OXIDATIVE STRESS AND INFLAMMATION: ARE THEY ALWAYS STRICTLY CORRELATED IN HEMODIALYSIS PATIENTS?

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INTRODUCTION AND OBJECTIVES

Patients affected by end-stage renal disease (ESRD) experience a condition of increased oxidative stress, which derives from comorbidities, decline of the renal function and hemodialysis itself.[1] The increased oxidative stress, acting in synergy with the inflammatory state, is a major risk factor for cardiovascular disease (CVD) and protein-energy malnutrition, and thus plays a crucial role in the high morbidity and mortality observed in this population.[2]

A fairly reliable evaluation of the inflammatory state is feasible through the measurement of C-reactive protein (CRP), which has become a routine test in hemodialysis units since it is easy to measure and is a good predictor of short term mortality.[3] However a similar quantification of the oxidative stress state is still not available in clinical practice.

The aim of our study was to investigate the difference in the oxidative state of hemodialyzed patients compared to healthy controls using three different oxidatively modified proteins (di-tyrosine, pentosidine and advanced oxidation protein products or AOPPs).

METHODS

The plasmatic concentrations of di-tyrosine, pentosidine and AOPPs were determined by spectrofluorimetry or spectrophotometry after high performance liquid chromatography separation in 35 hemodialyzed patients (age 69 ± 11) and 20 healthy controls (age 71 ± 8).

The inflammatory state of hemodialyzed patients was evaluated by measuring highly-sensitive CRP and the Malnutrition-Inflammation Score (MIS), a validated score for estimating protein-energy malnutrition.

All patients were dialyzed with high-flux synthetic membranes and ultrapure dialysis fluid. Patients with evident overt infections were not included.

RESULTS

In HD patients the average plasmatic levels of di-tyrosine, pentosidine and AOPPs were respectively 0,173 ± 0,045 AU, 0,089 ± 0,027 AU, 0,689 ± 0,175 AU, while in the control group the average plasmatic levels were respectively 0,084 ± 0,012 AU, 0,057 ± 0,008 AU, 0,42 ± 0,06 AU. In the first group CRP levels were 0,494 ± 0,476 mg/dL and the average MIS was 6,8 ± 3,3.

All three markers were significantly higher in HD patients ($p < 0,01$) compared to controls, however no significant correlation was found between CRP levels, MIS and the markers of oxidative stress.

Figure 1

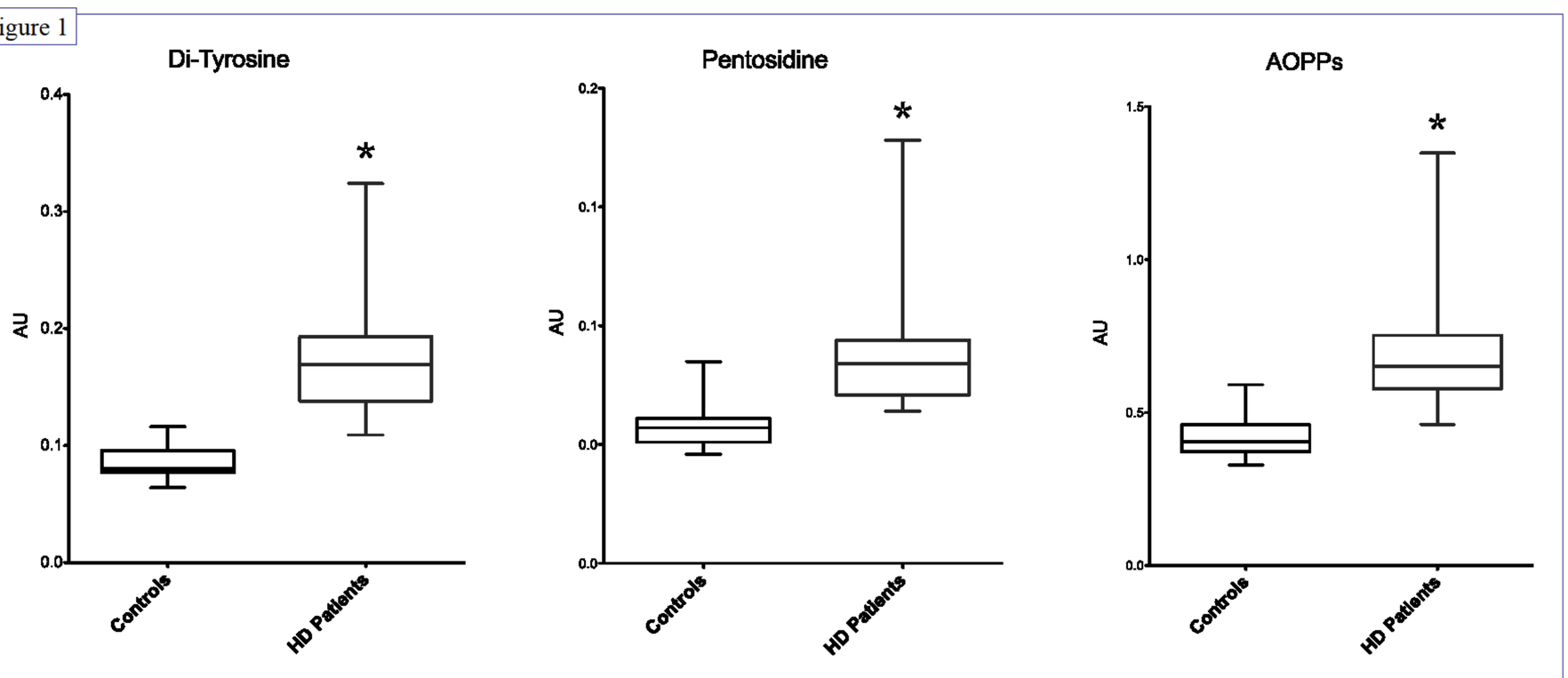

Figure 2

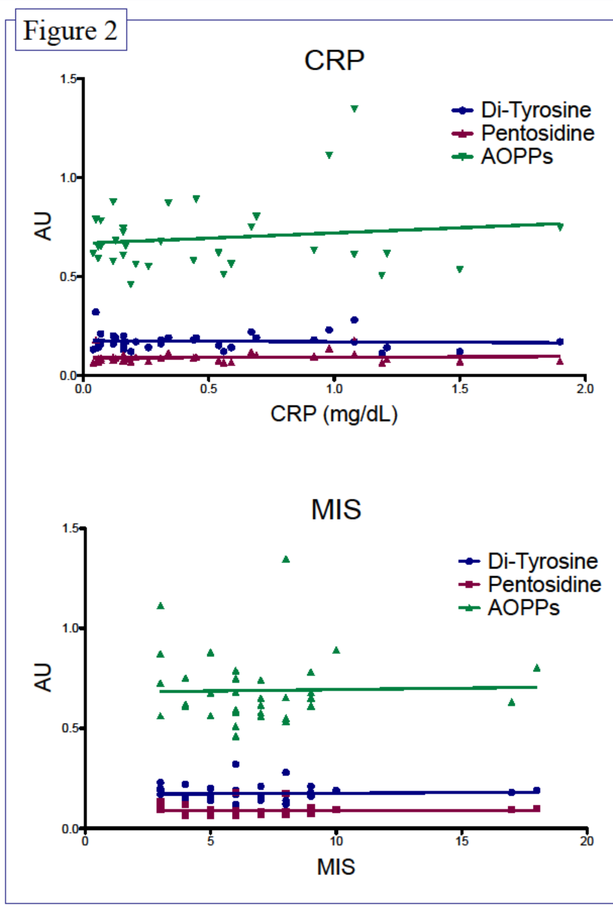

Figure 1. Average plasmatic levels of di-tyrosine, pentosidine and AOPPs in controls and hemodialyzed patients. (* $p < 0,01$).
Figure 2. Correlation between the markers of the inflammatory status (PCR and MSI) and oxidative stress ones.

CONCLUSIONS

From these data, the oxidative stress burden is higher in HD patients than in general population. However we did not observe a significant correlation between the markers of oxidative stress and inflammatory status ones. From these data it can be derived that oxidative stress and inflammatory status, although strictly related by pathogenic mechanisms, may also be in part independent from each other. Thus, the assessment of inflammatory status per se may not completely predict CVD risk in HD patients, since it does not take into account the influence of oxidative stress in CVD and protein-energy malnutrition pathogenesis. This assumption is strengthened by the finding of low CRP levels and acceptable MIS in HD patients, even though markers of oxidative stress were significantly higher compared to the general population.

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