IMPACT OF VITAMIN D RECEPTOR ACTIVATORS ON CARDIOVASCULAR RISK MARKER – KLOTHO IN CHRONIC KIDNEY DISEASE PATIENTS.

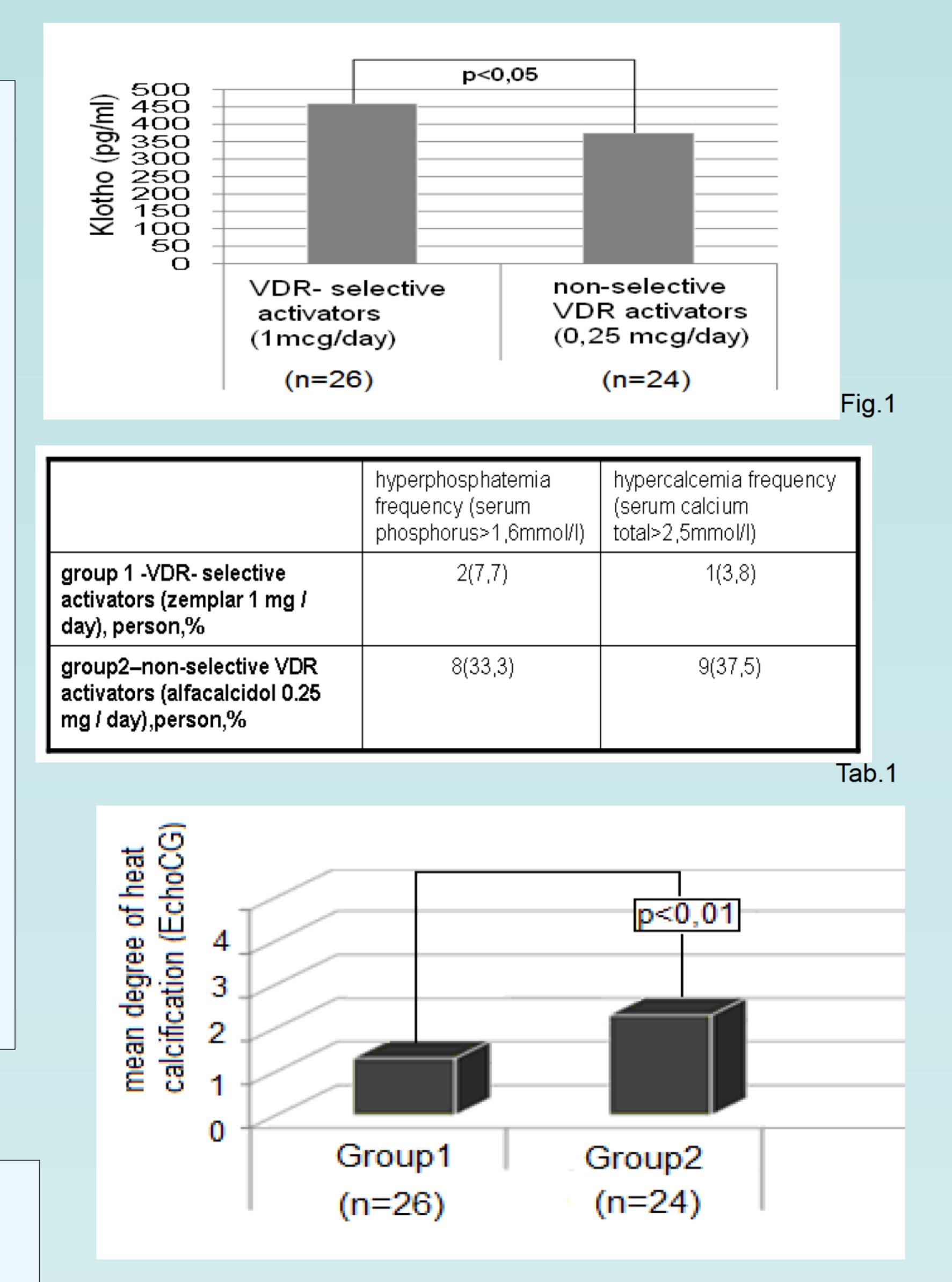
<u>Authors</u>: Kozlovskaya L., Milovanova L.Y., Dobrosmislov I.A. (<u>contact - Ludm.milovanova@gmail.com</u>)

<u>Institution:</u> I.M. Sechenov First Moscow State Medical University, Clinic of Nephrology, Internal and Occupational diseases, *Russia*

OBJECTIVES:. The aim of the study was to evaluate the impact of vitamin D receptor activators on cardiovascular risk marker - *Klotho* in CKD nondiabetic patients stage 3B-4

MATERIALS AND METHODS: The main group consisted of 50 CKD stage 3B-4 patients. In addition to standard clinical examination all patients were studied serum levels of parathyroid hormone (PTH), calcium total, phosphorus. ELISA was used for serum *Klotho* (Human alpha-KI ELISA kit with using anti-Klotho antibodies). Blood pressure (BP) including brachial and central (aortic) pressure were measured to all the patients, as well as Pulse Wave Velocity (PWV) with a Sphygmokor device (Australia), ECG, EchoCG, X-ray of the abdominal aorta in lateral projection (Kauppila method) were

RESULTS: Study included 50 CKD patients 3B - 4 stages who had elevated levels of PTH at screening time. From them, 26 patients – Group 1- started to treat with the selective activators of vitamin D receptor- VDR- selective activators (zemplar 1 mg / day), and 24 patients–Group2– started to treat with non-selective VDR activators (alfacalcidol 0.25 mg / day). After a year, we evaluated the results of the treatment. In patients who managed to achieve and maintain a target level of PTH in serum, higher rates of *Klotho* were marked. Patients, used selective VDR activators, had serum *Klotho* decreased and CKD progression less significant than patients treated with non-selective VDR activators [p<0,05; p<0,05] in



the same doses(Fig.1).

In addition, patients treated with alfacalcidol more than 6 months, more often observed hypercalcemia and hyperphosphatemia (2 vs 8 and 1 vs 9)- (Tabl.1).

Moreover, in Group 2 the degree of calcification of the heart and vessels was greater (p <0.01) according to the EchoCG (assessed by semiquantitative scale)-(Fig.2) and X-ray of the abdominal aorta (method Kauppila).

CONCLUSION: In patients with CKD, who managed to achieve and maintain a target level of PTH in serum, higher levels of serum Klotho was marked. Use of

selective VDR activators was associated with higher frequency achieve target values of PTH levels in serum and higher Klotho levels than the use of non-selective VDR activators.

The study showed the possibility of Klotho practical use as an early diagnostic markers of cardiovascular risk and that adequate correction of its changes including of parathyroid hormone overproduction therapy in predialysis CKD can reduce the risk of cardiovascular complications and increase the survival of CKD patients in general. Fig.2

REFERENCE: 1. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. KDIGO clinical practice guideline for the diagnosis, evolution, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). *Kidney Int*. 2009; 76 (Suppl.113): 1-130. 2. J. Donate-Correa, E. Martín-Núñez, C. Mora-Fernández et al. Klotho in cardiovascular disease: Current and future perspectives World J Biol Chem. 2015 Nov 26; 6(4): 351– 357.

doi: <u>10.4331/wjbc.v6.i4.351</u>

This work was supported by the Russian Science Foundation (grant № 14-15-00947 2014)

