Scintigraphic evaluation of radiation-induced gastrointestinal motility disturbance in micro-pig model

S.-S. Lee, K.M. Kim, J. Kim, W.-S. Jang, J.-E. Lee, N. Kim, S. Park, S.J. Lee, S.-Y. Cho, M. Kim, Y.H. Ji, G.J. Cheon and S.M. Lim

Korea Institute of Radiological & Medical Sciences, 215-4 Gongneung-dong, Nowon-ku, 139-706 Seoul, Republic of Korea

smlim328@kcch.re.kr

In the previous study, we have observed that micro-pigs showed similar clinicopathological responses to human in response to high-dose radiation exposure and that there are gastrointestinal (GI) motiltity disturbances even in less amount of irradiation causing acute GI syndrome. GI motiltity disturbances is a part of radiation-induced GI syndrome and may affect infectious progression from GI tract. The specific aims of this study is to evaluate objective evidence of GI motility disturbance employing scintigraphic evaluation and to develop biomarker in evaluating radiation-induced acute GI syndrome. PWG micro-pigs (6 month-old, BW 25Kg) were locally irradiated on whole abdomen with Co60 (δ-irradiation, 5Gy, 10 Gy and 15Gy). We compared gastric emptying time and small bowel transit time using 99mTc sulfur colloid (50mCi) and gamma camera, twice before (individual control) and sequential changes after irradiation (3, 7, 10, 14, 21 days). Endoscopic evaluation and biopsy followed scintigraphic evaluation in each experiment. With whole abdominal δ-irradiation (5Gy) in micro-pigs (n=2), small bowel transit time prolonged at day 3 (2.06 and 1.97 times in each), gradually recovered and normalized at day 10. In 10Gy, 15Gy-irradiated animals (n=2), GI motility prolongation were exaggerated. Endoscopy from stomach to upper jejunum showed no definite grossly identifiable mucosal changes in 5Gy and 10Gy irradiated animals, whereas microscopic mucosal changes were evident. At 4th day after irradiation, we observed shortening of mucosal villi, dilatation of microvessels, reduced proliferating activities (Ki67 labeling index) and marked increase of apoptotic bodies (TUNEL assay) at crypts and mucosal glands. The radiation-induced mucosal changes recovered till day 22. Microscopical changes preceded clinical manifestation and grossly identifiable changes, which suggests that treatment should be started prior to symptomatic manifestation. Scintigraphic evaluation of gastric emptying and small bowel transit gave objective evidence for GI motility disturbance after radiation exposure. It could be a useful biomarker for monitering treatment effects in acute GI syndrome, which may allow validation of newly developing therapeutics for acute radiation syndrome.

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