Abstract

Toxicological evaluation of Interleukin-2 and FPCR3 vaccine candidate in Sprague-Dawley rats, combined therapy in AIDS patients. Different types of vaccines have been developed in the search for new therapeutic formulas against the human immunodeficiency virus; among them, are those that stimulate cytotoxic T lymphocyte response against HIV antigens. After a vaccine candidate was obtained at the Center for Genetic Engineering and Biotechnology (Havana, Cuba) using a modified fowl pox virus with genes that express HIV proteins, a clinical trial combining the application of this product (FPCR3) with highly active antiretroviral therapy and low doses of human recombinant Interleukin-2 was designed. Before testing these biotechnological products in patients with acquired immunodeficiency syndrome, it was necessary to evaluate their safety by carrying out various toxicological assays. Two acute toxicity studies were designed in which the systemic and local responses of Sprague-Dawley rats given higher doses than the patients included in the pilot clinical study. Fifty rats of the Cenp subline: SPRD (Sprague-Dawley) were used in the acute toxicity study of hr-Interleukin-2 and 70 animals of this same species and subline were used for the vaccine candidate, FPCR3. The products were administered by subcutaneous and intramuscular routes respectively, at doses 30, 60 and 90 times higher than the therapeutic dose. Three groups were included in the FPCR3 vaccine candidate study, receiving repeated administrations to evaluate local tolerance for this product. In both studies a control group inoculated with placebo formula, was used. Daily clinical observation was carried out. A histopathological study of the target organs and the administration site was also carried out. No signs of toxicity or adverse effects were observed in the animals inoculated with the FPCR3 vaccine candidate or with IL-2. No deaths were reported during the studies and the animals showed an adequate response to stimuli, as well as a progressive increase in weight. The histopathological study showed a slight, local reaction characterized by the presence of granulation tissue in animals that received Interleukin-2. Macrophage granulomas of different intensities at the administration site were observed in the animals that received different doses of the vaccine candidate, FPCR3. No signs of toxicity were observed in the target organs. Even though other toxicological studies are necessary, these results suggest that the use of the vaccine candidate, FPCR3 and of Interleukin-2, against the human immunodeficiency virus, is safe and well tolerated when the doses studied are given, assuring adequate safety for its administration to patients infected with the acquired immunodeficiency syndrome included in the pilot clinical trial.
Keywords
Acute toxicity, DNA vaccines, VIH, Interleukin-2