Thyroid hormones associate with pentosidin hemodialysis (HD) patients

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Introduction and aim

Chronic overstimulation of advanced glycation end-products (AGE)–receptor for AGE (RAGE) pathway may increase the risk for cardiovascular disease (CVD) in chronic kidney disease (CKD) patients in whom low levels of T3 associate with CVD.

By stimulating RAGE, AGEs may exert their effects via NF-κβ, while activation of NF-κβ may down-regulate T3 production. We studied the relationship between pentosidine and thyroid hormones in HD patients.

Materials and Methods

In 218 prevalent HD patients (median (IQR) age 66 (51-75) years, 55% men, 26 % diabetes mellitus (DM), malnutrition 47%, median duration of dialysis 28 (14-57) months), we determined plasma pentosidine (by reversed-phase HPLC using fluorescence detection), advanced oxidation protein products (AOPP) (in a supernatant at 340 nm on a microplate spectrophotometer), and thyroid hormones T3, T4, and TSH (by immunometry) and subjective global assessment (SGA) of nutritional status.

Results:

Tabel 1. Baseline characteristics of hemodialysis patients according to pentosidine tertiles

Values are expressed as mean (SD), median (25 and 75 percentile) or % as appropriate.

Pentosidine (pmol/mL)	Tertile 1 (268-1323; n=75)	Tertile 2 (1340-2164; n=75)	Tertile 3 (2179-7281; n=74)	p-value
Age (yrs)	60.9 (14.5)	61.6 (13.6)	68.2 (14.0)	0.028
Male (%)	53	52	61	0.509
Diabetes (%)	29	29	19	0.248
Vintage (months)	22 (9-48)	29 (15-63)	31 (18-57)	0.055
AOPP (µmol/L)	151.3 (108.9-197.6)	155.0 (111.1-184.4)	165.2 (137.1-199.6)	0.072
Malnourishment (%)	50	53	38	0.147
T3 basal (nmol/L)	0.84 (0.70-1.06)	0.83 (0.68-1.10)	0.79 (0.60-0.98)	0.172
T4 basal (nmol/L)	71.70 (55.3-87.1)	70.80 (58.5-92.)	61.80 (45.3-74.6)	0.003
TSH basal (mU/L)	1.32 (0.73-2.25)	1.29 (0.8-2.8)	1.58 (1.08-2.63)	0.303

Table 2. Factors possibly associated with pentosidine.

Factor	Rho	p-value
Age	0.110	0.100
Gender	0.047	0.483
Diabetes	-0.094	0.162
AOPP	0.156	0.020
Duration of dialysis	0.175	0.009
T3 basal	-0.145	0.033
T4 basal	-0.185	0.006
TSH basal	0.080	0.236

Summary and conclusions

Levels of AGEs like pentosidine has been shown in to increase with GFR in CKD patients, while its receptor, RAGE, is upregulated. These could lead to an overstimulation of the AGE-RAGE pathway, stimulating different pathways, which in turn results in activation and translocation of nuclear transcription factors, including NF-κB. Others have demonstrated that NF-κB activation downregulates D1 mRNA in HepG2 cells, suggesting an involvement in the pathogenesis of Non-Thyreoidal Illness (NTI), a state which is mainly caused by a decrease in liver D1 mRNA and activity [1,2]. One could therefore hypothesize that AGEs may influence T3 levels in NTI in CKD patients by decreasing D1 activity via NF-κB activation.

The observed negative association between pentosidine and T3 and T4 levels supports the hypothesis that AGEs formation could be an additional cause of low thyroid hormone levels in HD patients.

References: *1. J Clin Invest 2000; 106(3):393-402, 2. J Endocrinol 2006;189(1):37-44.*

Table 3. Association between pentosidine and thyroid hormones levels in linear multiple regression model. Crude: unadjusted. Model 1: adjusted for age, diabetes and gender. Model 2: adjusted for age, diabetes, gender, AOPP, duration of dialysis and SGA.

Variable	Crude			Model 1			Model 2		
	β	SE	p	β	SE	p	β	SE	p
T3 basal	-0.140	0.000	0.038	-0.145	-0.000	0.031	-0.153	0.000	0.025
T4 basal	-0.220	0.002	0.001	-0.223	-0.002	0.001	-0.203	0.002	0.002
TSH basal	0.018	0.001	0.790	0.001	0.001	0.993	0.003	0.001	0.962

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