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25-Hydroxvitamin D concentrations are not lower in children with bronchial asthma, atopic dermatitis, obesity, or attention-deficient/hyperactivity disorder than in healthy children[☆]

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ABSTRACT

Vitamin D (vitD) is involved in immune regulation, and its receptor has been identified in several tissues including lung, adipose tissue, brain, and skin. Based on these observations, it has been suggested that vitD has an essential role not only in bone metabolism but also in other diseases such as atopic dermatitis (AD), bronchial asthma (BA), attention-deficit/hyperactivity disorder (ADHD), and obesity because the affected tissues express vitD receptors. Furthermore, obesity, AD, and BA are regarded as inflammatory diseases. Therefore, we hypothesized that vitD concentrations are lower in children with AD, BA, ADHD, and obesity compared to healthy children. We measured 25-hydroxyvitamin D concentrations in 235 children (60% boys, age 9.3±1.7 years) with obesity, BA, AD, or ADHD and compared them to those of 3352 children from a healthy population. Additionally, parathyroid hormone was measured in the children with obesity, ADHD, BA, and AD. VitD concentrations were not lower in children with obesity, ADHD, BA, and AD compared to healthy children. In multiple regression analyses adjusted to migration background, time period of blood sample, age, and sex, VitD levels correlated significantly with the severity of AD measured by SCORing Atopic Dermatitis index and attention deficit measured by Conners questionnaire in ADHD. VitD levels were not linked to hyperactivity in ADHD, the severity of BA measured as forced expiration volume in the first second, or body mass index standard deviation score.

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; BMI, body mass index; DSM, *Diagnostic and Statistical Manual of Mental Disorders*; FEV1%, forced expiration volume in the first second; IQR, interquartile range; KIGGS, bevölkerungsbezogene Kohorte des Kinder- und Jugendgesundheitsumfrage; PTH, parathyroid hormone; SCORAD, SCORing Atopic Dermatitis index; SDS, standard deviation score.

[☆] Declarations of interest: All authors declare that there is none.

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Parathyroid hormone was not associated with the activity of any analyzed disease. In conclusion, most of our findings do not support the hypothesis that vitD is involved in the pathogenesis of these entities.

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1. Introduction

Vitamin D is well known for its essential role in bone metabolism and calcium homeostasis [1]. Clinically relevant low vitamin D levels, as for example in rickets, are associated with an increase in the counterregulating hormone parathyroid hormone (PTH) [1]. Furthermore, vitamin D is involved in the regulation of the immune system [2–4], and its receptor has been verified in several tissues also including the lung, skin, brain, and adipose tissue [2,3,5]. Stimulation of the vitamin D receptor leads to gene transcription and the activation of a variety of signal transduction pathways [3,6]. Based on these observations, there is an ongoing discussion if the vitamin D endocrine system is related not only to bone diseases but also to several other conditions including obesity, atopic diseases such as bronchial asthma and atopic dermatitis, and attention-deficit/hyperactivity disorder (ADHD) [7–13]. Obesity, bronchial asthma, and atopic dermatitis seem to be promising candidates for diseases associated with the vitamin D status because they are all chronic inflammatory diseases and the affected tissues all express the vitamin D receptor. Because vitamin D deficiency alters behavior in mice and vitamin D receptors are also expressed in the brain, ADHD might be an example of a neuropsychiatric disorder related to the vitamin D status [3,14,15]. However, there is still a considerable disagreement regarding the role of vitamin D in the development or exacerbation of these diseases [16–19]. There are only a few longitudinal randomized controlled studies analyzing the effect of vitamin D supplementation on bronchial asthma, atopic dermatitis, and obesity with controversial findings [16,20–22].

Because of the challenging nature of conducting randomized controlled studies among minors, it is necessary to obtain more information about the role of vitamin D insufficiency or deficiency within the mentioned diseases before conducting further trials. One new approach would be measuring not only vitamin D but also the counterregulating hormone PTH within these entities. Furthermore, the relationships between severities of these diseases on the one hand and vitamin D as well as PTH concentrations on the other hand should be determined. Because such studies are largely missing in children with bronchial asthma, atopic dermatitis, ADHD, or obesity, we used data from the NIKI study (New Common Diseases During Childhood and Adolescence [*Neue Volkskrankheiten im Kindes- und Jugendalter*]) and a representative nationwide population-based study of children in Germany (KIGGS= bevölkerungsbezogene Kohorte des Kinder- und Jugendgesundheitsstudies) to compare the vitamin D levels between children with bronchial asthma, atopic dermatitis, obesity, and ADHD and healthy children. Furthermore, we analyzed the relationships between PTH or vitamin D and the severities of these diseases. Our primary hypothesis was that children with atopic dermatitis, bronchial asthma, obesity, or ADHD had lower vitamin D levels than healthy children. Secondary aims were to analyze whether the severities of bronchial asthma, atopic dermatitis, ADHD, and obesity are associated with both vitamin D and PTH concentrations.

2. Methods and materials

Written informed consent was obtained from all children and their parents. The study was approved by the local ethics committee of the University of Bochum.

2.1. NIKI cohort

The NIKI study was conducted to analyze new widespread diseases in children and adolescents. This multicenter study was performed between October 1, 2013, and September 30, 2016, at the Department of Pediatric Endocrinology, Diabetes, and Nutrition Medicine, Vestische Kinder- und Jugendklinik Datteln, University Witten/Herdecke, the University Children's Hospital, St Josef-Hospital Bochum, Ruhr University Bochum, the LWL-University Hospital for Child and Adolescent Psychiatry in Hamm, Ruhr-University Bochum, and the LVR-Klinikum Essen, Klinik für Psychiatrie, Psychosomatik und Psychotherapie des Kindes- und Jugendalters, Kliniken/Institut Universität Duisburg-Essen in Germany. In this study, children aged 6 to 13 years with bronchial asthma, atopic dermatitis, obesity, and ADHD were examined. A total of 611 (407 boys, 204 girls) children were screened, and 302 children (191 boys [63.2%], 111 girls [36.7%]) were included in the NIKI study (Fig. 1). Multiple variables were analyzed such as anthropometrics, questionnaire of the International Study of Asthma and Allergies in Childhood to determine the presence and the severity of the allergic diseases bronchial asthma and atopic dermatitis [23], the SCORing Atopic Dermatitis index (SCORAD) to quantify severity [24], blood parameters (including vitamin D and PTH), Conners questionnaire to determine symptoms of ADHD [25], as well as multiple other variables such as migration status. Children with diseases other than obesity, bronchial asthma, atopic dermatitis, or ADHD were excluded from the study.

2.2. Control group

The control group consisted of healthy children in the KIGGS study with vitamin D measurements in the age range of 6 to 13 years. The KIGGS study is a representative nationwide population-based study of children in Germany. The recruitment process has been described previously [26,27]. Children in the KIGGS study with bronchial asthma, atopic dermatitis, obesity, and ADHD were excluded from the analyses.

2.3. Definitions

Children not born in Germany with at least 1 parent not born in Germany or children with both parents not born in Germany were defined as having a migration background.

Bronchial asthma was diagnosed by specialized pediatric pneumologists by pathological lung function tests or typical

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