Psychiatry Research 230 (2015) 616–621

Contents lists available at ScienceDirect

Psychiatry Research

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

Vitamin D status in psychotic disorder patients and healthy controls – The influence of ethnic background

Mari Nerhus [a,*], Akiah Ottesen Berg [a], Sandra Rinne Dahl [b], Kristin Holvik [c], Erlend Strand Gardsjord [a], Melissa Authen Weibell [d], Thomas Doug Bjella [a], Ole A. Andreassen [a], Ingrid Melle [a]

[a] NORMENT, KG Jebsen Center for Psychosis Research, Institute of Clinical Medicine, University of Oslo, Norway; NORMENT, Division of Mental Health and Addiction, Oslo University Hospital, Ullevaal Hospital, Building 49, P.O.Box 4956 Nydalen, N-0424 Oslo, Norway
[b] Hormone Laboratory, Oslo University Hospital HF, Aker Hospital, P.O.Box 4956 Nydalen, N-0424 Oslo, Norway
[c] Division of Epidemiology, Norwegian Institute of Public Health, P.O.Box 4404, N-0403 Oslo, Norway
[d] Psychiatric Division, Regional Centre for Clinical Research in Psychosis, Stavanger University Hospital HF, P-O-Box 8100, N-4068 Stavanger, Norway

ARTICLE INFO

Article history:
Received 30 March 2015
Received in revised form
9 October 2015
Accepted 13 October 2015
Available online 20 October 2015

Keywords:
Early diagnosis
Calcitriol
Schizophrenia
Ethnicity
Seasons
Case-control studies

ABSTRACT

Vitamin D deficiency is common among patients with psychotic disorders and could be due to unknown disease mechanisms or contingent factors. However most studies are performed in chronic patients and have often failed to address the influence of ethnicity on vitamin D levels in clinical samples. We investigated serum concentrations of 25-hydroxy vitamin D (S-25 OH D) in first episode patients compared to patients with multi episodes and healthy controls; with a specific focus on differences between visible ethnic minorities and participants from the majority population. A total of 284 participants were included in this cross-sectional study. First episode patients with a DSM-IV psychotic disorder were matched on age, gender and ethnicity to participants from a multi episode patient sample (1:1) and healthy controls (1:2). We did not find any differences between either patient groups or the healthy controls, but participants from visible ethnic minorities had significantly lower S-25 OH D than participants from the majority population. This implies that S-25 OH D should be routinely measured in persons from visible ethnic minorities since low levels are associated with higher levels of depressive symptoms.

1. Introduction

The active metabolite of vitamin D is a steroid hormone with multiple functions. It binds to the vitamin D receptor (VDR) which is found in most parts of the body, including the immune system (Fernandes de Abreu et al., 2009) and the central nervous system (Stumpf, 2012). Vitamin D is involved in the proliferation, differentiation and growth of neurons and has an important role in neuroplasticity (Deluca et al., 2013) both in the developing and adult brain.

Two recent meta-analyses have indicated significantly lower serum–25 hydroxy vitamin D (S-25 OH D) in patients with established psychiatric disorders compared to healthy controls (Belvederi Murri et al., 2013; Valipour et al., 2014), in line with previous studies showing an association between lower S-25 OH D and having a diagnosis in the schizophrenia spectrum (Reay-Sanchez et al., 2009; Partti et al., 2010). Correspondingly, in a study of diagnostically diverse psychiatric out-patients the lowest S-25 OH D levels were found in patients with schizophrenia or autism spectrum disorders (Humble et al., 2010). There are thus relatively consistent indications of lower S-25 OH D in patients with psychotic disorders, especially schizophrenia. To what extent the low vitamin D levels are related to (hitherto unknown) disease mechanisms or secondary to poor nutrition, reduced self-care or medication use is not known. Most studies have included chronic patients, i.e. groups that probably will be more influenced by these types of contingent factors than patients with a recent onset of their disease. However only two earlier studies have up to now been conducted in first episode/first treatment samples and their findings are equivocal. One study ($N=138$) found significantly lower S-25 OH D in both white and black patients, but not in patients of Asian origin, compared to healthy controls (Crews et al., 2013). The other small study ($N=40$) did not find any patient/control differences (Graham et al., 2014).

The main source of vitamin D is ultraviolet B (UVB) radiation from the sun. Dark skin (high pigmentation), body-covering

* Corresponding author. Fax: +47 23 02 73 33.
E-mail address: mari.nerhus@medisin.uio.no (M. Nerhus).

http://dx.doi.org/10.1016/j.psychres.2015.10.015
0165-1781/

clothing and reduced outdoor activities, will interact with available UVB radiation, dependent on geographical latitude and season of the year, in affecting vitamin D levels in the body (Wacker and Holick, 2013). This is of interest for the study of psychotic disorders since there are consistent findings of a higher incidence of psychotic disorders in immigrants and visible ethnic minorities, in particular dark-skinned immigrants to countries with predominantly white majority populations, i.e. countries at high latitudes (Cantor-Graae and Selten, 2005). There are however few studies of the associations between ethnic background and vitamin D levels in psychotic disorders. In the current clinical cross sectional study we thus aimed to explore differences in S-25 OH D between a first episode psychosis patient sample, compared to a multi-episode patient sample and a healthy control sample matched for age, gender and ethnic background. We investigated if:

i. First episode patients and multi-episode patients have lower S-25 OH D than the healthy controls.
ii. Participants from visible ethnic minorities across the two patient groups and in the healthy control group have lower S-25 OH D than participants from the majority population.

2. Methods

Participants were recruited consecutively between May 2010 and April 2014 from in-and out-patient psychiatric units in the catchment areas of the four major hospitals in Oslo, as part of the larger Thematically Organized Psychosis (TOP) Study. The Regional Committee for Medical Research Ethics approved the study and our research methodology conformed to The Code of Ethics of the World Medical Association, Helsinki Declaration. All participants gave informed written consent to participate.

2.1. Participants

A power analysis based on group differences (means and standard deviations) from the previous vitamin D in FEP study (Crews et al., 2013) indicated that a group size of 46 participants would be sufficient to detect real differences given the expected differences and standard deviations. A total of 71 first episode patients (FEP) with a DSM-IV psychotic disorder (Schizophrenia spectrum i.e. schizophrenia, schizophreniform and schizoaffective, $N=46$; other psychosis i.e. delusional disorder, brief psychotic episode, psychotic depressive disorder and psychosis NOS, $N=25$) were included. Participants were defined as FEP if they gave consent to be recruited into the study within one year after start of their first adequate treatment (defined as admission to hospital or antipsychotic medication in adequate doses) for a psychotic episode (defined as at least one week with a score of four or more on Positive and Negative Syndrome Scale for Schizophrenia on items P1, P3, P5, P6 or G9). As a proxy for skin pigmentation the participants' ethnicity was used to divide the participants into two groups, one group including participants with European ancestry (majority population group), and one group with participants of Asian, Latin-American and African ancestry (visible ethnic minority group). The FEP sample was then matched 1:1 on visible ethnic minority status, age, gender and diagnosis to a multi episode sample (MEP) and then matched 1:2 to healthy controls (HC) drawn from the same catchment area in the following manner: Participants from the majority population were directly matched with HC from the control group of the TOP study. Due to a low number with visible ethnic minority status in this control group, participants with visible ethnic minority background (i.e. from Asia including Turkey ($N=17$), Africa ($N=17$) and Latin-America ($N=6$)) were matched with HC of visible ethnic minority background (Asia including Turkey) from a population-based health study including immigrants to the city of Oslo; the Oslo Immigrant Health Study (2002) (http://www.fhi.no/artikler/?id=53584).

2.2. Procedures

2.2.1. Clinical

All patients were assessed by trained clinical research personnel. Demographic and clinical variables and the use of medication were obtained by clinical interviews by protocol and by conferring the medical records. The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) was used for diagnostic purposes. In the FEP group, duration of untreated psychotic illness was measured in weeks. In the FEP and MEP groups total duration of illness (including treated and untreated phases) was measured in years and calculated as age minus age at onset. Current symptomatology was assessed by The Structured Interview for the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). At inclusion the participants went through a physical examination with blood sample withdrawal. Height and weight were measured by a standard procedure, and BMI was calculated by kg/m².

2.2.2. Biochemical

In the TOP sample; 25-OH D (25-OH D2 and 25-OH D3) serum concentrations were determined using a liquid chromatography–tandem mass spectrometry (LC–MS/MS) method developed at the Hormone laboratory (Oslo University Hospital, Norway) (Supplementary materials 1). In the Oslo Immigrant Health Study, S-25 OH D was measured by a radioimmunoassay (RIA kit from Diasorin) (Holvik et al., 2005). The equation LC-MS/MS = 1.16×(RIA)−9 was calibrated at the laboratory for comparisons and the calibrated values from the Oslo Immigrant Health Study are used in the current study.

2.3. Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics v. 22 (IBM corp. 2014). The level of significance was preset to $P<0.05$ (two tailed). Student *t*-tests and one way ANOVAs with Tukey post hoc tests were used for group comparisons of continuous variables, chi-square tests for categorical variables and Pearson's *r* for bivariate correlations. Normally distribution of the continuous variables was evaluated by normality plots and found to be satisfactory with the exception of the assessments of duration of untreated psychosis and total duration of illness where we used Spearman's correlations. For statistical purposes, season was dichotomized into winter (December–May) and summer (June–November) (Porojnicu et al., 2007). For PANSS we used the five factor model by Wallwork et al. (2012). Seven participants had missing values for BMI; five had missing values for age at onset, three had missing values for in-vs out-patient status and nine had missing values for regular use of antipsychotic medication or not. In the multivariate analyses missing values were replaced with group means for independent continuous variables and mode (most used value) for independent dichotomous variables. To investigate the potential influence of confounders, variables that were either statistically significantly associated with S-25 OH D or differed across groups (i.e. FEP, MEP or HC) or ethnicity (majority population or visible ethnic minority) in bivariate analyses were entered as covariates in an ANCOVA with S-25 OH D as the dependent variable; here group membership (FEP, MEP or HC) and ethnicity were fixed factors in the model. The analyses were then repeated in the subsample containing only patients with a narrow schizophrenia spectrum diagnosis (schizophrenia $n=77$, schizophreniform $n=8$, schizoaffective $n=15$). Finally we performed a second