A NEW POSSIBLE APPROACH FOR THERAPY AND FOLLOW UP OF BLADDER CANCER

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Introduction: The polymer PEI-MP (polyethyleneimine, functionalised with methylphosphonate groups) that might be labelled with ^{188}Re and ^{99m}Tc, have a strong potential for metabolic radiotherapy and diagnosis, respectively. The aim of this study was to evaluate the efficacy of ^{188}Re-PEI-MP as therapeutic agent for bladder carcinoma and ^{99m}Tc-PEI-MP for its follow up.

Material and Methods: Cytotoxicity of PEI-MP was investigated in bladder carcinoma cell line (CRL-1472) using the MTT test for different concentrations of PEI-MP (1 µM to 1000 µM) and incubation times (24h, 48h, 72h and 96h), and flow cytometry for a concentration of 1000 µM of PEI-MP (24h). Radiochemical purity of ^{188}Re-PEI-MP and ^{99m}Tc-PEI-MP was achieved using ascending microchromatography. Cellular uptake studies were performed using the complexes ^{188}Re-PEI-MP, ^{99m}Tc-PEI-MP, Na^{188}ReO$_4$ and Na^{99m}TcO$_4$. Cell samples were collected during four hours, centrifuged to separate supernatant and pellet. Subsequently, the radioactivity of each portion was counted to determine percentage of uptake. The *in vivo* studies were performed using eight groups of Balb/c nu/nu mice: four normal groups injected with Na^{188}ReO$_4$, ^{188}Re-PEI-MP, Na^{99m}TcO$_4$ and ^{99m}Tc-PEI-MP and four with bladder carcinoma xenotransplants injected with the same complexes. When tumour reached the appropriate volume, radiopharmaceuticals were administered by an intravenous injection in the tail vein (22-37MBq), with the animal anesthetized and previously placed on the gamma camera detector. After injection of the radiopharmaceuticals, were acquired dynamic and static images for 2 and 4 hours. For biodistribution proposes, mice were euthanized 2 and 4 hours after injection and organ samples where weighted and counted in a well-counter to obtain percentage injected activity per gram of organ (%ID/g).

Results: The MTT assay and flow cytometry tests showed that PEI-MP is not cytotoxic. The radiochemical purity of ^{188}Re-PEI-MP and ^{99m}Tc-PEI-MP was ≥85%. The uptake studies demonstrated that the uptake was higher for ^{188}Re-PEI-MP and ^{99m}Tc-PEI-MP in relation to their controls, and higher for ^{188}Re-PEI-MP e relation to ^{99m}Tc-PEI-MP. Biodistribution results, with $Na^{188}ReO_4$ and $Na^{99m}TcO_4$, showed a higher uptake by the thyroid, bladder and stomach, following a normal biodistribution. The biodistribution with ^{188}Re-PEI-MP and ^{99m}Tc-PEI-MP showed that the excretion of these complexes occurs primarily through the renal system, with a small fraction being eliminated by the hepatobilliary system. Tumour/muscle ratio for ^{188}Re-PEI-MP was greater than 1.5.

Conclusions: Considering the results, ^{188}Re-PEI-MP seems to be promising in the treatment of bladder cancer. Following the same biodistribution as ^{188}Re-PEI-MP, ^{99m}Tc-PEI-MP seems to be optimal for diagnosis and follow up of therapy.

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