552

DEVELOPMENT OF NEW THROMBUS IMAGING AGENT: ^{67}Ga-DFO-DAS-FIBRINOGEN.

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As a thrombus imaging agent, In-111 labeled platelet has been used, however, it has not been widely used in Japan because the special skills and complicated treatments are required prior to the administration. Therefore we developed a new thrombus imaging agent ^{67}Ga-DFO-DAS-Fibrinogen. Fibrinogen was conjugated with a reactive polymer(DAS), into which many bifunctional chelates(DFO) are introduced. DFO-DAS-Fibrinogen will be lyophilized and suplied with ^{67}Ga solution. Prior to the administration, lyophilized Fibrinogen should be simply dissolved in ^{67}Ga solution for ^{67}Ga labeling. The labeled soluion, ^{67}Ga-DFO-DAS-Fibrinogen, has high in vitro stability over 6 hours.

We established a sterile and pylogenic production system, without losing its physiological activity.

The toxity studies on DFO-DAS-Fibrinogen and final injectable solution indicated the toxicological safety of this agent.

Pre-clinical studies have been completed, and the clinical trials(IND) of ^{67}Ga-DFO-DAS-Fibrinogen is now in progress.

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553

DEVELOPMENT OF Tc-99m-DTPA-HSA AS A BLOOD POOL SCANNING AGENT

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A new HSA preparation, Tc-DTPA-HSA, was developed as a blood pool scanning agent. It shows higher labeling yield and higher blood retention than Tc-99m-HSA obtained from commercially available kits. The introduction of DTPA to HSA provides for the stable binding to Tc-99m. The preparation composed of 20mCi of Tc-99m at calibration time and 10mg of DTPA-HSA in a vial. After labeling, it had been stable for 24 hours at room temperature.

Biodistribution was studied using rats and rabbits. In rats, the half-lives of blood levels were 4 hours (rapid phase) and 13 hours (slow phase). The excreted rats of the radioactivity were 55% in urine and 14% in feces at 48 hours after i.v. administration.

Metabolized products observed in urine were free Tc-99m (coupled with some urinary constituents), reduced Tc-99m, Tc-99m-DTPA and so on.

In acute toxicity test in mice and rats, LD50 value was higher than 5000mg/kg assuring non-toxicity of this agent. The radiation dose for human was estimated by the MIRD technique based on the biodistribution results in rats.

These results suggested than Tc-99m-DTPA-HSA is an excellent agent for blood pool scanning. Its clinical trials will be started in the near future.

554

CENTOCOR 5D-3 RIA KIT MEASURING HBs ANTIGEN USING MONOCLONAL ANTIBODY.

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Recently we obtained new in-vitro diagnostic reagent Centocor 5D-3 RIA Kit measures hepatitis B surface antigen (HBs Ag). In 1981, J.R.Wands prepared and characterized high-affinity monoclonal IgM (5D-3) and IgG (5C-11) antibodies to specific determinants or epitopes on HBs Ag. These antibodies have been utilized to develop highly sensitive solid phase RIA for detection of HBs Ag in human serum. Measurement is so fast as finished in 4 hours reaction times by 1 step sandwitch method. Accuracies in intra and inter assays, and inter daily reproducibilities are quite well.Good results were obtained in recovery test as average recovery is 101%. In dilution test straight relationship was obtained till 32 times dilutions even if using patient serum with high antigen concentration, we also carried out some other test on specificity, standard curve, reaction conditions, and so on.

555

COMPETITIVE RADIOIMMUNOASSAY FOR ANTIBODY TO THE HEPATITIS DELTA ANTIGEN.

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The Hepatitis-B-Virus(HBV) associated Delta antigen was first detected in the liver of some patients with chronic HBV infection, by Rizzetto et al. in 1977. This Delta virus is transmitted by coinfection or superinfection of HBsAg carriers. In the case of coinfection, this Delta virus increases the severity of acute hepatitis. And in the case of superinfection, an asymptomatic HBsAg carrier state or a benign chronic persistent hepatitis is converted to chronic active hepatitis and cirrosis by this virus.

The prevalence of Delta infection in Japan have been reported, but the incidence is low. Delta infection is usually diagnosed by detecting of antibody to Delta antigen(anti-Delta), because circulating Delta antigen is only detectable in short time.

We have developed the competitive RIA for the detection of anti-Delta.

Within-assay and between-assay CV's were 3.7-10.2% and 1.0-11.0% respectively. And the dilution test showed a good result. In Japanese clinical study, anti-Delta was found in 1.2%(4/356) of HBsAg carriers. And Delta-antigen was also detected by immunofluorescence method in the liver from an anti-Delta positive patient. The patient was diagnosed fluminant hepatitis.