ASSOCIATION OF ANGIOTENSINOGEN GENE *(M235T)* POLYMORPHISM WITH ANTI-HYPERTENSIVE EFFICACY OF ACE INHIBITORS IN CHILDREN WITH STEROID-RESISTANT NEPHROTIC SYNDROME

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OBJECTIVE

Hypertension has been generally recognized as independent predictor of unfavorable long-term outcome in patients with various chronic kidney diseases (CKD).

Angiotensinogen *AGT (M235T)* gene single nucleotide polymorphism (SNP) associated with increased serum angiotensin level and hypertension.

The data on the potential association between *AGT (M235T)* gene SNP and BP-lowering efficacy of ACE inhibitors (ACE-i) in children with steroid-resistant nephrotic syndrome (SRNS) is limited.

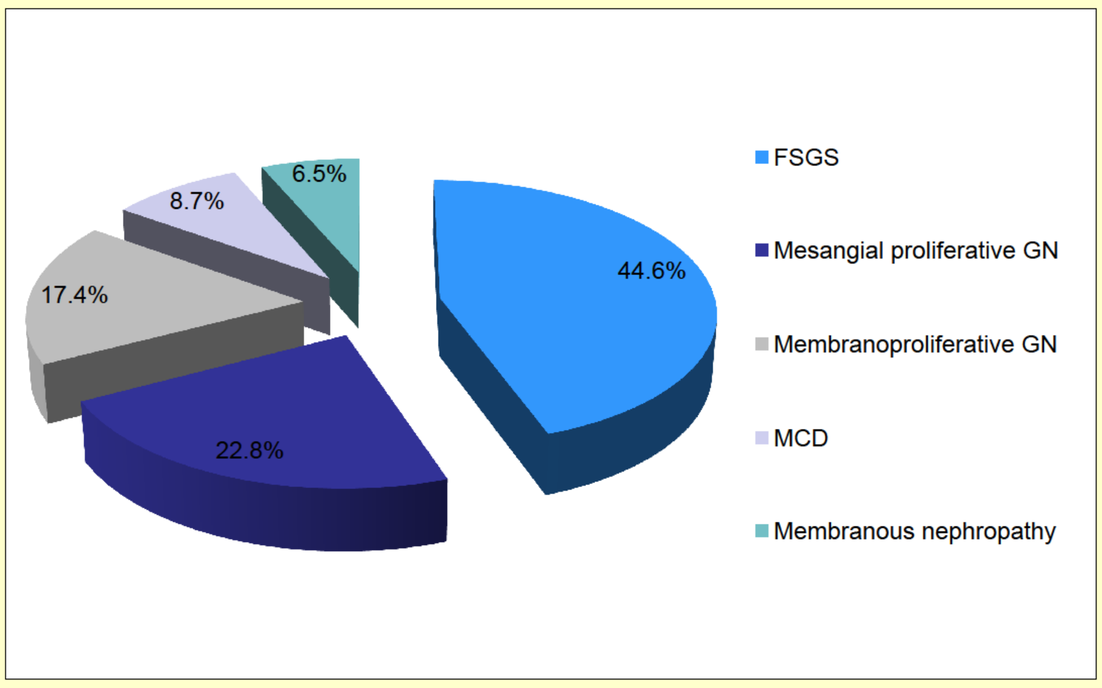
The study was conducted to determine whether *AGT (M235T)* gene SNP associated with efficacy of anti-hypertensive treatment in Russian children with idiopathic SRNS.

PATIENTS and METHODS

We performed a retrospective study of 92 children (40M/52F) aged 15.5 (IQR: 11.3; 17.0) years with idiopathic SRNS in relation to response to anti-hypertensive treatment with ACE-i subject to *AGT (M235T)* gene SNP. Histological findings were FSGS in 44.6%, MsPGN - 22.8%, MPGN - 17.4%, MCD - 8.7%, membranous nephropathy - 6.5% patients. Hypertension was determined during initial prednisolone treatment - 2 mg/kg/d (max 60 mg/d) for 6-8 weeks before using other immunosuppressive treatment. Anti-hypertensive effect of ACE-i treatment was defined as reduction of the BP ≤50th percentile for age, sex, and height of children. The *AGT* gene *(M235T)* SNP (rs699) was determined by PCR in SRNS patients and 50 healthy subjects as controls.

RESULTS

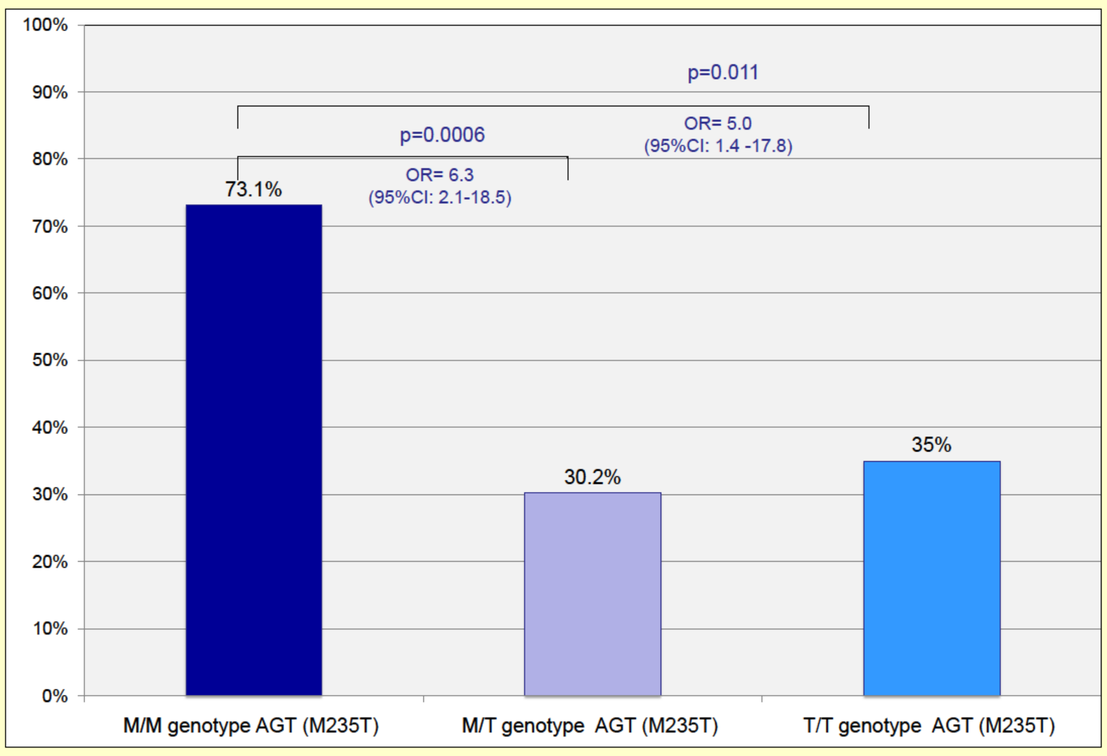
Histological diagnosis in children with SRNS (n=92)



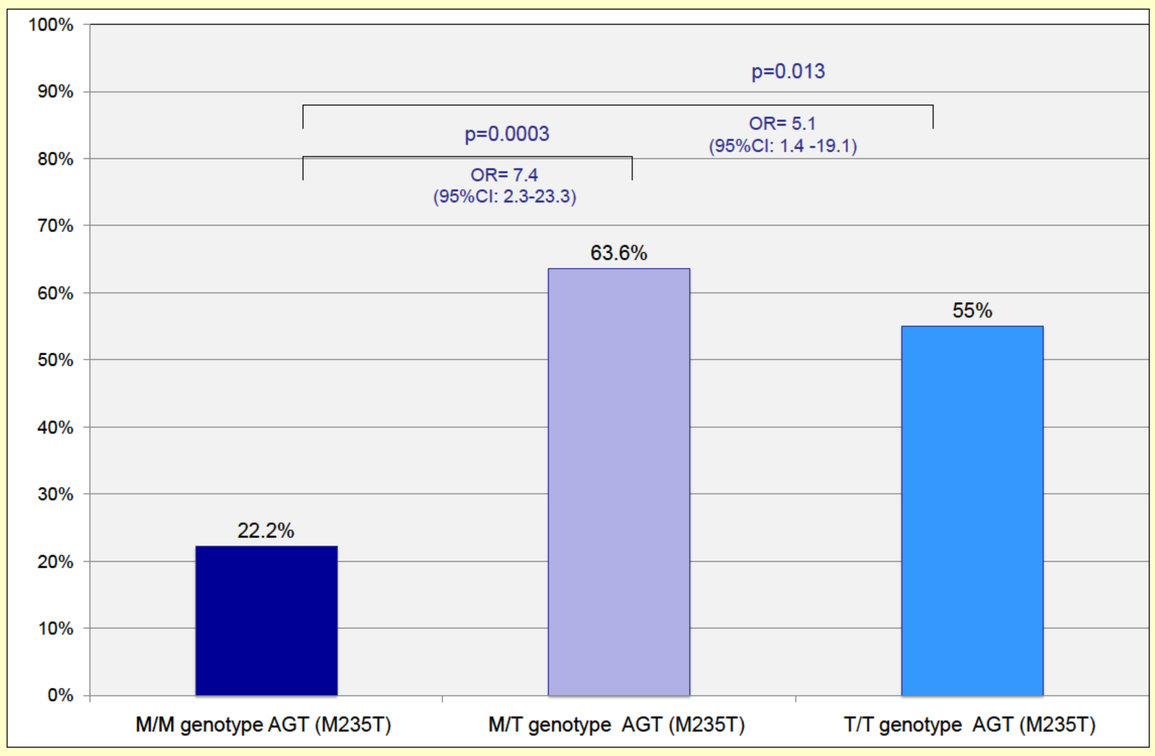
Distribution of alleles and genotypes of SNP *(M235T)* of *AGT* gene

Alleles & Genotypes	SRNS (n=92)	Control (n=50)	X^2	p
Allele *M*	99 (53.8%)	42 (42%)	3.61	0.06
Allele *T*	85 (46.2%)	58 (58%)		
Genotype *M/M*	27 (29.4%)	9 (18%)	3.5	0.17
Genotype *M/T*	45 (48.9%)	24 (48%)		
Genotype *T/T*	20 (21.7%)	17 (34%)		

Anti-hypertensive efficacy of ACE inhibitors in children with SRNS (n=92)



Proportion of combined anti-hypertensive therapy with inhibitors ACE and angiotensin-receptor blockers in children with SRNS



Allele frequencies and genotype distribution of the *AGT* gene *(M235T)* polymorphism in patients and controls were consistent with Hardy-Weinberg equilibrium (p>0.05). Median age, initial renal function, frequency of FSGS and hypertension did not differ significantly between patients with *AGT (M235T)* genotypes (p>0.05). Anti-hypertensive effect of treatment with ACE-i was identified significantly often in children with *M/M* genotype in comparison with patients with *T/T* and *T/M* genotypes of *AGT (M235T)* gene: 73.1% vs. 35% (p=0.011; OR=5.0, 95% CI: 1.4-17.8) and 30.2% (p=0.0006; OR=6.3, 95% CI: 2.1-18.5), respectively. Combined anti-hypertensive therapy with ACE-i and angiotensin-receptor blockers was needed significantly often in patients with *T/T* and *T/M* genotypes than in children with *M/M* genotype of *AGT (M235T)* gene: 55% vs. 22.2% (p=0.013), OR=5.1 (95% CI: 1.4-19.1) and 63.6% vs. 22.2% (p=0.0003), OR=7.4 (95% CI: 2.3-23.3).

CONCLUSION

Our results indicate that *AGT (M235T)* gene polymorphism associated with anti-hypertensive efficacy of ACE-i in children with SRNS. Patients with *M/M* genotype of *AGT (M235T)* gene had higher frequency of anti-hypertensive efficacy of therapy with ACE-i compared with children with *T/T* and *T/M* genotypes. This association can be speculated by severity of podocytes damage with involvement of expressed receptors to angiotensin.

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