants' perceived weight status, negative attitude toward their drugs and insight were the major factors associated with poor medication adherence. Of the participants who perceived themselves as being overweight, 86% believed that antipsychotics were responsible. Among those who had such beliefs, 72% had reduced their antipsychotic dosages on their own. About half of the participants had gained more than 7% of their baseline weight and 43.1% of the participants were found to be overweight after one year of treatment with antipsychotics. **Conclusions:** The results of this study indicate that medication adherence is associated with perceived weight status. Healthcare professionals should be aware of this relationship and address this issue early in the management of patients. Apart from weight management programs, education on a correct weight perception should be carried out with the promotion of proper drug attitudes and better insight for the improvement of medication adherence in the early course of psychotic disorder.

Introduction

Adherence to medication is to abide by the instructions given by a clinician in taking medication. Alarmingly, less than half of patients with first-episode psychosis adhere to their treatment plans (1). Poor adherence to antipsychotics has been found to be associated with relapse, hospital admission and persistent psychotic symptoms in patients with recent onset schizophrenia (2). In order to improve medication adherence, it is important to understand the reasons that patients do not follow their medication regimes. Factors that influence adherence include insight, attitude toward medication, medication-related side effects, severity of psychopathology, cognitive functioning, and practical issues such as financial difficulties (3). Amongst these factors, concern about body weight is an emerging problem, arguably

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Clinical Implications

Perceived overweight status instead of actual overweight status was associated with poor medication adherence in patients with first-episode psychotic disorder. There was significant weight gain after one year of antipsychotic treatment in this group of patients and most of them believed that antipsychotics were responsible for the weight gain. The concern about weight did not necessarily occur in those who were overweight, but was more of a problem for those who perceived themselves to be overweight. It is important to explore and discuss weight concerns of patients early in the course of illness with simple tools like the Figure Rating Scale, to provide advice and intervention on prevention of weight gain, and to implement weight management programs for reduction of harmful consequences associated with excessive weight gain, which include poor medication adherence. It may be better to use antipsychotics with a lower tendency to cause weight gain in patients who are very concerned about their weight if the other side effects profile is similar. Last, but not least, the message that even though antipsychotics are associated with different side effects including weight gain, they are beneficial in the preservation of mental health should be passed to patients. This is likely able to reduce the refusal rate and to improve medication adherence.

more so with individuals experiencing first-episode psychosis, especially those who are younger. Young people are more likely to be sensitive toward issues of body image (4) and display lower self-esteem if they are overweight (5). These sensitivities are exacerbated by the fact that the majority of patients are put on the newer second-generation antipsychotics, which are more likely to cause weight gain. It follows that, of young individuals, more of those with psychotic disorders are obese (56%) as compared to the general population (33%) (6). Clinicians are increasingly encountering patients who are distressed by their increased weight and, consequently, resistant to take further medications. This is particularly problematic in the younger patients who are suffering from first-episode psychotic disorder.

Weiden et al. found a significant positive association between subjective distress over weight and medication non-adherence, even accounting for other possible confounding factors including actual weight status, in a group of patients with schizophrenia (7). It seems that the actual body mass index (BMI) of a patient is not the major determining factor for adherence, but whether one cares about one's weight and whether one perceives that one is overweight. The study gathered information about height, weight, and adherence from patients at various stages of schizophrenia, but was limited in that it relied on self-reporting by patients via postal survey; and, while attitudes toward body size and preferences for a particular weight are mediated by substantial cultural factors (4), the situation in Chinese societies remains uncertain. In this study, we used more direct structured interviews to measure the association between weight dissatisfaction and medication adherence and focused on a group of patients with first-episode psychotic disorder.

Objectives and Hypotheses

The aim of this study is to examine the association between adherence with antipsychotics and subjective weight perception in individuals with first-episode psychotic disorder. It is hypothesized that if a patient with first-episode psychosis perceives that he is overweight, regardless of his actual weight, and if he believes that medications are responsible for his weight, he will have poorer medication adherence. Those who perceive themselves as overweight will be asked about their reasons for being overweight and any methods they have used for weight reduction.

Methods

Participants

Participants were recruited from the inpatient unit and the outpatient clinics of a psychiatric service, which covers a defined population (of approximately 1 million) in Hong Kong. Those who had a primary diagnosis under F20-29 (schizophrenia, schizotypal and delusional disorders) according to the Tenth Revision of the *International Classification of Disease (ICD-10)* (WHO, 1992) were identified from the case register and their case notes were reviewed to confirm the diagnoses and to make sure this was the first presentation of psychotic symptoms to a psychiatric service. Diagnoses including delusional disorder, unspecified psychosis and acute and transient psychotic disorders were included because patients with these conditions were also treated with antipsychotics, and they faced the same weight problem as those with schizophrenia. Also, it was not uncommon for these patients to have their diagnoses changed to schizophrenia over time. All eligible patients who presented with first-episode psychotic disorder between March and December 2007 were approached ten to twelve months after their diagnoses were made for recruitment into the study. Patients were included if they fulfilled the following criteria: 1) able to give informed consent; 2) ethnically Chinese and had adequate command and understanding of Chinese; 3) had a primary diagnosis under F20-29 according to the *ICD-10* criteria; and, 4) had taken antipsychotics

since their first presentation of acute psychotic symptoms to a psychiatric service ten to twelve months before the day of interview. They would be excluded if they: 1) were older than 65 years; 2) had past *ICD-10* diagnosis of a psychotic disorder; 3) had psychoactive substance (including alcohol) harmful use and/or dependence in the past one year; 4) had current or past *ICD-10* diagnosis of anorexia nervosa or bulimia nervosa, organic brain disorder, mental retardation, or mood disorder; 5) had prior treatment with antipsychotics for over two weeks in any one period before March 2007; 6) had discontinued antipsychotics according to formal doctor's orders due to remission of psychotic disorder; and, 7) were pregnant at the time of interview. Approval of the New Territories West Cluster Clinical and Research Ethics Committee was obtained before the study commenced. Informed written consent was obtained from each participant. The sample size was estimated to be 143 using the G*POWER (8) software to yield a power of 0.8 based on results of an earlier study (7).

Measurements

The BMI was calculated using weight and height (rounded up to the nearest 0.1 kilograms and 0.001 meters) of the participants in light clothing measured by a nurse. It is generally accepted that the BMI cut-off points defining overweight should be lower for Asians (9). Based on previous local studies, the proposed cut-off point to define overweight for Hong Kong Chinese is 23 kg/m^2 (10). The BMI was classified into three categories as follows: 1) smaller than 18.5 kg/m^2 as underweight; 2) 18.5–22.9 kg/m^2 as normal weight; and, 3) equal to or bigger than 23 kg/m^2 as overweight. Weights and heights before commencement of antipsychotics were measured for all the participants and recorded down in their case notes. The data were gathered from the case notes.

A body image questionnaire was used to assess the subjective weight perception (11). It was comprised of two parts: Figure Rating Scale (FRS) (12) and cognitive attitude toward body size. In the FRS, there are seven male/female contour drawings, numbered from 1–7, in increasing body size from left to right. Participants were asked to choose one figure drawing that most accurately represented the size of their own bodies and then one that represented their desired figure. Dissatisfaction with body figure could be calculated by the difference between the two chosen ratings ("current figure"–"desired figure"="body dissatisfaction score" [BDS]). For the cognitive attitude assessment, participants were asked whether they thought they were: 1) underweight; 2) of normal weight; or, 3) overweight. Those who perceived themselves overweight were asked about their reasons for being overweight and the method currently used, if any, for

weight reduction using standard questions developed based on literature review and interview with three groups of patients with psychotic disorder who attended a talk about weight management. The questions had been revised by an expert panel consisting of consultants and allied health workers, including occupational therapists, clinical psychologists and dieticians.

The Compliance Rating Scale (CRS) was used to assess medication adherence over the past two weeks (13). The scale consisted of ratings from 1–7, where 1 indicated complete refusal of medications and 7 indicated very good adherence in which the patient actively participates, readily accepts, and shows some responsibility for the regimen. This method of adherence measurement was validated against pill counts during community home visits and found to have satisfactory correlation (r_s=.78, p<.001). When rating the CRS, the investigator interviewed the participant and his caregiver separately and gathered as much information as possible from the case notes, nurses' reports, and reports from other people who were involved in his care. If there were discrepancies between reports from the participant and relatives/staff, information given by relatives/staff would be used for rating. It was unavoidable that the investigator (Dr. Wong), who rated the adherence, would have a rough estimation of the weight and height of the subjects during the interview. However, the actual measurements, as well as the amount of weight gain, the subjective weight perception of the subjects and other self-report measurement results would not be known by Dr. Wong.

With reference to existing literature on medication adherence in those with first-episode psychosis, all factors that had been found to have significant association with medication adherence in first-episode psychosis and those which were commonly examined were also assessed, including: 1) type of medication (conventional or atypical) prescribed to the participants; 2) positive and negative symptoms using the Scale for the Assessment of Positive Symptoms (SAPS) (14) and the Scale for the Assessment of Negative Symptoms (SANS) (15); 3) insight as assessed by the Cantonese-modified version Self-Rated Insight Scale (16), which was a self-report scale with ten questions, validated with Chinese patients with schizophrenia with satisfactory face, construct and concurrent validity, internal consistency and high test-retest reliability; 4) drug attitude as assessed by the 30-item Chinese version of the Drug Attitude Inventory (DAI-30) (17); and, 5) extrapyramidal side effects (EPS) as assessed by the Extrapyramidal Symptom Rating Scale (ESRS) (18). The FRS, body image questionnaire, CRS, Self-Rated Insight Scale, DAI-30 and ESRS were administered with permissions from the authors; the observer rated scales were rated by the investigator alone.

Data Analysis

Data were analyzed using SPSS (Windows version 16.0). For continuous data, variables were presented as means and standard deviations (SD) for normally distributed data or as medians (Mdn) and interquartile ranges (IQR) for skewed data. The Kolmogorov-Smirnov Test was used to test for normality. For categorical data, variables were presented as numbers and percentages.

Factors with significant association with adherence were put into a stepwise multiple regression model with the ratings of the CRS (1–7) as the dependent variable. Multicollinearity among factors was checked. The significance level was set at 0.05 and the power at 0.80. We assessed the cross-sectional associations between medication adherence (dependent variable) and demographic and clinical characteristics including the actual and perceived weight status (independent variables). The Mann-Whitney U test and the Kruskal-Wallis test were used for nonparametric variables. Spearman's rank correlation coefficients were computed between the compliance rating and the SAPS, SANS, DAI-30, ESRS, and the Self-Rated Insight Scale scores.

Results

Participants of the Study

From March to December 2007, 173 patients with psychotic disorders presenting for the first time were identified. Five of them were excluded: one had mental retardation; two had depression; and, two had histories of substance abuse. When the remaining 168 patients were approached ten to twelve months after their first presentation, five more were excluded: four because their diagnoses were changed to organic brain syndrome (one patient), drug-induced psychotic disorder (one patient), or bipolar affective disorder (two patients); and, a fifth patient because his clinician discontinued his prescription for antipsychotics. Two other patients could not be contacted as they left Hong Kong immediately after their hospital discharge. One patient refused to be interviewed. There was no statistically significant difference in sex (p=.87), age (p=.35) and baseline BMI (p=.45) between the patients who participated (160) and those who were excluded (13).

The final sample consisted of 160 participants (90 female and 70 male) with a mean age of 29.9 (SD=11.0), Mdn(IQR)=27.5(16), age ranges from 14 to 59. Of the patients meeting all inclusion criteria, 86.2% had achieved an education level of secondary school or higher and 91.3% were living with family. Their diagnoses at the time of the interview included schizophrenia (n=127), delusional disorder (n=19), unspecified psychosis (n=10), acute and transient psychotic disorder (n=3), and schizoaffective disorder

Table 1	**Association Between Baseline Demographic and Clinical Characteristics of Participants and Medication Adherence**			
	N=160		Compliance Rating (1–7)	
	N	%	Mdn (IQR)	P-Value
Sex				
Male	70	43.8	5 (3)	.02*
Female	90	56.3	4 (1)	
Age group				
<20	28	17.5	4 (1)	.24
20–29	67	41.9	4 (2)	
30–39	32	20.0	4 (2)	
>39	33	20.6	4 (1)	
Marital status				
Not married	127	79.4	4 (1)	.08
Married	33	20.6	4 (2)	
Living with others				
Yes	146	91.3	4 (1)	.57
No	14	8.8	4 (3)	
Employment status				
Employed†	109	68.1	4 (1)	.55
Unemployed	51	31.9	4 (1)	
Educational level				
Secondary and above	138	86.3	4 (1)	.23
Lower than secondary	22	13.8	4 (2)	
Diagnosis				
Schizophrenia	127	79.4	4 (1)	.37
Nonschizophrenia‡	33	20.6	4 (2)	
Second-generation antipsychotics				
Yes	85	53.1	4 (1)	.53
No	75	46.9	4 (2)	
Previous hospitalization				
Yes	107	66.9	4 (1)	.61
No	53	33.1	4 (2)	
Involvement of allied health workers§				
Yes	100	62.5	4 (1)	.47
No	60	37.5	4 (1)	
Overweight				
Yes	69	43.1	4 (1)	.83
No	91	56.9	4 (2)	
Perceived as overweight				
Yes	87	54.4	4 (0)	.001**
No	73	45.6	5 (2)	

	Mdn (IQR)	Correlation with CRS	P-Value
Number of concurrent medications use‖	1 (2)	.133	
Drug Attitude Inventory	18 (12)	.613	<.001**
Self-Rated Insight Scale	29 (3)	.395	<.001**
Body dissatisfaction score	1 (1.5)	-.238	.002**
Extrapyramidal Symptom Rating Scale	0 (0)	.101	.21
Scale for the Assessment of Positive Symptoms	0 (0)	-.172	.03*
Scale for the Assessment of Negative Symptoms	0 (7)	.100	.21

*p<.05; **p<.01. † Also included full-time students, housewives and those performing regular activities. ‡ Delusional disorder, unspecified psychosis, acute and transient psychotic disorder and schizoaffective disorder. § Case nurse, medical social worker, clinical psychologist and occupational therapist. ‖ Mood stabilizers, benzodiazepines, antidepressants, anticholinergics, beta-blockers and hypnotics.

Table 2	Multiple Linear Regression Analysis of the Factors Associated with Medication Adherence				
	Unstandardized Coefficients β	Standard Error	95% CI	Standardized Coefficients β	P-Value
Constant	0.68	0.78			
Drug attitude	0.08	0.01	(0.07, 0.10)	.66	<.001*
Perceived as overweight	-0.60	0.15	(-0.89, -0.31)	-.21	<.001*
Insight	0.08	0.03	(0.03, 0.14)	.17	.006*

R^2=.58, *p<.01

(n=1). None of them had comorbid medical diagnoses or took nonpsychiatric medication known to affect weight (such as steroids or medications for hypothyroidism or Cushing's syndrome). Concerning the adherence level, 16 participants had a CRS rating of 1, 4 had a CRS rating of 2, 12 had a CRS rating of 3, 63 had a CRS rating of 4, 39 had a CRS rating of 5, 25 had a CRS rating of 6, and 1 had a CRS rating of 7. 98 participants were prescribed other concomitant medications including anticholinergics, benzodiazepines, mood stabilizers, hypnotics, beta-blockers and antidepressants in addition to antipsychotics for the management of their psychotic disorder.

The final sample had a mean current BMI of 23.1 kg/m² (SD=4.3) while their mean baseline BMI was 21.0 kg/m² (SD=3.5). 123 participants had gained weight (Mdn=4.8 kg, IQR=8.3) after treatment with antipsychotics for 10–12 months. 57.5% of them gained more than 7% of their baseline weight. 11.9% of the participants were underweight, 45% of them had normal weight and 43.1% of them were overweight at the time of assessment. 10.6% of the participants perceived themselves as underweight, 35% of them perceived themselves as normal weight and 54.4% of them perceived themselves as overweight. Those who perceived themselves as overweight had a significantly greater median weight gain of 7.5 kg (IQR=7) comparing to 2 kg (IQR=5) in those who did not perceive themselves as overweight (p<.001).

Factors Associated with Medication Adherence

All 160 participants were included in the analysis of factors associated with medication adherence. Their CRS ratings ranged from one to seven. Female patients and those who perceived they were overweight had significantly lower CRS ratings, indicating poorer adherence (see Table 1). The scorings of the DAI, Self-Rated Insight Scale, BDS, and SAPS significantly correlated with the CRS ratings. Better drug attitude and insight were associated with better medication adherence while the presence of more severe positive symptoms was associated with poorer medication adher-

ence. Those who were more dissatisfied with their body size and who wanted to be thinner also reported poorer medication adherence.

Multiple Linear Regression Analysis of Factors Associated with Medication Adherence

The factors from Table 1 with p<.1 were entered for the stepwise multiple regression analysis associated with medication adherence. As the two factors "perceived as overweight" and "BDS" were highly correlated with each other (r_s=.85, p<.001), only "perceived as overweight" was used in the regression analysis. Those who perceived themselves as overweight (p<0.01) had worse medication adherence, while those who had better drug attitude (p<0.01) and insight (p=.006) had better medication adherence (see Table 2). The three factors accounted for 58% of the total variance. Drug attitude (β=.66, p<.001) was the most influential factor, followed by perceived overweight status (β=-.21, p<.001), and insight (β=.17, p=.006).

Causes of Overweight Status Perceived by the Participants and Methods of Weight Reduction Used

The 87 participants who perceived themselves as being overweight were asked about the reasons for being overweight. 75 participants considered antipsychotics as the cause. 72% of the participants (54 out of 75) who believed that antipsychotics led to their overweight status had reduced or omitted their dosages on their own in order to reduce weight (p<.001). This group has a significantly lower CRS rating than the other participants. 86 out of 87 of those who perceived themselves as overweight wanted weight reduction, signifying that they were not satisfied with their weight. Those who were put on concomitant medications that might also cause weight gain were analyzed separately, and no significant association was found between their use and weight gain, status of being overweight and perception of overweight status.

Discussion

Comment on the Level of Nonadherence as Compared to Other Studies

We found that patients with first-episode psychosis who perceived themselves as being overweight were dissatisfied with their weight and nearly all of them sought weight reduction. This contributed significantly to poor adherence. Our finding in first-episode patients was consistent with the initial finding of Weiden et al. (7) in a mixed group of patients. In particular, the finding that the perceived weight status, rather than the actual weight status, was associated with medication adherence was replicated in our study. Moreover, those who perceived themselves as overweight were more likely to have poor adherence, with other potential factors including drug attitude and insight being accounted for. As expected, attitude toward treatment and insight were also important factors associated with medication adherence in the early stages of antipsychotic treatment for patients with first-episode psychotic disorder. A Health Belief Model, which focuses on patient's perceptions, can be used to explain medication adherence (19). If a patient perceives that the benefit of taking medication exceeds that of the cost, the person is likely to adhere to treatment. However, if he perceives that the medication is responsible for his weight gain, he is unlikely to adhere to treatment. If a patient's perception of susceptibility and severity is heightened (i.e., he believes himself to be at high risk of becoming seriously unwell should he fail to adhere to treatment), then he will be more adherent.

Importantly, data from this study suggest a possible mechanism to explain how subjective perception of weight mediates medication adherence. Most participants who perceived themselves as overweight believed that their weight problem was caused by the antipsychotics they had been taking. Indeed half of the participants had experienced significant weight gain after one year of treatment. Those who perceived themselves as overweight experienced a significantly higher magnitude of weight gain over the study period compared to those who did not perceive themselves as overweight. Nearly all of them wanted to reduce their weight, and a significant number of participants had reduced their drug intake on their own in order to ameliorate their weight, as they believed that antipsychotics led to their overweight status. This further supported our hypothesis that those who believed medications were responsible for their weight problem would have poorer medication adherence.

Body weight perception is mediated by local social and cultural factors (4). It is likely affected by the sex, age, occupation, marital status and socioeconomic status of the participants. Further analysis of the association between body weight perception and these demographic characteristics was not among the objectives of this study. Among the demographic factors, only sex had a significant association with compliance rating. However, this association was not significant when doing the multiple regression analysis.

Being overweight is not uncommon in patients with first-episode psychosis who have been on antipsychotics for about one year. The baseline BMI was calculated with weight measured during the acute stage of the psychotic disorder. It is possible that these baseline measures were lower than the usual weights of the participants as a result of the mental illness (20). However, about half of the participants gained more than 7% of weight, which was compatible with an existing study (21), and some of them even became overweight after their first year of treatment. They were likely heavier than usual after one year of treatment. The perceived weight status was found to deviate considerably from the actual weight status of the participants. Patients tended to overestimate their weight by perceiving themselves as overweight when they were not according to BMI classification. Similar to what we found, Shih & Kubo (11) found that 57% of females and 12% of males overestimated their body size using the same body image questionnaire as used in this study. The type of antipsychotics used (first-generation vs. second-generation) did not show a significant difference in the compliance rating. The analysis of the extent of weight gain with individual antipsychotics would be presented in another paper (22).

The SAPS score was found to have a negative significant correlation with the CRS rating; however, they were not significantly associated with each other during the multiple linear regression analysis. Special attention was paid to any delusion related to weight distortion when doing the SAPS to ensure that the perception was not affected by the psychotic disorder of the participants. Controlled study done locally regarding weight perception in patients with first-episode psychotic disorder and their age-matched controls found that these patients, especially females, overestimated their weight status like their normal counterparts (23). This led to the findings in our study that a significant portion of participants overestimated their weight, a premise which agrees with what is happening in the general population and, therefore, is not a feature specific to the underlying psychotic disorder.

Limitations

This study has several limitations. The factors being studied, including medication adherence, were only measured at one time point. Therefore, it was impossible to comment on the causal effect of any change in the factors on adherence. In addition, there is no gold standard

for the measurement of adherence. On the other hand, the methods used in this study were simple, pragmatic, and easy to administer. Some participants even found participation engaging. Lastly, the BMI of the participants was only measured at two time points and any change within the one-year period would be missed.

Conclusions

Perceived overweight status instead of actual overweight status was associated with poor medication adherence in patients with first-episode psychotic disorder. There was significant weight gain after one year of antipsychotic treatment in this group of patients and most of them believed that antipsychotics were responsible for the weight gain. The concern about weight did not necessarily occur in those who were overweight, but was more of a problem for those who perceived themselves to be overweight. It is important to explore and discuss weight concerns of patients early in the course of illness with simple tools like the FRS, to provide advice and intervention on prevention of weight gain, and to implement weight management programs for reduction of harmful consequences associated with excessive weight gain, which include poor medication adherence. It may be better to use antipsychotics with a lower tendency to cause weight gain in patients who are very concerned about their weight if the other side effects profile is similar. Last, but not least, the message that even though antipsychotics are associated with different side effects including weight gain, they are beneficial in the preservation of mental health should be passed to patients. This is likely able to reduce the refusal rate and to improve medication adherence.

Acknowledgments

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