

Failure of human immunoresponse to N-glycolylneuraminic acid epitope contained in recombinant human erythropoietin

Abstract:

Recombinant human erythropoietin (rHUEPO) was produced by Chinese hamster ovary cells and commercially distributed to hospitals by two pharmaceutical companies in Japan ('ESPO' by Kirin Brewery Co. Ltd., and Sankyo Co. Ltd., and 'EPOGIN' by Chugai Pharmaceutical Co. Ltd.) These products contained about 1% N-glycolylneuraminic acid (Neu5Gc) in total sialic acid content. Since humans do not synthesize Neu5Gc, successive injection of Neu5Gc-containing products was feared to lead to allergic-like symptoms. Therefore, serum levels of antibodies of Neu5Gc epitope in 90 patients who received repeated i.v. injections of ESPO or EPOGIN were determined by an enzyme immunoassay using Neu5Gc alpha 2-3Gal beta 1-4Glc-Cer, GM3(Neu5Gc), as an antigen and compared with those in 100 healthy persons. Either no or low antibody levels were detected in both groups with no significant difference. In 40 patients who received s.c. injections of ESPO or EPOGIN, serum HD antibody levels were determined before and after weekly therapeutic injections carried out for one to several months, but no significant elevations were detected in all patients. The above results indicated that therapeutic administration of rHuEPO to patients with chronic renal failure is safe from allergic-like side effects associated with the production of Neu5Gc-specific antibodies, and it was concluded that Neu5Gc epitope of rHuEPO is minimally antigenic in humans