GSC Biological and Pharmaceutical Sciences

eISSN: 2581-3250 CODEN (USA): GBPSC2

Cross Ref DOI: 10.30574/gscbps

Journal homepage: https://gsconlinepress.com/journals/gscbps/

(RESEARCH ARTICLE)

Check for updates

Metabolic effects of risperidone on patients with psychosis in a tertiary care hospital of Myanmar

Aung Thet Soe and Kyaw Zwar Htoon *

Department of Pharmacology, Defence Services Medical Academy, Yangon, Myanmar.

GSC Biological and Pharmaceutical Sciences, 2024, 26(03), 183–189

Publication history: Received on 12 February 2024; revised on 23 March 2024; accepted on 26 March 2024

Article DOI: https://doi.org/10.30574/gscbps.2024.26.3.0105

Abstract

Background: Risperidone, a second generation antipsychotics, used to treat many psychotic conditions is related with obesity, hyperlipidemia, type 2 diabetes and hypertension.

Objective: To find out the metabolic effects of risperidone on patients with psychosis in a tertiary care hospital of Myanmar

Method: A hospital based before and after observational study was done on 37 male patients with psychosis who were treated with risperidone. Anthropometric parameters (weight, body mass index, waist hip ratio), clinical parameters (systolic and diastolic blood pressure), biochemical parameters (fasting total cholesterol, fasting high density lipoprotein, fasting low density lipoprotein, fasting triglyceride and fasting blood glucose) were determined before and at one, two, three months of risperidone therapy.

Results: After three months of treatment with risperidone at doses ranging from 2 to 6 mg, there were significant alterations in various anthropometric, clinical, and biochemical parameters among participants. Notably, there was a marked increase in body weight from an average of 55.8 kg to 61.6 kg ($p<0.001$) and in BMI from 20.5 to 22.5 ($p<0.001$). The waist-hip ratio rose from 0.84 to 0.89 ($p<0.001$), while systolic blood pressure increased from 119.7 to 125.7 ($p=0.001$) and diastolic blood pressure from 77.3 to 83.2 ($p<0.001$). Total cholesterol levels increased from an average of 169.4 to 185.7 ($p=0.027$), and triglyceride levels increased from 127.2 to 170.7 ($p=0.007$). However, there were no statistically significant changes observed in high-density lipoprotein, low-density lipoprotein, and fasting blood glucose levels.

Conclusion: The results of the study underscore the metabolic effects associated with risperidone therapy, necessitating vigilant monitoring by healthcare providers to manage potential adverse metabolic outcomes effectively.

Keywords: Anthropometric parameters; Biochemical parameters; Blood pressure; Metabolic effects; Risperidone

1. Introduction

According to the Myanmar Ministry of Health's 2020 Public Health Statistic Report, there has been a notable increase in reported cases of mental disorders between 2016 and 2019. In 2019, the prevalence rates per 100,000 population were 330 for alcohol use disorder, 16 for anxiety disorder, 12 for mental retardation, 12 for psychosis, and 7 for depression [1]. A 2020 study focusing on the Yangon Region found a mental distress prevalence of 18.0% among individuals aged 18-49, with women exhibiting a higher rate (21.2%) compared to men (14.9%) [2]. Psychotic disorders can manifest across various age groups but are relatively rare before puberty and after the age of 45. The highest incidence occurs

* Corresponding author: Kyaw Zwar Htoon

among late adolescents. Additionally, there is variation in the prevalence of psychotic disorders among different marital status groups, with a higher occurrence observed among single males and divorced or separated females [3].

Second-generation antipsychotic medications, also known as atypical antipsychotics, are commonly prescribed to manage psychotic conditions such as schizophrenia. They offer advantages over conventional antipsychotics by reducing the risk of extrapyramidal side effects. However, some atypical antipsychotics have been associated with significant drawbacks, including substantial weight gain and an elevated risk of dyslipidemia and type 2 diabetes mellitus [4]. These metabolic issues, compounded by factors like smoking and unhealthy lifestyle habits, are significantly more prevalent in individuals with psychosis compared to the general population, occurring between two to five times more frequently [5].

Significant variations exist among antipsychotic medications regarding their metabolic side effects. Olanzapine, clozapine and quetiapine are known for having the most adverse profiles in this regard, while aripiprazole, and ziprasidone tend to have milder profiles [5–8]. Certain factors such as higher baseline weight, male gender, and non-white ethnicity increase susceptibility to antipsychotic-induced metabolic changes, and improvements in psychopathology may be associated with metabolic disturbance [8].

Risperidone, classified as an atypical antipsychotic, primarily achieves its therapeutic effects by blocking dopamine D2 and serotonin 5-HT2A receptors. By doing so, it inhibits excessive dopaminergic activity in mesolimbic pathways, thereby alleviating positive symptoms of schizophrenia. However, risperidone is also known for its metabolic side effects, such as weight gain, dyslipidemia, and an elevated risk of developing type 2 diabetes mellitus. These metabolic effects are thought to stem from risperidone's affinity for histamine H1 and alpha-1 adrenergic receptors, which can result in increased appetite and reduced insulin sensitivity [9, 10]. To mitigate these risks, careful monitoring of metabolic parameters and lifestyle interventions are essential. By closely monitoring patients and implementing appropriate lifestyle modifications, healthcare providers can help minimize the metabolic complications associated with risperidone treatment [7, 9, 11, 12].

This study aimed to measure anthropometric, blood pressure and biochemical parameters of the psychotic patients within three months of risperidone therapy, and to study the metabolic effects of risperidone therapy in patients with psychosis attending to No (1) Defence Services General Hospital (1000-Bedded), Mingalardon, Yangon, Myanmar.

2. Materials and Methods

A hospital based before and after observational study was done on patients with psychosis from Psychiatric Ward and Out Patients Department of No (1) Defence Services General Hospital (1000-Bedded), Mingalardon, Yangon, Myanmar. Patients aged between 18-55 who were newly diagnosed with psychosis by consultant psychiatrist and were scheduled to treat with risperidone (2-6) mg were recruited following informed consent. The patients with high blood pressure (>160/90 mmHg), already diagnosed with diabetes, taking lipid lowering drugs, pregnant women and lactation mothers were excluded from the study. The study was conducted from March 2019 to August 2020.

Thirty-seven male patients participated in this study. After taking informed consent, before starting risperidone therapy, screening of the patients was done by history taking, clinical examinations (Blood Pressure (BP), weight, height, Waist Circumference (WC), Hip Circumference (HC), Waist-Hip Ratio (WHR)) and laboratory examinations (fasting total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), triglyceride and glucose). Anthropometric parameters (body weight, height, waist-hip circumference, BMI), blood pressure and biochemical parameters (fasting blood glucose (FBG)) were assessed at four different time points: time zero (T0) referring to the measurements before starting risperidone therapy, one month (T1), two months (T2) and three months (T3) of risperidone therapy. Biochemical parameters (fasting total cholesterol, HDL, LDL, triglyceride) were assessed before risperidone therapy (T0) and after three months (T3) of risperidone therapy.

Measuring body weight, height, WC, HC and WHR were done according to WHO guidelines by using measuring tape and balance. Calculation of the BMI was done by using Healthy Weight Guide BMI calculator. To calculate the BMI, the weight in kilogram was divided by the height in meters then divided the answer by the height again. Systolic and diastolic blood pressure were measured by using sphygmomanometer and stethoscope. For investigation of fasting lipid profile, after 8 hours of fasting, 3 mL of venous blood was collected under aseptic condition in K3 EDTA tube and lipid profiles were analyzed by Cobas C311 auto analyzer in Pathology Department of Defence Services Liver Hospital, Yangon. Measuring fasting blood glucose was done by taking blood sample from the tip of finger of the patient, and reading by glucometer and test strips naming Thada, TaiDoc Technology Corporation, Taiwan.

The data were collected in proforma and analyzed by using SPSS software version 22.0. P value < 0.05 was used to indicate statistical significance. The study was approved by the Academic Board of Post-graduate Studies (Pharmacology) of Defence Services Medical Academy, Yangon, Myanmar.

3. Results

The study involved thirty-seven male patients diagnosed with schizophrenia (n = 10), mood disorders (n = 15), or bipolar disorder with psychotic features (n = 12), who were treated with risperidone at doses averaging 3.4 mg for a duration of three months at the Psychiatric ward and Out Patients Department of No (1) Defence Services General Hospital (1000-Bedded), Mingalardon, Yangon, Myanmar. The mean age of the participants was 32.1 years. Baseline assessments revealed that 16% of patients had high lipid profiles, while 51% had elevated fasting blood glucose levels, classified as prediabetes. However, all these patients had haemoglobin A1C levels below 6.5%, indicating prediabetic status. Baseline anthropometric, clinical, and biochemical parameters were described in Table 1.

Table 1 Distribution of baseline anthropometric, clinical and biochemical parameters of study populations

Parameter	Frequency (n=37)	Percent (%)
BMI		
Under weight	9	24.3
Normal	27	73
Overweight	1	2.7
WHR		
Moderate risk	35	95
High risk	2	5
Total cholesterol		
Normal	31	83.8
High	6	16.2
Triglyceride		
Normal	31	83.8
High	6	16.2
HDL		
Normal	37	100
High	Nil	
LDL		
Normal	32	86.5
High	5	13.5
Fasting Blood Glucose		
Normal	18	48.6
High	19	51.4

Throughout the study period, there were progressive increases observed in mean body weight, BMI, waist-hip ratio, systolic and diastolic blood pressure, and fasting blood glucose levels at 1 month, 2 months, and 3 months of risperidone therapy. Specifically, the mean body weight increased from 55.8 ± 6.1 kg at baseline (T0) to 61.6 ± 6.3 kg after 3 months (T3), representing a 10.4% increase, which was statistically significant ($p < 0.001$). Similarly, BMI increased from 20.5 ± 2.3 kg/m2 at baseline to 22.5 ± 2.1 kg/m^2 at 3 months, indicating a 9.8% increase, which was also statistically

significant ($p < 0.001$). Waist-hip ratio increased from 0.84 ± 0.03 to 0.9 ± 0.03 (5.9% increase, $p < 0.001$), while systolic and diastolic blood pressure showed respective increases from 119.7 ± 6 mmHg to 125.7 ± 8 mmHg (5.1% increase, $p=0.001$) and from 77.3 ± 4.5 mmHg to 83.2 ± 5.8 mmHg (7.6% increase, $p < 0.001$). (Table 2 and 3)

Regarding biochemical parameters, fasting total cholesterol levels increased from 169.4 ± 31.6 mg/dL at baseline to 185.7 ± 30.5 mg/dL at 3 months (9.6% increase, $p < 0.027$), and fasting triglyceride levels increased from 127.2 ± 59.0 mg/dL to 170.7 ± 74.4 mg/dL (34.2% increase, $p < 0.007$). However, changes in high-density lipoprotein (HDL), low-density lipoprotein (LDL), and fasting blood glucose levels were not statistically significant. (Table 3)

Table 2 Anthropometric and biochemical parameters before, after 1 month, 2 months and 3 months of risperidone therapy

Parameters	**T0**	**T1**	**T2**	**T3**	**P Value**
	Mean±SD	**Mean±SD**	**Mean±SD**	**Mean±SD**	
Weight(kg)	55.8±6.1	57.7±6.6	59.6±6.5	61.6±6.7	0.001
BMI (kg/m^2)	20.5±2.3	21.1±2.3	21.7±2.3	22.5±2.1	0.002
WHR	0.84±0.03	0.86±0.03	0.88±0.03	0.89±0.03	<0.001
SBP (mmHg)	119.7±6	121.3±7.5	122.5±20.2	125.7±8	0.179
DBP (mm Hg)	77.3±4.5	79±5.1	81.1±5.7	83.2±5.8	<0.001
FBG (mg/dL)	119±28.2	116.6±23.4	123.8±26.2	133.1±43.6	0.114

Table 3 Changes of anthropometric, clinical and biochemical parameters before and after 3 months of risperidone therapy

Parameters	**T0**	**T3**	**% changes**	**P value**
	Mean ± SD	**Mean ± SD**		
Weight (kg)	55.8±6.1	61.6±6.7	10.4	<0.001
BMI (kg/m$^{2)}$	20.5±2.3	22.5±2.1	9.8	<0.001
WHR	0.84±0.03	0.89±0.03	5.9	<0.001
SBP (mm Hg)	119.7±6	125.7±8	5.1	0.001
DBP (mm Hg)	77.3±4.5	83.2±5.8	7.6	<0.001
FBG (mg/dL)	119±28.2	133.1±43.6	11.8	0.102
Total Cholesterol (mg/dL)	169.4±31.6	185.7±30.5	9.6	0.027
Triglyceride (mg/dL)	127.2±59	170.7±74.4	34.2	0.007
HDL (mg/dL)	43.5±11.6	44.2±14.5	1.6	0.825
LDL (mg/dL)	102.1±29.4	105.5±26	3.3	0.590

4. Discussion

Antipsychotic medications, such as risperidone, are crucial in the treatment of various psychotic disorders, including schizophrenia. However, these drugs often come with significant adverse effects, notably dyslipidemia and weight gain, which can be intolerable for many patients. Therefore, it is imperative to prioritize prevention, early detection, and treatment of these metabolic side effects to ensure the safe and effective use of risperidone therapy [4, 7, 8, 13, 14]. Therefore, the metabolic effects of risperidone were studied in patients with psychosis at psychiatric ward of No (1) DSGH (1000-bedded), Mingalardon for three months duration. The sample size in this study is small (n=37) and the

duration of the risperidone therapy is only three months. However, the metabolic effects of risperidone in short-term treatment had been detected in this study.

In a study by Nanotkar et al. [15], it was reported that the mean weight gain after two to six months of using risperidone was notably higher, with a mean weight gain of 1.75 kg. Similarly, Nagaraj and Madalageri [6] found that patients exhibited a mean weight gain of 2.67 kg within one year of risperidone use. In contrast, the present study observed a mean weight gain of 5.8 kg after three months of risperidone use, which exceeded the findings of the aforementioned studies. The primary mechanism of action of antipsychotic agents involves antagonism of serotonin ($5HT_2C$) receptors and dopamine (D_2) receptors, leading to increased appetite and subsequent weight gain [16].

The findings regarding BMI in this study slightly surpassed those documented in previous research [6, 15]. Throughout the present study, both body weight and BMI demonstrated incremental rises from baseline to one month, two months, and three months following initiation of risperidone therapy. Although establishing a direct correlation between weight gain or BMI and risperidone dosage is not definitive, it seems that the duration of risperidone treatment in the present study contributed to the gradual escalation in weight and BMI among participants.

The study observed a significant increase in the mean WHR from 0.84 at baseline (T0) to 0.89 at three months (T3), representing a 5.9% increase. This noteworthy elevation in WHR over the three-months monitoring period indicates the development of central obesity among individual patients. Central obesity, characterized by increased fat accumulation around the abdominal area, is associated with a higher risk of developing ischemic heart disease. According to a study in America, there was a low association between obesity and myocardial infarction rates, a moderate association with stroke rates and a strong association with high blood pressure rates [17]. The findings of the study revealed significant increases in both mean SBP and DBP following three months of risperidone therapy. This implies a heightened risk of hypertension associated with the use of risperidone. Furthermore, the mean FBG level exhibited a rise at the three-month mark post-risperidone treatment, although this change did not reach statistical significance. It's noteworthy that while some patients demonstrated above-normal blood glucose levels at baseline, none were diagnosed with diabetes after the three-month therapy period in this study. In the study by Nagaraj and Madalageri, FBG increased from 97.7 mg/dL to 105.27 at 6^{th} month and 110.13 at one year of risperidone treatment [6]. When the patients were given antipsychotic medication including risperidone, both fasting and postprandial blood glucose showed a continuous increasing trend on follow up according to another study [18].

In this study, significant increases were observed in the mean levels of total cholesterol and triglycerides following risperidone therapy for three months. However, the mean levels of LDL and HDL did not show statistical significance. A study by Nagaraj and Madalageri observed a significant rise in LDL and fall in HDL at the end of one year [6]. In the findings of another study, there was no significant changes in triglycerides and HDL values [15]. The mean fasting triglyceride levels in the patient cohort in this study significantly increased after three months of risperidone therapy. In the current study, the observed hypertriglyceridemia could be linked to several factors, including a refractory response to risperidone treatment and increased appetite. However, it is important to note that dietary habits were not investigated in this study, which could have contributed to the observed metabolic changes. Hypertriglyceridemia is a common form of dyslipidemia and is often associated with an increased risk of premature coronary artery disease [19]. Notably, the mean levels of HDL, LDL, and FBG did not exhibit statistically significant changes within the study period.

Accordingly in the present study, patients treated with risperidone might have the increase risk for the comorbidities like obesity, diabetes, dyslipidemia and hence periodic monitoring for metabolic abnormalities is required.

5. Conclusion

Risperidone has adverse effects including weight gain, higher BMI, increased WHR, FBG, and fasting lipids profile. It will be beneficial if the metabolic effects of risperidone in patients with psychosis receiving risperidone are early detected and treated accordingly.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

The study was approved by the Academic Board of Post-graduate Studies (Pharmacology) of Defence Services Medical Academy, Yangon, Myanmar. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Statement of informed consent

Informed consent was obtained from guardians of all individual participants included in the study as the participants were suffering from mental illness.

References

[1] MMR Ministry of Health. Public health statistics: 2017-2019. Internal Document., https://www.themimu.info/sites/themimu.info/files/documents/Report_Myanmar_Health_Statistics_2020_MOHS_Oct2020.pdf (2020, accessed 18 March 2024).

[2] Aye WT, Lien L, Stigum H, et al. The prevalence of mental distress and the association with education: A cross-sectional study of 18-49-year-old citizens of Yangon Region, Myanmar. BMC Public Health; 20. Epub ahead of print 22 January 2020. DOI: 10.1186/s12889-020-8209-8.

[3] Tin-Oo, Win-Aung-Myint. A study on clinical and social aspects of schizophrenia in Myanmar. University of Medicine 2, 2005.

[4] Newcomer JW, Haupt DW. The Metabolic Effects of Antipsychotic Medications. Can J Psychiatry 2006; 51: 480–485.

[5] Lambert T. Managing the metabolic adverse effects of antipsychotic drugs in patients with psychosis. Australian Presciber 2011; 34: 97–99.

[6] Nagaraj L, Madalageri NK. A comparative study of metabolic side effects of risperidone and olanzapine in the treatment of schizophrenia. Int J Basic Clin Pharmacol 2019; 8: 2561.

[7] Wong KCY, Leung PBM, Lee BKW, et al. Long-term Metabolic Side Effects of Second-Generation Antipsychotics in Chinese Patients with Schizophrenia: A Within-Subject Approach with modelling of dosage effects. DOI: 10.1101/2024.03.04.24303695.

[8] Pillinger T, McCutcheon RA, Vano L, et al. Comparative effects of 18 antipsychotics on metabolic function in patients with schizophrenia, predictors of metabolic dysregulation, and association with psychopathology: a systematic review and network meta-analysis. Lancet Psychiatry 2020; 7: 64–77.

[9] Leucht S, Corves C, Arbter D, et al. Second-generation versus first-generation antipsychotic drugs for schizophrenia: a meta-analysis. The Lancet 2009; 373: 31–41.

[10] Leucht S, Burkard T, Henderson J, et al. Physical illness and schizophrenia: A review of the literature. Acta Psychiatrica Scandinavica 2007; 116: 317–333.

[11] Waszak P, Piskorska N, Sarbiewska M, et al. Cardiovascular and metabolic side effects of second-generation antipsychotics - narrative review. Eur J Transl Clin Med 2019; 2: 70–77.

[12] Zhang Y, Liu Y, Su Y, et al. The metabolic side effects of 12 antipsychotic drugs used for the treatment of schizophrenia on glucose: A network meta-analysis. BMC Psychiatry; 17. Epub ahead of print 21 November 2017. DOI: 10.1186/s12888-017-1539-0.

[13] Schneider-Thoma J, Kapfhammer A, Wang D, et al. Metabolic side effects of antipsychotic drugs in individuals with schizophrenia during medium- to long-term treatment: protocol for a systematic review and network meta-analysis of randomized controlled trials. Syst Rev; 10. Epub ahead of print 1 December 2021. DOI: 10.1186/s13643-021-01760-z.

[14] Pérez-Iglesias R, Martínez-García O, Pardo-Garcia G, et al. Course of weight gain and metabolic abnormalities in first treated episode of psychosis: The first year is a critical period for development of cardiovascular risk factors. International Journal of Neuropsychopharmacology 2014; 17: 41–51.

[15] Nanotkar S, Choure B, Gosavi D. A comparative study of the effects of risperidone and olanzapine on metabolic parameters of schizophrenic patients. Int J Basic Clin Pharmacol 2016; 814–819.

[16] Strassnig M, Miewald J, Keshavan M, et al. Weight gain in newly diagnosed first-episode psychosis patients and healthy comparisons: One-year analysis. Schizophr Res 2007; 93: 90–98.

[17] Akil L, Ahmad HA. Relationships between Obesity and Cardiovascular Diseases in Four Southern States and Colorado. J Health Care Poor Underserved 2011; 22: 61–72.

[18] Wani RA, Dar MA, Margoob MA, et al. Diabetes mellitus and impaired glucose tolerance in patients with schizophrenia, before and after antipsychotic treatment. J Neurosci Rural Pract 2015; 6: 17–22.

[19] Berglund L, Brunzell JD, Goldberg AC, et al. Evaluation and Treatment of Hypertriglyceridemia: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2012; 97: 2969–2989.