CIRCULATINGPLASMA PENTOSIDINE IN PRE-DIALYSIS, PRE-TRANSPLANT, PERITONEAL DIALYSIS (PD) AND HAEMODIALYSIS (HD) PATIENTS (PTS)

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BACKGROUND AND OBJECTIVES

Circulating advanced glycated end products (AGEs) such as pentosidine associate with cardiovascular disease and other complications. AGE formation is enhanced by hyperglycemia, oxidative stress, inflammation and during aging. In chronic kidney disease (CKD), reduced renal disposal leads to accumulation of AGEs. We here describe factors potentially linked to increased plasma pentosidine level in patients across different stages of CKD and different dialysis treatment modalities and present the mortality predictive role of pentosidine among patients with impaired renal function.

METHODS

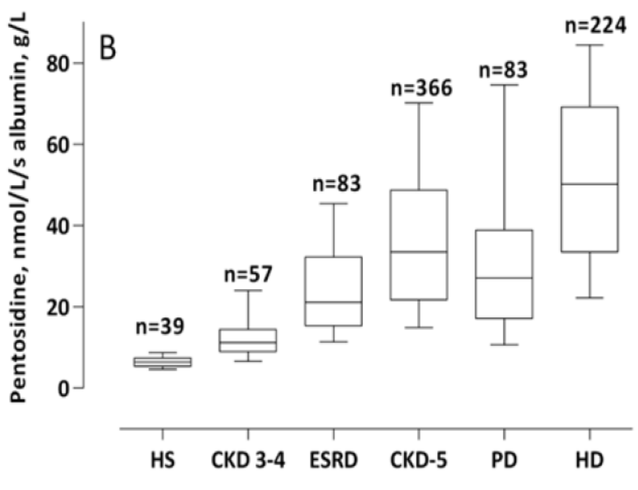
Plasma pentosidine (reversed-phase HPLC using fluorescence detection), other biomarkers and nutritional status (subjective global assessment, SGA) were measured at baseline in 6 cohorts (n=852) of: healthy subjects (HS; n=39), prevalent CKD3-4 patients (n=57), incident pre-dialysis patients (CKD5; n=366), patients undergoing LD transplantation (pre-Tx; n=83), prevalent HD (n=224) and prevalent PD (n=83). Cox regression model was used to analyze the mortality risk associated with increased levels of pentosidine.

RESULTS

Median pentosidine level (nmol/l) was higher in PD patients (899.5; 27.1) than in HS (243.2; 6.5), but lower or not different compared to HD patients (1733.2; 50.2), CKD5 patients (1095.1; 33.5), pre-Tx patients (752.1; 21.1) and CKD 3-4 (406.6; 11.2). After correction for albumin, the trend in all cohorts remained consistent (see Figure 1).

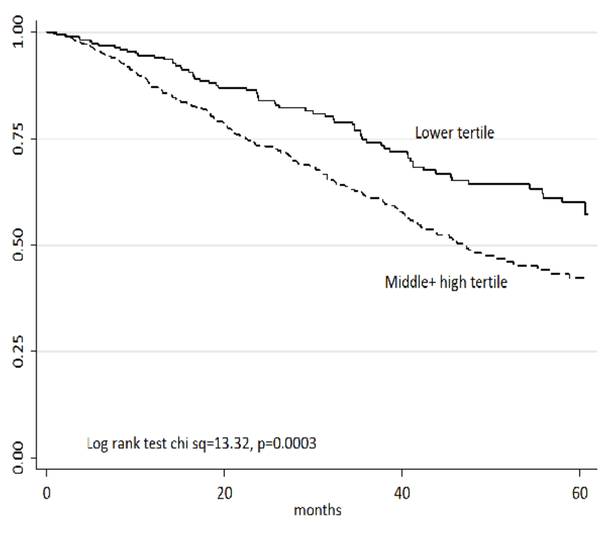
The combined analysis of mortality in 4 patients groups (CKD 3-4, CKD5, HD and PD) showed that the highest and middle versus lower tertile of pentosidine associated with increased mortality (see Figure 2).

Figure 1: Level of plasma pentosidine corrected for albumin level in all studied cohorts (n=852)



Pentosidine was higher in PD patients compared to HS and lower than in HD patients but not significantly different as compared to CKD5, CKD3-4 and pre-Tx patients.

Figure 2: All-cause mortality in combined cohorts during 5 year follow up time.



CORRELATIONS

The univariate analysis showed that in PD patients, pentosidine was positively correlated with **AOPP** (rho=0.55, p<0.001) and negatively with **GFR** (rho=-0.44, p<0.001). In HD patients the positive correlation of pentosidine was found with **age** (rho=0.16, p<0.05), **s-albumin** (rho=0.21, p<0.01), AOPP (rho=0.16, p<0.05) and **VCAM-1** (rho=0.01, p<0.05) whereas negative correlation with **BMI** (rho=-0.14, p<0.05). In pre-Tx patients the significant correlation was found with **8-OHDG** (rho=0.37, p<0.01). In CKD 5 patients starting dialysis pentosidine level correlated with age (rho=0.15, p<0.01), **s-albumin** (rho=0.19, p<0.001), **8-OHDG** (rho=0.22, p<0.001), **AOPP** (rho=0.30, p<0.01) and **VCAM-1** (rho=0.18, p<0.01) and negatively with **GFR** (rho=-0.14, p<0.05). Analysis of patients with CKD stage 3-4 showed that pentosidine is negatively correlated with **GFR** (rho=-0.70, p<0.001) and positively with **fibrinogen** (rho=0.27, p<0.05). The healthy controls showed correlation between pentosidine and age (rho=0.42, p<0.01) and **GFR** (rho=-0.44, p<0.01).

CONCLUSIONS

- Plasma pentosidine is markedly elevated in all categories of CKD patients.
- The results implicate factors such as oxidative stress, inflammation and low GFR.
- The latter may explain why pentosidine levels were higher in HD than in PD patients and other groups of patients.
- High plasma pentosidine can be a predictor of all-cause mortality in CKD patients.
- However, much of the variation of pentosidine remains unexplained and requires further investigations.

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