Schizophrenia Research xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Metabolic syndrome and aerobic fitness in patients with first-episode schizophrenia, including a 1-year follow-up

L. Nyboe [a,*], C.H. Vestergaard [a], M.K. Moeller [b], H. Lund [c,d], P. Videbech [a]

[a] The Research Unit, Department of Affective Disorders Q, Aarhus University Hospital, Risskov, Denmark
[b] Horsens Regional Hospital, Department of Medicine, Denmark
[c] SEARCH — Research Group for Synthesis of Evidence and Research, Research Unit for Musculoskeletal Function and Physiotherapy (FoF), Department of Sports Sciences and Clinical Biomechanics, University of Southern Denmark, Odense, Denmark
[d] Center for Evidence-based Practice, Bergen University College, Bergen, Norway

ARTICLE INFO

Article history:
Received 7 May 2015
Received in revised form 29 July 2015
Accepted 30 July 2015
Available online xxxx

Keywords:
First-episode schizophrenia
Metabolic syndrome
Aerobic fitness
Physical activity
Lifestyle habits

ABSTRACT

Objective: To compare the prevalence of metabolic syndrome (MetS) and metabolic abnormalities in patients with first-episode schizophrenia (FES) with sex- and age-matched healthy controls; to investigate changes in MetS during 1 year of treatment; and to investigate predictors of MetS.
Methods: Patients with FES (N = 99) and healthy controls (N = 50) were included in the study. MetS was defined according to IDF based on waist circumference (WC), blood pressure (BP), triglycerides (TG), high-density lipoprotein (HDL), and fasting-glucose. Data on physical activity, aerobic fitness, smoking, and dietary habits, sleeping disturbances, psychopathology and psychotropic medication were also obtained. Patients were assessed at baseline and at 1 year follow-up.
Results: Compared with healthy controls patients with FES had a higher baseline prevalence of MetS ($p = .07$), and metabolic abnormalities: WC ($p < .01$), TG ($p < .01$), HDL ($p = .017$), and fasting glucose ($p = .04$). Patients with FES had significantly increased prevalence of MetS ($p = .03$), WC ($p = .04$), and TG ($p = .01$) during the study period. Antipsychotics and low physical activity were significantly correlated with the increase in metabolic abnormalities. In multivariate analyses low aerobic fitness was the most consistent and significant predictor of metabolic abnormalities and MetS.
Conclusion: MetS and metabolic abnormalities are highly prevalent in patients with FES, and both increase significantly during 1 year of treatment. Apart from confirming the metabolic adverse effects of antipsychotics, our study highlights that low aerobic fitness is a significant risk factor for MetS. Promoting a healthier lifestyle should be part of psychiatric treatment and rehabilitation.

1. Introduction

Patients with schizophrenia have a 15- to 20-year shorter life expectancy than the general population (Laursen, 2011; Laursen et al., 2014). The higher mortality is mainly due to somatic illnesses such as cardiovascular disease (CVD), type 2 diabetes (T2D), and cancer (Brown et al., 2010; De Hert et al., 2009; Jin et al., 2011). Metabolic syndrome (MetS) — comprising abdominal adiposity, insulin resistance, increased blood pressure, elevated triglyceride (TG) levels, and low high-density lipoprotein (HDL) levels — significantly increases the risk for CVD and T2D (Alberti et al., 2006; Mottillo et al., 2010). The concept of MetS is useful when screening and monitoring cardiovascular risk factors in patients with schizophrenia.

The development of MetS is attributable to multiple factors, including genetic factors, physical inactivity, smoking, a high-calorie diet, and sleeping disturbances (Povel et al., 2011; Huang and Liu, 2014; Sun et al., 2012; Jennings et al., 2007). Moreover, patients with schizophrenia are also exposed to the well-known metabolic adverse effects of antipsychotic medication (Allison and Casey, 2001; De Hert et al., 2011). Weight gain has been given significant attention and both low baseline BMI and specific genetic factors prove to predict weight gain in patients with first-episode schizophrenia (FES) (Saddichha et al., 2008a; Boden et al., 2009; Srisawat et al., 2014).

The prevalence of MetS in multi-episode patients with schizophrenia is 35.3%, which is 2- to 4-fold higher than in the general population (Mitchell et al., 2011; Vancampfort et al., 2013). Patients with schizophrenia have a fourfold increased risk of abdominal obesity, and a

Abbreviations: BMI, body mass index; CVD, cardiovascular disease; FES, first-episode schizophrenia; FG, fasting glucose; GAF, Global Assessments of Function; HDL, high-density lipoprotein; MetS, metabolic syndrome; SANS, Scale for Assessment of Negative Symptoms; SAPS, Scale for Assessments of Positive Symptoms; T2D, type 2 diabetes; TG, triglycerides; WC, waist circumference; AP, antipsychotics; AD, antidepressants.

* Corresponding author at: The Research Unit, Department of Affective Disorders Q, Aarhus University Hospital, Skovagervej 2, Risskov DK 8240, Denmark.
E-mail addresses: lene.nyboe@ps.rm.dk (L. Nyboe), marianne.kleis@horsens.rm.dk (M.K. Moeller), h-lund@health.sdu.dk (H. Lund).

http://dx.doi.org/10.1016/j.schres.2015.07.053
0920-9964/

more than doubled risk of low HDL levels and hypertriglyceridemia (Lamberti et al., 2006; McEvoy et al., 2005; Boke et al., 2008; Cohn et al., 2004; Saari et al., 2005; Vancampfort et al., 2013).

A 2013 meta-analysis found that drug-naïve patients and patients with FES have comparable rates of MetS (~10%), although patients with FES have a significantly higher waist circumference (WC) and blood pressure (BP) (Mitchell et al., 2013). The significant increase of individual metabolic abnormalities early in the treatment of patients with FES have been confirmed in subsequent studies as comprising weight gain (Perez-Iglesias et al., 2014; Chiliza et al., 2015), dyslipidemia (Phutane et al., 2011; Wu et al., 2014), glycometabolism (Nielsen et al., 2010; Graham et al., 2008; Correll et al., 2014; Fleischhacker et al., 2013), and hypertension (Bensenor et al., 2012; Beary et al., 2012). Only a few studies have compared the rates of MetS in patients with FES and healthy controls, with divergent results. Some studies show no differences (Fleischhacker et al., 2013) but others do (Correll et al., 2014; Saddichha et al., 2008b; Bensenor et al., 2012). However, all studies have found a significantly higher prevalence of metabolic abnormalities in patients with FES compared with healthy controls, thereby also confirming a high metabolic risk early in the treatment of patients with FES.

The majority of studies describing an adverse metabolic effect of antipsychotics in patients with FES lack concurrent examination of non-pharmacological risk factors. Therefore, little is still known about how lifestyle factors such as physical inactivity, smoking, and poor diet contribute to the increased metabolic risk in patients with FES.

The aims of this study were to investigate the prevalence of MetS in patients with FES compared with healthy controls; to study how MetS and its individual metabolic abnormalities progress in these patients during the first year of treatment; and to examine predictors of MetS and metabolic abnormalities in patients with FES. We hypothesized that both antipsychotic medication and low physical activity would significantly increase the risk of MetS and metabolic abnormalities.

2. Methods and materials

This was a controlled, 1-year follow-up study, ending in 2014, of patients with FES (International Classification of Diseases-10 [ICD-10] diagnoses F.20) aged between 18 and 45 years. Patients were recruited from an outpatient clinic for patients with FES in the Central Region of Denmark. For comparison, we also included sex- and aged-matched healthy controls recruited via an advertisement in a local newspaper.

Only participants who spoke and understood Danish were included. Other exclusion criteria were physical disability or somatic illness impairing physical activity, pregnancy, mental retardation, or substance or alcohol abuse according to ICD-10 criteria, or coercion. For healthy controls, the use of any psychotropic medication or medical condition led to exclusion. All participants were included in the study after written, confirmed consent was obtained in accordance with the Declaration of Helsinki. The study protocol was approved by the local ethical committee and the study was registered with the Danish Data Protection Agency and ClinicalTrials.gov.PRS (NCT00957294).

Patients with FES were assessed at baseline and after 1 year of follow-up; healthy controls were only assessed at baseline. Apart for psychopathological data, all assessments were carried out by the same researcher (LN). All questionnaires were administered as structured interviews to account for cognitive deficits in the clinical population.

2.1. Socio-demographic data, smoking, and dietary habits

Socio-demographic data, smoking, and dietary habits were assessed, the latter using questionnaires adapted from the Danish Health Examination Survey 2007–2008 (Eriksen et al., 2011). Smoking habits were categorized as i) “nonsmoker”, comprising previous and nonsmokers, or ii) “smoker”, comprising daily and weekly smokers. Dietary habits were presented in sum scores from Likert-type scales, with a higher sum indicating a healthier diet, defined as having more regular meals, a more frequent intake of vegetables, fruits, whole-grain products, fish, and meat, and a less frequent intake of sweets, cakes, snacks, and soft drinks.

2.2. Metabolic measures

Metabolic measures comprised data from blood samples on level of fasting glucose (FG), TG, and HDL, measures of WC, weight, height, and body mass index (BMI), and BP. Participants were described as having MetS if they fulfilled the criteria defined by the International Diabetes Federation (IDF) (Alberti et al., 2006).

2.3. Physical activity

Physical activity was assessed by the Physical Activity Scale (Aadahl and Jorgensen, 2003; Andersen et al., 2010). All participants were asked to recall their activity level during the past week. Physical activity was presented in metabolic equivalents, with a higher score reflecting a higher level of physical activity. Aerobic fitness, defined as oxygen uptake (VO_2 max/kg), served as a proxy for physical activity level prior to inclusion and during the study period, and was measured using the Astrand–Rhyming test, a single-stage cycle ergometer test (Astrand, 1960). The test is designed to elicit a steady-state heart rate (HR) over a 6-min period. All tests were performed on a Monark 827 Ergometer cycle, and HR was measured during the entire test by a Polar HR monitor. Only patients who had a normal electrocardiogram were allowed to perform the test. Based on HR at a specific workload (Watt) the oxygen uptake (VO_2 max) was estimated using the Astrand–Rhyming sex- and age-sensitive nomogram. A recent study has proved The Aastrand–Rhyming test as valid and applicable for patients with schizophrenia (Vancampfort et al., 2014).

2.4. Sleeping disturbances

Sleeping disturbances were assessed by the Pittsburgh Sleep Quality Index (Buysse et al., 1989).

2.5. Psychopathological data

Psychopathological data included Global Assessment of Function (GAF), Scale for Assessment of Negative Symptoms (SANS) (Andreasen, 1984a), and Scale for Assessment for Positive Symptoms (SAPS) (Andreasen, 1984b). Data were assessed by trained psychiatric staff members.

2.6. Psychopharmacological data

Psychopharmacological data comprised names and dosages of prescribed antipsychotics (AP), antidepressants (AD), and benzodiazepines, and were registered for all patients. Data were obtained from patient's electronic medical records and included medical data from up to 6 months before inclusion and during the study period. Antipsychotic medication was described in defined daily dosages (DDD) and chlorpromazine equivalents based on the average doses given prior to and during study period, respectively.

2.7. Statistical analyses

For analyses of differences between the patients and the healthy controls a chi-squared test or Fischer's exact test was applied for categorical variables, and the Kruskal–Wallis test applied for continuous variables. The number of participants with MetS in each group was compared using the chi-squared test. The progression of the individual metabolic components of MetS was analyzed individually. For paired

Please cite this article as: Nyboe, L., et al., Metabolic syndrome and aerobic fitness in patients with first-episode schizophrenia, including a 1-year follow-up, Schizophr. Res. (2015), http://dx.doi.org/10.1016/j.schres.2015.07.053