Screening for metabolic syndrome in addiction care; quick, reliable and non invasive

A quantitative study into the effectiveness of waist circumference and blood pressure measurements as predictors of metabolic syndrome among patients being treated with second generation antipsychotics in addiction services

Research

It is well known that patients with schizophrenia have a reduced life expectancy of between 10 -15 years (Newman and Bland 1991). An increased risk of cardiovascular heart disease is the main cause of this excess mortality (Hansen, Jacobsen & Arnesen, 2001). When compared to the general population, patients with schizophrenia or bipolar disorder who are treated with antipsychotic medication, have been found to have a two to three times increased rate of obesity (Tirupati & Chua, 2007). Treatment with second generation antipsychotics (SGA's) has also been linked to an increased risk of weight gain, developing diabetes mellitus type II (Lindenmayer et al, 2003 and Tirupati & Chua, 2007) and an increased risk of developing hyperlipidaemia (Olfson, Marcus, Corey-Lisle, Toumari, Hines & L'Italien, 2006). These metabolic abnormalities are part of a cluster of risk factors that are collectively known as the metabolic syndrome. Metabolic syndrome gives rise to increased cardiovascular morbidity and mortality (Brown, 1997; Cohn, Prud'homme, Streiner, Kameh & Remington, 2004).

Patients with schizophrenia have a fourfold risk of developing metabolic syndrome (Meyer et al, 2005). They are more likely to smoke, they have a poorer diet and they are less physically active (Hert, Schreurs, Vancampfort & Winkel, 2009). Patients with metabolic syndrome have been found to have increased psychotic and depressive symptoms (Dixon et al, 1999) as well as lower compliance with treatment (Weiden et al, 2004). Despite these increased risks, patients with a severe mental illness, compared to the general population, are less likely to access primary health care, and their general health care needs are seldom addressed within psychiatric services (Hert et al, 2009).

Effective screening of patients for metabolic syndrome is impor-

tant in reducing the high morbidity and mortality rate of this patient group. There are currently several diagnostic definitions of metabolic syndrome which include the following metabolic abnormalities: raised blood pressure, abdominal obesity, raised body mass index, raised fasting blood glucose, raised fasting triglycerides and lowered high density lipoprotein. Strakker et al (2005) claimed that 100% of all cases of metabolic syndrome could correctly be identified by screening for abdominal obesity and raised fasting blood glucose levels only. This study also reported that abdominal obesity and raised blood pressure correctly identified 96.2% of all cases which the researchers suggest could be more acceptable in situations where it is difficult to measure fasting blood glucose levels. Tirupati & Chua (2007) reported that a BMI >25kg/m2 was 76.3% accurate in correctly predicting the presence of metabolic syndrome (sensitivity) and 80% accurate in correctly predicting that there was no metabolic syndrome (specificity).

Bouman GGZ is a provider of mental health services and is specialised in addiction care in the Rotterdam region (the Netherlands). The organisation is currently developing a new protocol for the systematic screening of patients who are at risk of developing metabolic syndrome. Within the organisation it is unclear how many patients being treated with SGA's have, or are at risk of, developing metabolic syndrome. The aim of this study is to identify if combined blood pressure and waist circumference measurements are reliable predictors of metabolic syndrome for this patient group.

Method

Research design

A descriptive correlational design was used to examine the sensitivity and specificity of screening techniques used to detect metabolic syndrome.

Study sample

Between January and April 2012 research was carried out of the electronic patient database of Bouman GGZ to identify patients who were being treated with one or more of the following second generation antipsychotics; clozapine, olanzapine, quetiapine, risperidone and aripiprazol. Fifty seven adult patients (18 year and older) were selected for the study.

Research context

Patients were recruited from a wide variety of inpatient and outpatient treatment settings within Bouman GGZ.

Procedures

Data were collected on gender, age, diagnosis, antipsychotic medication, treatment with a combination of antipsychotics (atypical plus atypical or atypical plus classic), and addiction to or misuse of alcohol. In order to gather these data a file review of all participating patients was conducted.

Data regarding waist circumference, body mass index (BMI) and blood pressure were collected of all participating patients. Fasting blood samples were taken and sent to independent laboratories for analysis of blood glucose, HDL and triglycerides levels.

If a patient had both abnormal waist circumference and abnormal blood pressure measurements the researcher then made diagnostic prediction of metabolic syndrome. A second diagnosis of metabolic syndrome was then made using all the collected data according to diagnostic criteria as defined by the Adult Treatment Panel III (National Cholesterol Education Program, 2002) and included:

- Central obesity; waist circumference ≥102 cm in males and >88 cm in females
- Raised fasting plasma glucose ≥5.6 mmol/L or history of diabetes mellitus II
- Raised fasting triglycerides ≥1.7 mmol/L or history of dyslipidaemia
- Lowered high density lipoprotein <1.03 mmol/L males, <1.29 females or history of dyslipidaemia
- Raised blood pressure ≥130 / 85 mm Hg or history of hypertension

Data analysis and methodological quality

The results of the predictive diagnosis and the diagnosis complying with all the criteria of the Adult Treatment Panel III (ATPIII) were analysed using a multiple regression analysis to test the sensitivity (ability to correctly identify a true case of metabolic syndrome) and specificity (ability to correctly identify the absence of metabolic syndrome) of the combination of waist circumference and blood pressure measurements as predictors for metabolic syndrome. Sensitivity, specificity, likelihood ratios (an index demonstrating the relationship between sensitivity and specificity) and positive predictive value (probability that result is correct) were calculated. Receiver Operator Characteristic (ROC) curves were plotted to establish appropriate cut of points for sensitivity and specificity. Bivariate analyses were carried out to assess the relationship between individual variables and metabolic syndrome. A linear regression analysis was carried out to calculate the predictive values of the multiple independent variables on the dependent variable metabolic syndrome. In order to be able to conduct a logistic regression analysis the outcomes of the metabolic screening were converted into dichotomised variables: 0 = No metabolic syndrome, 1 = Metabolic syndrome. The significance level (alpha) was set at .05.

Electronic blood pressure monitors were used and research staff received an update on correct measuring of waist circumference. To enhance internal validity it was decided not to include any data which were not complete and any blood data analysis which was not reported as fasting.

Ethical accountability

The research proposal was presented to and approved by the research and ethics committee of Bouman GGZ. Patients were informed of the research program. No written consent was requested because interventions carried out during the research may be considered as standard good practice in the treatment of patients taking atypical antipsychotic medication. Data were anonymised and Electronic Patient Database (EPD) numbers were used to record and catalogue data. Abnormal test results were reported to case coordinators and prescribing practitioners (e.g. psychiatrists) with advice for further interventions.

Results

Fifty seven patients were identified to take part in the study. Twenty five of them were being treated in community treatment settings and thirty two patients were being treated in an inpatient setting. Sixteen patients (28%) were eventually excluded due to discharge from treatment (N = 3), no show (N = 5), insufficient data (N = 5) and refusal to take part (N = 3). Of the excluded patients 75% were being treated in a community treatment setting. The final study group consisted of forty one patients of which 56.1% were male and 70% were inpatients.

The mean age of the group was 42.7, range 23-56, SD 8.0. Patients with a primary diagnosis of mood disorder made up 39% of the study group, schizophrenia spectrum disorder 34% and 27% other. Thirty two patients (78%) of patients were being treated with a single atypical antipsychotic medication. The most frequently used antipsychotic medication was quetiapine (56%). Olanzapine en risperidone both accounted for 17% and aripiprazol for 10% of the total use of antipsychotics. Twenty two patients (54%) met the criteria for metabolic syndrome (*see table 1*). Metabolic syndrome was not significantly associated with diagnosis, gender, antipsychotic medication or alcohol misuse/addiction. All 9 patients being treated with a combination of antipsychotic medications (atypical + atypical or atypical + typical) tested positive for metabolic syndrome ($r = 0.321$, $p = 0.041$). A significant association was also found between central obesity and metabolic syndrome ($r = 0.431$, $p = 0.005$), one third of all patients with central obesity tested positive for metabolic syndrome.

Table 1
Characteristics of Patients With or Without Metabolic Syndrome

	No metabolic syndrome (N= 19 [46.3%])		**Metabolic syndrome** (N=22 [53.7%])	
	N	%	N	%
Gender				
Male	11	57.9	12	54.5
Female	8	42.1	10	45.5
Primary diagnosis				
Schizophrenia spectrum disorders	9	47.4	5	22.7
Mood disorders	6	31.6	10	45.5
Other	4	21.0	7	31.8
Medication				
Olanzapine	4	21.1	3	13.6
Quetiapine	10	52.6	13	59.1
Risperidone	3	15.8	4	18.2
Aripiprazol	2	10.5	2	9.1
Combination therapy				
Single atypical	17	89.5	15	68.2
Atypical + atypical	2	10.5	2	9.1
Atypical + typical	0	0	5	22.7
Alcohol misuse or addiction				
No alcohol problem	5	26.3	8	42.1
Alcohol misuse	2	10.5	2	10.5
Alcohol addiction	12	63.2	9	47.4

In a linear regression analysis waist circumference in combination with blood pressure as predictors of metabolic syndrome were found to have a high significance as had BMI and blood pressure (*see table 2*). Moreover, when gender was added to the model also a significant association with central obesity was found (r = 0.314 p = 0.046) with 88% of the women in the sample having central obesity compared to 64% of the men.

The sensitivity, specificity, positive predictive value and likelihood ratios are presented in *table 3*. High blood pressure correctly identified 17 out of the 22 cases of metabolic syndrome and has a sensitivity value of 88%. Using central obesity as a measurement had a sensitivity of just 66% but a high positive predictive value meaning that 91% of the positive result will have metabolic syndrome. Combining blood pressure and central obesity as a measuring instrument creates a high sensitivity (93%) but a lower positive predictive value (64%). Combining blood pressure and body mass index resulted in a likelihood ratio of 5.1, a sensitivity of 63%, a specificity of 87% and a positive predictive value of 95%.

Table 2
Analysis of Predictive Value of Screening Instruments for Metabolic Syndrome

	R2	F	P=0.001
Predictive diagnosis: Central obesity, raised systolic/diastolic blood pressure or existing treatment for hypertension	0.395	5.887	0.001
Body mass index, raised systolic/ diastolic blood pressure or existing treatment for hypertension	0.380	5.509	0.001

Table 3
Criteria of Metabolic Syndrome and their Predictive Values

	Sensitivity	Specificity	PPV*	+LR**
High blood pressure (≥130/85 mmHg) or history of hypertension	88%	73%	73%	3.4
Raised fasting blood glucose (≥5.6 mmol/L) or a history of diabetes mellitus	75%	60%	55%	1.9
Raised fasting triglycerides (≥1.7 mmol/L 4)	84%	72%	73%	3.1
Lowered High Density Lipoprotein (m. < 1.03 mmol/L, f. <1.29 mmol/L)	88%	71%	68%	3.0
Central obesity (m. ≥102cm, f. >88cm)	66%	81%	91%	3.6
Body Mass Index (BMI)	63%	72%	86%	2.3
High blood pressure and central obesity	93%	69%	64%	3.0
High blood pressure and BMI	63%	87%	95%	5.1

* PPV = Positive Predictive Value
** +LR = Positive Likelihood Ratio

n = 41 patients of which 22 positive cases of metabolic syndrome.

Discussion

Major findings

To the best of the author's knowledge this is the first study so far that has researched metabolic syndrome in patients with addiction and comorbid psychiatric disorders. Inpatients were recruited for this research from a variety of different wards including acute admission and longer stay psychiatric wards. The findings reveal a high prevalence of metabolic syndrome (53.7%) among the study population. In a study examining metabolic syndrome in patient with schizophrenia, Heiskanen et al (2003) reported a prevalence rate of metabolic syndrome of 37% and a study looking at cost-effective screening for metabolic syndrome, Straker et al (2005) reported a rate of 29%. In this study metabolic syndrome was also not associated with any specific antipsychotic.

In the study group a significant association was found between central obesity and metabolic syndrome. Central obesity alone however was not associated with metabolic syndrome. Cerit, Ozeten & Yildiz (2008) also reported that females were significantly more likely to have central obesity and Tirupati & Chua (2007) observed the same rate of 88% of females in their study had central obesity.

As expected, all the individual diagnostic criteria that were separately added to the analysis model were significantly associated with the metabolic syndrome. Blood pressure measurements alone had a high sensitivity of 88%. Combined blood pressure and central obesity were found to have a significant association with metabolic syndrome and had a sensitivity of 93%, which is almost similar to the 96% Straker et al (2005) reported. Specificity, that is the ability to use a combined blood pressure and waist circumference measurement to correctly identify the absence of metabolic syndrome, was however lower than 69%, which can result in a high number of false positive diagnostic results.

There are also some limitations to the study that have to be discussed.

The large attrition rate is one of the limitations of this study and may have compromised the external validity. The small number of subjects in this study is also a limitation which may have seriously compromised the measuring of sensitivity and specificity. Furthermore the attrition rate was at its highest amongst patients being treated in community settings, which may indicate self-selection. Patients who were not concerned about their weight and general health may have

chosen not to take part in the study or treatment in a clinical setting may have an association with abnormalities in metabolic functioning. Further research with a larger study population is needed to determine if waist circumference and blood pressure measurements alone are reliable diagnostic predictors in clinical and community settings.
The results of this study may also have been limited by the cross-sectional nature of the design. Blood pressure for example was measured only once. Diagnosing hypertension from one high blood pressure reading lacks sensitivity and specificity. Finally, results may have been modified by variables that were not controlled for, such as length of time on medication, dose of medication, side effects of medication, and interactions with other medications.

Conclusion

This study has clearly demonstrated that combined waist circumference and blood pressure measurements may be clinically useful as a quick reliable and nonintrusive method to identify patients with metabolic syndrome who are unwilling or unable to provide fasting blood samples. Providing a fast, easy and acceptable method of initially screening patients would significantly increase our knowledge of the prevalence of metabolic syndrome among this patient group as well as inform and improve treatment. Patients who test positive could be referred for the full diagnostic test. By identifying patients with risk factors for metabolic syndrome, clinicians will be able to effectively target interventions to reduce or manage these risks factors.

References

Brown, S. (1997). Excess mortality of schizophrenia: a meta-analysis. *British Journal of Psychiatry*, 171, 502-508.

Cerit C., Ozeten, E. & Yildiz, M. (2008). The prevalence of metabolic syndrome and related factors in patients with schizophrenia. *Turkish Journal of Psychiatry*, 19, nr. 2, 1-8.

Cohn, T., Prud'homme, D., Streiner, D., Kameh, H. & Remington, G. (2004). Characterizing coronary heart disease risk in chronic schizophrenia: High prevalence of metabolic syndrome. *Canadian Journal of Psychiatry*, 49, nr. 11, 753-760

Dixon, L., Postrado, L., Delahanty, J., Fischer, P. J. & Lehman, A. (1999). The association of medical comorbidity in schizophrenia with poor physical and mental health. *Journal of Nervous Mental Disease*, 187, nr. 8, 496-502.

Hansen, V., Jacobsen, B., K. & Arnesen, E. (2001). Cause-specific mortality in psychiatric patients after deinstitutionalisation. *British Journal of Psychiatry*, 179, 438-443.

Hert, M. de, Schreurs, V., Vancampfort, D. & Winkel, R. van (2009). Metabolic syndrome in people with schizophrenia: a review. *World Psychiatry*, 8, 15-22.

Heiskanen T., Niskanen L., Lyytikainen R., Saarinen P. & Hintikka J. (2003). Metabolic syndrome in patients with schizophrenia. *Journal of Clinical Psychiatry*, 64, 575-579.

Lindenmayer, J. P., Czobor, P., Volavka, J., Citrome, L., Sheitman, B., McEvoy, J. P., Cooper, T. B., Chakos, M. & Lieberman, J. A. (2003). Changes in glucose and cholesterol levels in patients with schizophrenia treated with typical or atypical antipsychotics. *American Journal of Psychiatry*, 160, nr.2, 290-296.

Meyer, J. M., Nasrallah, H. A., McEvoy, J. P., Golf, D. C., Davis, S. M., Chakos, M., Patel, J. K., Keefe, R. S., Stroup, T. S. & Lieberman, J. A. (2005). The clinical antipsychotic trails of intervention effectiveness (CATIE) schizophrenia trail: Clinical comparison of subgroups with and without metabolic syndrome. *Schizophrenia Research*, 80, 9-18.

Newman, S.C. & Bland, R.C. (1991). Mortality in a cohort of patients with schizophrenia: a record linkage study. Canadian Journal of Psychiatry, 36(4), 239-45

National Cholesterol Education Program (2002). 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). Final report. Consulted 09-10-2011 via http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3_rpt.htm.

Olfson, M., Marcus, S.C., Corey-Lisle, P., Toumari, A.V., Hines, P. & L'Italien, G. (2006). Hyperlipidemia following treatment with antipsychotic medications. *American Journal of Psychiatry, 163*, 1821-1825.

Straker, D., Correll, C.U., Kramer-Ginsberg, E. K., Abdulhamid, N., Koshy, F., Rubens, E., Saint-Vil, R., Kane, J. M. & Manu, P. (2005). Cost-effective screening for the metabolic syndrome in patients treated with second generation antipsychotic medication. *American journal of Psychiatry*, 162, nr. 6, 1217-1221.

Tirupati, S. & Chua, L-E (2007). Obesity and the metabolic syndrome in a psychiatric rehabilitation service. *Australian and New Zealand Journal of Psychiatry*, 41, 606-610.

Weiden, P. J., Mackell, J. A. & Mc Donnell, D. D. (2004). Obesity as a risk factor for antipsychotic noncompliance. *Schizophrenia Research*, 66, nr. 1, 51-57.

Summary

Objective To identify if combined blood pressure and waist circumference measurements are reliable predictors of metabolic syndrome.
Method A descriptive correlational design was used to examine the sensitivity and specificity of screening techniques used to detect metabolic syndrome. Data were collected regarding waist circumference, body mass index, blood pressure, fasting blood glucose, triglycerides and high density lipoproteins
Results Blood pressure and waist circumference measurements demonstrated high significance, sensitivity and specificity as screening methods for metabolic syndrome.
Conclusion Combined waist circumference and blood pressure measurements may be clinically useful for a quick and reliable detection of metabolic syndrome in patients with addiction and comorbid mental health problems.