VITAMIN K ANTAGONISTS IN HEMODIALYSIS PATIENTS: IMPACT ON THE PLASMA LEVELS OF DEPHOSPHO-UNCARBOXYLATED MATRIX GLA-PROTEIN

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Background:

Matrix Gla-protein (MGP) could act as an inhibitor of vascular calcifications. Its physiological action is highly dependent of vitamin K which is necessary for the activation of Gla-proteins via a carboxylation process. Measurement of the inactive form of the protein, namely the desphospho-uncarboxylated matrix Gla-protein (dp-ucMGP), is now available (IDS, Boldon, UK). In the general population and in chronic kidney disease patients, it has been suggested that plasma concentrations of dp-ucMGP are higher in patients treated by vitamin K antagonist compared to non-treated. In this work, we tested if this hypothesis was also observed in hemodialysis patients.

Materials and methods:

Prevalent hemodialysis patients from three centers were recruited for this study. We separated patients treated, or not, by acenocoumarol. Clinical (age, gender, BMI, dialysis vintage, status of hypertension and diabetes, smoking status, presence of vascular antecedents) and biological variables were then compared between these two groups. Among biological variables, we compared classical data of the phosphorus-calcium metabolism (calcium, phosphorus, parathormone, 25-OH vitamin D), bone biomarkers [bone-specific alkaline phosphatase (b-ALP), C-terminal telopeptide of collagen type I, intact amino-terminal propeptide of type I procollagen (P1NP), tartrate-resistant acid phosphatase 5b, osteoprotegerin] and various biomarkers of interest (albumin, magnesium, C-reactive protein, troponin T, homocysteine, interleukin-6, TNFα, FGF-23, fetuin and dp-ucMGP). We used the Mann-Whitney test or independent samples t-test according to the distribution.

Results

Results: clinical data

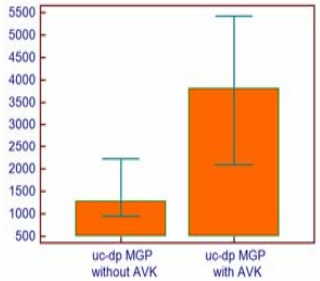
	Total	Without AVK	With AVK	p
Sample	165	143	20	NS
Age	74 [63;80]	74 [64;80]	71 [59;80]	NS
Gender (% of male)	44	44	45	NS
BMI	26±7	26±7	27±6	NS
Dialysis Vintage (months)	22 [11;43]	21 [10;44]	26 [18;39]	NS
HTA (%)	87	85	100	NS
Diabetes (%)	44	45	40	NS
Smoking (%)	21	21	20	NS
CV diseases	65	65	70	NS

Results: biological data (1)

	Total	Without AVK	With AVK	p
Calcium (mmol/L)	2.16±0.16	2.16±0.15	2.14±0.21	NS
Phosphorus (mg/dL)	4.6 [4.0;5.9]	4.6 [4.0;6.0]	4.8 [4.3;5.7]	NS
PTH (ng/L)	295 [134;478]	297 [137;466]	290 [112;537]	NS
Albumin (g/L)	38 [36;40]	38 [36;40]	40 [36;40]	NS
25-OH vitamine D (ng/mL)	23±13	23±13	21±11	NS
b-ALP (µg/L)	16 [11;22]	15 [10;23]	22 [17;34]	p=0.004
P1NP (µg/L)	218 [112;381]	206 [107;342]	330 [173;519]	p=0.04
TRAP-5b (U/L)	5.3 [4.0;7.0]	5.2 [3.9;6.9]	6.3 [4.4;8.0]	NS
CTX (µg/L)	1587 [1033;2355]	1602 [1037;2255]	1478 [959;2886]	NS

Results: biological data (2)

	Total	Without AVK	With AVK	p
CRP (mg/L)	5.0 [2.6;13.0]	5.0 [2.6;13.1]	5.5 [2.6;13.9]	NS
IL-6 (pg/mL)	9 [5;15]	9 [5;15]	10 [7;14]	NS
TNFα (pg/mL)	16 [11;35]	16 [11;35]	15 [9;27]	NS
Fetuin A (µg/mL)	237±72	241±72	208±71	NS
FGF-23 (U/mL)	2902[1018;7365]	2733[855;7486]	3152[2242;6085]	NS
OPG (pmol/L)	12 [9;16]	12 [9;16]	12 [9;18]	NS
uc-dpMGP (pmol/L)	1462 [994;2448]	1280 [955;2178]	3802 [2274;5232]	p<0.0001
Homocytein (µmol/L)	25 [20;34]	25 [19;33]	27 [21;35]	NS
Troponin T (µg/L)	0.04 [0.02;0.07]	0.04 [0.02;0.07]	0.04 [0.03;0.13]	NS



Conclusion:

- In this study, we confirmed that levels of desphospho-uncarboxylated matrix Gla-protein (dp-ucMGP) were strongly influenced by vitamin K antagonist therapy in hemodialysis.
- The moderate effect of vitamin K antagonist on b-ALP and P1NP deserve further studies.