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Preparation of A Novel Potential Perfusion Imaging Agent and Animal Study

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Purpose: To search for a novel potential SPECT cerebral blood flow perfusion imaging agent of our country knowledge property right, and to prove its SPECT cerebral perfusion imaging characteristics by animal studies. **Methods:** Tridentated MBPDA with N_2S obtained form chemical synthesis and characterized by IR, ^{1}H, ^{13}C NMR, element analysis and MS, and ECD provided by Shanghai Hongqi Medicinal Factory were labeled with technetium-99m under optional conditions, respectively. Biodistribution in 40 Kung Ming mice was measured at different time points after intravenous injection of 555～ 740 KBq $^{99}Tc^{m}$-MBPDA. The uptake percent dose per organ (%ID/organ) and per gram tissue (%ID/g) were calculated. Dynamic imaging of 30 scintigrams at a rate of 2 s/frame, 28 at 30 s/frame, and 50 at 60 s/frame using GE Starcam 400 AC/4000i SPECT in 2 monkeys was immediately acquired after rapid injection of 218.3～333 MBq of $^{99}Tc^{m}$-MBPDA or $^{99}Tc^{m}$-ECD, and SPECT monkey whole body and cerebral tomographic imaging were performed at 70 min postinjection, and images were processed and reconstructed to be transverse, coronal and sagittal sections. Acute toxic animal trials using 2 groups of mice (n=5, each group) and apyrogen experiment in 3 rabbits were studied respectively. **Results:** The radiochemical purity of $^{99}Tc^{m}$-MBPDA abd $^{99}Tc^{m}$-ECD was more than 95% and 97% Biodistribution results in mice showed high brain uptake and good retention, and the brain uptake percents at 2, 5, 15, 30 and 60 min postinjection were 1.85±0.38, 1.80±0.02, 1.32±0.02, 1.16±0.23, and 1.17±0.05 %ID. Sixty-three point two percent of initial activity remained in brain 60 min postinjection. The blood clearance half time was less than 15 min (6.19±0.07%ID). The brain/blood ratio was 7.3 at 60 min postinjection. The cerebral dynamic blood flow perfusion imaging in monkey demonstrated at 2 min after administration to attain the maximum radioactivity of $^{99}Tc^{m}$-MBPDA in the brain. In comparison with activity at 2 min ($^{99}Tc^{m}$-MBPDA) and 5 min ($^{99}Tc^{m}$-ECD) postinjection, eight-three percent ($^{99}Tc^{m}$-MBPDA) and sixty-two point eight (ECD) percent of initial activity remained in brain at 60 min images. The brain uptake of 2.7 %ID for $^{99}Tc^{m}$-MBPDA and 2.9 %ID for $^{99}Tc^{m}$-ECD were obtained at 70 min postinjection from the whole body imaging. The tomographic images showed that the activity remained in gray matter was higher than in white matter. The radioactive distribution in cerebral cortex showed uniform and symmetric, with good contrast of imaging. No death and side-effects during 48 h observation was found in acute toxic study and pyrogen experiment showed negative. **Conclusion:** $^{99}Tc^{m}$-MBPDA possessed similar property to $^{99}Tc^{m}$-ECD, and the initial high brain uptake combining with ideal brain retention in monkey was favorable for SPECT imaging. This proposed compound as a radiopharmaceuticals showing safe and reliable in vivo appeared to be a novel potential cerebral flow perfusion imaging agent.