CARDIO-RENOPROTECTIVE EFFECTS, INCLUDING IMPACT ON FGF-23 AND sKLOTHO, OF PROTEIN RESTRICTION DIET SUPPLEMENTED BY ESSENTIAL AMINO ACIDS KETOANALOGS, IN CKD 3B-4 STAGES RUSSIAN PATIENTS

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OBJECTIVES: The aim of the study was to evaluate the effects of low protein diet (LPD) supplemented by essential amino acids ketoanalogs (KA) on serum FGF-23 and Klotho (sKlotho) in CKD.

***METHODS*:** A total of 51 non-diabetic patients in stage 3B-4 CKD were included in the study. The cohort was divided into 2 groups depending on the diet type. The group 1 patients (n=25) got LPD-0.6 grams/kg of body weight/day and KA (Ketosteril) 1 pill /5 kg of weight/day during 14 study months; the group 2 (n=26) matched to the 1st group, took LPD without KA. In addition to routine lab tests, FGF-23 (Human Fibroblast Growth Factor-23 (FGF-23) ELISA, using monoclonal antibodies to the native human FGF-23 molecule, Merk Millipore), alpha - Klotho (Human soluble alpha-Klotho Assay, IBL-Takara), phosphorus, total calcium, parathyroid hormone (PTH) serum levels, as well as eGFR, were examined. Bioimpedance analysis, echocardiography (the valvular calcification score (VCS) and LVMMI) and sphygmography by "Sphygmacor" device (stiffness (augmentation) indices (AI), were hold.

RESULTS: A muscle body mass decrease in men (p=0.027) and women (p=0.044) was observed in the LPD alone group to the end of the study (14th month) – Tabl.1. In addition, lower sFGF-23 (p=0.029) and higher sKlotho (p=0.037) were detected in the LPD+KA group compared to the LPD one – Tabl.2, Fig.1. The increase of AI (p=0.034**)**, VCS (p=0.049), and LVMMI (14.3% vs 67.6 %) values were observed more often in the LPD group as compared to the LPD+KA group – Tabl.3. In addition, the average eGFR some higher (p=0.047) was obtained at the end of study in the LPD+KA group (Table 1, Fig.2). The statistically significant decreasing of serum total protein level (from 76.2 to 65.6 and transpherin (3.0 to 2.1) were in the 2-nd group, while average values of serum albumin levels remained in normal range in both groups. Serum phosphate (p=0.037) and PTH (p=0.042) were higher in 2-nd group at the end of study, which increased the need for phosphate binders and vitamin D use (Table 2, Fig.1, Tabl.4).

Table 1

Determinant		Group 1 LPD+KA (n=25)	Group 2 LPD (n=26)	P Value
eGFR (ml/min/1,73m²)	baseline	35.1 (19.8.6-43.4)	34.9 (20.1-44.1)	0.571
	end of study	29.1 (16.6-40.1)	26.6 (14.7-39.9)	**0.047**
Mean central systolic BP (mm/Hg)	baseline	113.0 (109.5-128.0)	111.0(107.0-129.5)	0.632
	end of study	118.0 (115.0-133.3)	131.0 (117.5-146.5)	**0.049**
Body mass index (kg/m²)	baseline	24.4 (23.2-25.4)	24.9 (23.4-25.6)	0.783
	end of study	24.2 (23.0-25.1)	19.6 (19.1-21.9)	**0.046**
Muscle body mass, %	baseline	M 35.1 (33.4-38.9) F 27.2 (25.1-29.4)	M 35.4 (33.5-39.1) F 26.9 (24.9-29.7)	0.821 0.792
	end of study	M 35.4 (33.7-39.0) F 26.9 (24.8-29.2)	M 27.9 (26.2-31.9) F 20.1 (19.0-24.6)	**0.027** **0.044**

Table 2

Determinant *Laboratory values*		Group 1 LPD+KA (n=25)	Group 2 LPD (n=26)	P Value
Serum phosphorus (mmol/l)	baseline	1.41 (1.21-1.55)	1.39 (1.2-1.58)	0.824
	end of study	1.24 (1.22-1.57)	1.55 (1.39-1.87)	**0.037**
Calcium total (mmol/l)	baseline	2.27 (2.19-2.37)	2.29 (2.21-2.36)	0.713
	end of study	2.42 (2.28-2.51)	2.12 (1.9-2.42)	**0.041**
Albumin (g/l)	baseline	38.48 (36.7-40.1)	39.43 (36.9-40.2)	0.911
	end of study	37.97 (36.4-38.9)	36.10 (35.9-37.7)	0.482
Total protein (g/l)	baseline	76.6 (74.9-83.4)	77.3 (75.6-84.1)	0.893
	end of study	76.2 (74.4-82.7)	65.6 (63.8-77.8)	**0.039**
Transpherin (g/l)	baseline	3.1 (2.8-3.6)	3.0 (2.7-3.6)	0.983
	end of study	3.0 (2.4-3.4)	2.1 (1.9-2.5)	**0.048**
Parathyroid hormone (pg/ml)	baseline	67.0 (39.0-115.6)	69.0 (55.5-127.6)	0.631
	end of study	75.0 (45.6-132.4)	120.0 (78.0-295.0)	**0.042**
FGF-23 (pg/ml)	baseline	97.0 (67.0-360.5)	89.9 (59.0-337.5)	0.648
	end of study	110.3 (78.4-478.5)	422.0 (110.0-792.9)	**0.029**
Klotho (pg/ml)	baseline	409.9 (268.8-537.6)	413.2 (271.1-544.3)	0.914
	end of study	402.1 (261.3-522.2)	201.2 (174.1-294.7)	**0.037**

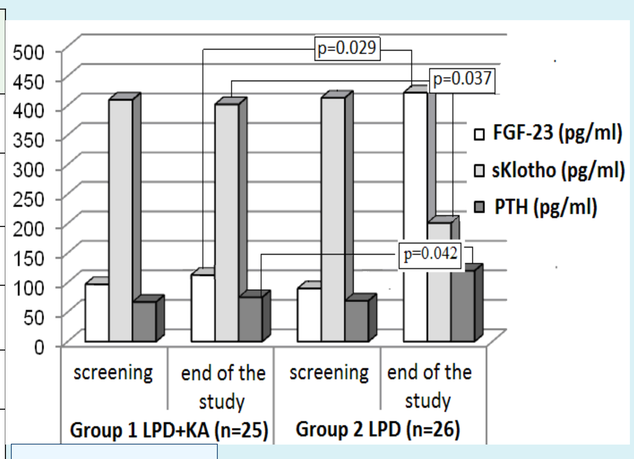

Figure 1

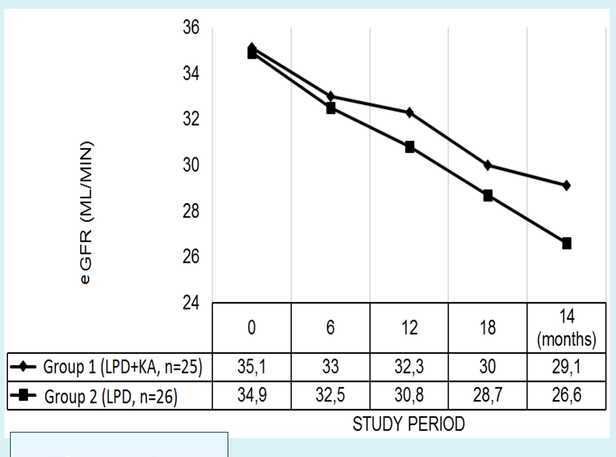

Figure 2

Table 4

Parameter *Medications (patients, %)*		Group 1 LPD+KA (n=25)	Group 2 LPD (n=26)	P Value
Antihypertensive drugs, n (%)	baseline	21 (83.3)	22 (84.0)	0.571
	end of study	22 (88.0)	26 (100)	0.051
Phosphorus binders, n (%)	baseline	4 (16.2)	4 (16.4)	0.944
	end of study	5 (21.4)	11 (43.2)	**0.034**
Ca contained PB, n (%)	baseline	1 (4.7)	1 (5.4)	0.673
	end of study	1 (4.7)	2 (8.1)	0.072
Vitamin D therapy (n, %)	baseline	6 (23.8)	6 (24.3)	0.920
	end of study	10 (40.0)	18 (69.2)	0.053

Table 3

Determinant		Group 1 LPD+KA (n=25)	Group 2 LPD (n=26)	P value
Augmen-tation Index, %	baseline	19.7 (16.0-25.00)	19.4 (15.4-25.00)	0.734
	end of study	21.2 (17.5-27.00)	29.9 (19.5-36.9)	**0.034**
Cardiac (valvular) calcification score, (patients) (%)				
«0 points»	baseline	5 (20.0)	6 (23.0)	0.68
	end of study	4 (16.0)	0 (0)	**0.049**
«0.5-1 points»	baseline	18 (72.0)	17(65.4)	0.47
	end of study	18 (72.0)	23 (88.5)	0.086
«1.5> points»	baseline	2 (8.0)	2 (7.7)	0.89
	end of study	3 (12.0)	5 (19.2)	0.51
Increasing of LVMMI, n (%) to the end of study		4 (14.3)	18 (67.6)	**0.020**

***CONCLUSIONS*:** The LPD+KA diet not only supports the nutrition status, but also contributes to more efficient correction of sFGF-23 and sKlotho abnormalities that may result in decreasing of cardiovascular calcification and cardiac remodeling in stage 3B-4 CKD patients.

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