

INFLAMMATORY and OXIDATIVE STRESS MARKERS in HEMODIALYSIS PATIENTS with PERMANENT SUBCUTANEOUS CATHETER. EFFECT of PARICALCITOL and ATORVASTATIN COMBINED TREATMENT.

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INTRODUCTION AND AIMS:

Cardiovascular disease remains the most common cause of morbidity and mortality in CKD patients related to oxidative stress, inflammation and endothelial dysfunction. In addition, Permanent Subcutaneous Catheter (PSC) is an inflammatory stimulus in these patients. The aim of the current study was to evaluate the effect of different oral treatments, paricalcitol (P), paricalcitol plus atorvastatin (P+A), and atorvastatin (A) alone on the release of pro-inflammatory cytokines and oxidative stress.

METHODS:

30 patients age 71.21 ± 16.88 in Hemodialysis (HD) treatment 3 times per week for 48.53 months ± 64.24, were randomized into a 12 weeks period study. Group 1 (n=10) was treated with P; Group 2 (n=11) was treated with P+A; Group 3 (n=9) received A alone. Blood samples were collected two weeks before treatment (T-2), at baseline (T0), 6 weeks (T6) and 12 weeks after treatment (T12) and 2 weeks post treatment (T14). CD3, CD4, CD8, CD19, CD25, CD56, CD69 and CD95 lymphocytes blood markers and serum levels of IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12p70, IL-1β, TNF-β, TNF-α, and IFN-γ were analyzed by flow cytometry. Serum levels of PEG-2, COX-2, iNOS and FGF-23 were analyzed by ELISA.

RESULTS:

Treatment with P+A significantly reduced the expression of CD25, CD56, CD25/CD56 double positive, and CD69 compared with the treatment with P and A alone. A reduction in the release of IFNγ, IL-1β, IL-2 and IL-5 was also observed, mainly in Groups 1 and 2; and a reduction in COX-2 p<0.012 in T0vsT12. Moreover treatment with P+A significantly reduced the plasma level of FGF23 (T0 vs T12: p=0.044).

CONCLUSIONS:

The combined treatment with Paricalcitol and Atorvastatin elicits an early and significant decrease of inflammation and oxidative stress, and FGF23 in HD patients. These effects could have a considerable impact in reducing the risk of progressive atherosclerotic cardiovascular disease in patients using PSC.

DISCLOSURE: SENPARIC Clinical Trial was supported by AbbVie Inc. Chicago, USA

INOS	T0	T6	T12	T14
G 1	0.93± 0.56	0.75± 0.45	0.71± 0.87	0.58± 0.90
G 2	0.76± 0.84	0.74± 0.77	0.71± 0.87	0.44± 0.68
G 3	0.68± 0.35*	1.17± 1.41	1.04± 0.59	0.49± 0.58

*p=0.041 vs Group 2.

COX-2	T0	T6	T12	T14
G 1	16.5±2 .0	17.3± 1.2	13.3± 18.1**	19.6± 1.4***
G 2	16.4±1 .1	16.8± 1.1	18.1± 1.9*,****	17.8± 6.0****
G 3	16.35± 0.8	16.9± 0.7	17.2± 0.4	18.5± 2.1

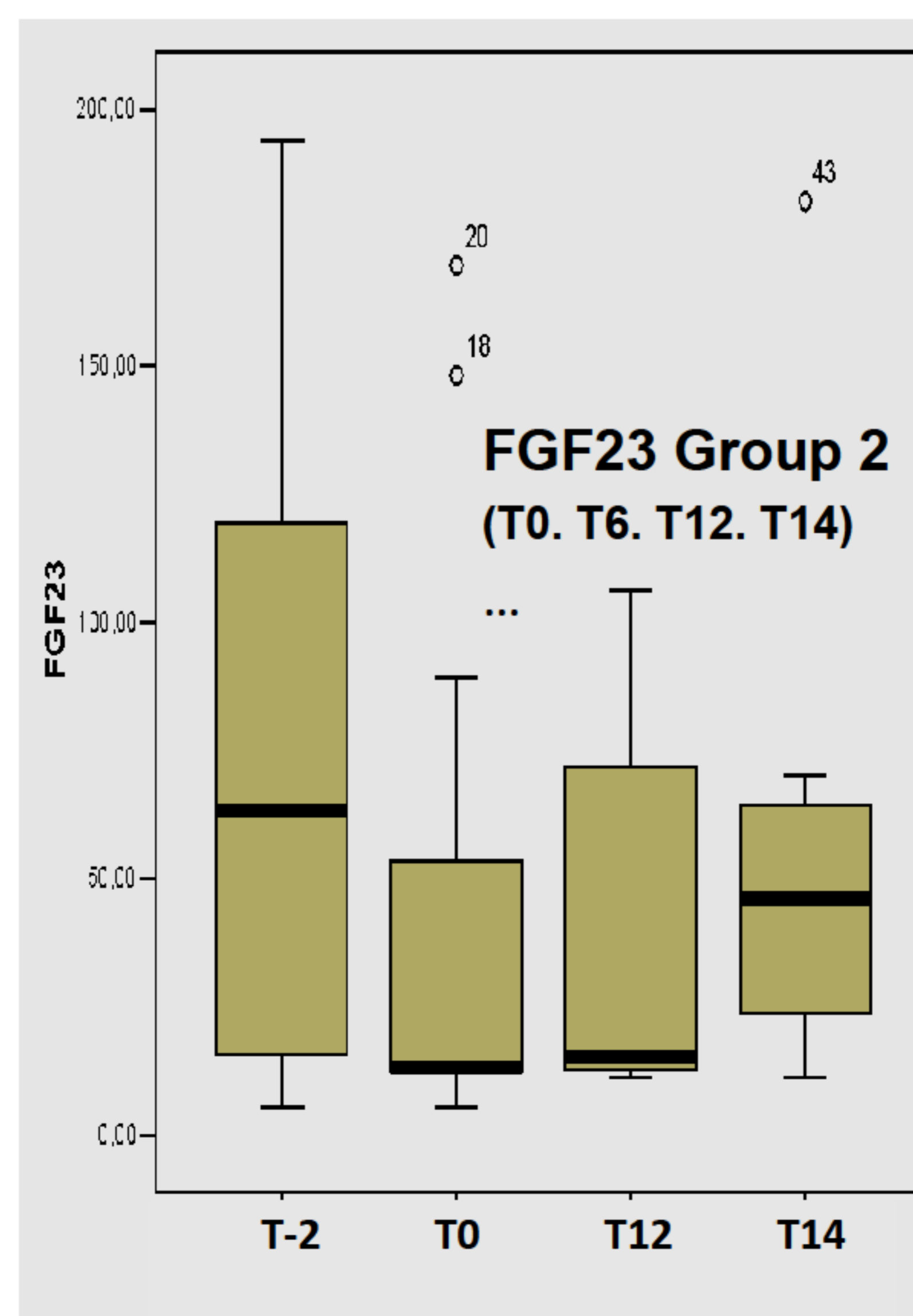
*p=0.007 vs Group 1 ; **p=0.012 T6 vs T0 Group 1; **p=0.004 T12 vs T6 Group 1; ***p=0.006 T14 vs T12 Group 1; ****p=0.027 T12 vs T0 Group 2; ****p=0.044 T12 vs T6 Group 2; ****p=0.011 T14 vs T12 Group 2.

L M	CD25 (T6)	CD56 (T6)	CD25/CD56 (T6)
G 1	23.3± 7.4	30.6± 12.3	2.7± 2.0
G 2	25.4± 9.3	26.8± 5.4*	3.1± 2.7**
G 3	20.6± 4.6	23.0± 10.8***	1.5± 1.0****,*****

L M = LYMPHOCYTE MARKERS
*p=0.004 vs G1; **p=0.028 vs G1; ***p=0.04 vs G2; ****p=0.039 vs G1; *****p=0.000 vs G2.

C R	IL12-p70 (T12)	IFN-γ (T12)	IL2 (T12)
G 1	1.9 3.3	16.3 19.7	73.5 55.0
G 2	23.2 50.4*	15.8 35.0	64.2 52.8
G 3	10.8 18.1**	18.2 28.3	73.2 61.3

C R = CYTOKINE RELEASE
*p=0.019 vs G1;
**p=0.002 vs G1.



FGF 23	T0	T6	T12	T14
G 1	22.4± 21.4	55.9± 92.6	39.5± 39.3	97.7± 160.8
G 2	76.4± 65.0*	46.1± 60.5	40.2± 39.8	53.3± 47.7
G 3	25.8± 26.3**	103.4± 167.3	42.9± 59.9	58.7± 58.6

*p=0.001 vs Group 1; **p=0.044 vs Group 2.