URINARY VITAMIN D-BINDING PROTEIN EXCRETION IN CHILDREN WITH DIABETES MELLITUS TYPE 1

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Introduction

The main function of Vitamin D binding protein (VDBP) is to transport vitamin D metabolites through the circulation. VDBP is filtered by the glomerulus and subsequently reabsorbed by proximal tubular cells through receptor-mediated uptake. This process is energy-consuming, tubular injury would be expected to result in urinary VDBP (uVDBP) loss. Experimental studies have shown that uVDBP may be a novel urinary biomarker of tubulointerstitial damage. These data need to be confirmed in clinical research.

Objective

To assess the relation between uVDBP and established tubular damage markers in children with type 1 diabetes.

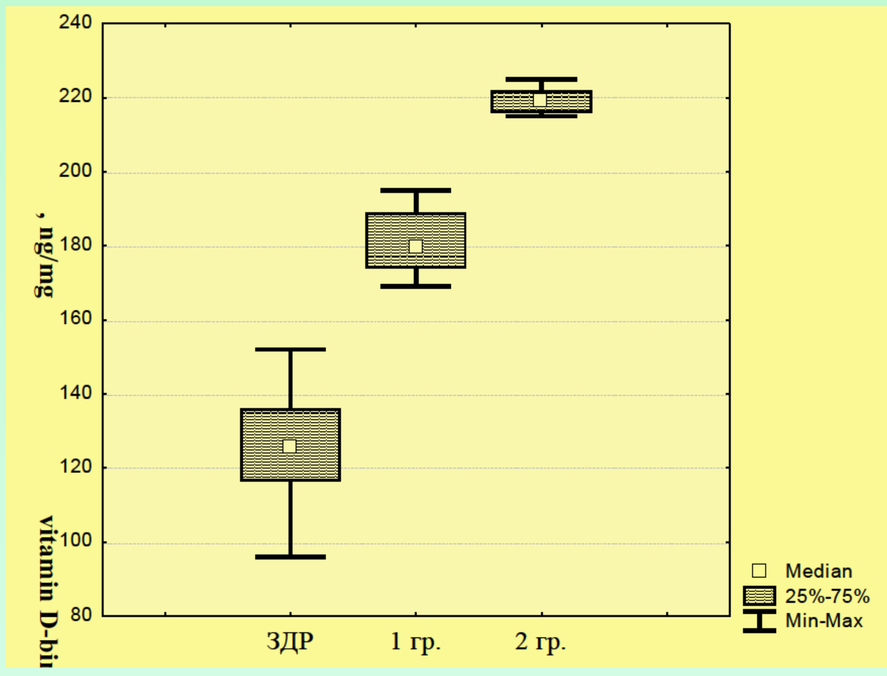
Material and Methods

42 children aged 6 to 17 years suffering from type 1 diabetes (T1D) were examined, among them 24 nornoalbuminuric patients (1st group) and 18 microalbuminuric (2nd group). 15 healthy children were included in control group. uVDBP was measured with a commercially available sandwich ELISA (Immundiagnostik, catalog # K2314, Bensheim, Germany), according to the manufacturer's instructions. The established proximal tubular damage markers kidney beta-2-microglobulin (uB2M) and alanine aminopeptidase (uAAP) were determined in urine. The levels of uB2M were measured by indirect solid phase enzyme immunometric assay (ELISA, ORG 5BM, ORGENTEC DIAGNOSTIKA Gmbh, Mainz, Germany). uAAP activity was determined by the colorimetric reaction (wave length 405 nm) on the hydrolysis of L-alanine 4-nitroanilide. Statistical analyses were performed with StatSoft STATISTICA Version 8 (Tulsa, OK). Non-parametric variables are given as median (interquartile range). Differences between groups were tested using Mann-Whitney test. Multivariate regression modeling was performed to address the association between uVDBP and parameters of tubulointerstitial damage and diabetic course. The clinical studies from which materials were obtained for the current study were approved by the Medical Ethics Committee of the Kharkiv National Medical University and conducted in accordance with the guidelines of the Declaration of Helsinki. All participants and their parents gave written informed consent.

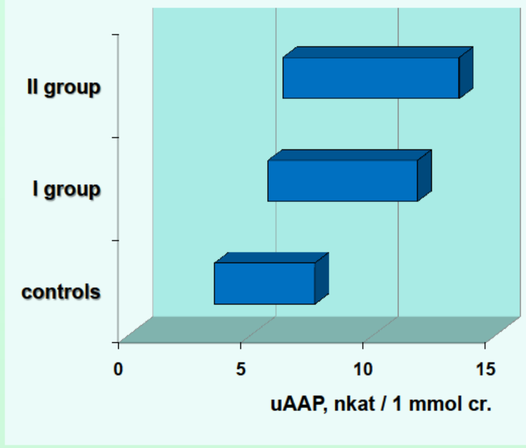
Results

uVDBP levels were significantly elevated in the patients of the 1st and 2nd groups, compared with control group ((179.5 (174.0; 189.0) and 219.0 (216.0; 222.0), compared with 125.0 (116.5;136.0) ng/mg, respectively) ($P<0.001$)). A marked increase in the uVDBP excretion was apparent in subjects with microalbuminuria, compared with normoalbuminuric diabetic patients ($P<0.001$). Using multivariate regression modeling, significant correlates of uVDBP excretion included microalbuminuria ($P = 0.004$), glycosylated hemoglobin ($P = 0.010$), uB2M ($P = 0.007$), and uAAP ($P = 0.037$).

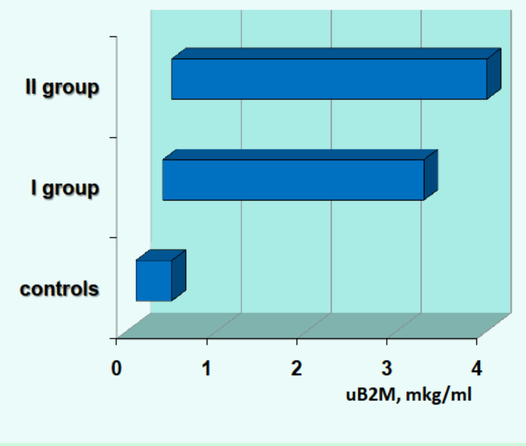
Levels of Vitamin D binding protein in urine at investigated children



Activities of alanine aminopeptidase in urine at investigated children



Levels of beta-2-microglobulin in urine at investigated children



Conclusions

Children with TD1 exhibit altered catabolism and concentrations of uVDBP. There is an important impact of their underlying disease. The level of uVDBP increased with increasing severity of renal damage. uVDBP excretion is increased early after renal injury, and is associated with tubulointerstitial damage.

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