MATERIALS AND METHODS: Radiation sensitive (C57BL/6 female) mice and radiation resistant (C3H/Hej female) mice were treated with a single dose of irradiation to the thorax of 5 Gy or 12.5 Gy and mice were sacrificed at 1, 7, and 14 days post irradiation. Total lung RNA was prepared, immobilized by northern and slot blots, and hybridized with ^{32}P radiolabelled probes encoding for the messages of: collagen I (C I), collagen III (C III), collagen IV (C IV), fibronectin (FN), interleukin-1 (IL-1β), transforming growth factor beta$_{1,2,3}$ (TGFβ_1, TGFβ_2, TGFβ_3), and normalized to glyceraldehyde-3-phosphate dehydrogenase (GAPDH) mRNA abundance. Autoradiographic data were analyzed by video densitometry.

RESULTS: Changes in mRNA abundance in IL-1β TGFβ_1,β_2,β_3,collagen I/III/IV and fibronectin can show differences as great as 10 fold comparing the sensitive and resistant strains. Generally dose response patterns were found at either 1, 7 or 14 days. Although large variations within strains were noted at these different dose and time points. The increase in all components of TGFβ_1 and IL-1β at most time points, especially at 14 days, indicates an incremental fibrogenic stimulus persists after irradiation over the first 2 weeks. The alterations in collagen 1/3 ratios were particularly evident in radiosensitive mice at 14 days as compared to radioresistant mice where ratios were relatively normal at all times studied.

CONCLUSIONS: Changes in collagen I/III ratios are often considered as underlying causes of fibrosis. The results suggest a large imbalance in the radiosensitive C57BL/6 mice may be a major reason why they are more likely to develop fibrosis as compared to the radioresistant C3H/Hej mice. Furthermore, the different responses at the two doses utilized in the sensitive and resistant strains indicates that more than one mechanism may be involved in the development of fibrosis.

1050

EFFECT OF COENZYME Q_{10} AND AZELASTINE ON PROTECTING RADIATION PNEUMONITIS IN PATIENTS WITH LUNG CANCER

Kazufumi Imanaka, M.D., Toshiya Sakaguchi, M.D., Takeyuki Kushima, M.D., Yoshiaki Okamoto, M.D., Takahisa Hashimura, M.D., Michio Kono, M.D.,

Department of Radiology , Kobe University School of Medicine , Kobe 650 , Japan

Purpose: In experimental study, we have already suggested that initial damage of irradiated lung was induced by lipid peroxidase and leukotriens which were produced by the radiation-induced free radicals. Furthermore, we studied that an antioxidant (coenzyme Q_{10}) and an inhibitor of leucotrienes (azelastin HCl) could reduce radiation pneumonitis (RP).The purpose of this study is to investigate the effect of coenzyme Q_{10} and azelastin HCl for prevention of RP.

Materials and Methods: We performed a retrospective analysis of 41 patients with lung cancer to compare the severity of RP in two groups. Twenty patients was administered coenzyme Q_{10}(90mg) and azelastin HCl (4mg) every day during and after radiotherapy for 6 months (group A). Historical controls of 21 patients were irradiated without these drugs(group B). The criteria entered to evaluate RP was as follows ; 1) more than 40 Gy irradiation, 2) field size of 70 - 140 cm^2, 3) chest X - ray follow-up was taken at least for 6 months 4) without evidence of regrowth, pleural effusion and atelectasis. According to the findings of chest X-ray taken at the completion of radiotherapy, 1,3 and 6 months after radiotherapy , the severity of RP was divided into 4 grade (negative, mild, moderate, severe).

Results: Background and RP grade in two groups are shown in table 1 and 2. Severe RP was observed more frequently in group B than in group A. Severe cases in group A were all irradiated more than 60 Gy and their field size were more than 100 cm^2. On the other hand , in group B, 7 of 9 severe cases were irradiated less than 60 Gy and their field size were less than 100 cm^2.

Table 1

	dose(Gy)	field size(cm^2)
A	61.5 ±5.9	109.5 ±20.3
B	52.9 ± 10.5	88.6 ± 16.1
	p<0.001	p<0.005

Table 2

	Neg.	Mild	Mod.	Sev.	Total
A	0	7 (35)	10 (50)	3 (15)	20
B	2 (9.5)	4 (19)	6 (28.5)	9 (41)	21

cases (%)

Conclusions : These results strongly suggested that preventive administration of coenzyme Q_{10} and azelastin HCl was effective in reducing severe radiation pneumonitis.