

Vascular Wall and Endothelium

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J. Martins e Silva
Carlota Saldanha

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VASCULAR WALL AND ENDOTHELIUM

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FIBRINOLYTIC ACTIVITY AND VASCULAR ACCESS IN CHRONIC RENAL FAILURE PATIENTS UNDER HAEMODIALYSIS

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ABSTRACT

Our aim was to study the relationship between fibrinolytic activity and the type of vascular access in haemodialysis patients. We measured the circulating antigen levels of plasminogen activator inhibitor type-1 (PAI-1), tissue plasminogen activator (tPA) and D-dimers. This study was performed in 50 CRF patients under regular haemodialysis, 11 with central venous dialysis catheter and 39 with AV-fistula, and in 25 healthy controls.

Compared with controls, CRF patients presented significantly lower levels of tPA and with higher levels of D-dimers. In CRF patients, the levels of D-dimers correlated positively and significantly ($r=0.359$, $p=0.01$) with rhEPO doses (rhEPO/Kg/week) and negatively with haemoglobin levels ($r=-0.335$, $p=0.017$). When comparing the two groups of CRF patients, we found that those with central venous catheter vascular access presented a statistical significant rise in D-dimer and tPA plasma levels. No difference was found between the two groups of patients concerning the plasma levels PAI-1.

Our results showed an altered haemostasis in CRF patients, as suggested by the rise in D-dimer, an index of fibrin turnover and intravascular thrombogenesis. The increased levels of D-dimer and tPA in CRF patients, particularly in those using central venous dialysis catheters, led us to propose a relationship between the type of vascular access chosen for the haemodialysis procedure, and the risk of thrombogenesis. It seems reasonable to assume that these patients present an increased risk for cardiovascular disease events.

Key-Words: fibrinolytic activity, Chronic Renal Failure, Vascular access, D-dimers.

INTRODUCTION

Cardiovascular disease events are the main cause of death in chronic renal failure (CRF) patients. Disturbances in coagulation and fibrinolysis have been reported in patients with chronic uremia, and are known to contribute to the pathogenesis of cardiovascular diseases. However, studies about coagulation and fibrinolysis in CRF patients under regular hemodialysis have yielded conflicting results. Some studies reported a suppressed fibrinolysis and others an increased fibrinolysis¹⁻³. These controversial results may be related to the type of vascular access (central venous dialysis catheter or AV-fistula) chosen for the haemodialysis procedure, and may associate a different risk of thrombosis³⁻⁵.

Our aim was to study the relationship between fibrinolytic activity and the type of vascular access in haemodialysis patients.

MATERIALS AND METHODS

Subjects

We studied 50 CRF patients under regular haemodialysis (32 males, 18 females; mean age 64.5 ± 15.4), 11 with Central Venous Dialysis Catheter and 39 with AV-Fistula.

CRF patients were under therapeutic haemodialysis three times per week, for 3 to 5 h, for a median period of time of 36 months. All patients used the high-flux polysulfone FX-class dialysers of Fresenius, 25 with FX60, 23 with FX80 and 2 with FX100 dialyser type.

The causes of renal failure in patient's population were as follows: diabetic nephropathy (n=16), chronic glomerulonephritis (n=6), polycystic kidney disease (n=5), hypertensive nephrosclerosis (n=3), obstructive nephropathy (n=3), pyelonephritis associated with neurogenic bladder (n=1), nephrolithiasis (n=1), chronic interstitial nephritis (n=1), Alport syndrome (n=1), renal vascular disease due to polyarteritis (n=1) and chronic renal failure of uncertain aetiology (n=12).

Patients with autoimmune disease, malignancy, haematological disorders, and acute or chronic infection were excluded. All patients gave their informed consent to participate in this study.

The control group included 25 healthy volunteers presenting normal haematological and biochemical values, with no history of renal or inflammatory diseases, and, as far as possible, age and gender matched with CRF patients.

Assays

Plasma levels of plasminogen activator inhibitor type-1 (PAI-1), tissue plasminogen activator (tPA) and D-dimers were evaluated by enzyme immunoassays (TintElize PAI-1, TintElize tPA and TintElize D-dimer, Biopool-Trinity Biotech Company, respectively).

Data analysis

For statistical analysis, we used the Statistical Package for Social Sciences, version 14.0. Kolmogorov Smirnov statistics were used to evaluate sample normality distribution. Comparisons between groups were performed using Kruskal-Wallis test and Mann-Whitney U (data with a non-Gaussian distribution) or Student's t-test (data with a Gaussian distribution). Spearman's rank correlation coefficient was used to evaluate relationships between sets of data. Significance was accepted at p less than 0.05.

RESULTS

Compared with controls, CRF patients presented significantly lower levels of PAI-1 and with higher levels of D-dimers (Fig. 1). In CRF patients, the levels of D-dimers correlated positively and significantly ($r=0.359$, $p=0.01$) with rhEPO doses (rhEPO/Kg/week) and negatively with haemoglobin levels ($r=-0.335$, $p=0.017$) (Fig.2). When com-

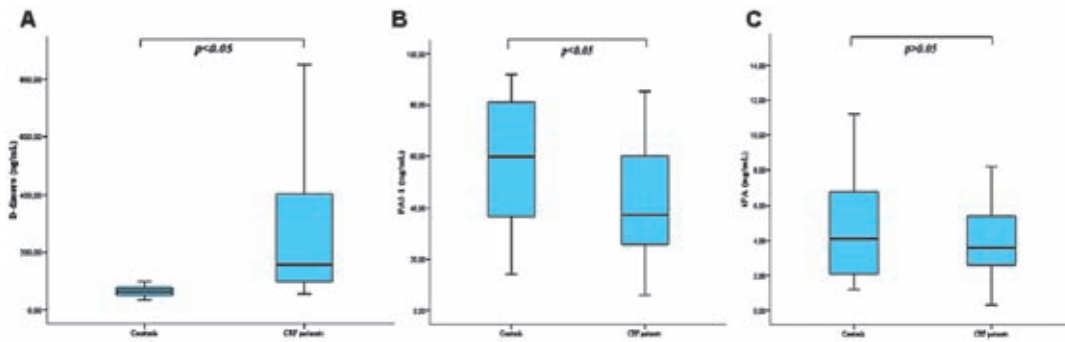


Fig. 1 – Compared with controls, CRF patients presented significantly higher levels of D-dimers (A) and lower levels of PAI-1 (B). No difference between these two groups was found for tPA levels (C).

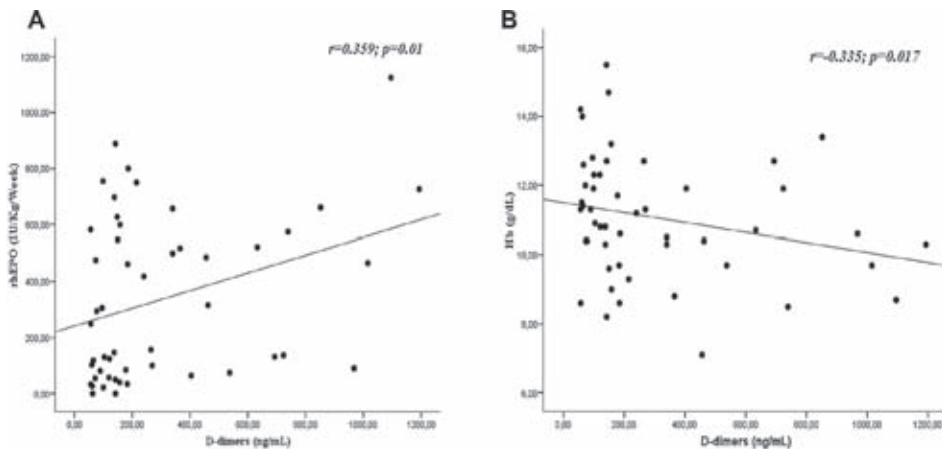


Fig. 2 – Correlation between D-dimers levels and rhEPO doses (A) and hemoglobin levels (B) in CRF patients.

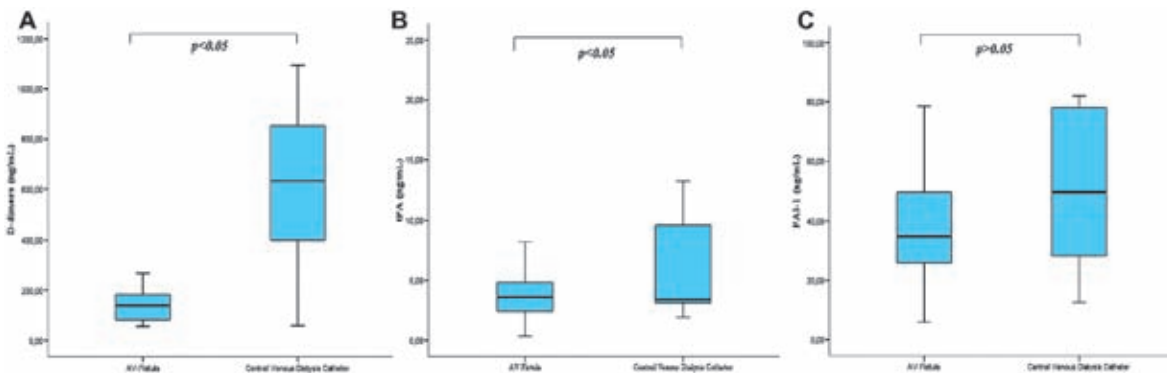


Fig. 3 – CRF patients with Central Venous Catheter as vascular access presented a statistical significant rise in D-dimers (A) and tPA (B) plasma levels, when compared with those using AV-Fistula as vascular access. No difference was found between the two groups of patients concerning the plasma levels of PAI-1 (C).

paring the two groups of CRF patients, we found that those with central venous catheter vascular access presented a statistical significant rise in

D-dimer and tPA plasma levels. No difference was found between the two groups of patients concerning the plasma levels PAI-1 (Fig.3).

DISCUSSION

Our results showed an altered haemostasis in CRF patients, as suggested by the rise in D-dimer, an index of fibrin turnover and intravascular thrombogenesis. The increased levels of D-dimer and tPA in CRF patients, particularly in those using central venous dialysis catheters, led us to propose a relationship between the type of vascular access chosen for the haemodialysis procedure, and the risk of thrombogenesis. It seems reasonable to assume that these patients may present an increased risk for cardiovascular disease events.

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