Proceedings of the Nutrition Society (2017), **76 (OCE3)**, E48 doi:10.1017/S0029665117001203

Irish Section Meeting, 21–23 June 2017, What governs what we eat?

Interaction between vitamin D and parathyroid hormone on perinatal outcomes highlights significance of calcium metabolic stress in pregnancy

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There is a high global prevalence of vitamin D deficiency in pregnant women[(1)]. Clinical data and biological plausibility warrant exploration of a potential role for vitamin D in prevention of adverse perinatal outcomes, specifically hypertensive disorders of pregnancy. However, systematic reviews have highlighted substantial heterogeneity in studies to date, and while the evidence for vitamin D is conflicted, calcium is acknowledged as protective against pre-eclampsia (PE)[(2,3)]. Despite the long-established metabolic interactions between vitamin D and calcium, the two nutrients are often examined in isolation[(4)]. Stress to the calcium metabolic system, typified by elevated parathyroid hormone (PTH) levels, may arise from low calcium intake and/or low vitamin D status and has been associated with PE and small-for-gestational age (SGA) birth[(5,6)]. We have previously shown a reduced risk of the combined prevalence of SGA+PE with serum 25-hydroxyvitamin D (25(OH)D) >75 nmol/L in the SCOPE Ireland pregnancy cohort[(7)]. The aim of the current study was to test the concept of calcium metabolic stress in this cohort by exploring associations of vitamin D and PTH with mean arterial pressure (MAP), PE and SGA.

Serum intact PTH was measured in 1714 white, primiparous gravidae at 15 weeks gestation in the SCOPE study by ELISA (MD Biosciences Inc, Minnesota, USA) and serum 25(OH)D was analysed by LC-MS/MS. MAP was calculated as diastolic blood pressure (BP)+[(systolic BP-diastolic BP)/3]; elevated MAP was defined as >90 mmHg. Geometric mean (95 % CI) PTH was 7·8 (7·6, 8·0) pg/mL and mean (SD) 25(OH)D was 57·1 (25·8) nmol/L. Participants were stratified according to PTH and 25(OH)D status. Following exclusion of women >97·5th percentile (to minimise potential confounding from undiagnosed primary hyperparathyroidism), high PTH was defined as >80th percentile.

		Prevalence (%)			
25(OH)D threshold nmol/L	PTH percentile pg/mL	Elevated MAP	SGA	PE	SGA+PE
<30	⩽80	8·3	10·6	5·0	15·0
	>80	19·1	16·0	4·3	18·1
<50	⩽80	8·7	11·5	4·5	14·9
	>80	15·4	11·8	2·6	13·3
⩾75	⩽80	9·7	6·7	1·9	8·6
	>80	8·3	11·7	5·0	15·0

While there were inconsistencies in the prevalence of PE across stratified 25(OH)D/PTH thresholds, the highest prevalence of elevated MAP (19 %), SGA (16 %) and PE+SGA (18 %) was in women with a 25(OH)D <30 nmol/L and PTH >80th percentile. The lowest prevalence of SGA (7 %), PE (2 %) and SGA+PE (9 %) was in participants with 25(OH)D ⩾75 nmol/L and PTH ⩽80th percentile. In conclusion, these results highlight the importance of considering vitamin D status within the broader calcium metabolic system in future explorations of nutrition and perinatal outcomes.

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