

Short Communication

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The association between vitamin D levels and precocious puberty: a meta-analysis

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Abstract: The objective of this short communication was the relationship between vitamin D and precocious puberty (PP). In this study, a comprehensive search of multiple databases was performed to identify studies focused on the association between vitamin D deficiency and PP. Studies that compared serum vitamin D levels between patients with PP and controls were selected for the systematic meta-analysis. The main outcome was the mean difference in serum vitamin D levels between PP and controls. Vitamin D-deficient subjects were more likely to develop PP. Our findings suggest that PP may be linked to vitamin D deficiency. Thus, providing supplements of vitamin D to PP patients may improve their nutritional status and prevent diseases. But, the amount of vitamin D required is uncertain, so it is important to be careful when taking vitamin D supplements.

Keywords: meta-analysis; precocious puberty; vitamin D.

Introduction

Precocious puberty (PP) is when a child's body begins to change to that of an adult too early; this might be caused by abnormal sex hormone production or exposure occurring earlier than normal given an individual's sex, race and ethnic background. PP is often accompanied by abnormal gonadotropin-releasing hormone (GnRH)

secretion and luteinizing hormone (LH) and follicle-stimulating hormone (FSH) production. PP is a common problem affecting up to 29/100,000 girls and 3/100,000 boys per year [1]. Vitamin D plays a critical role throughout children's growth and development. Vitamin D deficiency is associated with many disorders, including immune dysfunction, obesity, metabolic syndrome, insulin resistance, infection, cancers and cardiovascular abnormalities. Moreover, vitamin D is suggested to have a regulatory role in reproductive organ development and function. Previous studies evaluating the prevalence of vitamin D deficiency in the serum of patients with PP did not reach a consistent conclusion [2]. This study was designed for the systematic meta-analysis of the relationship between the prevalence of serum vitamin D deficiency and PP.

Materials and methods

All studies published prior to April 26, 2019 that met the inclusion criteria for this analysis were included. The inclusion criteria were as follows: (1) cross-sectional, case-control or cohort studies; and (2) the relationship between vitamin D deficiency and the risk of PP was evaluated. Case reports, review articles and meeting reports were excluded. We used odds ratios (ORs) to compare the prevalence of vitamin D deficiency in patients with PP and controls. In addition, fixed-effects models were used in all analyses due to the low heterogeneity. All analyses were performed using the Stata 12.0 software (StataCorp LLC, College Station, TX, USA). The electronic databases searched were PubMed, MEDLINE, Web of Science and Google Scholar. Cochran's Q statistic and the I² statistic were used to assess the statistical heterogeneity in the meta-analysis [3]. Heterogeneity was analyzed via subgroup analyses. Egger's test was used to evaluate the publication bias.

Results

Six studies, including 3016 PP patients and 8296 healthy individuals, met the inclusion criteria. Six studies provided data on the prevalence of vitamin D deficiency; vitamin D-deficient subjects were more likely to develop PP (OR=2.02 [95% confidence interval (CI) 1.65–2.46]) (Figure 1).

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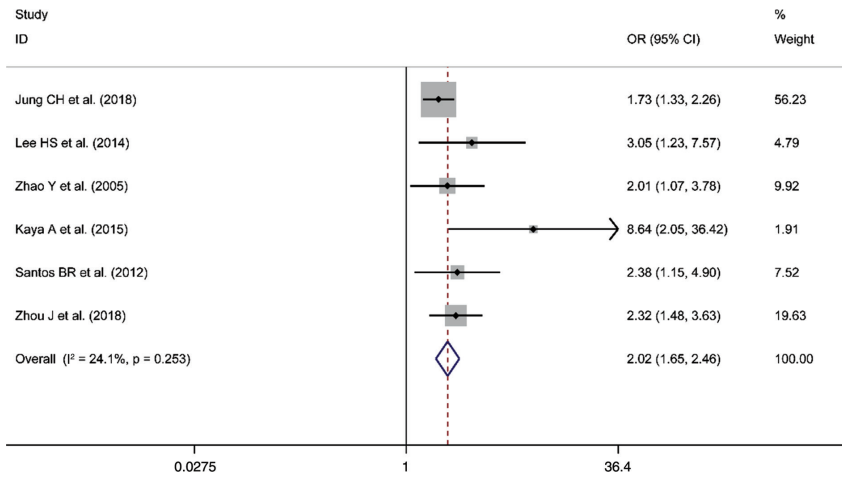


Figure 1: Six studies provided data on the prevalence of vitamin D deficiency; vitamin D-deficient subjects (OR = 2.02 [95% confidence interval (CI) 1.65–2.46]) are more likely to develop PP than normal people.

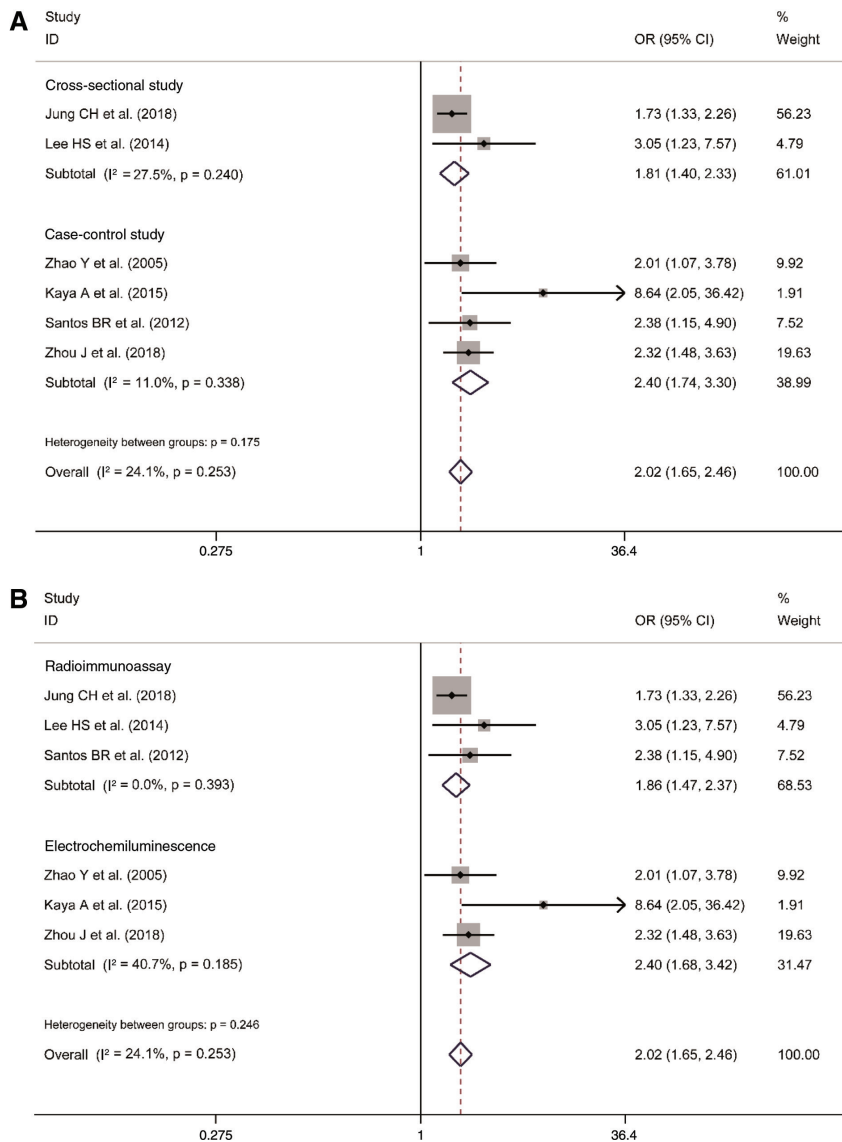


Figure 2: Subgroup analysis was performed according to the assay method and type of study.

(A) There were two types of study included in the literature: cross-sectional studies and case-control studies. The subgroup analysis revealed no significant differences between the two study types. (B) Two types of assay methods were used: radioimmunoassay and electrochemiluminescence. There was no significant difference between these two methods.

Subgroup analyses according to the assay method and type of study were performed. There were two types of study included in the literature: cross-sectional studies and case-control studies. The subgroup analysis revealed no significant differences between the two study types (Figure 2A). In addition, two types of assay methods were used: radioimmunoassay and electrochemiluminescence. There was no significant difference between these two methods (Figure 2B). Because the number of included studies was small, meta-regression was not performed.

Discussion

Vitamin D deficiency has an effect on the neuroendocrine axis. The vitamin D receptor (VDR) is expressed by the hypothalamic-pituitary-gonadal axis [4], suggesting a role for VDR signaling in reproductive functions. Vitamin D deficiency attenuated preovulatory LH surges. Attenuated preovulatory LH release is associated with reduced GnRH neuron density [5]. GT1-7 cells (hypothalamic neuronal cells), which are immortalized GnRH neurons, express the VDR. Alternatively, a possible mechanism through which the VDR may regulate GnRH neuron function is by affecting calcium channel signaling. More specifically, calcium is important for GnRH neuron function, and GnRH neurons express L-type calcium channels that are regulated by the VDR. It is possible that early life vitamin D deficiency dysregulates GnRH neuron activity through programmed effects on L-type calcium channel function [6]. Our research has several limitations. All of the included studies were designed as either cross-sectional or case-control studies, which are types of observational studies that are usually used when a randomized controlled trial (RCT) or cohort study will be difficult and the number of previous studies is small. More research is needed in this area.

Vitamins are closely related to endocrine disorders. During the perinatal period of receptor development, vitamin D may play a real hormonal role, affecting receptor development when it is deficient. However, the required dose of vitamin D is uncertain, so caution must be taken with the supplement of vitamin D [7].

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Ethical statement: This article has no ethical issues.

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