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Hospital General Universitario
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PHARMACOGENETIC STUDY ABOUT POLYMORPHISM INFLUENCE OF THE GENE TRAILR1 IN RESPONSE TO TREATMENT WITH INLFIXIMAB IN PATIENTS WITH CROHN's DISEASE (CD)

M. De Andres Bautista, D. Lacruz Guzmán, V. Dominguez Leñero, P. Perez Cañadas, M. Martínez Penella, H. Garcia Lagunar, E. Ferris Villanueva, R. Guerrero Bautista
Santa Lucia University Hospital, Cartagena (Murcia) Spain

BACKGROUNG

Anti-TNF drugs show high interindividual variability in efficacy and toxicity. Currently there are not genetic, biochemical or enviromental markers to predict response to treatment.

PURPOSE

To assess the influence of gene polymorphism rs2230229 TRAILR1 as genetic marker in response to treatment with infliximab in patients diagnosed with Cronh´s disease (CD) will allow us to predict response and improve the effectiveness of the drug.

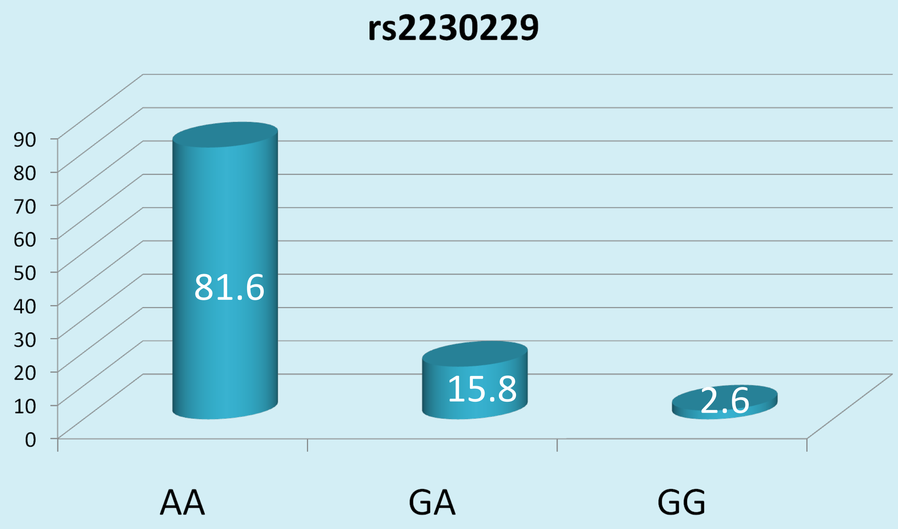
MATERIAL AND METHODS

Prospective observational study. The clinical response to therapy in CD was assessed after three moths of infliximab initiation (4th infliximab infusion). The therapy was considered as effective when CDAI (Crohn Disease Activity Index) decreased in more than 70 points compared to the pre-infliximab (basal) score or clinical remission when CDAI index was below 150 points. Biological response was evaluated at 3, 6 and 12 months after infliximab commencement by measuring the CRP (C-reactive protein) level and considering a positive response when CRP decreased in more than 25% compared to basal levels. Gene polymorphism was determined using the Kbioscience chemistry based on competitive allele-specific PCR (KASPAR). A 7500F real time termocycler was used for PCR and plate reading (Applied Biosystems, Foster City, CA, USA). All patients included in the study received a starting dose of infliximab 5 mg / kg at 0, 2 and 6 weeks after the start and then a maintenance dose every 8 weeks. Statistical analysis of the data was performed using the Epidat 3.1 program considering p <0.05 as statistically significant.

RESULTS

40 patients were included, 61.1% female. Mean age: 38.66±13.98 years

GENOTYPE DISTRIBUTION



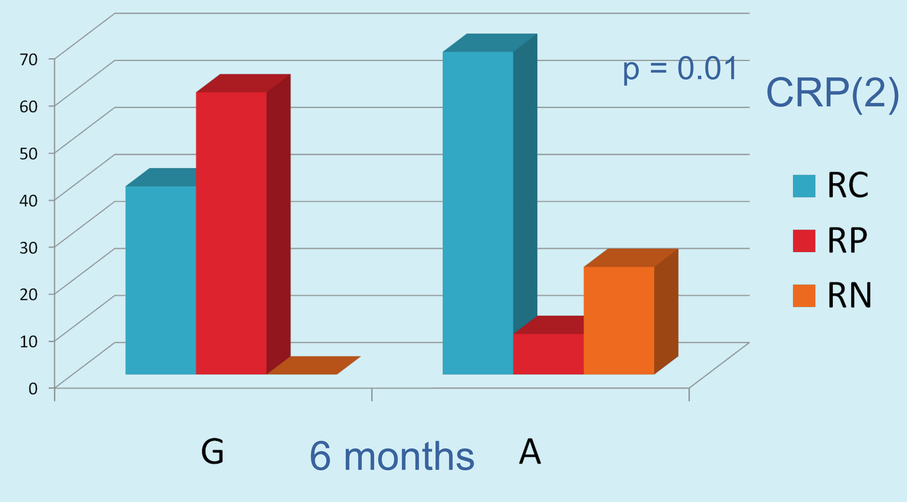
Association of genotypes GA +AA opposite GG in the polymorphism of TRAIL R1 rs2230229 according to the biological response criteria in CD

CD		TRAIL R1 rs2230229		P
		GG	GA/AA	
CRP (1) (6 months)	PR	0	11 (84.6%)	0.047
	NR	1 (100%)	2 (15,4%)	

Response to treatment according to alleles of TRAIL R1 polymorphism rs2230229 in CD

(CRP (1) was considered when the distribution of patients was between responders and no responders; CRP (2) was considered when distribution of patients was between responders, partial responders and no responders)

CD		TRAIL R1 rs2230229		P
		G	A	
CRP (1) (6 months)	RP	1 (4.5%)	2 (33.3%)	0.043
	RN	21 (95.5%)	4 (66.6%)	



Response to treatment according to genotypes of TRAIL R1 polymorphism rs2230229 in CD

CD		TRAILR1 rs2230229			
		GG	GA	AA	P
CRP (2) 12 months	CR	0	0	4 (66.6%)	0.044
	PR	0	1 (100%)	0	
	NR	1 (100%)	0	2 (33.3%)	

CONCLUSIONS

The results of our study show an association of this polymorphism with response to infliximab. The worst response rates were observed in patients carriying allele G. However, more studies on this polymorphism with a larger sample size are needed to confirm these findings.