PP504

THE SERUM LEVELS OF CARBOXYLATED AND UNDERCARBOXYLATED OSTEOCALCIN IN CHILDREN WITH CYSTIC FIBROSIS

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Introduction

Osteocalcin (OC) is a noncollagenous protein of bone matrix produced by osteoblasts that plays an important role in bone metabolism. In its carboxylated form (c-OC) osteocalcin binds to hydroxyapatite in bone and plays a regulatory role in bone formation and mineralization. In contrast, undercarboxylated OC (uc-OC) binds less effectively to hydroxyapatite and hence a significant association has been found between fracture incidence and uc-OC in elderly subjects. Undercarboxylated OC is recognized as a functional marker of vitamin K status. Deficiency in vitamin K, observed in subjects with cystic fibrosis (CF) may play an important role in bone pathology of these patients.

The aim of this study was to assess the serum levels of total osteocalcin as well as carboxylated and undercarboxylated forms of osteocalcin in children with cystic fibrosis.

Materials and Methods

The study included 25 children with CF and 25 healthy controls aged 5-9 years. The diagnosis of cystic fibrosis was done on clinical findings, positive sweat chloride test (>60mEq/L) and gene mutation analysis. No studied patients were treated with corticosteroids during the study. All CF children, except one were pancreatic insufficient and were taking pancreatic enzyme supplements (6000 U lipase/kg/day). They were on unrestricted high caloric diet in accordance with the standard recommendations for cystic fibrosis care. Anthropometric parameters (weight, height) were performed for all children and body mass index (BMI) was calculated. The severity of CF disease was evaluated by the Shwachman-Kulczycki (S-K) scoring system. Pulmonary function was assessed by spirometric measurements (including Forced Expiratory Volume in one second - FEV_1), which were performed during routine check-up visits at three to six month intervals.

Concentrations of calcium, phosphate and 25-hydroxyvitamin D were measured in serum by standard methods. Serum levels of bone metabolism markers were determined using immunoenzymatic ELISA assays. Concentrations of BALP were measured using kit from Quidel (USA), total OC and CTX - kits from IDS (UK), cOC and ucOC - kits from Takara (Japan). Statistical analyses were performed using the Statistica software program, version 10.0 PL.

Results

- There were no significant differences regarding age, gender, weight, height and BMI between the cystic fibrosis and control groups. Our patients were in clinically stable condition without recent acute pulmonary infections. According to the clinical Shwachman-Kulczycki score they had mild/moderate disease severity (Table 1).
- Mean serum calcium and phosphate levels were within normal range in both studied groups, but the concentration of 25-hydroxyvitamin D was significantly lower in patients with CF compared to the control children ($p<0.05$). Children with CF had significantly higher activity of BALP and slight increased concentration of CTX than in healthy ones (Table 2).
- Despite the similar total osteocalcin levels, we observed lower carboxylated form of osteocalcin and higher undercarboxylated osteocalcin concentrations in CF patients as compared to the controls (Fig. 1). Hence, the ratio of ucOC/cOC was significantly higher in children with CF than in the healthy children ($p<0.05$) (Fig 2).

Conclusions

- In patients with cystic fibrosis an imbalance between bone formation and resorption processes can be present from the early stages of life, even in prepubertal period.
- Decrease in concentration of cOC and increase in ucOC may relate to vitamin K deficiency and lead to abnormal bone formation in these patients.
- A careful follow up on bone status, including periodic measurement of bone turnover markers is required to prevent osteopenia and osteoporosis in patients with cystic fibrosis.

Table 1.
Clinical, anthropometric and genetic characteristics of cystic fibrosis patients and healthy children

	Cystic fibrosis group	Control group
n	25	25
Gender (F/M)	13/12	12/13
Age (years)	7.0 ± 1.6	7.1 ± 1.9
Body weight (kg)	22.2 ± 5.4	24.8 ± 6.3
Body height (cm)	122.4 ± 10.8	125.8 ± 11.9
BMI (kg/m^2)	14.9 ± 1.3	15.7 ± 1.6
CF genotype		
ΔF508 homozygote *n* (%)	15 (60%)	
ΔF508 heterozygote *n* (%)	8 (32%)	
Non ΔF508 mutation *n* (%)	2 (8%)	
Pancreatic insufficiency *n* (%)	24 (96%)	
Shwachman-Kulczycki clinical score	87.4 ± 6.9	
FEV_1 (%)	88.9 ± 11.9	

Data are presented as mean values ± SD; BMI - body mass index; FEV_1 - forced expiratory volume in 1 s

Fig. 1.
Serum concentrations of total osteocalcin and its carboxylated and undercarboxylated forms in patients with cystic fibrosis and in control children.

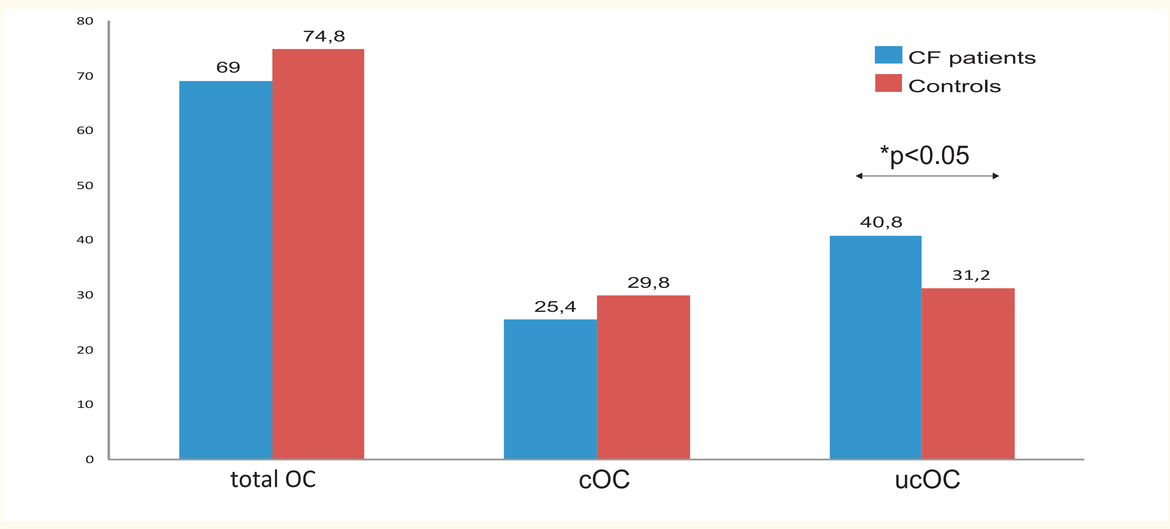
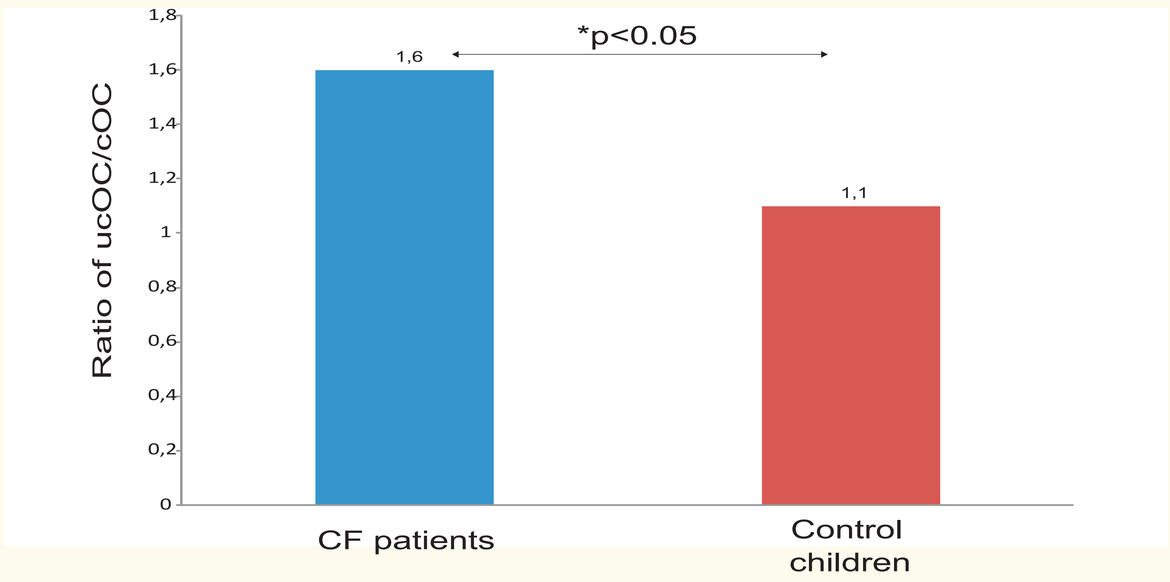


Table 2.
Serum fat soluble vitamins and bone metabolism parameters in CF and healthy children

	Children with CF	Healthy children	P value
Calcium (mmol/l)	2.39 ± 0.12	2.44 ± 0.13	0.1548
Phosphate (mmol/l)	1.54 ± 0.17	1.50 ± 0.12	0.3004
25OH vitamin D (ng/ml)	21.9 ± 7.3	28.3 ± 7.6	**0.0412***
BALP (U/L)	158.9 ± 26.1	130.8 ± 27.0	**0.0065***
CTX (ng/ml)	1.816 ± 0.599	1.680 ± 0.528	0.3202

Data are presented as mean values ± SD; *Statistically significant

Fig.2.
The ratio of ucOC/cOC in patients with cystic fibrosis and in control children.



Conflict of Interest
The authors have stated that they have no conflict of interest.