Low bone mineral density is associated to poor glycemic control and increased dickkopf-1 (DKK-1) serum levels in children and adolescents with type 1 diabetes

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The authors disclose any conflict of interest

BACKGROUND

Decreased bone mineral density (BMD) and increased fracture risk have consistently been observed in type 1 diabetes mellitus (TIDM). The influence of TIDM on BMD seems to depend on gender or age of patients and to occur early after TIDM diagnosis. The mechanisms of decreased BMD in TIDM patients are still unknown. Dickkopf-1 (DKK-1) is a Wnt signaling inhibitor which decreases bone formation and increases bone resorption (fig. 1), thus it strongly affects BMD in murine models and human diseases.

OBJECTIVE AND HYPOTHESES

We aimed to investigate the serum levels of DKK-1 in TIDM children and adolescents and to evaluate the relationship with glycemic control, BMD and bone biomarkers.

METHODS

This cross-sectional study included 53 TIDM children and adolescents (mean age 12.1 ± 3.3 years) and 50 sex and age-matched controls (Table 1). Phosphorus, calcium, osteocalcin, alkaline phosphatase (ALP), PTH and 25(OH)-Vitamin D values were determined. DKK-1 was measured in the sera of TIDM patients and controls by ELISA. Bone mineral status was measured by Quantitative ultrasonography (QUS), and reported as AdSos-Z-score and BTT-Z-score.

RESULTS

TIDM patients showed a lower BMD than controls (p<0.01) (Fig. 2). Higher DKK-1 levels were found in patients than in controls (3344±961 vs 2450±684 pg/ml, p<0.001) (Fig. 3). The DKK-1 levels directly correlated with HbA1c values (r=0.353, p=0.01) (Fig. 4A) and inversely with AdSos-Z-score (r=0.201, p<0.0001) (Fig. 4B). Furthermore, with adjustment for age, HbA1c inversely correlated with BTT-Z-score, AdSos-Z-score, osteocalcin, 25(OH)-Vitamin D (Fig. 5) and ALP (r=-0.35, p<0.0001), as well as directly correlated with daily insulin dosage (r=0.32, p=0.01) and TIDM duration (r=0.22, p<0.01). Multiple regression analysis showed that DKK-1 serum levels were best predicted by AdSos-Z-score, ALP, 25(OH)-vitamin D and HbA1c (r=0.61, p<0.0001) (Table 2).

CONCLUSIONS

In conclusion, children and adolescents with TIDM showed a reduction of bone mineral status associated to poor glycemic control and increased DKK-1 serum levels.