African Journal of Medical Case Reports Vol. 1 (1), pp. 004-009, December, 2013. Available online at www.internationalscholarsjournals.org © International Scholars Journals

Full Length Research Paper

Metabolic syndrome in Japanese patients with mental retardation

Shunya Hoshino[1], Kenji Yamamoto[1]*, Shingo Miyaji[1], Yoshiro Sakai[1,2], Hiroaki Yamamoto[1], Masami Inui Yukawa[1] and Hitoshi Miyaoka[1]

[1]Department of Psychiatry, Kitasato University School of Medicine Kitasato 1-15-1, minami-ku, Sagamihara, Kanagawa 252-0374, Japan.
[2]Hatano Kousei Hospital, Minamiyana 2-12-1, Hatano, Kanagawa 257-0003, Japan.

Accepted 16 May, 2013

To conduct a study on metabolic syndrome (MetS) observed in patients with mental retardation (MR) to clarify the factors associated with its prevalence and incidence. During the period from October 2006 to March 2007, for 302 cases of patients with MR who were admitted to or visited 2 support facilities for people with intellectual disabilities in Japan, we reviewed the patients' admission records and nursing records regarding their clinical data and profiles. The prevalence of MetS in Japanese patients with MR was 29 cases among 203 males (14.3%) and 12 cases among 99 females (12.1%). There was a significant association between the distribution of the severity of MR and MetS, and regarding treatment drugs, there was a significantly large number of patients who were taking antidepressants or atypical antipsychotics in the MetS group. MetS is prevalent in patients with MR. A significant correlation was observed between MetS and the severity of MR and treatment drugs, and this seems to be an important factor when considering MetS in patients with MR.

Key words: Mental retardation, metabolic syndrome, antipsychotics, antidepressants.

INTRODUCTION

Metabolic syndrome (hereinafter abbreviated as MetS) has been drawing attention recently, and it is a clinical condition in which visceral lipid accumulates due to overeating and lack of exercise which leads to insulin resistance, and it is accompanied by several lifestyle diseases such as hypertension, hyperlipidemia, and diabetes (Committee to Evaluate Diagnostic Standards for Metabolic Syndrome., 2005). Furthermore, MetS is considered to be a risk factor of coronary artery diseases, and there have already been some reports on the relationship between MetS and coronary artery diseases in Japan and in other countries (Lakka et al., 2002; Takeuchi et al., 2005). On the other hand, it has been reported that people with psychiatric diseases such as schizophrenia have a shorter average life expectancy than those without psychiatric diseases and that coronary artery diseases are a significant cause of death in such people, which is believed to be due to elevated glucose and lipid levels induced by side effects of antipsychotics (Newcomer, 2007). In particular, atypical antipsychotics cause an increase in appetite due to their histamine H1-receptor antagonistic action and serotonin 5-HT2A, 5-HT2C-receptor antagonistic action, leading to increases in body weight and insulin resistance. It is believed that this causes patients to present abnormal glucose tolerance and abnormal lipid metabolism (Wirshing et al., 1999).

People with mental retardation are highly likely to suffer from psychiatric disorders and behavioral disorders, and thus take psychotropic agents (Branford, 1994; Corbett, 1979; Linaker, 1990). In addition, they may develop eating disorders due to an inability to control their impulses, and it is expected that their risk of MetS is also high, as is the case in patients with psychiatric disorders. To date, as an investigation of the relationship between MetS and mental retardation, Mckee and colleagues conducted a study focusing on the relationship between

*Corresponding author. E-mail: keny@kitasato-u.ac.jp. Tel: +81-42-778-8111. Fax: +81-42-778-9579.

MetS and switching of atypical antipsychotics (Mckee et al., 2005); however, other than this study, there have been few reports on the relationship between people with mental retardation and MetS, and at present, the relationship between the prevalence of MetS and administered drugs has not yet been clarified. We conducted a study to clarify the factors associated with the prevalence and incidence of MetS that is observed in people with mental retardation in support facilities for people with intellectual disabilities, and our report thereof is as follows.

SUBJECTS

The subjects included 302 patients that were admitted to or visited 2 support facilities for people with intellectual disabilities in Kanagawa Prefecture (where is located next to Tokyo, and the second-most populated prefecture after Tokyo) between October 2006 and March 2007, and were diagnosed with mental retardation based on the International Classification of Disease, 10th Edition (hereinafter referred to as ICD-10). The capacity of the facilities was respectively 150 and 102 persons for long-term admission, and 10 persons for short-term admission at both facilities. Although one of the facilities also has an outpatient center for 58 persons, the other does not have an outpatient center. The 302 subjects of this study include 255 long-term and short-term admission subjects who resided at the 2 facilities during the study period and 47 outpatient subjects.

METHODS

Patient information

The admission records and nursing records were reviewed regarding the age, gender, medications, and coexisting physical diseases, etc.

Psychiatric diagnosis and evaluation of intellectual function

Two psychiatrists with over 5 years of experience each individually made a diagnosis of psychiatric disorder accompanied by mental retardation based on the ICD-10. In addition, an experienced psychologist conducted the Tanaka-Binet intellectual test at the time of admission to the support facility. According to the intelligence quotient (hereinafter referred to as IQ) measured thereby and the subordinate classifications of the ICD-10, the intellectual function of each subject was classified into one of 4 groups including mild (IQ 50-69), moderate (IQ 35-49), severe (IQ 20-34), and profound (IQ less than 20).

Diagnosis of MetS

There are several diagnostic criteria of MetS, and among them, the major diagnostic criteria are those of the National Cholesterol Education Program's Adult Treatment Panel III (hereinafter abbreviated as NCEP-ATP III) (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol In Adults, 2001) and the International Diabetes Federation (hereinafter abbreviated as IDP) (Alberti et al., 2005). However, since these are numerical values wherein the waist circumference diameter conforms to a BMI of 30, which is the obesity standard in the US, the diagnostic criteria of the Japanese Society of Internal Medicine have been employed in many cases in Japan. Table 1 shows the major diagnostic criteria for MetS. In this study, since the subjects were Japanese, diagnoses were made by employing the diagnostic criteria of the 8 conferences associated with the Society of Internal Medicine, which have been recommended by the Japanese Society of Internal Medicine (2005) (Committee to Evaluate Diagnostic Standards for Metabolic Syndrome, 2005).

Regarding the items of blood pressure and abdominal circumference that are required for diagnosing MetS, we used the results of regular health checkups conducted during the study period, and for the laboratory values such as Triglyceride (hereinafter referred to as TG), High Density Lipoprotein - Cholesterol (hereinafter referred to as HDL-Chol), fasting glucose level, etc., we used values measured within ±6 months from the time when the abdominal circumference was measured as the diagnostic criteria.

Statistical analysis

Statistically, based on the study results, the subjects were classified into a MetS group and a non-MetS group and comparisons were made between the 2 groups. The Pearson $\chi 2$ test was used for comparing the nominal scales, while the Student t test was used for comparing the serial scales. In all of the tests, a less than 5% level in the two-sided test was determined to be significant. Furthermore, in order to eliminate the influence of confounding factors when discriminating between the presence or absence of MetS, we considered items in which a statistically significant difference was observed in the comparison between the 2 groups as explanatory variables and considered the presence or absence of MetS as an objective variable, and conducted logistic regression analysis through the step-down procedure. Under loading conditions of $p<0.05$, items with large p values were eliminated sequentially to obtain the optimal odds ratio and the 95% confidence interval. We used the SPSS statistical program (version 13.0 for Windows, SPSS Inc., Chicago, Ill.) for all of the statistical analyses.

The present study was performed with the consent of each facility, and personal information was managed based on the Personal Information Protection Law, which has been enforced in our country to protect individual's rights and interests in considering the usefulness of individual information since 2005. Regarding the ethical aspects, personal data was all coded at the time of input to be used for analysis such that the individual names and the person could not be identified.

RESULTS

Table 2 shows the case profile. Among 302 cases with mental retardation, 203 cases (67.2%) were males, and 99 cases (32.8%) were females. The prevalence of MetS was 41 (13.6%) out of 302 cases, including 29 males and 12 females. The gender, age, degree of mental retardation, psychiatric diagnosis, and treatment mode of the MetS group and the non-MetS group were compared. Therein, a significant difference was observed in the degree of mental retardation; however, no obvious significant difference was observed in the other items.

Table 3 shows the results of the comparison between

Table 1. MetS diagnostic criteria.

	International criteria				
	Diameter of waist circumference (cm)	***HDL – cholesterol (mg/dl)***	***Triglyceride (mg/dl)***	***Blood pressure (mmHg)***	***Glucose (mg/dl)***
NCEP-ATPII† (2001)	Male: > 102 Female: >88	Male: <40 Female: <50	>150	>130/85	>110
IDF‡ (2005)	Male: >85 Female: >90	Male: < 40 Female: < 50	>150	>130/85	>100
	Domestic criteria				
	Diameter of waist circumference (cm)	***Triglyceride and HDL-cholesterol (mg/dl)***	***Blood pressure (mmHg)***	***Glucose and hemoglobin A1C***	
JSIM§ (2005)	Male: >85 Female: >90 (equivalent to the visceral fat area >100 cm^2)	Triglyceride > 150 and/or HDL-cholesterol <40	Systolic: >1 30 and/or Diastolic: > 85	Fasting glucose level >110 mg/dl	
MHLW ¶(2006)	Male: >85 Female: >90	Triglyceride >150 and/or HDL-cholesterol <40	Systolic: >130 and/or Diastolic: >85	Hemoglobin A1C >5.5%	

† NCEP-ATPIII (National Cholesterol Education Program Adult Treatment Panel III (ATPIII): Those who satisfy at least 3 items described in the columns are diagnosed with MetS. ‡IDF (International Diabetes Federation): The abdominal circumference is set according to race, and those taking medication are also included. Including the abdominal circumference as a required item, those who satisfy at least 2 out of 4 items described in the right columns are diagnosed with MetS. §JSIM (Japanese Society of Internal Medicine): In addition to the descriptions in the Diameter of waist circumference, when at least 2 items in the right columns are satisfied. Even if the test results do not satisfy the criteria on the left, those receiving medication for hyperlipidemia, hypertension, and diabetes are considered to be included in each of the items. ¶MHLW (Ministry of Health, Labor and Welfare): In addition to the descriptions in the diameter of waist circumference, when 1 of the items in the right columns is satisfied, the case is determined as suspicious, and when at least 2 items are satisfied, the case is determined as highly suspicious. Even if the test results do not satisfy the criteria on the left, those receiving medication for hyperlipidemia, hypertension, and diabetes are considered to be included in each of the items.

the MetS group and the non-MetS group for each item of the laboratory values and physical measurements that are required for the diagnosis of MetS, including blood pressure, diameter of waist circumference, triglyceride, HDL-Chol, and glucose level. Although some laboratory results were missing in some cases, this did not influence the diagnosis of MetS. Among the results, a significant difference was observed in the items of blood pressure, diameter of waist circumference, and triglyceride.

Table 4 shows the results of the comparison between the MetS group and the non-MetS group regarding the use group and the non-use group of treatment drugs including antidepressants, antiepileptic drugs, and antipsychotics. The antidepressants taken by the MetS group included 4 cases of fluvoxamine and 2 cases of milnacipran, while the non-MetS group included 6 cases of trazodone and 3 cases of fluvoxamine. The atypical antipsychotics taken by the MetS group included 7 cases of risperidone and 2 cases of quetiapine, while the non-MetS group included 19 cases of risperidone and each 3 cases of quetiapine and olanzapine. A significant difference was observed between the 2 groups with respect to the antidepressants and atypical antipsychotics.

Table 5 shows the results of logistic regression analysis employing the presence or absence of MetS as an explanatory variable regarding the items in which a significant difference was observed in the comparison between the MetS group and the non-MetS group. The items in which a significant difference was observed included the degree of mental retardation, the use or non-use of antidepressant medication, and the use or non-use of atypical antipsychotic medication, and as a result of performing a logistic regression analysis, a significant difference was observed in all 3 items. Regarding the degree of mental retardation, the group corresponding to “mild mental retardation” and “moderate mental retardation” in the ICD-10 was compared with the group corresponding to “severe mental retardation” and “profound mental retardation”.

DISCUSSION

The results of this study revealed the following: (1) The prevalence of MetS in Japanese people with mental retardation was 29 case among 203 males (14.3%) and 12 cases among 99 females (12.1%); (2) It was suggested that there was a significant relationship

Table 2. Profile of each group.

Group		MetS (n = 41)	non-MetS (n = 261)	p value
Gender	Male	29	174	0.61
	Female	12	87	
Age		38.4	38.5	0.96
	S.D.	13.8	13.1	
	Lowest age-highest age	19-68	18-69	
Mental retardation	Mild (IQ 50~69)	9 (22.0)	31(11.9)	0.01
	Moderate (IQ 35~49)	14(34.2)	50(19.2)	
	Severe (IQ 20~34)	9 (22.0)	57(21.9)	
	Profound (less than IQ 20)	9 (22.0)	122 (46.9)	
ICD-10 F code†	F60 (Personality disorder)	1(2.4)	5(1.9)	0.08
	F20 (Schizophrenia)	3(7.3)	19 (7.3)	
	F32 (Depression)	1(2.4)	0 (0)	
	F84 (Pervasive developmental disorder)	7 (17.1)	19 (7.3)	
	F90 (Hyperactivity disorder)	0 (0)	2(0.8)	
	F91 (Behavioral disorder)	1(2.4)	5(1.9)	
	N/A	28(68.3)	211 (80.8)	
ICD-10 G code‡	G40	11 (27.5)	101 (38.7)	0.17
	N/A	29(72.5)	160 (61.3)	
Outpatient/Inpatient	Outpatient	10	37	0.09
	Inpatient	31	224	

( ) refers to %, †icd-10 f code: the international statistical classification of diseases and related health problems 10th revision(ICD-10) Chapter V: mental and behavioural disorders, ‡ICD-10 G code: ICD-10 Chapter VI: diseases of the nervous system.

Table 3. Comparison between the laboratory values and the physical measurements.

Variable	n		MetS (n = 41)	non-MetS (n = 261)	p value
Blood pressure (mmHg)	295	Systolic	126.4	117.4	0.002
		S.D.	16.4	17.0	
		Diastolic	80.9	76.4	0.11
		S.D.	12.2.	16.8	
Diameter of waist circumference (cm)	285		88.8	76.9	<0.001
		S.D.	10.0	8.0	
Triglyceride (mg/dl)	285		140.8	91.6	<0.001
		S.D.	97.3	42.5	
HDL-Cholesterol(mg/dl)	298		61.6	63.8	0.45
		S.D.	18.4	16.6	
Glucose (mg/dl)	298		104.9	94.2	0.16
		S.D.	20.3	47.5	

between distribution of the severity of mental retardation and MetS; (3) Compared to the non-MetS group, the MetS group included a significantly larger number of patients who took atypical antipsychotics and

Table 4. Comparison among treatment drugs.

Treatment drug	n		MetS (n = 41)	non-MetS (n = 261)	p value
Antidepressants	302	User	7 (17.1)	14(5.4)	0.006
		Non-user	34 (82.9)	247(94.6)	
Antiepileptics	282	User	27 (73.0)	138(56.3)	0.06
		Non-user	10 (27.0)	107(43.7)	
Typical antipsychotics	282	User	22 (59.5)	108(44.1)	0.08
		Non-user	15 (40.5)	137(55.9)	
Atypical antipsychotics	301	User	11 (26.8)	28 (10.8)	0.004
		Non-user	30 (73.2)	232(89.2)	
Chlorpromazine equivalent dose	128 (MetS = 23, non-MetS = 105)	mg	340.5	383.4	0.60
		S.D.	290.0	362.2	

( ) refers to %.

Table 5. Logistic regression analysis in the MetS group and the non-MetS group.

Variable	Odds ratio	95%CI	p value
Degree of mental retardation†	2.51	1.26-5.04	0.009
Antidepressant (taken)	3.06	1.05-8.26	0.03
Atypical antipsychotic (taken)	2.39	1.02-5.35	0.04

†Comparison between the mild/moderate group and the severe/profound group.

antidepressants.

Prevalence of MetS

There have been various reports on the prevalence of MetS to date, and it is clear that the results are different depending on the race and age (Ford et al., 2002; Gu et al., 2005; Shiwaku et al., 2005). In Japan, the Ministry of Health, Labor, and Welfare conducts a large scale survey every year, called the National Health and Nutrition Examination Survey (Ministry of Health, Labour, and Welfare, 2008-2009), of approximately 7000 to 8000 individuals (the minimum - maximum number of individuals who could be surveyed regarding their physical condition was 7278-8060 individuals for the past 5 years) from approximately 3500 households (the minimum - maximum number of households was 3421-3838 households for the past 5 years) in 300-unit divisions extracted in a stratified random manner from the survey area of the National Livelihood Survey. As a result, it has been reported that for the last 5 years, individuals 20 years and older for which MetS is strongly suspected make up 21.2 to 26.9% of male and 8.9 to 10.6% of female. In this study of patients with mental retardation, individuals 18 years and older for which MetS is strongly suspected comprised 29 cases among 203 males (14.3%) and 12 cases among 99 females (12.1%).

Relationship between the severity of mental retardation and MetS

Upon classifying the severity of mental retardation into the group of mild/moderate mental retardation and the group of severe/profound mental retardation according to the ICD-10, it was found that the prevalence of MetS in the mild/moderate group was 23 out of 104 cases (22.1%), the prevalence of MetS in the severe/profound group was 18 out of 197 cases (9.1%), and a significant difference was observed between the 2 groups. There have been no reports thus far on the relationship between the degree of mental retardation and the prevalence of MetS, and therefore, our report is the first to address this phenomenon.

The management system in the support facilities for people with intellectual disabilities may be one reason for the difference in the prevalence of MetS depending on the degree of mental retardation. In the facilities, when the severity of mental retardation is milder, the

management is more open, leaving the choice of snacks etc. up to the individual to some degree. However, due to the characteristics of people with severe/profound mental retardation, the management system is much less open, and their diets and snacks are all under management. We believe that this difference in the management system led to a significant difference in the prevalence of MetS between the mild/moderate group and the severe/profound group.

Relationship between the administration of atypical antipsychotics/antidepressants and MetS

There have been many reports on the relationship between antipsychotics and MetS. DeHert et al. (2008) reported that, among patients showing initial onset of schizophrenia, upon prospective comparison between the group of those treated with typical antipsychotics only and the group of those treated with atypical antipsychotics only, it was found that the incidence of MetS was approximately 3 times in the latter group than in the former group. In addition, there are some reports that the use of atypical antipsychotics increases the risk of MetS in schizophrenic patients (Newcomer, 2007; DeHert et al., 2008; Rege, 2008; Padmavati, 2010). The results of our study showed that a significantly large number of mentally handicapped patients with MetS were treated with atypical antipsychotics, although the prevalence of MetS was not high compared to general population. Accordingly, these results suggest that the treatment with atypical antipsychotics could be an important risk factor for MetS in the patients with mental retardation.

In addition, the results of this study showed that a significantly large number of patients in the MetS group were taking antidepressants. However, because there were few patients taking antidepressants and there are various types of antidepressants, it cannot be categorically concluded that antidepressants have an influence on MetS at this stage. Serotonin agonists such as fenfluramine and difenfluramine have been used in the past in the treatment of obesity (Mathus-Vliegen, 1992); however, the serotonin/noradrenalin reuptake inhibitor sibutramine has been drawing attention recently as a treatment drug for obesity in the future (Bray et al., 1996). However, since antidepressants may increase body weight and appetite as side effects, further study on the relationship between antidepressants and obesity or appetite will be necessary in the future.

Since the present study has some limitations, the following cautions are necessary for interpreting the results. Firstly, the subjects were mostly those who stayed in the facilities and lived their lives under considerable restrictions. In actual home life, there are less dietary restrictions, and therefore, the prevalence of MetS in patients with mental retardation who stay at home without visiting a care facility may be higher than the results of this study. The results of this study include 47 home-care patients; however, no significant difference was observed in any of the items between the home-care patients and the patients in the facilities (data not shown). However, in order to further strengthen the results of this study, it will be necessary to study an even larger number of cases in the future. Secondly, there is a problem of age. It is known that the prevalence of MetS differs by age. The age distribution of our patients did not match to the general population. Thirdly, a detailed study was not conducted regarding the duration of psychotropic therapy and the type of psychotropic agents. The present study provides cross-sectional results for a certain period and analysis based on the medication at the time of survey, and thus it is possible that a bias such as differences in the duration of medication, type of drug, dose, etc. had an influence on the results. In addition, the drugs were only classified broadly into antipsychotics and antidepressants, and thus the influence of the individual drug agent was not sufficiently examined. The fourthly, there is a methodological problem regarding a time lapse between the physical measurements and a blood test when diagnosis of MetS. Although the physical measurements and a blood test were done simultaneously in most cases, a time lapse (the maximum: six months) was recognized in some cases. However, the physical measurements have been done every month, and there was no case that showed a rapid change of physical measurements which could influence our results.

ACKNOWLEDGEMENTS

The authors report no financial or other relationship relevant to the subject of this article.

REFERENCES

Alberti KG, Zimmet P, Shaw J (2005). IDF Epidemiology Task Force. Consensus Group. The metabolic syndrome new worldwide definition. Lancet., 366: 1059-1062.

Bray GA, Ryan DH, Gordon D, Heidingsfelder S, Cerise F, Wilson K (1996). A double-blind randomized placebo-controlled trial of sibutramine. Obes. Res., 4: 263-270.

Branford D (1994). A study of the prescribing for people with learning disabilities living in the community and in National Health Service care. J. Intellect. Disabil. Res., 38: 577-586.

Committee to Evaluate Diagnostic Standards for Metabolic Syndrome (2005). Definition and the diagnostic standard for metabolic syndrome. J. Jpn. Soc. Int. Med., 94: 794-809.

Corbett JA (1979). Psychiatric morbidity and mental retardation. In: FE James and RP Snaith (Ed.), Psychiatric illness and mental handicap, Gaskell, London, pp. 11-25.

De Hert M, Schreurs V, Sweers K, Van Eyck D, Hanssens L, Sinko S, Wampers M, Scheen A, Peuskens J, Van Winkel R (2008). Typical and atypical antipsychotics differentially affect long-term incidence rates of the metabolic syndrome in first-episode patients with schizophrenia: A retrospective chart review. Schizo. Res., 101: 295-303.

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol In Adults (2001). Executive Summary of The Third Report of The National Cholesterol Education Program(NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol In Adults(Adult Treatment Panel III). JAMA, 285: 2486-2490.

Ford ES, Giles WH, Dietz WH (2002). Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA, 287: 356-359.

Gu D, Reynolds K, Wu X, Chen J, Duan X, Reynolds RF, Whelton PK, He J (2005). Inter ASIA Collaborative Group. Prevalence of the metabolic syndrome and overweight among adults in China. Lancet, 365: 1398-1405.

Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, Salonen JT (2002). The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. JAMA, 288: 2709-2716.

Linaker OM (1990). Frequency and determinants for psychotropic drug use in an institution for the mentally retarded. Br. J. Psychiatry., 156: 525–530.

Mathus-Vliegen EM, van de Voorde K, Kok AM, Res AM (1992). Dexfenfluramine in the treatment of severe obesity: a placebo-controlled investigation of the effects on weight loss, cardiovascular risk factors, food intake and eating behaviour. Am. J. Intern. Med., 232: 119-127.

Mckee JR, Bodfish JW, Mahorney SL, Heeth WL, Ball MP (2005). Metabolic Effects Associated With Atypical Antipsychotic Treatment in the Developmentally Disabled. J. Clin. Psychiatry, 66: 1161-1168.

Ministry of Health, Labour and Welfare (2008-2009). Annual Health, Labour and Welfare Report 2008-2009, Measures for National Health Promotion.Available from [http://www.mhlw.go.jp/english/wp/wp-hw2/],[http://www.mhlw.go.jp/bunya/kenkou/kokumin-kenkou.html].

Newcomer JW (2007). Metabolic Syndrome and Mental Illness. Am. J. Manage. Care, 11: 170-177.

Padmavati R, McCreadie RG, Tirupari S (2010). Low prevalence of obesity and metabolic syndrome in never treated chronic schizophrenia. Schizophr. Res., 121: 199-202.

Rege S (2008). Antipsychotic induced weight gain in schizophrenia: mechanisms and management. Aust NZ J Psychiatry., 42: 369-381.

Shiwaku K, Nogi A, Kitajima K, Anuurad E, Enkhmaa B, Yamasaki M, Kim JM, Kim IS, Lee SK, Oyunsuren T, Yamane Y (2005). Prevalence of the metabolic syndrome using the modified ATP III definitions for workers in Japan, Korea and Mongolia. J. Occup. Health, 47: 126-135.

Takeuchi H, Saitoh S, Takagi S, Ohnishi H, Ohhata J, Isobe T, Shimamoto K (2005). Metabolic syndrome and cardiac disease in Japanese men: applicability of the concept of metabolic syndrome defined by the National Cholesterol Education Program Adult Treatment Panel III to Japanese men-the Tanno and Sobetsu study. Hypertens. Res., 28: 203-208.

Wirshing DA, Wirshing WC, Kysar L, Wirshing WC, Kysar L, Berisford MA, Goldstein D, Pashdag J, Mintz J, Marder SR (1999). Novel antipsychotics: Comparison of weight gain liabilities. J. Clin. Psychiatry, 60: 358-363.