

New bone-seeking agent: Animal study of Tc-99m-incadronate

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Objective: Disodium cycloheptylaminomethylenediphosphonate monohydrate (incadronate disodium) is a third-generation bisphosphonate compound which potently inhibits bone resorption, and a highly effective drug in the treatment of metastatic bone disease. We first labeled incadronate disodium with ^{99m}Tc , and examined its biodistribution and bone uptake after intravenous injection in rats to assess its potential for clinical use as a bone-seeking agent for judgment of the therapeutic effect of incadronate on bone metastases. Bone scan with ^{99m}Tc -labeled incadronate (^{99m}Tc -incadronate) may yield important information prior to the use of incadronate for treatment of bone metastases. **Methods:** Synthesis of ^{99m}Tc -incadronate was carried out by reduction of ^{99m}Tc -pertechnetate in the presence of SnCl_2 and N_2 gas. Normal rats were injected with 18.5 MBq (0.5 mCi) ^{99m}Tc -incadronate in a volume of 0.1 ml intravenously and then sacrificed at 15 min, 30 min, 1 h or 2 h (six rats at each time point) after injection. Samples of muscle, stomach, small intestine, kidney, liver and bone (femur) were taken and weighed. In addition, a 1-ml sample of blood was drawn from the heart, and urine was taken from the urinary bladder immediately after sacrifice. Samples were measured for radioactivity and expressed as percent uptake of injected dose per gram or per milliliter (% ID/g or ml). Bone-to-blood and bone-to-muscle uptake ratios were determined from the % ID/g or ml values for these organs. **Results:** The greatest accumulation of ^{99m}Tc -incadronate was found in bone. Radioactivity in bone was as high as $3.22 \pm 0.68\%$ ID/g at 2 hours after injection. Scintigraphic images of ^{99m}Tc -incadronate in normal rats revealed highly selective skeletal uptake. **Conclusion:** ^{99m}Tc -incadronate exhibited high uptake in bone, and relatively low uptake in soft tissue, suggesting that it may be useful as a bone-seeking agent for judgment of the therapeutic effect of incadronate on bone metastases, by determining the degree of its accumulation in metastatic bone lesions.

Key words: bone-seeking agent, bisphosphonate, ^{99m}Tc , incadronate, rats