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LETTER TO THE EDITOR

Vitamin D levels in primary growth hormone deficiency disorder Prader–Willi syndrome

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To the Editor,

We read with interest the research article by Savanelli et al. (*Endocrine*, October 2015) [1], in which the authors report that low vitamin D levels predict dyslipidaemia and hypertension in patients with growth hormone (GH) deficiency. Given that vitamin D modulates gene expression of the GH/IGF-1 pathway and its administration augments circulating IGF-1 [2], the relationships of vitamin D and GH with cardiovascular risk are likely to intersect.

Individuals in their study cohort had GH deficiency with disparate causes (including numerous types of pituitary tumours and idiopathic GH deficiency) and, presumably, age of onset. It is therefore of interest to investigate whether vitamin D levels are similarly affected in a cohort in which GH deficiency arises from a common cause which is present from early life.

Prader–Willi syndrome (PWS) is a genetic imprinting disorder associated with hyperphagia, muscular hypotonia and endocrine dysfunction. Hypothalamic GH deficiency is a hallmark of PWS, contributing to the short stature, poor muscular development and low bone mineral density in individuals with this disorder. Many children and (in recent years) adults with PWS now receive GH replacement therapy, which has beneficial effects on height, muscle mass, obesity and physical activity. Individuals with PWS have increased risk of adverse cardiovascular events independent of obesity status; low-grade inflammation, low GH/IGF-1 levels and impaired autonomic function have been suggested as possible mechanisms but to our knowledge no research into vitamin D in PWS has been conducted.

Approval for this study was obtained from the St Vincent's Hospital Human Research Ethics Committee. Study participants or their parents/guardians gave written informed consent prior to participation. To determine vitamin D status in a cohort with GH deficiency and increased cardiovascular risk, we assessed 10 GH-naïve adults with PWS (age 27.9 ± 2.7; BMI 37.0 ± 2.9) in comparison to 12 obese controls (age 31.9 ± 2.5; BMI 34.3 ± 1.2) and 10 lean controls (age 28.9 ± 1.3; BMI 21.3 ± 0.5). Blood samples were collected after an overnight (10 h) fast, and plasma was obtained by centrifugation and stored at −80 °C prior to being assayed. Circulating 25(OH) vitamin D levels were measured in plasma by ELISA (Enzo Life Sciences, Farmingdale, USA). Group means were compared using ANOVA (GraphPad Prism 6.0, GraphPad Software, San Diego, CA, USA) and classified according to the guidelines established by Nowson et al. [3].

25(OH) vitamin D levels in the three groups are shown in Fig. 1. While group differences were not statistically significant, group means fell within different categories of vitamin D status. The lean group had a mean plasma 25(OH) vitamin D concentration of 23.4 ± 4.4 ng/mL, placing them in the optimal range for adults in Australia and New Zealand [3]. Obese subjects had mean levels of 18.6 ± 3.1 ng/mL, placing them in the mild vitamin D deficiency category. The individuals with PWS, with mean levels of 12.7 ± 1.5 ng/mL, exhibited mild-to-moderate vitamin D deficiency.

From this cross-sectional study, we cannot conclude whether the low levels of vitamin D in individuals in the PWS group are an intrinsic feature of the disease or secondary to environmental factors. Sunlight accounts for 90–95 % of vitamin D in Australians; as the PWS group,

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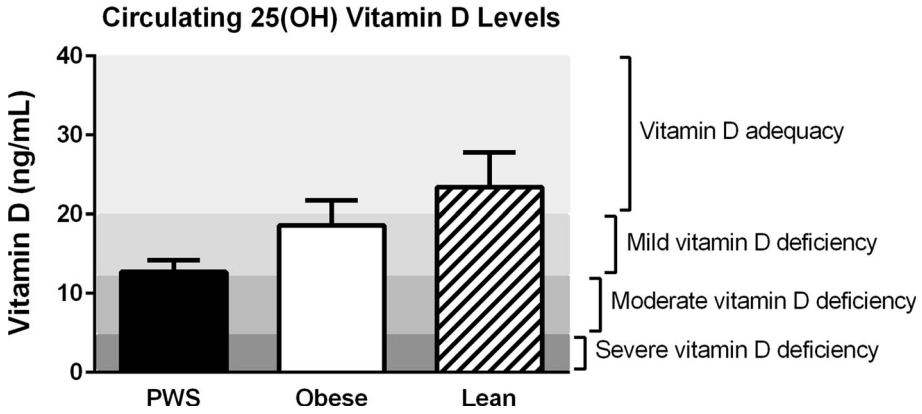

Fig. 1 Circulating 25(OH) vitamin D levels in PWS ($n = 10$; *black bar*), obese ($n = 12$; *white bar*) and lean ($n = 10$; *striped bar*) individuals. Categories of vitamin D status as per Nowson et al. [3]

along with the obese control group, reported a sedentary physical activity pattern, a lack of outdoor exercise could contribute to their vitamin D deficiency. Given that the obese control group also exhibited vitamin D deficiency, albeit to a lesser extent, adiposity itself may be a contributing factor.

This study shows for the first time evidence of hypovitaminosis D in adults with PWS. It is possible that correcting this deficiency by vitamin D supplementation could help to prevent osteoporosis and be beneficial to metabolic and cardiovascular health. Additionally, if in future studies vitamin D replacement is found to increase GH levels in PWS, this supplementation may induce further beneficial effects through the GH pathway.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to declare.

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