[S2-4] [10/10/2003(Fri) 13:00-13:30/ Grand Ballroom 103]

Development and Applications of Radiopharmaceutical "Milican inj."

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Purpose

Radiation therapy has been used for the cancer treatment externally or internally. The external radiation therapy has been widely used, but for the lack of its selectivity it requires strong radiation dose causing the dermal irritation and radiation effect of the normal tissues or organs. So we investigate non-clinical and clinical studies of "Milican inj.", in which chitosan is chelated with 166-Holmium, as an anticancer agent for internal radiation therapy.

Methods

Physicochemical properties, toxicity and biodistribution of "Milican inj." were performed in non-clinical experiments with medical preparation of a Holmium166-chitosan complex injection fluid. After that, Clinical Phase I and early phase II study were designed with 19 patients of hepatoma on 3 dose escalating steps[10mCi/cm(1step), 20mCi/cm(2step), 30mCi/cm(3step)], and late phase II study were performed with 62 patients of hepatoma (dosage; 20mCi/cm). For the extension of application, efficacy and/or biodistribution studies for the prostate cancer and skin cancer in animal model were performed. And clinical studies for rheumatoid arthritis is being performed.

Results

A clear solution of low pH was made by mixing "Milican inj.", but it converts to a gel under basic conditions. The biodistribution study of intrahepatic or intratumoral administration of "Milican inj."in rats revealed that 1) the effective biological half-life of the administration site is much longer than that of other tissues; 2) the administration site-to-tissue ratios are extremely high; and 3) the activity in the organs rather than the administration site is very low. In case of clinical phase I and IIa study, the responses of the tumors to the treatments for 1, 2 and 3 step were 50%, 85.7% and 66.7% respectively at CT imaging. The radioactive concentrations in blood were extremely low, and cumulative urinary

excretions upto a period of 0-72hr were below 0.1%. Administered "Milican inj."was well localized within tumors without distribution to the other organs or tissues on gamma camera imaging. Any toxicity to the bone marrow or liver function except an allergy (skin rash) related "Milican inj."in 3 of 19 patients was not observed significantly, but the skin rash recovered within 3days after treatment. And during clinical phase IIb study, we can find 49 case(77.7%) of CN(complete necrosis) or PN(partial necrosis, more than 50%) among 63 patients.

Conclusion

These results indicate strongly that "Milican inj." can be a highly effective and safe new radiopharmaceutical agent for internal radiation therapy against hepatoma. And it can be applied to another diseases such as rheumatoid arthritis, prostate cancer and skin cancer.