

CORTICOSENSITIVITY IN INFLAMMATORY BOWEL DISEASE: ROLE OF GLUCOCORTICOID RECEPTOR POLYMORPHISMS

De Iudicibus S.^{1,2}, Stocco G.^{1,2}, Drigo I.^{1,2}, Norbedo S.², Bartoli F.¹, Decorti G.^{1,2}, Martellosi S.², Ventura A.²

¹ Department of Biomedical Sciences, University of Trieste

² Department of Paediatrics, I.R.C.C.S. Burlo Garofolo Trieste

Glucocorticoids (GC) are used as first line anti-inflammatory and immunosuppressive drugs in many inflammatory and autoimmune diseases and are effective in most patients with inflammatory bowel disease (IBD). However different clinical responses have been observed among patients suffering from such diseases. Three common polymorphisms (*BclII*, N363S and ER22/23EK) in the glucocorticoid receptor gene (hGR) may be involved in the large inter-individual variations in sensitivity to GCs and could hence cause different clinical response to steroid treatment, and alteration of hypothalamus-pituitary-adrenal (HPA) axis. The aim of this study was to evaluate the impact of hGR polymorphisms on GC sensitivity in IBD patients.

The hGR polymorphisms were studied by polymerase chain reaction-restriction fragment length polymorphism assay in 112 young patients, 60 with Crohn's disease (CD) and 52 with ulcerative colitis (UC), and 100 healthy volunteers. Of the 112 patients, 45 were GC-dependent, as GC therapy was needed to control the disease, and 67 were defined GC-responsive, if GC withdrawal was possible without steroid requirement during at least one year.

The homozygous mutated genotype for *BclII* was significantly more frequent in CD patients (21.7%) than controls (8.00%; $p=0.04$). This mutation was found to be associated with GC hypersensitivity and could therefore lead to an increased sensitivity in peripheral and central glucocorticoid receptors, determining a raised susceptibility to feedback inhibition of GCs on the HPA axis.

A significant higher frequency of *BclII* mutated genotype was also observed in the GC-responsive patients, compared with GC dependent group ($p=0.0075$). Hence, patients with this polymorphism, respond well to the steroids and do less often need additional courses of this therapy, at least during the first year considered. No differences were observed for the other hGR gene polymorphisms