32

Radioiodinate Labeling of Atherosclerotic Plaque Imaging Agent SP-4 and Preliminary Experiments

Y. Zhang, Z. Wu

Union Hospital, Tongji Medical University, Wuhan, China

Objective: SP-4 was oligopeptide contained 18 amino-acid. It was a part of apolipoprotein B. To study labeling SP-4 with ^{131}I and its clinical prospect as an atherosclerotic plaque imaging agent. Methods: SP-4 was synthesized by solid phase method and identified by amino acid analysis after purification with preparation-model HPLC. SP-4 was labeled with ^{131}I by the Chloramine-T method and purified through Sephadex G-25, then the radiochemical purity of ^{131}I-SP-4 and its stability in vitro were analyzed. 12 New Zealand rabbits were divided into atherosclerosis group (n=7, group A) and control group (n=5, group B). All of them were administrated with bovine serum albumen through i.v. ,then the rabbits of group A were fed on high cholesterol and high fat diet and group B, on normal diet. Purified ^{131}I-SP-4 was injected intravenously. %ID/g in blood and thoracic aorta and abdominal aorta at 4 hrs after injection and biodistribution of ^{131}I-SP-4 was investigated. Results: The amino acid formation of the pure product was identified to be correct through amino-acid analysis. The radiochemical purity of ^{131}I-SP-4 was 96.2% after being purified, but less than 90% after being stored for 20 hrs. One of 7 rabbits in group A died after being fed for three weeks, the others were alive and atherosclerotic lesions were found after being fed for two mon. On the contrary, 5 rabbits in group B were visualized not to have atherosclerotic lesions. The uptakes of group A and group B at 4 hr after injection were 0.0378 ± 0.0028 and 0.0371 ± 0.038 in blood ($p>0.05$), 0.0882 ± 0.0101 and 0.0276 ± 0.0044 in abdominal aorta ($p<0.01$), 0.0544 ± 0.0026 and 0.0220 ± 0.0021 in thoracic aorta ($p<0.01$). The radioactive accumulation of atherosclerotic lesions were significantly higher than that of normal rabbits. The disappearance of radioactivity from plasma was very rapid. The radioactivity in plasma at 4 hr was 8.22% of that at 2 min after injection. ^{131}I-SP-4 was mainly excreted through kidneys. Conclusions: SP-4 remained its biological activity after radioiodination and was located at atherosclerotic lesions. It was potentially useful as an atherosclerotic plaque imaging agent.

33

Synthesis and Biodistribution of ^{188}Re-labeled Phosphonic Acid Derivatives

K.S. Won[2],*, S.J. Oh[1], D.H. Moon[1], J.H. Cheon[1], H.K. Lee[1]

Department of Nuclear Medicine, Asan Medical Center[1], Asan Kangnung Hospital[2], University of Ulsan, Seoul, Korea

In this study, we synthesized ^{188}Re-labeled phosphonic acid derivatives; ethylenediaminetetramethylene phosphonate (EDTMP), 3,3-diphosphono-1,2-propanedicarboxylic acid (DPD) and dichloromethy lidene-1,1-bisphosphonate (Chlodronate), and compared in vivo biodistribution of ^{188}Re-EDTMP with that of ^{188}Re-HEDP. EDTMP 43 mg, DPD 13 mg, or chlodronate 20 mg was used. 50 μg NH_4ReO_4 and 0.7 mg, 1mg, and 3mg of $SnCl_2$ was used and it was incubated 15, 30, and 30 min at 100 °C for ^{188}Re-EDTMP, DPD and Chlodronate, respectively. All compounds were synthesized at pH=1, and adjusted to pH=6 with 3 M sodium acetate. Radiochemical purity and stability were checked by ITLC and Whatman paper 1. ^{188}Re-HEDP was synthesized using established method, which is HEDP 15mg, $SnCl_2$ 3 mg, gentisic acid 4 mg, and NH_4ReO_4 50 μg at 100 °C, 15 min. Animal experiment for ^{188}Re-EDTMP and ^{188}Re-HEDP was performed. After injection, organs were dissected and %ID/g was obtained at 4, 24, and 48 h (n = 4 for each group). ^{188}Re complexes of all ligands showed > 95 % radiochemical yields. Uptake (%ID/g) of ^{188}Re-HEDP and EDTMP in femur was 1.11 ± 0.07, 1.18 ± 0.21 at 4 h ; 0.79 ± 0.07 and 0.87 ± 0.24 at 24h; and 0.77 ± 0.14 and 0.77 ± 0.12 %ID/g at 48 h, respectively ($p>0.05$). For spine, 1.39 ± 0.17, 1.15 ± 0.15 ; 0.85 ± 0.12, 0.81 ± 0.04; 0.75 ±0.05, 0.64 ± 0.10, respectively ($p>0.05$). The ^{188}Re-EDTMP uptake in the kidney was 0.629 %ID/g at 4 h but decline to 0.250 and 0.184 at 24 and 48 h, respectively. The radioactivities for ^{188}Re-EDTMP in the lung, liver, muscle, and heart were all lower than 0.07 %ID/g at 4 h and also decline rapidly. Uptake of blood was slightly higher for ^{188}Re-EDTMP at only 4 hours (0.036 vs 0.054 for ^{188}Re-HEDP and EDTMP, respectively, $P < 0.05$), and it decline to 0.01 and 0.004 %ID/g at 24 and 48 h, respectively. The ligands complexed with ^{188}Re in high yield and all complexes showed good stability. ^{188}Re-EDTMP showed similar or higher bone uptake with ^{188}Re-HEDP.