GRONINGEN KIDNEY CENTER

Plasma somatostatin is not associated with disease severity or rate of disease progression in patients with ADPKD

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Introduction

Somatostatin (SST) has a wide range of inhibitory effects on metabolic pathways. In the epithelial cells of the renal tubulus it inhibits cyclic adenosinemonophosphate (cAMP) production.

In autosomal dominant polycystic kidney disease (ADPKD), high levels of cAMP are a pivotal step in the cascade leading to cyst formation and growth. Therefore, SST analogues are suggested to be beneficial to reduce disease progression in ADPKD.

Moreover, the disease course of ADPKD is highly variable between affected subjects. Identification of biomarkers that are able to predict prognosis and to select patients with a high likelihood of rapid disease progression that may benefit from early interventions is therefore important.

Study aims

We investigated in ADPKD patients, whether fasting plasma concentrations of SST

1. are comparable to healthy controls
2. are associated with parameters of disease severity
3. are associated with the rate of disease progression

Methods

At baseline fasting concentrations of SST were measured in 127 ADPKD patients and 15 healthy controls using an immunoassay with an intra- and inter CV of 7.7 and 31.8% resp.

Kidney function was measured (mGFR) by (125)I-iothalamate, and total kidney volume (TKV) was measured by classical volumetry on MRI.

Disease progression was expressed as annual change in mGFR and height-adjusted (ht)TKV.

Multivariable linear regression was used to assess the association between SST concentrations and disease parameters.

Results

Subject characteristics

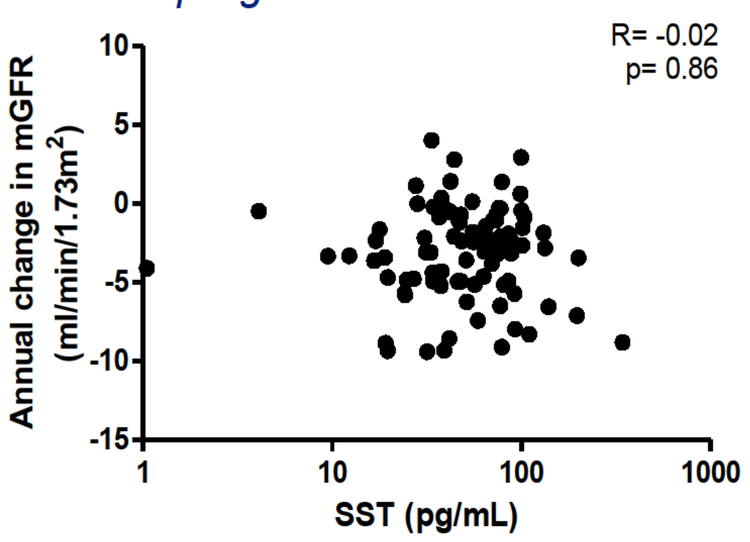
Baseline			
	ADPKD	**Controls**	**p**
N	127	15	
Age (yrs)	40.9 ± 11.0	34.7 ± 12.3	0.04
Female (%)	44.1	53.3	0.5
Body Service Area (m^2)	2.03 ± 0.25		
eGFR (ml/min/1.73m^2)	72.2 ± 31.5	101 ± 13.4	<0.001
mGFR (ml/min/1.73m^2)	75.2 ± 32.0		
htTKV (mL/m)	826 (521-1296)		
SST (pg/mL)	48.5 (34.3-77.8)	50.2 (23.1-60.0)	0.2
Follow-up			
N	99		
Follow-up time (yrs)	3.85 ± 1.26		
Annual change in			
- mGFR (ml/min/1.73m^2)	-3.17 ± 2.99		
- htTKV (%)	6.37 ± 5.79		

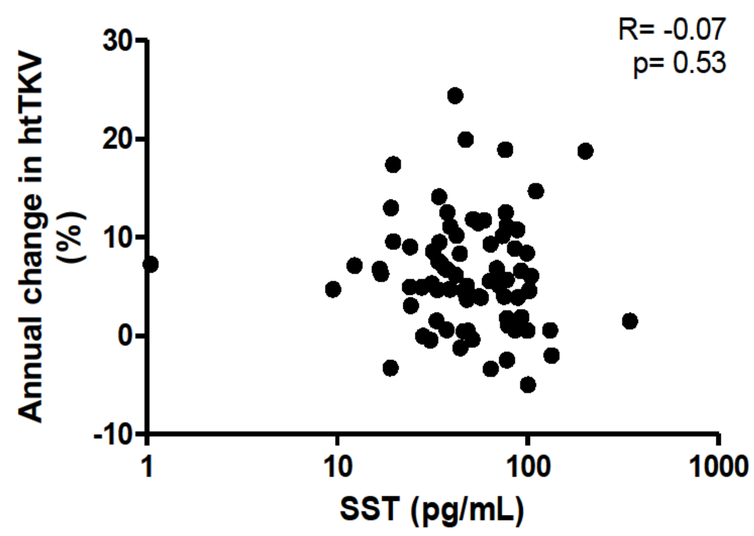
Disease severity

	Crude		**Model 1**		**Model 2**	
	St. β	**p**	**St. β**	**p**	**St. β**	**p**
mGFR (ml/min/1.73m^2)						
SST	-0.3	0.005	-0.1	0.06	-0.1	0.1
Sex*			0.03	0.7	-0.05	0.5
Age			-0.6	<0.001	-0.6	<0.001
htTKV					-0.3	<0.001
htTKV (mL/m)						
SST	0.2	0.02	0.1	0.2	0.09	0.3
Sex*			-0.3	0.003	-0.3	<0.001
Age			0.2	0.05	-0.1	0.2
mGFR					-0.5	<0.001

Dependent variables are mGFR or log transformed htTKV, the independent variable is the log transformed SST concentration.
*Female vs. male
Model 1: adjusted for age and sex
Model 2: adjusted for age, sex and htTKV or mGFR

Disease progression





Conclusion

Fasting plasma concentrations of SST were neither associated with disease severity nor with rate of disease progression in ADPKD patients. Since SST analogues have been suggested to be beneficial to slow the rate of disease progression in these patients, in which SST reaches higher concentrations, we hypothesize that fasting plasma SST concentrations may be too low to result in pathophysiological effects in ADPKD.

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