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The Effects of Antipsychotic Drugs (Olanzapine and Risperidone) on Body Weight, Body Fat Percentage and Lipid Profiles of Patients with Psychotic Illness

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ABSTRACT

Approximately 50% patients with psychotic illnesses on antipsychotic drugs have an increased risk of obesity. This study aimed to determine changes in body weight, body fat percentage and lipid profiles and to stress the importance of early nutrition intervention in the management of psychotic illness patient treated with antipsychotic drugs. This is a prospective longitudinal study conducted for 3 months in Hospital Mesra Bukit Padang, Kota Kinabalu, Sabah. A total of 150 patients with Diagnostic and Statistical Manual IV (DSM-IV) diagnosis of psychotic illness (either Olanzapine or Risperidone only at any dosage) first started or restarted after a treatment gap of at least 6 months were recruited. Weight, height and body fat percentage were measured using Bioelectrical Impedance Analysis (BIA) (Model Omron HBF-375) and blood fasting lipid test were taken from the point of starting medication for 12 weeks. Data were analysed using repeated measures of ANOVA for statistical method. All variables showed significant mean differences ($p < 0.05$) in increasing pattern throughout the 12 weeks of treatment. However, the total cholesterol of risperidone patients had no significant mean difference from initial to week 6 ($p = 0.282$). It was proven that there was increase in body weight, body fat percentage and lipid profiles among patients on olanzapine and risperidone. The limitation of this study might relate to the drugs' dosage and method used in assessing the body composition. It is suggested that early nutrition intervention is needed to control unnecessary gain of weight, body fat and lipid profiles in the management of patient with psychotic illnesses.

INTRODUCTION

The common treatment given to patients with psychosis illness is antipsychotic drugs (APDs). Antipsychotic drugs have two generations, namely the "first-generation" or conventional and the "second-generation" or atypical antipsychotic. Atypical antipsychotics are preferable over conventional antipsychotics[1, 2, 3]. Among the atypical antipsychotics, Olanzapine is the intermediate D2 antagonist and Risperidone is the high D2 antagonist. However, other side effects such as induced weight gain have rapidly become more evident[4, 5, 6]. This is concerning since these weight gains have been proven to lead the patients into exhibiting obesity[7, 8, 9]. Antipsychotic drugs (olanzapine and risperidone) are the most common APDs that prescribed in Hospital Mesra Bukit Padang, Kota Kinabalu, Sabah according to the pharmacy unit.

DSM-IV defines psychotic illness as a clinically significant behavioural or psychological syndrome or pattern that occurs in an individual. It is associated with present distress, disability or with a significantly increased risk of suffering death, pain, or an important loss of freedom. According to National Health and Morbidity Survey 2015, in Malaysia, 29.2% adults and 12.1% children aged 5 to 15 are diagnosed with mental illness[10]. In East Malaysia, Sabah and Sarawak, there is lack of study that that could provide information on the prevalence rate of mental illness among residents in Sabah[11].

Many studies have been carried out to show the relationship between the consumption of antipsychotic drugs and obesity among patients with psychotic illnesses. Despite its low prevalence, psychosis illness can be an economic burden to a country, especially developing country[12, 13]. Malaysian doctors have been urged to provide these people with treatments and solution[14]. These treatments include the usage of APDs, whether in long term or short term. This, unfortunately, only increases the prevalence of obesity in Malaysia if the usage goes unmanaged.

This study aimed to determine the changes in anthropometric measurement, body composition as well as blood lipid profile among patients treated with olanzapine and risperidone. This study contributes as an empirical research. It provides an insight for future researchers to understand the importance of early nutrition intervention in the management of psychotic illness patients. This study could further explore how APDs can affect the anthropometric measurement and body fat percentage of patients. Since APDs are known to induce weight gain in most psychotic patients, the potential of inducing weight gain between Olanzapine and Risperidone is investigated. Thus, the objectives of the study were to analyse the changes in body composition among the patients when treated with Olanzapine and Risperidone.

MATERIALS AND METHODS

This study was conducted between 2015 and 2017 in terms of recruitment of patients and each eligible patient was following up for 3 months for this study at the Hospital Mesra Bukit Padang. This prospective longitudinal study was conducted over a period of three months involving 150 patients (76 males and 74 females). The number of subjects was calculated based on GLIMMPSE (General Linear Multivariate Model Power)[15]. The patients were aged between 18 and 45 years old diagnosed with psychotic illness based on the DSM-IV diagnostic criteria. Their treatment started with either Olanzapine (5 – 30 mg per day) or Risperidone (0.5 – 6 mg per day) which was assigned randomly according to the patients' medical condition and patients were experiencing either their first episode of psychosis or had not taken antipsychotic drugs in the last six months. The patients who were diagnosed with drug induced psychosis, affective disorders and having other medical problems that can affect the lipid profile or body fat composition, including diabetes, hyperlipidaemia and other endocrine disorders, on other medication which affect

the lipid profile or body fat composition (e.g. statins) and have an abnormal level of total cholesterol (more than 5.7 mmol/l), and TG (more than 2.3 mmol/l) and with a BMI of more 24.9 kg/m^2 and in Overweight and Obese range[2, 3, 4] were excluded from the study.

The data collection was approved by the National Medical Research Registry (NMRR-15-1006-26514) and all patients provided written informed consent before participating in this study. Opinion from professionals such as psychiatrists and medical officers will be considered to determine the ability of patient to give consent. The data will only be taken after consent given by the patient.

Information on patients' demographic data and current medications were obtained from their medical records. The researcher obtained access for patients' medical records as a health professional in the hospital. Patients' height was determined without shoes on a portable stadiometer with the Frankfort plane parallel to the floor according to National Health and Nutrition Examination Survey (NHANES) The head is in the Frankfort plane when the horizontal line from the ear canal to the lower border of the orbit of the eye is parallel to the floor and perpendicular to the vertical backboard. Body fat percentage was measured using the Body Fat Analyzer OMRON HBF 375 Weight Scale with correction for light indoor clothing. Fasting Lipid Profile (Total Cholesterol, triglycerides, high-density lipoprotein and low-density lipoprotein) of every patient in this study was obtained. All measurements mentioned were taken upon admission (Initial), week 6 and week 12.

The demographic characteristics of the patients were presented using frequencies, percentage and counts. To compare the main demographic and clinical characteristics among patients, repeated measures ANOVA was used to means of these variables at initial, week 6 and week 12. To further examine the relationship between APDs and the appetite of the patients, a chi-square analysis was performed. All these data were analysed using the Statistics-PC-software for Windows, Version 25.0.

RESULTS

There were 76 (51%) male patients and 74 (49%) female patients recruited for this research while 33 patients dropped out. The age distribution among the 150 recruited patients was normal with mean value of 32.65 $\pm$ 6.37 years old (Table 1).

Table 1 Socio-demographic characteristics of subjects (*n* = 150)

Variables		Overall (*n*)	Olanzapine *n* (%)	Risperidone *n* (%)
Gender	Male	76	44 (57.9)	32 (42.1)
	Female	74	37 (50.0)	37 (50.0)
Age	21 – 25	25	10 (40.0)	15 (60.0)
	26 – 30	41	24 (58.5)	17 (41.5)
	31 – 35	47	27 (57.4)	20 (42.6)
	36 – 40	11	7 (63.6)	4 (36.3)
	41 – 45	26	13 (50.0)	13 (50.0)

The research reported that 61 Olanzapine patients claimed to have increased appetite during the medication, 8 patients claimed decreased appetite while the remaining of 12 have no changes in appetite. While for Risperidone patients, 23 of them have increased appetite, 16 with decreased appetite and 30 of them with unchanged appetite (Figure 1).

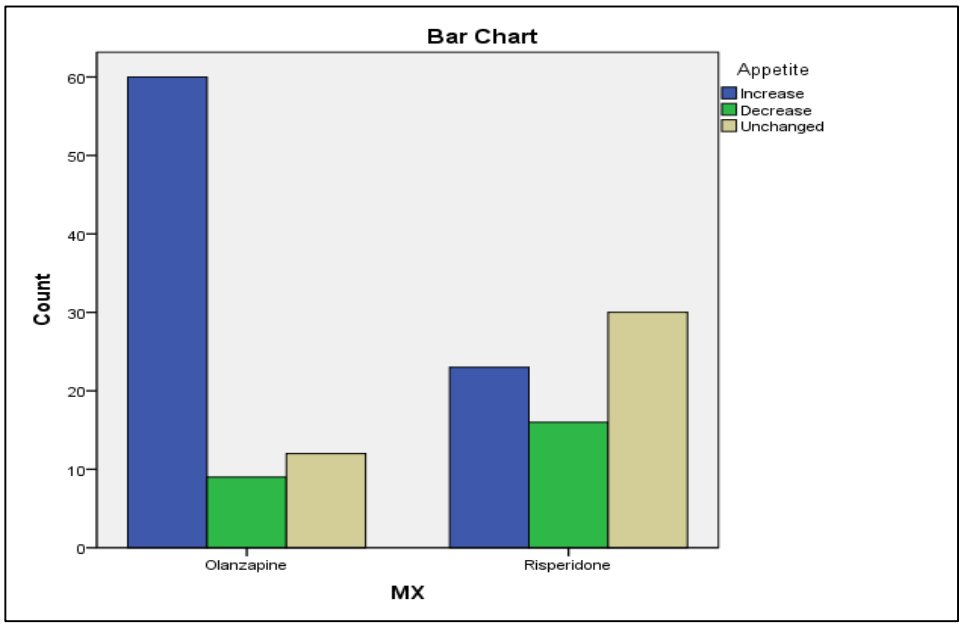

Figure 1 Distribution of appetite among patients taking Olanzapine and Risperidone

The means for Olanzapine and Risperidone patients' initial body weight were 56.11 ± 7.77 kg and 55.50 ± 8.00 kg respectively. For body fat, the means recorded for Olanzapine and Risperidone patients were 21.97 ± 4.26 % and 23.00 ± 4.54 % respectively while the results also revealed that the mean and standard deviation for waist were 28.59 ± 2.53 inch and 28.88 ± 2.88 inch respectively. The mean and standard deviation for hip were 32.77 ± 2.82 inch and 33.35 ± 2.75 inch respectively.

Table 2 Initial body composition among Olanzapine and Risperidone patients (*n* = 150)

Treatment	Variables	Minimum	Maximum	Mean	Std. Deviation
Olanzapine	Weight (kg)	36.0	72.0	56.11	7.77
	Body Fat (%)	12.7	29.0	21.97	4.26
	Waist (inch)	23.0	34.5	28.59	2.53
	Hip (inch)	27.0	41.0	32.77	2.82
Risperidone	Weight (kg)	38.0	73.0	55.50	8.00
	Body Fat (%)	14.2	33.8	23.00	4.54
	Waist (inch)	24.0	34.0	28.88	2.88
	Hip (inch)	25.0	38.0	33.35	2.75

The minimum triglycerides among patients is 0.04 and the maximum is 2.00. The mean for triglycerides cholesterol for Olanzapine and Risperidone patients is 1.16 with standard deviation of 0.29 and 1.13 ± 0.32. The minimum HDL among patients is 0.60 and the maximum is 1.90. The means for HDL of Olanzapine and Risperidone patients are 1.04 ± 0.22 and 1.05 ± 0.21 respectively. As for Low Density Lipoprotein (LDL), the minimum LDL among patients is 0.09 and the maximum is 4.10. The means of LDL for Olanzapine and Risperidone patients are 2.92 ± 0.75 and 2.88 ± 0.66 respectively. Table 3 illustrates that the minimum total cholesterol among patients is 3.00 and the maximum is 5.50. The means for total cholesterol are reported to be 4.29 ± 0.65 for Olanzapine and 4.29 ± 0.66 for Risperidone patients respectively. (Table 3).

Table 3 Initial Blood Lipid Profile among Olanzapine and Risperidone patients (*n* =150)

Treatment	Variables	Minimum	Maximum	Mean	Std. Deviation
Olanzapine	Triglycerides (mmol/L)	0.44	1.80	1.16	0.29
	HDL (mmol/L)	0.60	1.90	1.04	0.22
	LDL (mmol/L)	0.90	4.10	2.92	0.75
	Total Cholesterol (mmol/L)	3.00	5.30	4.29	0.65
Risperidone	Triglycerides (mmol/L)	0.04	2.00	1.13	0.32
	HDL (mmol/L)	0.60	1.70	1.05	0.21
	LDL (mmol/L)	1.50	4.00	2.88	0.66
	Total Cholesterol (mmol/L)	3.00	5.50	4.29	0.66

Table 4 and Table 5 summarize the mean and standard deviation for all the variables at initial, week 6 and week 12 for Olanzapine and Risperidone patients. The tables also reported that there were increasing patterns across the means of the dependent variables, except for HDL which displayed decreasing pattern from initial to week 6 and to week 12 for both Olanzapine and Risperidone patients. However, the results also revealed that there are no significant mean differences in HDL among patients treated with Olanzapine or Risperidone after week 6 (p = 0.143). In addition, the total cholesterol among Risperidone patients also show no significant mean difference from initial to Week 6 (p = 0.282). On the other hand, there is a significant mean difference from Week 6 to Week 12 which means the mean for total cholesterol increases only after week 6 of Olanzapine or Risperidone.

Table 4 BMI, weight, body fat at Initial, Week 6 and Week 12 for Olanzapine and Risperidone Patients (*n* = 150)

Variable	Medications	Mean Difference		Std. Error	95% Confidence Interval for Difference[a]	
				Lower Bound	Upper Bound	
BMI	Olanzapine	At week 6 vs initial	1.184*	.075	1.001	1.367
		At week 12 vs initial	2.347*	.118	2.059	2.634
		At week 12 vs at week 6	1.163*	.67	.999	1.327
	Risperidone	At week 6 vs initial	1.328*	.116	1.042	1.613
		At week 12 vs initial	2.626*	.155	2.245	3.007
		At week 12 vs at week 6	1.299	.080	1.102	1.495
Body weight (kg)	Olanzapine	At week 6 vs initial	3.069*	.367	2.172	3.966
		At week 12 vs initial	6.037*	.423	5.001	7.073
		At week 12 vs at week 6	2.968*	.167	2.559	3.377
	Risperidone	At week 6 vs initial	3.396*	.300	2.659	4.132
		At week 12 vs initial	6.641	.398	5.663	7.619
		At week 12 vs at week 6	3.245	.209	2.732	3.758
Body fat (%)	Olanzapine	At week 6 vs initial	1.820*	.163	1422	2.218
		At week 12 vs initial	3.473*	.220	2.936	4.010
		At week 12 vs at week 6	1.653*	.122	1.355	1.951
	Risperidone	At week 6 vs initial	1.777*	.201	1.282	2.271
		At week 12 vs initial	3.413*	.240	2.824	4.002
		At week 12 vs at week 6	1.636*	.127	1.324	1.948

* The mean difference is significant at the 0.05 level

Table 5 Blood Lipid Profile Parameters at Initial, Week 6 and Week 12 for Olanzapine and Risperidone Patients (n = 150)

Variable	Medications	Mean Difference		Std Error	95% Confidence Interval for Difference[a]	
				Lower Bound	Upper Bound	
Triglycerides (mmol/L)	Olanzapine	At week 6 vs initial	.314*	.040	.216	.411
		At week 12 vs initial	.482*	.043	.377	.588
		At week 12 vs at week 6	.168*	.022	.113	.223
	Risperidone	At week 6 vs initial	.233*	.034	.150	.317
		At week 12 vs initial	.339*	.048	.222	.456
		At week 12 vs at week 6	.106*	.037	.014	.197
Total Cholesterol (mmol/L)	Olanzapine	At week 6 vs initial	.560*	.063	.406	.715
		At week 12 vs initial	1.044*	.074	.864	1.225
		At week 12 vs at week 6	.484*	.048	.367	.601
	Risperidone	At week 6 vs initial	.806	.475	–.359	1.971
		At week 12 vs initial	1.254*	.473	.092	2.415
		At week 12 vs at week 6	.448*	.058	.306	.590
LDL (mmol/L)	Olanzapine	At week 6 vs initial	.478*	.060	.330	.625
		At week 12 vs initial	.953*	.068	.786	1.120
		At week 12 vs at week 6	.475*	.051	.352	.599
	Risperidone	At week 6 vs initial	.309*	.059	.164	.453
		At week 12 vs initial	.665*	.061	.516	.815
		At week 12 vs at week 6	.357*	.044	.249	.464
HDL (mmol/L)	Olanzapine	At week 6 vs initial	–.44*	.016	–.084	–.004
		At week 12 vs initial	–.091*	.020	–.141	–.042
		At week 12 vs at week 6	–.047*	.023	–.104	.010
	Risperidone	At week 6 vs initial	–.047*	.017	–.090	–.004
		At week 12 vs initial	–.064*	.018	–.108	–.021
		At week 12 vs at week 6	–.017	.017	–.060	.026

*The mean difference is significant at the 0.05 level

DISCUSSION

The weight gain can be seen through the mean differences of the patients' weight throughout the duration of the treatment. As revealed by the repeated measures ANOVA, there are significant mean differences for body weight of Olanzapine and Risperidone patients from initial to week 6 of treatment and week 6 to week 12 of treatment. This finding reaffirms the finding which indicated an association of APDs with weight gain among psychotic illness patients[16, 17]. Besides weight gain, that study also revealed differences in body composition among those that were induced by APDs compared to the control group[17].

From the statistical findings, all variables show significant mean differences in increasing pattern throughout the 12 weeks of treatment. However, the total cholesterol of Risperidone patients has no significant mean difference from initial to week 6 (p = 0.282). The results indicate the mean difference is only significant after the 6th week. The findings from repeated measures ANOVA indicate that there is no significant reduction HDL from week 6 to week 12 of treatment. The findings are also

consistent with a study where Risperidone was revealed to induce weight gain[16] among psychiatric patients with a mean weight gain of 4.3 kg after 12 weeks of treatment[18].

The patients are at risk of dyslipidaemia and cardiovascular as findings revealed increasing pattern for LDL and triglycerides from initial to week 12 while decreasing pattern of HDL from initial to week 6. The variation in patients' appetite does not help in predicting the APDs-induced body weight gain among the patients since some of the patients were reported to experience decreased appetite. It does however, shows that Olanzapine patients experienced higher increased appetite than the group that received Risperidone for their treatment[19].

The finding of this research seems to be in contrary with other studies that used a comparison of Olanzapine and Risperidone to determine their potential in inducing changes in weight gain and other body composition[20]. A study shows that Olanzapine induced more weight gain than Risperidone[21], however, for LDL, Risperidone seems to induce a significant change in LDL as compared to those treated with Olanzapine[22]. Lastly, although the result shows that patients prescribed Risperidone have higher weight gain compared to Olanzapine but there is no significant difference between the mean weight of Olanzapine and Risperidone, except on Low Density Lipoprotein (LDL) and Triglycerides.

Factors that could influence the side effect of APDs in inducing body weight gain among patients include its dosage and the demographic characteristics of patients[23]. Olanzapine has been known to be a dose-dependent drug, but the effects of Risperidone are less well known[24, 25, 26, 27]. Demographic characteristics such as age, gender and appetite were discussed to give a clearer picture on the confounding factors that could predict the body weight gain among patients[28].

The limitation of this study can be related to the drugs' dosage. In this study, the dosage of both Olanzapine and Risperidone were assigned by the clinicians according to the patients' needs. Hence, the dosage is not constant but varies with different patients. Next, there is a need to have control group, a control group is an essential element to allow the researchers to examine if the intended effects of the applied drugs are produced only by the drug[29].

CONCLUSION

It is proven that antipsychotic drugs induce changes in body weight, body fat percentage and lipid profiles among patients prescribed with Olanzapine and Risperidone. It is recommended that early nutrition intervention is crucial to control unnecessary weight, body fat and lipid profiles in the management of patient with psychotic illnesses that treated with antipsychotic drugs such as Olanzapine and Risperidone. Dietary counselling and monitoring of body weight and body fat may help to minimize the risk of obesity among psychotic patient on antipsychotic drugs.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this article.

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