Marked vitamin D deficiency in patients with diabetes in the UK

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pretreatment levels after approximately 1.5 years. Puberty is usually associated with deterioration in glycaemic control, but age was not a significant determinant of the changes seen. Differences in glycaemic control and the pattern observed between centres that cover areas with a similar socio-economic background suggest that the approach of the local diabetes team is of great importance. It is of note that the number of patients in some contributing units was relatively small.

Few studies have investigated the longer-term effects of insulin pump use in young people. The initial improvements in HbA_{1c} described are generally modest, with some groups also reporting a return to baseline HbA_{1c} values [3]. No study to date has used a robust method of modelling repeated measurements and hence their estimates of effectiveness may be subject to bias [4].

The limitations of our study include the retrospective nature of the data collected and that we only measured HbA_{1c} which, it can be argued, is only part of what continuous subcutaneous insulin infusion has to offer. Other potential benefits include an improved quality of life and a reduction in hypoglycaemia. It is of note that the patients in this study had a broad range of HbA_{1c} values at baseline and National Institute of Health and Clinical Excellence (NICE) guidelines may not have been rigorously adhered to.

These data underline the need for well-designed, prospective, randomized trials of continuous subcutaneous insulin infusion therapy in children, so that the true impact and cost-effectiveness can be determined.

Competing interests

Nothing to declare.

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Marked vitamin D deficiency in patients with diabetes in the UK: ethnic and seasonal differences and an association with dyslipidaemia

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At least 1 billion people worldwide have vitamin D deficiency [1]. Whilst levels of 25-hydroxyvitamin D [25(OH)D] ≥ 30 ng/ml are considered optimal for bone health [2], the levels in diabetes and cardiovascular disease, which have also been linked to vitamin D deficiency, are not established [3].

We assessed the 25(OH)D status in a cross-sectional study of 563 unselected subjects with diabetes and 44 subjects without diabetes to establish the prevalence of vitamin D deficiency and its association with ethnicity, season, lipids and cardiovascular disease.

Ethical approval was not required as the data were extracted retrospectively and did not extend beyond the standard clinical practice of a biannual diabetes clinic review. All participants were aged ≥ 18 years old and attended clinics at the Central Manchester Foundation Trust, Manchester, UK, from August 2009 to July 2010. Subjects with chronic kidney disease stages 4 and 5, granulomatous diseases and malabsorption syndromes were excluded.

Clinical demographic data were analysed from medical records and a medical record database (Diamond database; Hicom, Woking, UK). Serum for 25(OH)D was stored at -20°C and assayed using an automated platform (Immuno-Diagnostic Systems Ltd, Bolden, UK) based on chemiluminescence technology.

Data were assessed for normality and appropriate statistical analyses were employed using Statsdirect (Statsdirect Ltd, Altrincham, UK). A P -value of < 0.05 was considered to be statistically significant and was maintained in multiple comparison tests. All values are presented as mean $\pm$ standard deviation (SD).

The mean serum 25(OH)D concentration was 15.7 ± 9.1 ng/ml in subjects with diabetes and 21.3 ± 14.6 ng/ml in subjects without diabetes, although the latter cohort was significantly smaller. The two cohorts were matched for age (59.7 ± 13.3 vs. 58.1 ± 15.6 years) and ethnicity (59 vs. 61% white European).

Table 1 Characteristics by categories of 25(OH)D in 563 unselected subjects with diabetes

	Serum 25(OH)D				P-value
	Category 1	Category 2	Category 3	Category 4	
25(OH)D status	< 10 ng/ml	10 to < 20 ng/ml	20 to < 30 ng/ml	≥ 30 ng/ml	—
<i>n</i> (%)	179 (32)	233 (41)	99 (18)	52 (9)	< 0.0001
Men (%)	53	57	48	48	NS
Type 2 diabetes (%)	85	75	69	52	< 0.0001
% free of cardiovascular events	79	80	77	84	NS
Age (years)	58.8 ± 13.7	59.6 ± 13.5	61.0 ± 12.4	60.2 ± 13.0	NS
Duration of diabetes (years)	15.4 ± 9.4	17.9 ± 11.9	19.1 ± 11.1	22.3 ± 15.1	0.03
BMI (kg/m ²)	31.2 ± 6.5	30.5 ± 6.4	31.5 ± 7.0	29.1 ± 6.4	NS
Systolic blood pressure (mmHg)	129 ± 17	129 ± 16	133 ± 18	131 ± 17	NS
Diastolic blood pressure (mmHg)	69 ± 10	70 ± 9	69 ± 9	71 ± 11	NS
HbA _{1c} (mmol/mol)	69 ± 24	68 ± 20	66 ± 17	73 ± 21	NS
(%)	8.6 ± 1.9	8.4 ± 1.7	8.2 ± 1.5	8.8 ± 1.9	
Total cholesterol (mmol/l)	4.2 ± 1.3	4.1 ± 1.2	4.2 ± 0.9	4.5 ± 1.6	NS
HDL cholesterol (mmol/l)	1.3 ± 0.7	1.3 ± 0.4	1.4 ± 0.5	1.6 ± 0.6	0.003
Triglycerides (mmol/l)	2.2 ± 2.8	1.7 ± 1.5	1.5 ± 0.9	1.6 ± 1.3	0.04

Data are presented as mean ± SD unless specified as %.
25(OH)D, 25-hydroxyvitamin D; NS, not significant.

Subjects were divided into four categories of 25(OH)D levels (Table 1). Our data confirm widespread vitamin D deficiency among people with diabetes in the UK; 511 (91%) subjects had vitamin D insufficiency (< 30 ng/ml), with severe (< 10 ng/ml) deficiency in 179 (32%) individuals, and in over half (54%) of South Asian/Middle Eastern subjects. Despite deficiency in vitamin D there were no significant alterations in either alkaline phosphatase (ALP) or corrected calcium. These data argue against guidance suggesting that we only test those with symptoms of osteomalacia or altered calcium or ALP levels. This highlights the need for routine testing of vitamin D status and the subsequent treatment with vitamin D3.

There were significant differences in HDL cholesterol ($P = 0.003$) and triglycerides ($P = 0.04$) between categories. However, after adjusting for BMI, season, ethnicity and lipid medication use, regression analyses remained significant only with HDL cholesterol ($r = 0.12$, $P = 0.006$), although the clinical significance of this may be questionable.

7-Dehydrocholesterol is a precursor for both cholesterol and vitamin D, providing a potential mechanistic link between vitamin D and cardiovascular disease [4], although there was no association of 25(OH)D levels with manifest cardiovascular disease.

South Asian/Middle Eastern subjects ($n = 179$) had significantly lower levels of 25(OH)D (11.3 ± 9.6 ng/ml) compared with white Europeans ($n = 334$) (18.0 ± 7.0 ng/ml), Afro-Caribbean ($n = 32$) (16.4 ± 7.8 ng/ml) and Far East Asian groups ($n = 18$) (14.5 ± 4.5 ng/ml) ($P < 0.0001$). There was a clinically questionable but statistically significant seasonal variation in the 25(OH)D status in the white European group [spring (17.2 ± 9.9 ng/ml) vs. summer (20.1 ± 8.8 ng/ml) vs. autumn (17.8 ± 9.9 ng/ml) vs. winter (16.0 ± 6.1 ng/ml), ($P = 0.009$)], which was absent in the South Asian/Middle

Eastern group [spring (10.6 ± 6.1 ng/ml) vs. summer (11.0 ± 5.5 ng/ml) vs. autumn (10.9 ± 6.8 ng/ml) vs. winter (12.5 ± 8.9 ng/ml)]. Seasonal variation in vitamin D levels are often cited as reasons for overestimation of vitamin D deficiency, yet in the present study a minimal difference of only 4.1 ng/ml was observed in white Europeans, and even this small variation was absent in South Asian/Middle Eastern subjects.

In conclusion, we demonstrate widespread vitamin D deficiency among people with diabetes in the UK. Whether supplementation will benefit glycaemic control [5] and lower cardiovascular risk is not known [3], particularly as the limited interventional studies have failed to conclusively show improvements in metabolic control. However, randomized placebo controlled trials are underway (<http://www.vital-study.org/>) of vitamin D supplementation assessing cardiovascular outcomes as primary endpoints; the results are eagerly awaited.

Competing interests

Nothing to declare.

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