



Very Low Protein Diet reduces serum levels of indoxyl sulfate and p-cresyl sulfate in Chronic Kidney Disease

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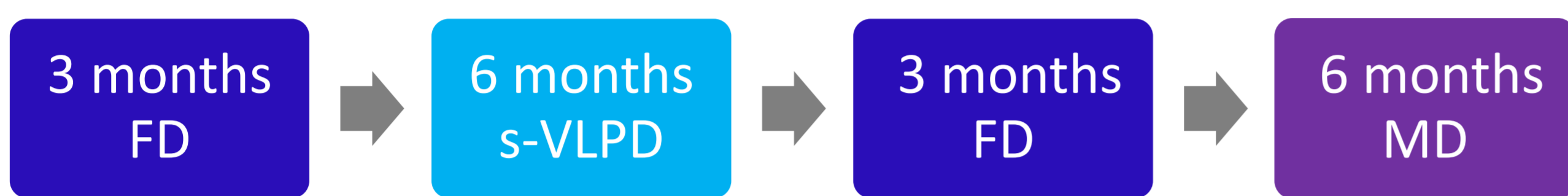
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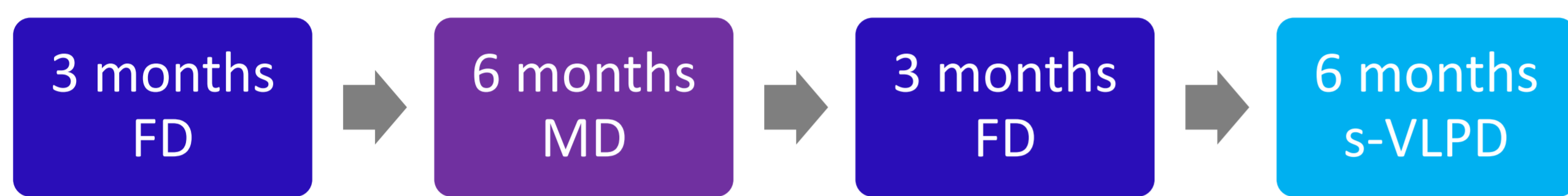
INTRODUCTION AND OBJECTIVES: High serum levels of uremic nephrovascular toxins, indoxyl sulfate (IS) and p-cresyl sulfate (PCS), are associated with chronic kidney disease (CKD) progression and increased risk of cardiovascular disease and mortality in CKD patients¹. IS and PCS cannot be efficiently removed by conventional haemodialysis, due to their high binding affinity for albumin. The aim of this pilot study was to assess whether a Mediterranean Diet (MD) and a Very Low Protein Diet supplemented with amino acids and ketoacids (s-VLPD)² would reduce serum concentrations of IS and PCS in CKD patients.

METHODS: This is a prospective randomized cross-over controlled trial that investigated 60 CKD grade 3B-4 patients (46 males, mean age of 67 years). The enrolled CKD patients were randomly assigned (1:1) to 2 different nutritional schemes, A and B.

Scheme A: 30 patients alternatively undergoing 3 dietary schemes as follows:



Scheme B: 30 patients alternatively undergoing 3 dietary schemes as follows:



FD: proteins 1 g/body weight/day; s-VLPD: proteins 0.3-0.5 g/body weight/day + 0.05 g/body weight/day ketoacids supplementation; MD: proteins 0.7-0.8 g/body weight/day.

Total and free IS and PCS were quantitatively and simultaneously measured, at baseline and at the end of each dietary scheme, by liquid chromatography/electrospray ionization–tandem mass spectrometry (LC/ESI-MS/MS). Differences between IS and PCS serum levels were tested by Wilcoxon test.

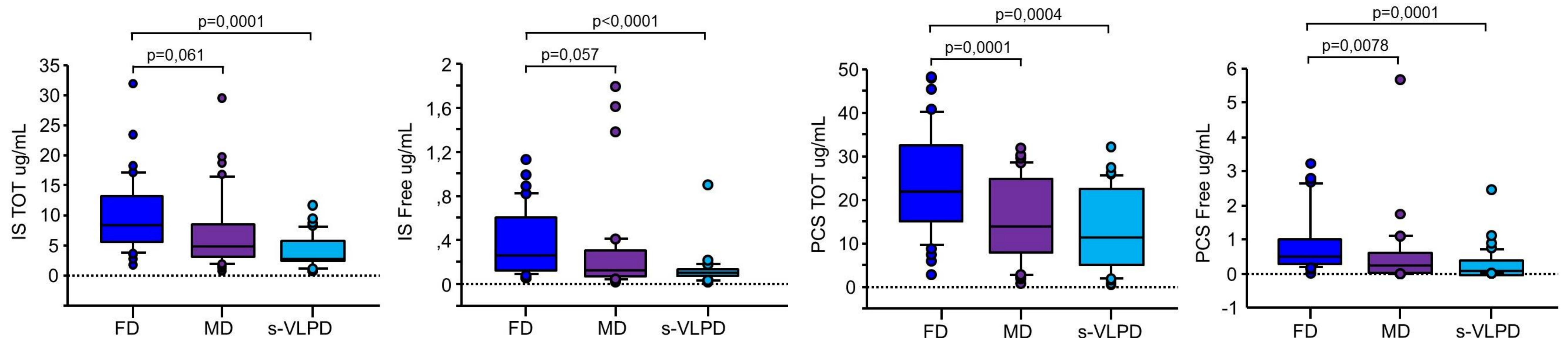
RESULTS AND CONCLUSIONS: Preliminary data on 40 out of 60 CKD patients show that s-VLPD diet is very effective in reducing total ($4.1 \pm 2.8 \mu\text{g/mL}$, $p=0.0001$) and free ($0.2 \pm 0.1 \mu\text{g/mL}$, $p<0.0001$) IS and total ($12.9 \pm 9.4 \mu\text{g/mL}$, $p=0.0004$) and free ($0.3 \pm 0.4 \mu\text{g/mL}$, $p=0.0001$) PCS serum levels compared to FD (IS total $10.3 \pm 6.5 \mu\text{g/mL}$; IS free $0.4 \pm 0.3 \mu\text{g/mL}$. PCS total $23.8 \pm 11.7 \mu\text{g/mL}$; PCS free $0.8 \pm 0.8 \mu\text{g/mL}$). Serum levels of total ($7.3 \pm 6.5 \mu\text{g/mL}$, $p=0.061$) and free ($0.3 \pm 0.4 \mu\text{g/mL}$, $p=0.057$) IS after administration of MD show the same trend of s-VLPD compared to FD, although the decrease of IS is not statistically significant.

Table 1. Demographic, Clinical and biochemical data of patients according to each nutritional intervention.

	FD	MD	VLPD
Number		60	
Sex (M)		46	
Age, years		66±16	
Diabetes (n°)		24	
Body Weight, kg	70.0±12.8	69.8±13.1	70.0±12.9
Systolic Blood Pressure, mm Hg	129±19	128±19	124±10
Diastolic Blood Pressure, mm Hg	73±11	71±9	69±7 *
Urea, mg/dl	175±22	137±26#	64±19*
Uricemia	5.4±1.6	5.2±1.6	5.1±1.7
Na, mmol/L	141±2	141±2	138±4*
K, mmol/L	5.1±0.6	5.0±0.8	5.1±0.7
Phosphate, mg/dl	4.5±0.7	4.1±0.7	3.6±0.7*
Bicarbonates, mmol/L	20±3	23±3#	25±3*
PTH, pg/ml	200±123	180±105	165±111*
Hb, g/dl	11.4±1.0	11.7±1.7	12.1±0.7*
Albumin, g/dl	3.6±0.4	3.6±0.4	3.6±0.8
CRP, mg/L	3.4±3.3	3.0±2.9	2.7±2.9
Na-u, mmol/day	164±47	151±50	127±48 *
K-u, mmol/day	44±16	49±17*	57±21 *
Cl-u,	115±28	112±22	94±16 *
P-u	706±198	499±201#	281±140 *
UUN, g/day	23±6	17±6#	8.2±2.9 *
Prot-u, mg/day	1587±1072	1543±1398	935±1059 *
Creatinine-u, mg/day	1.0±0.4	1.0±0.4	0.9±0.3
Creatinine Clearance, ml/min	22.1±13.9	23.7±13.1	23.2±16.7
Protein intake, g/kg/day	1.21±0.23	0.90±0.20#	0.48±0.14*
P intake, mg/day	989±271	799±264#	368±194*
Na intake, g/day	10.2±2.3	9.1±2.7	8.5±3.4
Urinary Pr/Cr ratio	1.5±1.2	1.5±1.4	1.0±0.91*

*Bonferroni test $p<0.05$ versus FD and MD

#Bonferroni test $p<0.05$ versus FD



Instead, the MD diet decreased total ($15.1 \pm 9.3 \mu\text{g/mL}$, $p=0.0001$) and free ($0.67 \pm 1.2 \mu\text{g/mL}$, $p=0.0078$) PCS, even to a lesser extent than s-VLPD diet. The preliminary results of this pilot study show for the first time, to the best of our knowledge, that both MD and, to a greater extent, s-VLPD, are effective in reducing serum levels of microbiota-generated uremic toxins, specifically IS and PCS, in CKD patients.

Bibliography

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