ACUTE PARICALCITOL ADMINISTRATION REDUCE INFLAMMATION IN CKD PATIENTS *IN VIVO* AND *IN VITRO*

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Objectives:

Micro-inflammation state is a pathologic feature of chronic kidney diseases (CKD).
Recent evidence suggests that vitamin D deficiency, common in CKD patients, has a role in the modulation of immune response and inflammation.(1) Evidence is also mounting that Paricalcitol, a synthetic vitamin D analogue, is renoprotective in different inflammatory nephropathies.(2-3)
Neutrophil gelatinase-associated lipocalin (NGAL), a protein with a key role in the innate immune response, is upregulated in presence of inflammation.
The aim of our study was to evaluate the anti-inflammatory action in acute of Paricalcitol in CKD patients *in vivo* and *in vitro*.

Methods:

The study was conducted on 40 patients with IV-V stage of CKD (20 males and 20 females) and a control group (HS). We measured serum levels of calcium (Ca), phosphorous (P), vitamin D, parathyroid hormone (PTH), erythrocyte sedimentation rate (ESR), high-sensitivity C-reactive protein (hsCRP), interleukin-17 (IL-17), interleukin-1beta (IL-1β), interferon-gamma (IFN-γ), tumour necrosis factor-alpha (TNF-α) and plasmatic and urinary NGAL before and after 24 hours of an intravenous bolus of Paricalcitol 5 mcg. *Human peripheral blood mononuclear cells* were isolated and stimulated with phytohaemagglutinin. In the culture medium we measured: NGAL, IL-1β, IL-17, TNF-α and IFN-γ. Albuminuria and proteinuria were also measured.

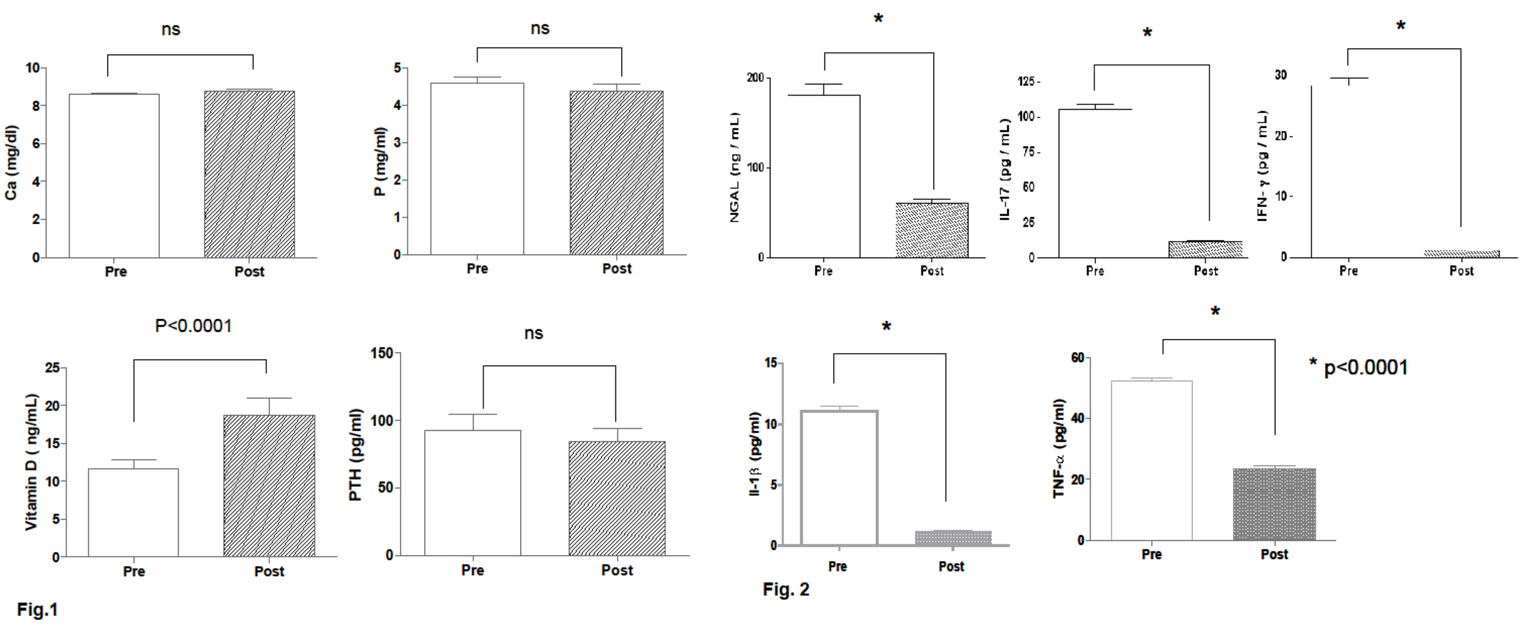

Fig.1

Fig. 2

Univariate and multiple regression analysis of NGAL in CKD patients

In vivo

Variable	Partial R	β	P-value
ESR	**0.35 (P= 0.02)**	**0.32**	**0.001**
hs-CRP	**0.81 (P<0.0001)**	**0.81**	**<0.0001**
IL-17	**0.64 (P<0.0001)**	**0.32**	**0.006**
IFN-γ	**0.90 (P<0.0001)**	**0.75**	**< 0.0001**
TNF-α	**0.59 (P< 0.0001)**	**0.76**	**< 0.0001**
Il-1β	**0.51 (P =0.0007)**	0.23	0.13

In vitro

Variable	Partial R	β	P-value
ESR	**0.35 (P= 0.02)**	0.75	0.4
hs-CRP	**0.36 (P=0.002)**	0.35	0.3
IL-17	**0.97 (P<0.0001)**	0.41	0.07
TNF-α	**0.96 (P< 0.0001)**	**0.43**	**0.0002**
Il-1β	**0.97 (P<0.0001)**	**0.08**	**0.001**
Vitamin D	**- 0.48 (P =0.001)**	**- 0.28**	**0.001**

Dependent variable: NGAL; β: standardized coefficient of correlation

Fig.3

Results:

Patients with CKD have alterations of Ca/P metabolism. Vitamin D values were significantly lower in these patients than in HS ($p < 0.0001$), while the amounts of inflammatory markers such as cytokines levels were significantly higher ($p<0.0001$). [Figure1]
After Paricalcitol, in CKD patients, there was a significant increase in 25(OH)D levels ($p<0.0001$) associated with a reduction of PTH, but not in a statistically significant way. NGAL and cytokines amounts were significantly down-regulated ($p < 0.0001$) both in *vivo* and *in vitro.* [Figure2]
At univariate analysis, *in vivo* NGAL was found to be directly correlated with ESR, IL-17, INF-γ, IL-1β, TNF-α and hsPCR. *In vitro* NGAL was found to be directly correlated with ESR, hsPCR, IL-17, IL-1β, TNF-α, while an inversion correlation was found with 25(OH)D levels.
No significant correlation was found for albuminuria, proteinuria, PTH, Ca or P.
In a multivariate model using NGAL as a dependent variable, i*n vivo* significance was maintained for the correlation between NGAL and ESR, hsCRP, IL-17, and IFN-γ, and TNF-α.
In vitro significance was maintained for NGAL and Vit D, IL-1β and TNF-α. [Figure3]

Conclusions:

Studies have shown an involvement of Paricalcitol in the regulation of immune and inflammatory processes. These effects appear to be mediated by non-PTH mechanisms. Paricalcitol can be used for anty-inflammatory therapeutic purposes.

References:

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