**Impact of the stopping of vitamin K antagonist treatment on concentrations of dephosphorylated and uncarboxylated Matrix Gla protein**

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**Introduction**

Several experimental and clinical studies suggest that vitamin K antagonist (VKA) therapy is a risk factor for the development of vascular calcifications and calciphylaxis. Until recently, few alternative strategies were available . Recent data in hemodialysis suggested that fondaparinux, an indirect factor Xa inhibitor, could be safely used in these patients 1. Matrix Gla protein (MGP) is an 11 kDa protein secreted by vascular smooth muscle cells (VSMCs), acting as a potent local inhibitor of vascular calcification. In order to be fully active, MGP must be phosphorylated and carboxylated. This carboxylation is highly dependent on availability of vitamin K. Recent data have shown that dephosphorylated-uncarboxylated (dp-ucMGP) MGP concentrations, the inactive form of MGP, were higher in hemodialysis patients treated by AVK and that dp-ucMGP could be associated with vascular calcifications 2. In this study, we have measured dp-ucMGP in patients directly after switching from AVK to fondaparinux.

**Methods**

We included in the analysis hemodialysis patients treated by AVK in our University center. Switching from AVK (acenocoumarol) to fondaparinux was considered only in patients anticoagulated for atrial fibrillation. Seven patients, dialyzed three times a week were considered. Two measurements (T1 and T2) were obtained at the beginning of the dialysis session before stopping AVK. The patients stopped AVK therapy the day before the first dialysis session of the next week. Five measurements were then obtained at the beginning of each dialysis session (T3 to T7). dp-ucMGP was quantified by the only automated method available on the market (IDS, Boldon, UK). dp-ucMGP concentrations were compared by Wilcoxon tests.

**Results**

Before switching from AVK to fondaparinux, median concentrations of dp-ucMGP obtained at two different times (T1 and T2) were very high but not different: T1 6316 [5485;8693] and T2 6150 [4911;7325] pmol/L. In the first 24 hours following the switch (T3), the median concentration did not still change significantly: 5902 [4842;9165] pmol/L. However, all measurements obtained after significantly decreased in comparison to T1: T4 4505 [3295;6791] (p=0.0156), T5 3810 [2331;4979] (p=0.011), T6 3850 [2159;4586] (p=0.0156), and T7 2948 [1644;3721] (p=0.007) pmol/L. Concentrations at T4 were also higher than at T5, T6 and T7 but after this time interval, a steady state was reached and concentrations at T5, T6 and T7 were not different.

**Conclusions**

Stopping AVK in hemodialysis patients is associated with a rapid reduction of dp-ucMGP concentrations. If this reduction of dp-ucMGP is associated with a better evolution of vascular calcifications remains to be proved.



Reference List

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