Original Article CNPT11(2020)15-22

CNPT The Japanese Society of Clinical Neuropsychopharmacology Clinical Neuropsychopharmacology and Therapeutics scnp

Association of selected antipsychotics on the triglyceride levels in patients with schizophrenia in inpatient and outpatient settings

Shin Ono, M.D., Ph.D.[1], Takuro Sugai, M.D., Ph.D.[2], Yutaro Suzuki, M.D., Ph.D.[2], Manabu Yamazaki, M.D., Ph.D.[3], Kazutaka Shimoda, M.D., Ph.D.[4], Takao Mori, M.D., Ph.D.[3], Yuji Ozeki, M.D., Ph.D.[5], Hiroshi Matsuda, M.D., Ph.D.[3], Norio Sugawara, M.D., Ph.D.[4], Norio Yasui-Furukori, M.D., Ph.D.[4], Kurefu Okamoto, M.D., Ph.D.[3], Toyoaki Sagae, M.S.[6], Toshiyuki Someya, M.D., Ph.D.[2]

[1]*Department of Community Psychiatric Medicine, Niigata University Graduate School of Medical and Dental Sciences, Japan*

[2]*Department of Psychiatry, Niigata University Graduate School of Medical and Dental Sciences, Japan*

[3]*Japan Psychiatric Hospital Association, Japan*

[4]*Department of Psychiatry, Dokkyo Medical University School of Medicine, Japan*

[5]*Department of Psychiatry, Shiga University of Medical Science, Japan*

[6]*Department of Health and Nutrition, Yamagata Prefectural Yonezawa University of Nutrition Sciences Faculty of Health and Nutrition, Japan*

ABSTRACT

Objective: Patients with schizophrenia have higher morbidity and mortality rates than the general population and a shorter life expectancy. While increased plasma triglyceride levels constitute a risk factor for cardiovascular diseases, metabolic disturbances are seen in patients with schizophrenia and in those on antipsychotics. This study assessed the triglyceride levels of patients with schizophrenia who were administered antipsychotic monotherapy in various treatment settings as a post-hoc analysis of a previous nationwide survey.

Methods: The final study population comprised 2416 inpatients and 1159 outpatients selected using questionnaire surveys were administered at facilities within the Japan Psychiatric Hospitals Association. Analysis of covariance was performed to compare the triglyceride levels among the three antipsychotic groups: olanzapine, risperidone or aripiprazole.

Results: The triglyceride levels of inpatients were significantly different among the three antipsychotic groups after adjusting for body mass index, age, sex and chlorpromazine-equivalent dosage. In the post-hoc analysis, inpatient triglyceride levels were significantly higher in the olanzapine group (106.5 ± 61.8 mg/dL) than the risperidone group (97.1 ± 50.4 mg/dL). In contrast to inpatient hospitalisations, outpatient settings may mask the antipsychotic treatment effects on triglyceride levels.

Conclusions: Triglyceride levels differ based on the type of antipsychotic treatment in inpatients but not outpatients.

Keywords: antipsychotics, hospitalization, metabolic syndrome, schizophrenia and triglyceride

Corresponding Author: Toshiyuki Someya, 757 Asahimachidori-ichibancho, Niigata 951-8510, Japan; Tel: +81-25-227-2213, Fax: +81-25-227-0777, E-mail: psy@med.niigata-u.ac.jp

Received January 28, 2020 / Accepted February 27, 2020 / Published April 7, 2020.

INTRODUCTION

Patients with schizophrenia have higher morbidity and mortality rates compared with the general population and a life expectancy that is approximately 20% shorter [1]. They also have an increased prevalence of cardiometabolic risk factors, such as obesity, dyslipidaemia and diabetes [2]. High plasma triglyceride levels are a risk factor for cardiovascular diseases in the general population [3, 4]. Previous studies have attributed the metabolic disturbances associated with schizophrenia to poor lifestyle choices, such as a sedentary lifestyle, smoking, poor diet, prolonged stress, use of antipsychotic drugs and genetic susceptibility [5].

Recently, a meta-analysis reported higher triglyceride levels in patients with antipsychotic-naïve schizophrenia compared with controls [6]. Another study reported that antipsychotic-treated patients had significantly higher levels of triglycerides compared with drug-naïve, first-episode patients and healthy subjects [7]. In a previous study that evaluated the relationship between antipsychotics and triglyceride levels in patients with schizophrenia, clozapine or olanzapine was each found to be associated with increased triglyceride levels [8, 9].

Serum lipid levels are affected by other confounding lifestyle factors that are unrelated to smoking, such as exercise and alcohol intake. Smoking habits, diet and exercise habits differ between inpatient and outpatient settings. Generally, triglyceride levels are susceptible to diet. The results of previous reports on the effects of antipsychotics on triglyceride levels may not be consistent because many such studies used subjects who were outpatients and their diet was not controlled. However, in Japan, the diets of hospitalised schizophrenic patients are controlled to some extent. In addition, there is often no smoking in the hospital environment; as such, the effect of smoking on triglyceride levels may be small in hospitalised patients. Therefore, it is important to investigate the effects of antipsychotics on triglyceride levels in hospitalised patients as this has not been previously studied. However, since schizophrenic patients are also treated in outpatient settings, it is important to investigate the comparative effects of antipsychotics on triglycerides levels in outpatient and inpatient settings.

In Japan, there are approximately 795,000 people with schizophrenia. The majority of such patients are treated in hospitals within the Japan Psychiatric Hospitals Association. To assist patients with schizophrenia, a joint project between the Japanese Society of Clinical Neuropsychopharmacology and the Japan Psychiatric Hospitals Association was formed in 2012. A large-scale investigation of the prevalence of metabolic syndrome with schizophrenia was previously conducted [10]. In this study, we investigated the effects of antipsychotic monotherapy on triglyceride levels in Japanese patients with schizophrenia in different treatment settings by hospitalisation or outpatient analyses as a post-hoc analysis of a previous nationwide survey.

SUBJECTS and METHODS

Participants

This study was a post-hoc analysis of a previous survey [10]. Of the 23,116 subjects in the original survey, only those who received monotherapy with olanzapine, risperidone, or aripiprazole were included in the present study. Olanzapine, risperidone, and aripiprazole have different pharmacological profiles, and differences in metabolic side effects have been reported in previous studies. Therefore, we extracted and studied these three drugs. The original sample included 15,461 inpatients and 7655 outpatients who were diagnosed with schizophrenia on the basis of the International Statistical Classification of Diseases and Related Health Problems version 10 [11] or the Fourth edition of the Diagnostic and Statistical Manual of Mental Disorders [12]. The study protocol and informed consent procedure were approved by the Ethics Committee of the Japan Psychiatric Hospitals Association in accordance with the Declaration of Helsinki. All participants gave written informed consent before all study procedures.

The original questionnaire survey was conducted between January 2012 and July 2014. For the current study, we excluded the following patients: those aged below 20 years; patients whose sex, body mass index (BMI) and triglyceride data were not recorded and patients medicated with either multiple antipsychotics or drugs other than olanzapine, risperidone or aripiprazole. Using these criteria, 3575 individuals were finally included in the study.

Table 1. Comparison of triglyceride levels and clinical characteristics between outpatients and inpatients

		Inpatients (n = 2416)	Outpatients (n = 1159)	p value
Age	years	61.7 ± 12.9	51.9 ± 13.8	< 0.001
Female (male)	n	1228 (1188)	530 (629)	0.004
BMI	kg/m^2	22.1 ± 4.0	25.3 ± 4.7	< 0.001
Triglyceride levels	mg/dL	100.9 ± 56.2	140.9 ± 99.5	< 0.001
CP-equivalent dosage of current AAP	mg	479.0 ± 285.8	435.0 ± 263.1	< 0.001
Antipsychotic agent				< 0.001
Olanzapine	n	864	378	
Risperidone	n	1155	528	
Aripiprazole	n	397	253	
Concomitant drugs				
Benzodiazepines	n	45	22	0.941
Mood stabilizer	n	54	12	0.107
Antidepressant	n	8	3	0.759

Data are presented as the mean ± standard deviation of the number of subjects.
Age, BMI, triglyceride levels, and the CP-equivalent dosage of current AAP were compared between the outpatients and inpatients. The Chi-square test was used to compare differences in sex, types of antipsychotic agent and concomitant drugs.
BMI: body mass index; CP: chlorpromazine; AAP: atypical antipsychotic.

Assessments

A brief questionnaire was created to assess demographic data (age and sex) and triglyceride levels after reviewing the relevant literature and guidelines. Body weight and height were measured and the BMI was calculated as weight (kg)/height squared (m^2). Triglyceride levels were measured by standard analytical techniques in fasting.

Statistical Analyses

The demographic and clinical variables were expressed as the mean ± standard deviation. To compare the clinical characteristics between the outpatients and inpatients, the t-test was used for continuous variables and the Chi-square test was used for categorical variables. Analysis of covariance was carried out with BMI, age, sex and chlorpromazine-equivalent dosage of current atypical antipsychotics as confounding variables for inpatients and outpatients to compare triglyceride levels among the three antipsychotic groups (olanzapine, risperidone, or aripiprazole). Post-hoc analyses were performed using the Bonferroni method. The threshold for significance was set at $p < 0.05$. SPSS Statistics 24 for Mac OS (IBM Japan, Tokyo, Japan) was used for statistical analyses.

RESULTS

A total of 2416 inpatients and 1159 outpatients with schizophrenia met the inclusion/exclusion criteria for participation in this study and were included in our analyses. All the participants were Japanese, with a mean age of 58.4 ± 14.1 years and a mean BMI of 23.2 ± 4.5 kg/m^2. For the overall participants, significant differences in age, sex, BMI, triglyceride levels, chlorpromazine-equivalent dosage of current atypical antipsychotics and antipsychotic medication were found among the inpatients and outpatients (Table 1). The inpatients were older than the outpatients ($p < 0.001$) (Table 1). The BMI and triglyceride levels in the inpatients were lower compared to that of the outpatients ($p < 0.001$) (Table 1). Chlorpromazine-equivalent dosages of current atypical antipsychotics in the inpatients were higher than those of the outpatients ($p < 0.001$). Concomitant drugs for antidepressants, mood stabilizers and benzodiazepines did not differ in distribution (Table 1).

The triglyceride levels of the inpatients were significantly different among the three antipsychotic groups ($p < 0.001$) after adjusting for BMI, age, sex and chlorpromazine-equivalent dosage of current atypical antipsychotics (Table 2). For post-hoc analysis of triglyceride levels in inpatients among the groups, triglyceride levels were significantly higher in the olanzapine group (106.5 ± 61.8 mg/dL) than in the risperidone group (97.1 ± 50.4 mg/dL) ($p < 0.001$) (Table 2). The triglyceride levels in

Table 2. Comparison of triglyceride levels of inpatients in the three antipsychotic groups

		Olanzapine (n = 864)	Risperidone (n = 1155)	Aripiprazole (n = 397)	p value	Post-hoc test (p value)
Triglyceride level	mg/dL	106.5 ± 61.8	97.1 ± 50.4	99.8 ± 58.7	< 0.001	Olanzapine > risperidone (< 0.001)

Data are shown as mean ± standard deviation of number of the subjects.
Analysis of covariance among the three antipsychotics was performed for triglyceride levels, with age, sex, body mass index and CP-equivalent dosage of current AAP as confounding variables.
Post-hoc analyses were performed using the Bonferroni method.

the outpatients were not significantly different among the groups (Supplemental table).

DISCUSSION

Our study showed that the schizophrenic inpatients had significant differences in triglyceride levels based on the type of antipsychotic treatment. However, the outpatients showed no differences in triglyceride levels.

Regarding the effects of antipsychotic treatment on triglyceride levels, a previous sequence symmetry analysis using data from health insurance claims reported that olanzapine was significantly associated with an increased risk of hyperlipidaemia (adjusted sequence ratio, 1.56; 95% confidence interval, 1.25-1.95) [13]. A case-control analysis was performed on patients with schizophrenia using pharmacy and claims data [14]. That study reported that patients with schizophrenia who were treated with clozapine, olanzapine, or risperidone, but not aripiprazole, showed an increased incidence of hyperlipidaemia compared with patients who were not treated with an antipsychotic agent. In a randomised study of 112 patients with first-episode schizophrenia, fasting triglyceride levels were significantly increased in patients who were treated with clozapine or olanzapine [9]. Olanzapine was also associated with increased triglycerides levels in the CATIE study [8]. Consistent with these studies, we found that triglyceride levels in hospitalised, olanzapine-treated patients were higher than those in patients who were treated with risperidone. However, we found no differences in triglyceride levels between olanzapine and aripiprazole in inpatients. There was possibility that aripiprazole may have been prescribed for patients who need to be aware of metabolic problems in general clinical settings. The reason why the no differences between olanzapine and aripiprazole on triglyceride levels might be that this study was an observational study and antipsychotics are not randomly assigned for study participants. we also found that the outpatients did not show any differences in triglyceride levels among the three antipsychotic groups.

BMI and triglyceride levels are positively correlated in the general population. Li et al. [15] reported that the prevalence of obesity was approximately two times higher in female patients with chronic schizophrenia compared with male patients. Their study used the stepwise multiple regression to determine which factors contributed to obesity in male and female patients. They found that type 2 diabetes mellitus and triglyceride levels were significantly associated with obesity in female patients but only triglyceride levels were associated with obesity in male patients. Lipid metabolism is thought to be regulated by sex hormones. Indeed, plasma triglyceride levels during fasting and fed conditions are lower in premenopausal women than in age-matched men in the general population [16]. The effects of menstruation on triglyceride levels were not evaluated in this study. Several studies have investigated the relationship between sex and triglyceride levels in schizophrenia. In patients with first-episode schizophrenia, triglyceride levels were higher in men compared with women who were being treated with clozapine or olanzapine [17]. Similarly, higher triglyceride levels were observed in male patients with first-episode schizophrenia compared with female patients [18]. In our study, a difference in triglyceride levels between antipsychotics was shown by analysis of variance with adjustment of factors such as sex and BMI. However, because the association between sex hormones and triglyceride levels was not examined in this study, further investigation is required.

A previous meta-analysis reported that drug-naïve patients with schizophrenia showed higher triglyceride levels than control subjects [6]. However, another study reported that antipsychotic-treated patients had significantly higher triglyceride levels compared with drug-naïve, first-episode patients

and normal subjects [7]. A further study reported that triglyceride levels did not differ between drug-naïve patients, drug-free patients, siblings, or controls [19]. The current study only included subjects who were treated with antipsychotics. Therefore, we did not investigate the direct effects of schizophrenia on triglyceride levels. Future studies should include control subjects within the different treatment environments to provide a better understanding of the effects of antipsychotic treatment on triglyceride levels.

In the current study, triglyceride levels in the outpatients were higher than what were observed in the inpatients, though there were no differences due to the choice of antipsychotics in the outpatients (Table 1, Supplemental table). The system for psychiatric treatment in Japan is different from that of other countries because Japan has more psychiatric hospitals than any other OECD country [20]. Indeed, the current study included more inpatients than outpatients. The average length of stay in a psychiatric bed in Japan is long [21], which is thought to be longer than the length of stay in other countries. Notably, a previous study by our group reported that differences in high-density lipoprotein cholesterol could be detected in obese schizophrenic inpatients but not in obese outpatients [22].

Concomitant drugs for antidepressants, mood stabilizers and benzodiazepines did not differ in distribution in this study. Regarding the combination of antipsychotics with mood stabilizers, Meltzer HY et al. reported triglyceride levels of the augmentation with valproic acid. Significantly higher triglyceride levels were observed with olanzapine plus valproic acid compared with olanzapine without valproic acid. Risperidone plus valproic acid and risperidone without valproic acid groups did not differ significantly with respect to triglyceride levels. The olanzapine plus valproic acid group had significantly higher triglyceride values than the risperidone plus valproic acid group [23]. We conducted additional analysis on triglyceride levels between antipsychotics without concomitant of mood stabilizers, benzodiazepines and antidepressants. Results of significant difference of triglyceride among the three antipsychotic groups in inpatients, post-hoc analysis of triglyceride levels in inpatients among the groups and no significant difference among the group in outpatients was not changed (additional analysis data was not shown).

In the inpatient setting, diet is more strictly controlled and patients are more likely to adhere to recommended medical treatment. Additionally, many hospitals prohibit smoking. In contrast, diet and exercise are irregular and patients are less likely to adhere to recommended medical treatment in the outpatient setting. In the current study, we did not assess factors, such as smoking, diet and exercise, which are known to affect plasma triglycerides levels. However, differences in treatment environments could reasonably be assumed to affect these factors, and consequently, triglyceride levels. Indeed, no differences were observed in terms of the choice of antipsychotics in the outpatients in this study. This could be ascribed to the masking effect of the treatment environment in outpatient settings.

The present study has several limitations. First, antipsychotic treatments were not administered randomly; hence, a bias in prescription may have occurred. Second, this study was a post-hoc analysis of a larger dataset and had a post-hoc design. Therefore, there was a possibility of type I error. Our findings should be confirmed in other well-designed clinical studies before firm conclusions can be drawn. Third, this study did not include a comparison with unmedicated patients with schizophrenia or healthy controls. Fourth, we did not evaluate the effect of smoking, duration of medication and other medical conditions that have been shown to affect triglyceride levels. Fifth, we did not assess psychiatric symptoms or severity using the Brief Psychiatric Rating Scale, Positive and Negative Symptom Scale or Clinical Global Impressions in this study. Psychiatric symptoms might be related to body weight, physical activity, or antipsychotic drugs. Finally, the causal relationship between antipsychotics and triglyceride levels could not be indicated as this study was a cross-sectional observational study. Although there might be a relationship between antipsychotics and triglyceride levels from other prospective studies, it is meaningful to detect significant differences in large samples, though the observed effect is small in this study.

CONCLUSION

In conclusion, this study shows that triglyceride levels differ based on antipsychotic treatment in the inpatient, but not outpatient. However, because this study is an observational data derived from a nationwide study, further study was needed such as a

randomised control trial on antipsychotics, specifically designed to evaluate long-term metabolic effects.

Funding

This work was partially supported by Eisai Co. Ltd., Yoshitomi Pharmaceutical Industries, Dainippon Sumitomo Pharma Co. Ltd., Astellas Pharma Inc., Meiji Seika Pharma Co. Ltd., Eli Lilly Japan K.K., Otsuka Pharmaceutical Co. Ltd., GlaxoSmithKline K.K., Janssen Pharmaceutical K.K., MSD K.K., Shionogi & Co. Ltd., Asahi Kasei Pharma Corp., Novartis Pharma Co. Ltd., Takeda Pharmaceutical Co. Ltd., Ono Pharmaceutical Co. Ltd., and Tsumura & Co. The funders had no role in the study design, data collection and analysis, decision to publish or preparation of the manuscript.

Competing Interests

Toshiyuki Someya has received research support or honoraria from Asahi Kasei Pharma Corp., Astellas Pharma Inc., Daiichi Sankyo Co. Ltd., Dainippon Sumitomo Pharma Co. Ltd., Eisai Co. Ltd., Eli Lilly Japan K.K., GlaxoSmithKline K.K., Janssen Pharmaceutical K.K., Meiji Seika Pharma Co. Ltd., Mitsubishi Tanabe Pharma Co. Ltd., Mochida Pharmaceutical Co. Ltd., MSD K.K., Otsuka Pharmaceutical Co. Ltd., Pfizer Japan Inc., Shionogi & Co. Ltd., Tsumura & Co., and Yoshitomi Pharmaceutical Industries. Norio Yasui-Furukori has received research support or honoraria from Dainippon Sumitomo Pharma Co. Ltd., Mochida Pharmaceutical Co. Ltd., MSD K.K., Otsuka Pharmaceutical Co. Ltd. Shin Ono has received grant or research support from the Hospitals Bureau Niigata Prefecture Government and a Grant-in-Aid for Scientific Research (C): KAKENHI, the Grant-in-Aid for Scientific Research of the Ministry of Education, Culture, Sports, Science and Technology (MEXT) of Japan. There are no patents, products in development or marketed products to declare. The other authors declare no potential conflicts of interest.

ACKNOWLEDGEMENT

We are grateful to the study participants and the facilities of the Japan Psychiatric Hospitals Association that cooperated with this investigation. The authors would like to thank Enago (www.enago.jp) for the English language review.

REFERENCES

[1] Harris, E.C. & Barraclough, B. Excess mortality of mental disorder. British Journal of Psychiatry 1998; 173: 11-53.

[2] McEvoy, J. P., Meyer, J. M., Goff, D. C., et al. Prevalence of the metabolic syndrome in patients with schizophrenia: baseline results from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Schizophrenia Trial and comparison with national estimates from NHANES III. Schizophrenia Research 2005; 80: 19-32.

[3] Hokanson, J.E., & Austin, M.A. Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies. Journal of Cardiovascular Risk 1996; 3: 213-219.

[4] Asia Pacific Cohort Studies Collaboration. Serum triglycerides as a risk factor for cardiovascular diseases in the Asia-Pacific region. Circulation 2004; 110; 2678-2686.

[5] De Hert, M., Schreurs, V., Vancampfort, D., et al. Metabolic syndrome in people with schizophrenia: a review. World Psychiatry 2009; 8: 15-22.

[6] Misiak, B., Stańzykiewicz, B., Łaczmański, Ł.,et al. Lipid profile disturbances in antipsychotic-naive patients with first-episode non-affective psychosis: a systematic review and meta-analysis. Schizophria Research 2017; 190: 18-27.

[7] Zhang, B., Deng, L., Wu, H., et al. Relationship between long-term use of a typical antipsychotic medication by Chinese schizophrenia patients and the bone turnover markers serum osteocalcin and β-CrossLaps. Schizophria Research 2016; 176: 259-263.

[8] Lieberman, J. A., Stroup, T. S., McEvoy, J. P., et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. New England Journal of Medicine 2005; 353: 1209-1223.

[9] Wu, R. R., Zhao, J. P., Liu, Z. N., et al. Effects of typical and atypical antipsychotics on glucose-insulin homeostasis and lipid metabolism in first-episode schizophrenia. Psychopharmacology (Berl) 2006; 186: 572-578.

[10] Sugai, T., Suzuki, Y., Yamazaki, M., et al. Difference in prevalence of metabolic syndrome between Japanese outpatients and inpatients with schizophrenia: a nationwide survey.

Schizophria Research 2016; 171: 68-73.
[11] World Health Organization. (2004) International statistical classification of diseases and related health problems (10th revision, 2nd ed.). Geneva: World Health Organization.
[12] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4 th edn. 1994; Washington, DC: APA.
[13] Takeuchi, Y., Kajiyama, K., Ishiguro, C., et al. Atypical antipsychotics and the risk of hyperlipidaemia: a sequence symmetry analysis. Drug Safety 2015; 38: 641-650.
[14] Olfson, M., Marcus, S. C., Corey-Lisle, P., et al. Hyperlipidemia following treatment with antipsychotic medications. American Journal Psychiatry 2016; 163: 1821-1825.
[15] Li, Q., Chen, D., Liu, T., et al. Sex differences in body mass index and obesity in Chinese patients with chronic schizophrenia. Journal of Clinical Psychopharmacology 2016; 36: 643-648.
[16] Wang, X., Magkos, F. & Mittendorfer, B. Sex differences in lipid and lipoprotein metabolism: it's not just about sex hormones. Journal of Clinical Endocrinology and Metabolism 2011; 96: 885-893.
[17] Wu, R. R., Zhao, J. P., Zhai, J. G., et al. Sex difference in effects of typical and atypical antipsychotics on glucose-insulin homeostasis and lipid metabolism in first-episode schizophrenia. Journal of Clinical Psychopharmacology 2007; 27: 374-379.
[18] Chen, S., Broqueres-You, D., Yang, G., et al. Male sex may be associated with higher metabolic risk in first-episode schizophrenia patients: A preliminary study. Asian Journal of Psychiatry 2016; 21: 25-30.
[19] Darcin, A. E., Cavus, S. Y., Dilbaz, N., et al. Metabolic syndrome in drug-naive and drug-free patients with schizophrenia and in their siblings. Schizophria Research 2015; 166: 201-206.
[20] Organisation for Economic Co-operation and Development (2017) OECD health statistics.
[21] Ministry of Health, Labour and Welfare. Summary of Static/Dynamic Surveys of Medical Institutions and Hospital Report 2010 [Ministry of Health, Labour and Welfare Web site]. Retrieved 12 January 2019, from https://www.mhlw.go.jp/english/database/db-hss/mih_report_2010.html.
[22] Ono, S., Sugai, T., Suzuki, Y., et al. High-density lipoprotein-cholesterol and antipsychotic medication in overweight inpatients with schizophrenia: post-hoc analysis of a Japanese nationwide survey. BMC Psychiatry 2018; 18: 180.
[23] Meltzer, HY., Bonaccorso, S., Bobo, WV., et al. A 12-month randomized, open-label study of the metabolic effects of olanzapine and risperidone in psychotic patients: influence of valproic acid augmentation. J Clin Psychiatry 2011 ;72(12): 1602-10.

Supplemental Table. Comparison of triglyceride levels of outpatients in the three antipsychotic groups

		Olanzapine (n = 378)	Risperidone (n = 528)	Aripiprazole (n = 253)	p value	Post-hoc test (p value)
Triglyceride level	mg/dL	141.0 ± 96.7	138.3 ± 96.5	146.2 ± 109.6	0.183	

Data are shown as mean ± standard deviation of the number of subjects.
Analysis of covariance among the three antipsychotics was performed for triglyceride levels, with age, sex, body mass index and CP-equivalent dosage of current AAP as confounding variables.