Exploratory case-control study on ACE2 expression in children with short stature

LB-18

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BACKGROUND

Short stature is one of the most common presentations to paediatric endocrinologists. It is estimated that despite all the exams, in 50–90% of cases, children are labeled as having idiopathic short stature. It has been recently reported that genetic ACE2 deficiency is associated with reduced body weight as well as with impaired gestational weight gain and fetal growth restriction in pregnancy. It has been argued that ACE2 deficiency, which is usually associated with an increase of tissue Angiotensin II, could be associated with uterine artery dysfunction. Based on these premises, the aim of our study was to evaluate whether there was a difference of ACE2 expression in children with short stature as compared to age-matched controls.

METHODS

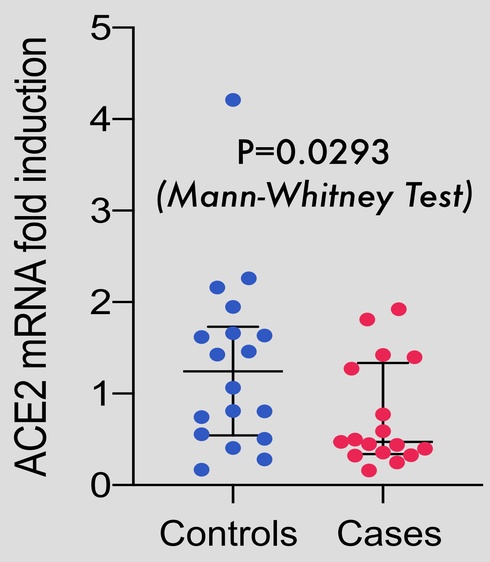
We designed an exploratory case-control study aiming at recruiting consecutively 40 children with short stature (cases) and 40 controls presenting at the Endocrinology Service, aged 2-13 years, excluding those with acute intercurrent diseases, diabetes, renal insufficiency, syndromes and/or on medications. After signing the informed consent to participating in the study, children underwent a medical visit and a fasting blood sampling. Peripheral blood mononuclear cells (PBMC) were isolated to extract mRNA for gene expression analyses. Sera were collected for protein measurements.

RESULTS

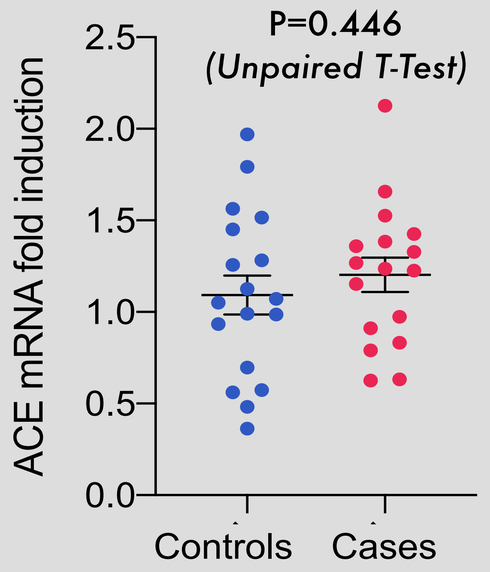
Children with short stature presented with lower height and body weight as compared to controls.
Our preliminary data show that children with short stature exhibited a significant reduction of ACE2 gene expression, and a significant increase of ACE/ACE2 ratio in PBMC. This was associated with a modest increase of Angiotensin II/ Angiotensin 1-7 ratio.
Our multivariate analysis showed that across the groups ACE2 was independently associated with height but not with body weight.

	Controls (n=18)	Cases (n=17)	p value
Age (years)	**6.502±0.683**	**10.095±0.772**	**0.0014**
Birth weight (grams)	3250 (3527.5-3085)	3080 (3250-2890)	0.0516
Height (SDS)	**0.09±0.179**	**-2.518±0.100**	**<0.0001**
Weight (SDS)	**-0.087±0.203**	**-2.374±0.147**	**<0.0001**
BMI (SDS)	**0.249±0.189**	**-1.270±0.144**	**<0.001**
SH/H	-0.376±0.246	0.190±0.175	0.3611
U/L ratio	1.154±0.028	1.101±0.017	0.1212
Arm span/H	0.97 (0.98-0.96)	0.98 (1-0.96)	0.3316
Systolic BP (mmHg)	102.8±2.966	99.0±3.433	0.409
Diastolic BP (mmHg)	62.89±1.637	61.76±2.261	0.6872

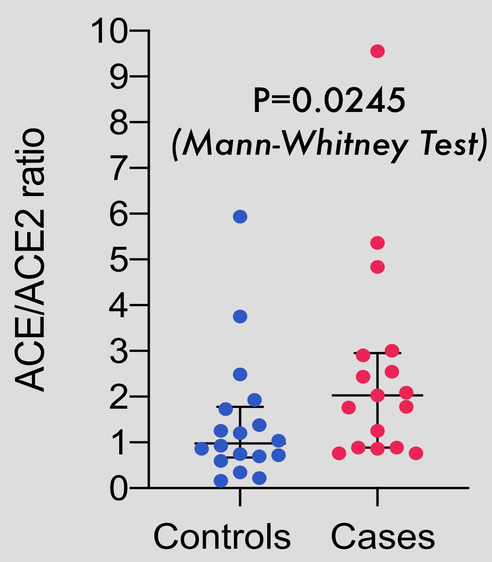
ACE2 gene expression



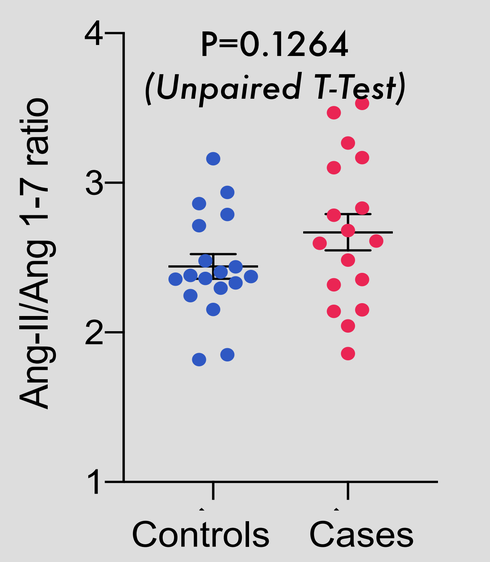
ACE gene expression



ACE/ACE2 ratio



Proteins expression



CONCLUSIONS

Our results, despite being preliminary with recruitment still ongoing, suggest - for the first time in vivo on children - a correlation between the reduction of ACE2 and the short stature - in line with our hypothesis and literature - which could play a causative role in growth reduction through IGF-1-dependent as well as IGF-1-independent mechanisms.
If these results will be confirmed, this study could be the basis for subsequent investigations aimed at confirming the causal relationship between ACE2 defect and growth impairment, with subsequent diagnostic-therapeutic perspectives.

References

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