MOLECULAR DYSREGULATION IN PLASMA FROM NON DIALYTIC PATIENTS WITH CHRONIC KIDNEY DISEASE

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Background

Cell-free plasma DNA (cfDNA) is short double-stranded DNA originates from necrotic and apoptotic cells reflecting inflammation. It has been documented that cfDNA is present in blood and urine in healthy and pathological conditions. cfDNA has been found in many clinical conditions in which apoptosis and necrosis were involved suggesting that such events are the main source for its presence. High levels of cfDNA have been also reported in pathological conditions involving kidneys (HD, PD, severe sepsis) and there are few data about the role of cfDNA in CKD patients.

Aim

The aim of this study was to evaluate plasma cfDNA and Caspase-3 in patients with different stages of CKD. Furthermore, we evaluated indices of inflammation and ox stress in this population.

Methods

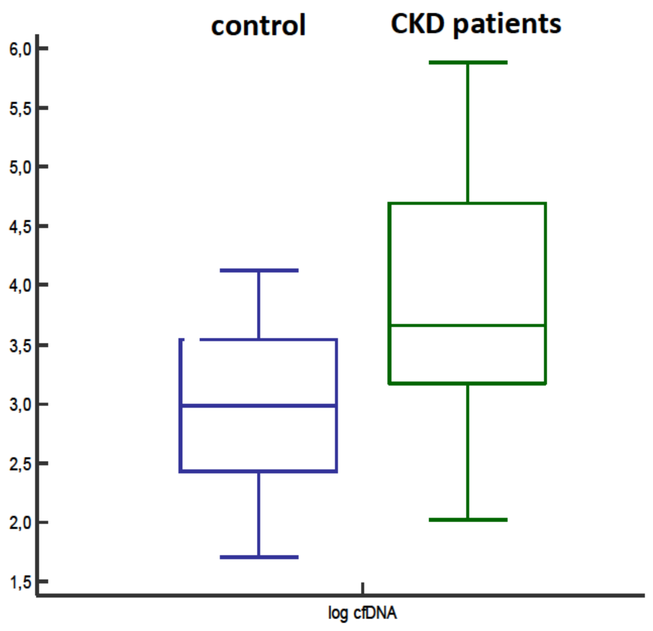
We enrolled 40 nondialytic CKD patients who came to our center for routine visit and we divided them depending on CKD stage (CKD-EPI creatinine equation). 29 healthy volunteers were enrolled as control. cfDNA was extracted from plasma and quantified by Real Time PCR for the β-actin gene. Quantitative plasma level of Casp3, IL-6/18/1β, EPA (Eicosapentaenoic acid), MPO (Myeloperoxidase) and NO (Nitric Oxide) were also performed by ELISA assay.

Results

Quantitative analysis showed significantly higher levels of cfDNA in CKD patients compared with control (p=0.001) (FIGURE A). Furthermore, cfDNA distinguished CKD patients from healthy controls with a sensitivity of 81.4% (p<0.0001) (FIGURE B). The increase of apoptotic events in CKD group was confirmed by Caspase-3 activation (p=0.003) (FIGURE C) and a significant positive correlation was observed between cfDNA and Caspase-3 levels (rho=0.779, p<0,0001). Positive correlations were observed between cfDNA and urea (rho=0.340, p=0.043) and between Caspase-3 and urea (rho=0.564, p=0.015). cfDNA levels were significantly different depending on CKD stages (p=0.025); furthermore, we observed an increasing levels of cfDNA from CKD stage 1 to CKD stage 5. Inflammatory status of CKD patients (plasma concentrations of IL-6/1b/18), and ox stress status (plasma concentrations of MPO, EPA and NO), were statistically different from control population. Furthermore there was a positive correlation between cfDNA and IL-6 (rho=0.363, p=0.0070).

	Control		CKD patients		
	Median	25 - 75 P	Median	25 - 75 P	p-value
MPO	10,164	5,745 to 20,550	5986,979	3712,773 to 11540,468	<0.000001
NO	13,414	12,793 to 14,745	710,102	565,559 to 798,015	<0.000001
pIL-18 (pg/ml)	20,429	17,702 to 23,599	161,296	129,046 to 246,450	0.000014
pIL-1b (pg/ml)	10,461	10,049 to 11,261	7,850	6,982 to 8,599	0.000877
pIL-6 (pg/ml)	7,780	4,953 to 16,719	30,184	27,025 to 39,219	<0.000001
EPA	5,903	2,287 to 9,975	1963,550	1064,771 to 2795,337	< 0,000001

A



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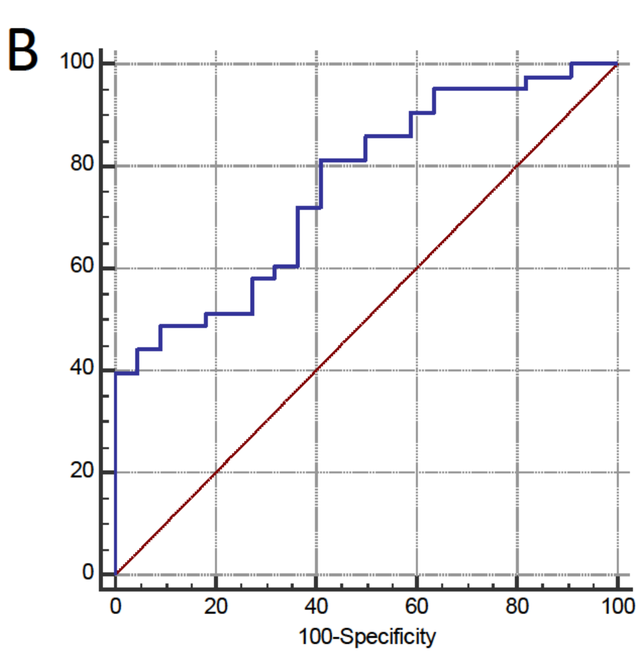

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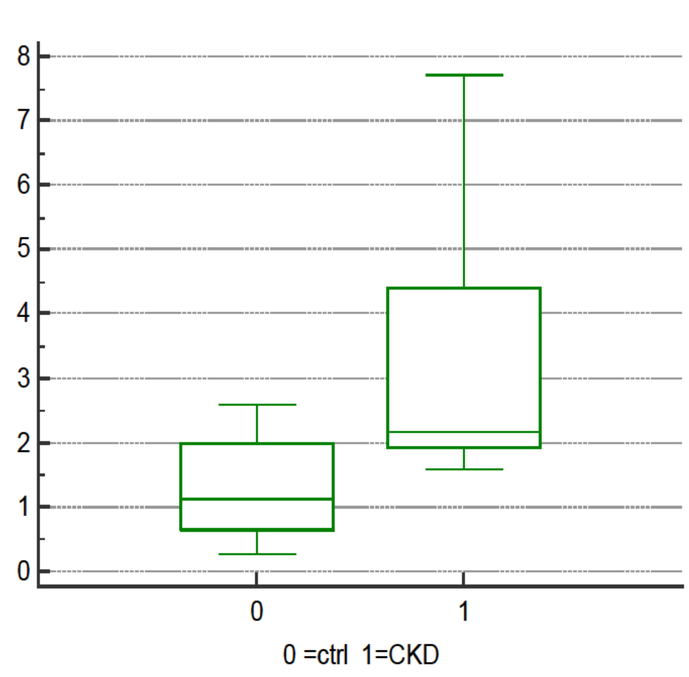

Conclusions

Our data suggest that cfDNA is increased in the plasma of CKD patients and cell apoptosis could be one of its potential source. CKD patients enrolled in the study were non-dialytic patients, and we hypothesize that cfDNA could be influence by urine elimination and could be find and detect in urine. Further experiments are necessary to our confirm this hypothesis. We concluded that inflammation, ox stress, apoptosis and higher levels of cfDNA could be potential causes of cytotoxicity could be implicated in the pathological mechanism involved in CKD.

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