OBSERVATIONS

No Difference in Vitamin D Levels Between Children Newly Diagnosed With Type 1 Diabetes and Their Healthy Siblings: A 13-Year Nationwide Danish Study

The causes of the worldwide increase in type 1 diabetes (T1D) in children are still largely unknown. In Denmark, the increase in incidence is steep at 3.4% annually and does not appear to be leveling out (1). Lower levels of 25-hydroxyvitamin D [25(OH)D] have been found in patients with newly diagnosed T1D compared with healthy control subjects, implying that 25(OH)D might play a role in the pathogenesis of T1D (2,3). We aimed to elucidate the possible association between low levels of 25(OH)D and T1D by measuring 25(OH)D levels in children with newly diagnosed T1D and their healthy siblings in Denmark across a 13-year study period (1997–2009).

We included 1,803 children (907 T1D patients and 896 siblings) in the data analyses. The children were aged 0–18 years (mean [SEM] 10.6 [0.13] years for patients and 9.9 [0.12] years for siblings). Of the 1,803 children included, 859 were females and 944 were males. Siblings were matched with the T1D patients for age, sex, month of sampling, and sample year. Blood was sampled within 3 months after onset.

Vitamin D status was measured as serum 25(OH)D by high-performance liquid chromatography, and parathyroid hormone (PTH) level was measured with Siemens Immulite 2000. Table 1 shows the geometric mean and range of 25(OH)D, PTH, and calcium levels.

In the univariate model, 25(OH)D levels were 2.6% (95% CI −3.2 to 8.9%, $P = 0.38$) higher in patients than in siblings, and in the adjusted model, levels were −5.2% (−14.9 to 3.4%, $P = 0.22$) lower in patients. When sample year was forced as a linear variable, there was no sign of a decrease in 25(OH)D per year in patients or siblings, whereas when year was tested as a categorical variable in a joint model of patients and siblings, 25(OH)D varied significantly by year, with the highest levels in 1997 and in 2004–2006 ($P = 0.02$). The PTH levels were not significantly different in patients and siblings in either the univariate analysis (−7.0% [−15.0 to 1.8%], $P = 0.12$) or the adjusted model (−5.3% [−13.5 to 3.7%], $P = 0.24$).

The present findings are somewhat contradictory to previous studies of 25(OH)D levels in patients with newly onset T1D (2,3) and years after (4). In contrast with other studies, we compared patients with siblings as a way to eliminate genetic confounding but which could result in overmatching on environmental factors (e.g., exposure to sunlight, vitamin supplementation, and exercise). The present study is larger than prior studies, where 25(OH)D levels were found to be 15–43% lower in patients (2–4). PTH is a valuable indicator of vitamin D status, and because PTH levels mirrored 25(OH)D levels in both patients and siblings, it supports the main finding.

In summary, the results show year-to-year variation in 25(OH)D levels, probably as a result of change in the "hours of bright sunshine" (5), and no association between 25(OH)D levels and T1D around onset in children and adolescents. The role of 25(OH)D levels in utero or in early childhood and a later risk for developing T1D needs further investigation.

Table 1—*Association between 25(OH)D, PTH, and total calcium levels and case subject status by sex*

		Sibling		Patient	
	All (n = 1,803)	Female (n = 423)	Male (n = 473)	Female (n = 436)	Male (n = 471)
Age (years)	10.26 (0.09)	10.58 (0.19)	10.71 (0.18)	9.42 (0.18)	10.29 (0.17)
25(OH)D (nmol/L)	57.77	58.00	54.02	57.00	61.82
Q1; Q3	37.07; 86.64	36.99; 89.00	36.17; 80.65	37.16; 85.00	38.25; 90.75
PTH (pmol/L)	0.73	0.82	0.74	0.75	0.64
Q1; Q3	0.16; 1.51	0.16; 1.61	0.16; 1.51	0.16; 1.41	0.16; 1.47
Calcium (mmol/L)	2.54	2.49	2.52	2.56	2.57
Q1; Q3	2.40; 2.66	2.29; 2.64	2.36; 2.64	2.47; 2.68	2.43; 2.68

Data are mean (SEM) or median unless otherwise indicated.

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