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Apolipoprotein e2 allele – a genetic risk factor for nocturnal blood pressure elevations in Type 1 diabetes

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Introduction

We aimed to look for an association of the apoE genotype with blood pressure in adolescent patients with type 1 diabetes. Arterial hypertension, a precursor of cardiovascular disease in type 1 diabetes, is known to start as early as in childhood[1]. The prognosis of type 1 diabetes is highly dependent on the occurrence of cardiovascular complications[2]. Former reports have yielded contradictory results regarding the role of the apoE isoforms, probably due to different genetic background of the investigated populations. Modified by gender and environmental factors, genetic variants of the apolipoprotein E (apoE) have been shown to influence the susceptibility to hpertension. Therefore, we aimed to study the distribution of the apoE alleles in our population of german children and adolescents with type 1 diabetes and to look for an association of the different apoE variants with susceptibility for elevated blood pressure.

Methods

A total of 219 patients were recruited from the diabetes outpatient clinic. The local allele frequency of the ApoE gene was established in all patients and in a control population consisting of 181 healthy subjects (adult blood donors from the same region). All ambulatory blood pressure measurements were performed with the SpaceLabs 90207 monitor (SpaceLabs, Kaarst, Germany) based on an oscillometric method with the appropriate cuff size. Normal ranges for 24 h blood pressure in healthy children and adolescents were evaluated formerly in 130 patients in our clinic (age 7±23 years), which constituted part of a large multicenter study[3]. From 0600 to 2200 hours blood pressure was measured every 20 min, night measurements were performed every 40 min. ApoE genotypes were determined by PCR and mass spectrometry analysis. Ambulatory blood pressure values were compared with the genotype.

Results

The apoE genotypes did not differ regarding age distribution, duration of the diabetes or the gender distribution; whereas the BMI (sds) differed significantly, being lowest in the e2/3 and highest in the e3/3 group (p=0.035). Patients with the e2/3 vs. the e3/4 genotype had higher nocturnal systolic blood pressure (mean sds 1.07 vs. 0.12, p = 0.022).

	e2/3 (n=13)		e3/3 (n=75)		e3/4 (n=31)		p value*
		SD		SD		SD	
Sys BP day (sds)	-0.093	0.542	0.002	0.585	-0.191	0.632	0.81
Dia BP day (sds)	-0.198	1.371	-0.344	0.983	-0.548	0.835	0.82
Mean BP day (sds)	0.050	1.271	-0.123	0.878	-0.459	0.656	0.8
Sys BP night (sds)	1.029	0.945	0.651	1.116	0.248	1.137	0.022
Dia BP night (sds)	0.828	1.209	0.587	1.167	0.540	0.814	0.32
Mean BP night (sds)	1.149	1.341	0.698	1.334	0.397	1.065	0.047
Sys % day	12.51	18.66	10.94	15.25	7.68	9.8	0.089
Sys % night	7.26	15	3.33	9.03	1.07	4.37	0.0045
Dia % day	8.14	14.03	7.62	9.72	5.02	5.25	0.19
Dia % night	4.74	10.82	2.21	7.03	1.54	4.73	0.017

Table 1 ApoE genotype vs. blood pressure values (sds)

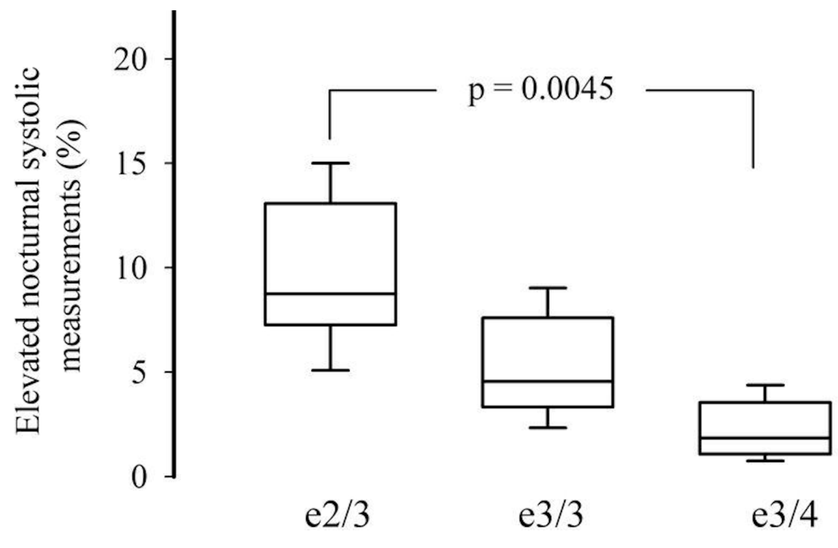

Figure 1 ApoE genotype vs. % of elevated nocturnal systolic blood pressure measurements

Moreover, patients with this genotype showed a higher percentage of elevated measurements of nocturnal systolic (7.26% vs. 1.07%, p=0.0045) and diastolic (4.74% vs. 1.54%, p=0.017) blood pressure measurements. Interestingly, this association was confined to male and to non-obese patients.

Conclusion

The apoE e2/3 genotype is associated with elevated nocturnal blood pressure in a German male and non-obese population with type 1 diabetes. Former reports have shown that genetic influence on the phenotype might be gender dependent[4]. Apart from environmental factors this genetic variant may increase susceptibility for cardiovascular morbidity and mortality. The molecular basis for the genotype-phenotype interaction and the preference of male gender still remains to be elucidated. Apart from accurate clinical surveillance, identifying genetic risk factors is of interest as this would aid follow-up and treatment of these patients.

References

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