STUDY OF IGF-1 RECEPTOR (IGF1R) GENE IN SMALL FOR GESTATIONAL AGE (SGA) PATIENTS WITH SHORT STATURE TREATED WITH rhGH.

FERRER LOZANO M., MARTINEZ DE ZABARTE JM, DE ARRIBA MUÑOZ A, BARRIO OLLERO E, LABARTA AIZPUN JI, FERRANDEZ LONGAS A.

Paediatric Endocrinology Unit. CHILDREN'S UNIVERSITY HOSPITAL MIGUEL SERVET. ZARAGOZA (SPAIN).

BACKGROUND

IGF1 is essential for pre and postnatal growth. Mutations in IGF1 R gene have been described in patients with intrauterine growth retardation and other anomalies.

OBJECTIVE

To study IGF1R gene in SGA patients treated with rhGH and correlate the results with clinical presentation and response to rhGh treatment.

METHODS

-Longitudinal retrospective study of 69 SGA patients with short stature registering weight, height, adult height, target height, height at start of rhGH and height gain after tratment.
-Genetic analysis consisted in DNA amplification, sequencing and electrophoresis.
-Statistics SPSS V20.0 ($p<0.05$)

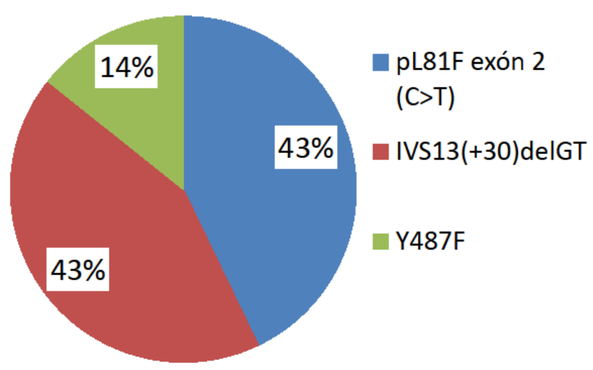
RESULTS:

-From the total cohort (79,7% female), 10,1% showed mutations in IGF1R, 81,4% polymorphisms and 13% were normal. Most prevalent polymorphisms were E1013E and IVS(+72) A/G.

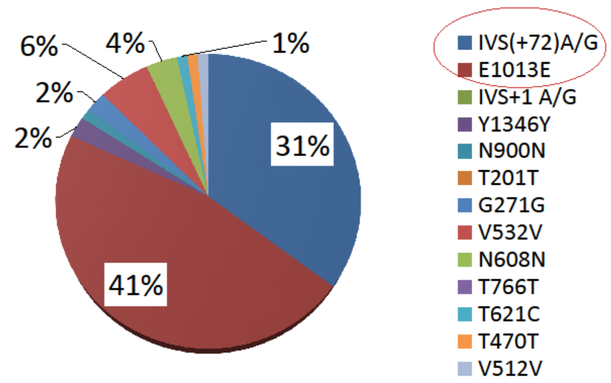
- Patients with **mutations** were significantly smaller at birth (lower weight, length and cephalic circumference), and presented with maternal short stature.

-Patients with **polymorphisms** showed lower length and weight at birth, target height and adult height compared with those with normal IGF1R analysis (ns).

-Analyzing **response to rhGH** in patients with the most prevalent polymorphisms, those with IVS(+72)A/G initiated before rhGH (6,4 ±2,6 vs 8,9±2,9 years; p=0,03), with more affected height (-3,32±0,6 vs -2,54±0,6 SDS; p=0,04), lower levels of IGF1(117±71 vs 264±130 mg/d; p=0,03)l and showed a better response in the first year of treatment (Δ0,94±0,8 vs Δ0,38±0,3 SDS; p=0,01) than patients with E1013E.



Mutations (n=7)

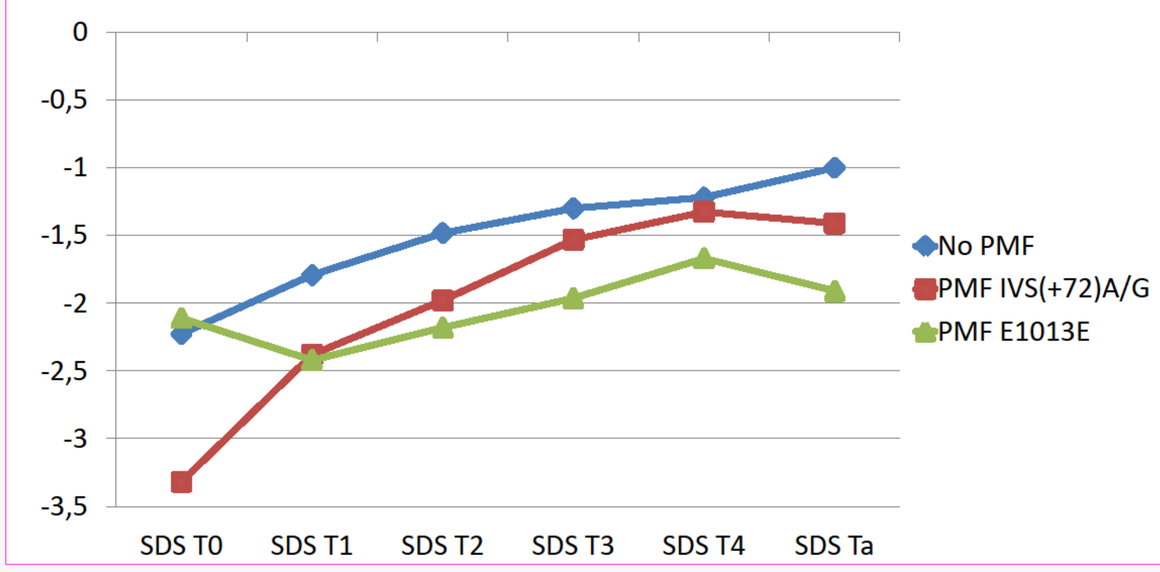


Polymorphisms

PERINATAL DATA

	MUTATION (-) (n=62)			MUTATION (+) (n=7)			p
	n	X̄	DS	n	X̄	DS	
Weight at birthkg)	50	2,54	0,52	4	2,32	0,6	0,280
Weight SDS		-1,46	1,3		-2,48	1,8	0,128
Lenght at birth (cm)	49	45,44	2,54	4	43,63	0,95	0,021
Lenght SDS		-2,53	1,03		-3,96	0,54	0,002
Cephalic circumference (cm)	40	32,48	2,74	4	30	1,83	0,036
Cephalic circumference SDS		-1,02	1,56		-2,8	1,39	0,025

RESPONSE TO rhGH TREATMENT



CONCLUSIONS:

- IGF-1 R gene mutations cause severe prenatal growth failure and are usually associated with familial short stature.
- Polymorphisms in this gene (E1013E and IVS(+72)A/G) have been found in SGA patients with short stature.
- The presence of different polymorphisms can influence the response to rhGH treatment in these patients.

ESPE 2015 393--P2

GH and IGF Physiology

Marta Ferrer

DOI: 10.3252/pso.eu.54espe.2015

Poster presented at: ESPE 2015 BARCELONA European Society for Paediatric Endocrinology

PosterSessionOnline.com