THE EFFECT OF *PANAX GINSENG* ON THE POSTOPERATIVE RADIATION COMPLICATION IN CERVICAL CANCER PATIENTS

Yoon Seok Chang, Charn Il Park and Hyoung Ill Noh
College of Medicine, Seoul National University, Seoul, Korea

Radiation therapy has proved to be effective in the management of malignant tumors which is one of the leading causes of death. And it can be useful alone in the cases of poor surgical and medical risk for palliation, or in combination with surgery, chemotherapy and immunotherapy.

But radiation therapy is not possible without some clinical complications, one of which is the frequent depression of bone marrow. Therefore, a variety of drugs have been studied to enhance the hematopoietic activity of the depressed bone marrow.

Several studies have suggested that saponin extracted from Panax ginseng enhance the hematopoietic activity in the depressed bone marrow caused by radiation therapy.

Ginseng has traditionally been considered a medicinal plant of mysterious powers since about 2,000 years before. Fujiya[2], Asahina and Tanaka[3] etc. have determined the chemical structure of saponin, believed to be the main component of Panax ginseng, since Garrignes's first report of Panax ginseng in 1854[1]. And many experimental and clinical reports have been published for its pharmacological actions on central nervous system, cardiovascualar system, hematopoietic system, endocrine system, and various malignant diseases.

Yamamoto[4] reported that Panax ginseng especially enhances the synthesis of protein and lipid by stimulating mitosis in the bone marrow. And Yonezawa[5] also published an article that the administration of ginseng extract to the irradiated rats resulted in remarkable decrease in mortality, suggesting the recovery effect of hematopoietic activity in the depressed bone marrow.

In our effort to clarify the recovery effect of Panax ginseng on the depressed bone marrow due to radiation therapy, we administered Panax ginseng to a total of 50 cervical cancer patients undergoing radiation therapy, and analyzed its recovery effect by their hematological pictures before and after treatment of ginseng.

Materials and Methods

Between May and October, 1979, a total of 50 cervical cancer patients requiring radiation therapy alone or postoperative radiation therapy were included in this study. They were randomly divided into the experimental and control group of 25 patients, respectively. The experimental group was treated with 5.0 g of red ginseng powder per day for 5 weeks from the day before the initiation of radiation therapy, whereas the control group with placebo.

Hematologic examinations and blood chemistry were performed once or twice a week from the 2 days before radiation therapy. The laboratory data involved RBC and WBC counts with differential count, platelet count, and the serum levels of protein and bilirubin.

Radiation therapy was given by cobalt-60 units to the pelvic radiation field of 15 × 15 cm, and a tumor dose of 175–200 rads was delivered daily for a total of 4,500 to 5,075 rads. The age distribution of 50 patients was shown at Table 1.

Table 1. Age distribution in control and treated group.

Age	Control		Treated	
	No.	%	No.	%
21 ~ 30	0	0	2	8
31 ~ 40	4	16	4	16
41 ~ 50	8	32	8	32
51 ~ 60	8	32	8	32
60 or more	5	20	3	12
Total	25	100	25	100

Results

We assessed the differences of laboratory data between the experimental and control groups with their statistical significance. The results of hematologic and blood chemistry data are shown in Table 2.

The average counts of RBC in both experimental and control groups after medication were 375.2 × 10^4/mm^3 and 366.9 × 10^4/mm^3 respectively, slightly lower than those before medication by 11.6 × 10^4/mm^3 and 21.3 × 10^4/mm^3 respectively. In the experimental group, the RBC count was elevated within 2 weeks after medication of ginseng, whereas within 4 weeks in the cases of the control group, suggesting more potent recovery effect of red ginseng (Table 3 and Figure 1).

The mean hemoglobin values of both the experimental and control groups after medication were 12.00 g/100 ml and 11.67 g/100ml respectively, lower than those before medication by 0.22 g/100 ml and 0.39 g/ 100ml respectively without any statistical significance. The control group showed an increasing tendency from 2 weeks after placebo medication but the experimental group didn't (Table 4 and Figure 2).

The average WBC counts of both the experimental and control groups after medication

Table 2. Analysis of experimental data

Variables	Control (N = 25)			Treated (N = 25)		
	Pre-Tx.	Post-Tx.	Difference	Pre-Tx.	Post-Tx.	Difference
RBC (10^4/*mm*^{3})	388.8 ±30.8	375.2 ±30.6	−11.6 ±21.3	382.0 ±38.6	366.9 ±25.2	−21.3 ±19.6
Hb. (gm/100m*l*)	12.16 ±0.66	12.00 ±0.80	−0.22 ±0.23	12.17 ±1.15	11.67 ±0.99	−0.39 ±0.36
WBC (No./*mm*^{3})	5,305 ±1,246	3,640 ±675	−1,571 ±1,233	5,193 ±817	3,913 ±743	−1,341 ±743
Seg (%)	59.20 ±7.90	66.25 ±7.22	+7.08 ±7.74	54.07 ±16.39	66.93 ±7.72	+13.92 ±10.85
Lymphocyte (%)	32.50 ±7.83	21.40 ±5.12	−11.08 ±7.31	35.54 ±13.12	21.85 ±6.95	−13.92 ±16.71
Platelet (10^3/*mm*^{3})	266.0 ±90.6	229.0 ±56.4	−42.1 ±54.5	256.4 ±53.0	244.7 ±54.9	−21.0 ±29.7
Protein (gm/100m*l*)	8.03 ±0.41	7.98 ±0.39	−0.10 ±0.10	7.77 ±0.43	7.68 ±0.43	−0.10 ±0.35
Albumin (gm/100m*l*)	4.69 ±0.50	4.65 ±0.32	−0.04 ±0.28	4.62 ±0.44	4.78 ±0.41	+0.11 ±0.16
Bilirubin (mg/100m*l*)	0.58 ±0.33	0.51 ±0.31	−0.07 ±0.27	0.49 ±0.03	0.48 ±0.01	−0.11 ±0.10

Table 3. RBC count of both groups in pre-treatment and post-treatment. (× $10^4/mm^3$).

		Control (N = 25)	Treated (N = 25)
Pre-Tx.		388.8 ± 30.8	382.0 ± 38.6
Post-Tx	1 week	374.7 ± 43.3	375.3 ± 40.1
	2 weeks	369.1 ± 33.3	363.1 ± 29.7
	3 weeks	381.0 ± 43.7	372.4 ± 36.7
	4 weeks	362.7 ± 32.3	369.7 ± 30.5
	5 weeks	379.4 ± 37.1	383.2 ± 16.5

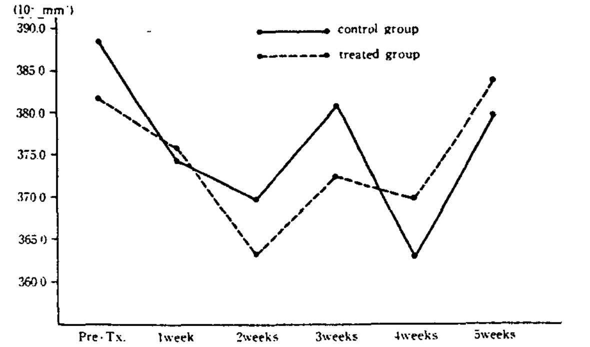

Fig. 1. Changes in RBC count in pre-treatment and post treatment.

Table 4. Hemoglobin value of both groups in pre-treatment and post-treatment. (gm/100m*l*)

		Control (N = 25)	Treated (N = 25)
Pre-Tx.		12.15 ± 0.66	12.17 ± 1.15
Post-Tx	1 week	12.07 ± 1.04	11.86 ± 1.15
	2 weeks	11.86 ± 0.77	11.84 ± 1.18
	3 weeks	11.92 ± 1.22	11.75 ± 1.24
	4 weeks	11.97 ± 0.75	11.76 ± 1.11
	5 weeks	11.92 ± 1.07	11.66 ± 1.12

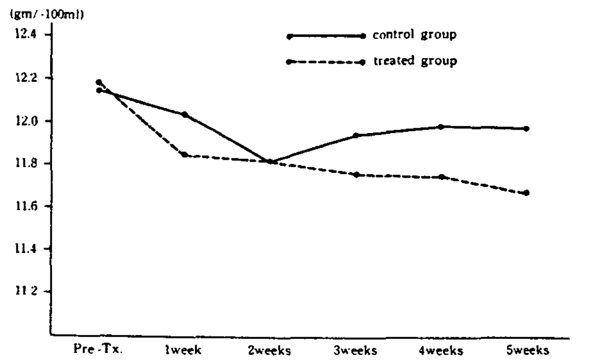

Fig. 2. Changes in hemoglobin value in pre-treatment and post-treatment

were $3640/mm^3$ and $3913/mm^3$, lower than those before medication by $1571/mm^3$ and $1341/mm^3$ respectively. The experimental group showed a little higher values than those of the control group, but statistically significant difference was not found.

The patterns of changes in laboratory values were similar in both groups during the period of study. The tendency of recovery was noticed from 4 weeks after medication with ginseng and placebo. On occasion of irradiation, the recovery of granulocyte count was found earlier than that of lymphocyte, because lymphocyte is more sensitive and labile to radiation injury (Table 5 and Figure 3).

The mean platelet levels were $229.0 \times 10^3/mm^3$ and $244.7 \times 10^3/mm^3$ respectively in both groups after treatment. And those values were lower than those before medication by $42.1 \times 10^3/mm^3$ and $21.0 \times 10^3/mm^3$ respectively, suggesting the inhibitory effect of ginseng on the decreasing tendency in platelet levels after radiation therapy.

Table 5. WBC count of both groups in pre-treatment and post-treatment. (No./mm^3).

		Control (N = 25)	Treated (N = 25)
Pre-Tx.		5,305 ± 1,246	5,193 ± 817
Post-Tx	1 week	3,847 ± 882	4,083 ± 760
	2 weeks	3,606 ± 904	3,766 ± 1,141
	3 weeks	3,618 ± 960	3,983 ± 972
	4 weeks	3,423 ± 585	3,325 ± 949
	5 weeks	3,809 ± 852	3,800 ± 1,053

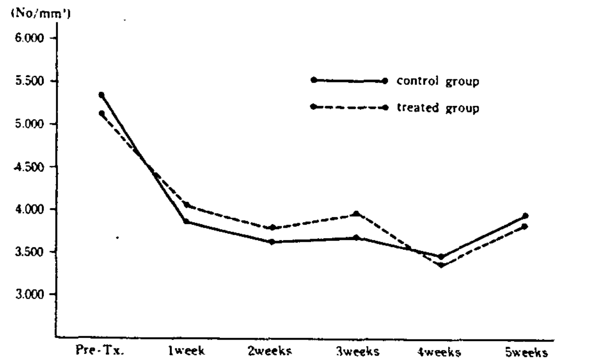

Fig. 3. Changes in WBC count in pre-treatment and post-treatment.

The changing pattern of platelet count in the experimental group was noticed from 3 weeks after the administration of ginseng whereas the control group didn't show any recovery pattern (Table 6 and Figure 4).

Table 6. Platelet count of both groups in pre-treatment and post-treatment. ($10^3/mm^3$).

		Control (N = 25)	Treated (N = 25)
Pre-Tx.		266.0 ± 90.6	256.4 ± 53.0
Post-Tx.	1 week	250.4 ± 93.1	254.6 ± 81.0
	2 weeks	232.1 ± 93.1	227.3 ± 74.2
	3 weeks	235.2 ±102.5	207.6 ± 64.6
	4 weeks	219.8 ± 53.8	233.7 ± 43.2
	5 weeks	220.8 ± 84.4	239.3 ± 68.2

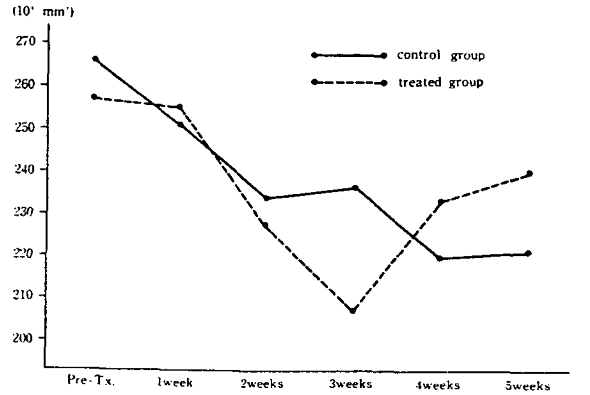

Fig. 4. Changes in platelet count in pre-treatment and post-treatment.

The mean levels of total serum protein after medication were 7.98 g/100ml and 7.68 g/100 ml respectively in both experimental and control groups, lower than those before medication by 0.1 g/ml in both groups. The serum levels began to increase from 1 week after medication in both groups without any significant difference (Table 7 and Figure 5).

The average serum albumin levels of the both experimental and control groups after medication were 4.65 g/100ml and 4.78 g/100 ml respectively. The albumin level of the experimental group in post-treatment was higher than that of pre-treatment by 0.11 g/ 100ml, whereas that of the control group was lower by 0.04 g/ 100 ml, but without statistical significance. And

Table 7. Serum protein content of both groups in pre-treatment and post-treatment. (gm/100 ml)

		Control (N = 25)	Treated (N = 25)
Pre-Tx.		8.03 ± 0.41	7.77 ± 0.43
Post-Tx	1 week	7.63 ± 0.48	7.68 ± 0.48
	2 weeks	7.60 ± 0.35	7.71 ± 0.43
	3 weeks	7.75 ± 0.42	7.76 ± 0.56
	4 weeks	7.74 ± 0.45	7.64 ± 0.53
	5 weeks	7.90 ± 0.37	7.84 ± 0.30

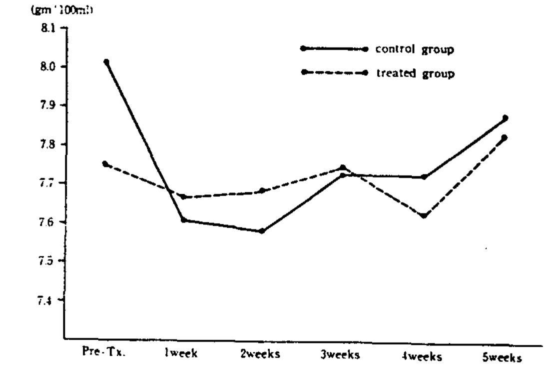

Fig. 5. Changes in protein content in pre-treatment and post-treatment.

the changing pattern of serum albumin levels was the variable one in the control group. In the experimental group the serum albumin levels increased until 3 weeks after medication and then rather decreased afterwards (Table 8 and Figure 6).

The mean serum bilirubin levels after medication were 0.51 mg/100 ml and 0.48 mg/100 ml respectively in both experimental and control groups and lower than those before medications by 0.07 mg/100 ml and 0.11 mg/100 ml respec-

Table 8. Serum albumin content of both groups in pre-treatment and post-treatment (gm/100m*l*)

		Control (N = 25)	Treated (N = 25)
Pre-Tx.		4.69 ± 0.50	4.62 ± 0.44
Post-Tx	1 week	4.71 ± 0.42	4.70 ± 0.51
	2 weeks	4.68 ± 0.38	4.74 ± 0.42
	3 weeks	4.64 ± 0.32	4.82 ± 0.44
	4 weeks	4.74 ± 0.31	4.67 ± 0.31
	5 weeks	4.70 ± 0.07	4.62 ± 0.53

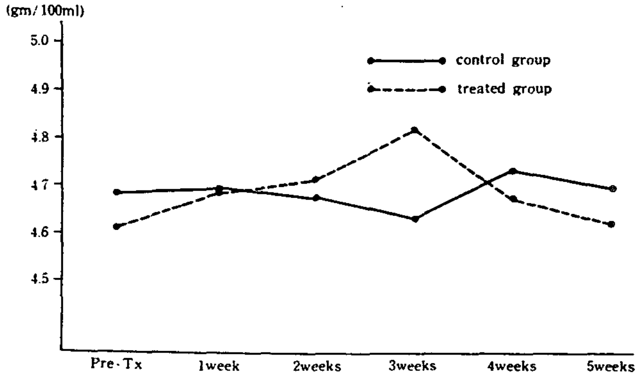

Fig. 6. Changes in serum albumin content in pre-treatment and post-treatment.

tively, but statistical significance was not found. Considering the overall changing patterns for 5 weeks, the recovery effect of the experimental group rather decreased from 1 week after administration of ginseng, whereas the control group didn't show any constant one (Table 9 and Figure 7).

The other common complications accompanying radiation therapy such as anorexia, fatigability, nausea and vomiting occurred in

Table 9. Serum bilirubin content of both groups in pre-treatment and post-treatment (mg/100m*l*)

		Control (N = 25)	Treated (N = 25)
Pre-Tx		0.58 ± 0.33	0.49 ± 0.03
Post-Tx	1 week	0.48 ± 0.20	0.54 ± 0.21
	2 weeks	0.49 ± 0.21	0.45 ± 0.12
	3 weeks	0.44 ± 0.12	0.40 ± 0.15
	4 weeks	0.60 ± 0.17	0.61 ± 0.19
	5 weeks	0.42 ± 0.20	0.35 ± 0.14

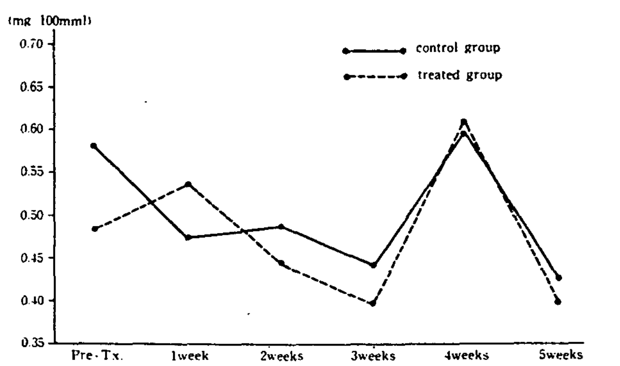

Fig. 7. Changes in serum bilirubin content in pre-treatment and post-treatment.

both groups without statistically significant difference in incidence.

Discussion

Recent trend in the management of malignant tumors has been multi-disciplinary approach using surgery, radiation and chemotherapy in combination. Therefore, considerable clinical complications are inevitable during treatment. Of those complications the depression or derangement of hematopoietic activity of bone marrow has been thought to be an obstacle delaying the treatment of malignancies.

According to Lee[6] et al., radiation injury such as bone marrow depression seems to be caused indirectly by Hydroxy radical (OH), Hydroperoxy radical (HO_2) or Hydrogen radical (H) which are the ionizing products of tissues by irradiation, or by direct effect of radiation on the molecules of tissues.

The severity of radiation-induced bone marrow depression usually depends upon the intensity of radiation, radiation site and individual immunocompetency. Particularly, irradiation to a large field such as in uterine cancer, bone marrow depression is more frequently complicated. Although we often evaluate the bone marrow function on the basis of WBC and platelet counts, but any definite corelationship between them is not still confirmed.

According to Philip[7], radiation dose required to produce the death of bone marrow is approximately 500 rad by a single whole body irradiation. And on occasion of using the fractional irradiation, the lowest dose to produce bone marrow depression is ranged from 3,000 rad/3 weeks to 6,000 rad/5 weeks, but varied with radiation site or area given irradiation. The recovery from the radiation-induced bone marrow depression usually requires at least one or two months, and sometimes even six or seven months.

Radiation dose for the treatment of cervical cancer is high enough to cause bone marrow depression. So the development of drugs to prevent or minimize the bone marrow dysfunction would contribute to improve the cancer mortality. Many pharmacological agents have already been found to induce alteration of cellular function on radiation and are classified into the 2 groups: one for the prevention of radiation-induced complication, the other for the enhancement of radiosensitivity of cells.

Bacq[8] found that the chemical substances such as histamine, cyanide, catecholamine, tryptamine, antioxidants, thiols and disulfide compound prevent radiation hazards more or less, and the possible mechanism of those substances, according to Eldjarn[9] et al. and Bacq[8], seems to be a radiation eliminator on irradiation.

Recently numerous reports have documented various purified chemical constituents from ginseng with their pharmacological actions. Saito[10] et al. and Takaki[11] et al. reported that ginseng increased the ability of exercise in rats, and Oura[12] found that ginseng stimulated the RNA synthesis in liver.

Yokozawa[13] et al. and Kwon[14] et al. suggested that it also enhanced lipid synthesis with suppression of serum glucose level. Petkov[15] et al. also suggested that ginseng would increase the adaptability to the external environment via stimulating corticosteroid secretion from adrenal cortex. Park[16] reported that ginseng had some therapeutic effects on atherosclerosis and hypertension.

In addition, according to the dose, ginseng was found to have some tranquilizing or stimulating action on central nervous system[17,18]. And it is believed to have some enhancing the ability and thinking power in addition to anti-inflammatory and anticancerous effects.

Bone marrow is the most metabolically active organ in which DNA synthesis and production of RBC, WBC, and platelet occur. Among the various effects of ginseng, its recovery one on the postirradiational or postchemotherapeutic bone marrow depression is particularly of great concern to medical field.

Yamamoto[4] et al. administered ginseng extracts to rats per oral or intraperitoneally and found that both erythroid and myeloid series showed increased mitosis with enhanced synthesis of nucleic acids, protein and lipid. Oura[22] et al. reported that administration of ginseng extracts intraperitoneally resulted in the increased production of serum albumin and gamma-globulin.

In his animal experiment, Lee[6] observed that there was a significant decreasing tendency of post irradiational injury in ginseng-treatment group. Yonezawa also found the survival rate of rats improved in the ginseng-treatment group in his animal experiment.

In 1977, Kato[23] et al. assessed the recovery effect of ginseng on bone marrow depression by hematologic data including RBC, WBC and platelet counts with the weight of spleen. In cases without irradiation, the hematologic data was similar in both groups. But in the cases given radiation, statistically significant increase in the weight of spleen was noticed with elevation of RBC, WBC, and platelet counts in the ginseng-treatment group.

To exclude the influence of hematopoietic organs, Kato[24] et al. studied the ginseng effect on the survival rate after irradiation in the splenectomized and unsplenectomized groups. The survival rate was significantly improved in the cases given ginseng without regard to splenectomy. Considering the hematologic data of splenectomized ginseng-treatment group, RBC and WBC counts didn't show any statistically significant increase but platelet significantly increased. Consequently platelet count would be more of importance in the determination of the recovery effect of ginseng rather than that of RBC or WBC. And they concluded that spleen seemed to have a considerable effect on the recovery of erythrocyte.

But Yonezawa et al. and Kato et al. limited their animal experiments to the cases given a single whole body irradiation, so the application of their findings to the radiation therapy of cervical cancer using longterm fractional radiation seems to have some drawbacks.

In the present study, we compared hematologic data of the ginseng-treatment group with that of the control group to assess the recovery effect of ginseng on the radiation-induced bone marrow depression. The result was that any statistically significant difference was not found in the laboratory data except in platelet count between both the experimental and control groups. Such a result seems to be contrary to Oura's[22] report and our previous observation that the administration of ginseng extracts increased serum albumin and gamma-globulin levels. The platelet count increased from 3 weeks after initiation of the administration of red ginseng powder in the experimential group. The increment of platelet count was also observed in Kato's report and the changing patterns of RBC and WBC counts were identical with those seen in Kato's experiment of splenectomized animal but with the results of unsplenectomized cases[23),24)].

Although it has some drawbacks to determine the recovery effect of ginseng on the bone marrow function only on the basis of the platelet count, the increment of platelet suggests that Panax ginseng has somewhat recovery effect on bone marrow depression, considering Kato's report[24] that a rise in platelet count was thought to be the main contributing factor in the recovery of the depressed bone marrow due to radiation.

Although the exact mechanism of recovery effect of ginseng is still unknown, a further study will be necessary to determine whether the presumed recovery effect is the result of the fact that ginseng produces a generalized hypoxic state such as the predescribed radiation eliminators, or acts as a potent antioxidant compound containing -SH radical, or the result from unknown mechanism quite different from the aboves.

Yamamoto[4] et al. also tried to explain the mechanism in terms of C-AMP theory, but it also requires a further study to back up.

Conclusions

To determine the recovery effect of Panax ginseng on the radiation-induced bone marrow depression, we divided a total of 50 cervical cancer patients, diagnosed at the Department of Obstetrics and Gynecology, and Therapeutic Radiology of Seoul National University Hospital, into the experimental and control groups, 25 patients respectively. They were all given radiation therapy alone or in combination with surgery. The experimental group was medicated with 5.0 g of red ginseng powder per day for 5 weeks, whereas the control group with placebo.

The results were summarized as followings:

1. RBC counts didn't show any statistically significant difference in both experimental and control groups although a slightly higher level noticed in the experimental group from 4 weeks after administration of ginseng.
2. The mean hemoglobin values was lower in the experimental group rather than in the control group although not statistically significant.
3. The changing patterns of WBC counts were similar in both groups in which progressive increase had been found from 4 weeks after treatment.
4. Platelet counts had showed progressive increment in the experimental group and statistically significant difference was apparent from 3 weeks after initiation of medication ($p < 0.05$).
5. The serum protein levels were similar in both groups in which progressive recovery was found from 2 weeks after initiation of medication.
6. The mean serum albumin values showed no statistically significant difference between the two groups although in the experimental group some decrement was seen from 3 weeks after medication.
7. The difference between the mean serum bilirubin levels of both groups was not statistically significant. In the experimental group, the decreasing tendency was found from 1 week after initiation of medication whereas the control group didn't show significant change.

In conclusion, we couldn't find any statistically significant differences between laboratory data of both groups except the mean platelet counts which increased significantly from 3 weeks after initiating of administration of ginseng in the experimental group.

Therefore, as far as platelet is concerned, it can be said that red ginseng powder has the protective effect on the radiation injury.

In this study, radiation dose was too small to depress the bone marrow significantly to discontinue the radiation for a while. Therefore, it was assumed that red ginseng might have showed more effective action for the recovery of depressed bone marrow by radiation if dose of radiation were high enough to depress bone marrow markedly.

Chairman: Now the time is open to discussion.

Fulder: I am wondering whether in the clinical situation in which you tested with your red ginseng, whether wouldn't be suitable to try more sensitive parameters on the general health and well being of your patient, because clearly the control group will not suffer from radiation damage as you have said yourself as much as to demonstrate a clear effect if there is one of red ginseng in this situation. So, what would have been most suitable try more sensitive measures of vitallity, energy well being of your patients rather than the blood parameters. We didn't find any changing blood parameters either in our studies. It would seem that that's why we forward rather than using patients receiving very high density of radiation.

Chang: I am sorry I can't quite get the exact question. You mean beside this data, you are talking about some general condition?

Fulder: You failed to show significant result on the blood parameters. My question is maybe it would be best to use other parameters such as general health and performance parameters and psycological parameters because they are more sensitive to the well being of the patients.

Chang: As you know it is very difficult to judge the difference in the mood or some behavior or some general health. Some kind of data which can be expressed in exact number like this. So, we compare the two groups that it is hard to say about that.

Fulder: Well, there might be some very sophisticated what we call general mood questionnaire, general health questionnaire administered by the patient's doctor or even by the nurses. As the daily records patients well being this questionnaires exist and may be useful to try them.

Chang: Yes, I understand. In the following experiment as I told you I will try to make that kind of experimental design in the future experiment. When I do a similar experiment, they are much higher dose of radiation.

References

1. Garriques : Panax Quinquefolia L. Annal. d. Chem. W. Pharmac. Bd. 90 : 231, 1854.
2. Fujiya : Research on Korean ginseng and Unchon ginseng. Kyoto-Igakkai-Zatsi 2 : 43, 1905.
3. Asahina and Tanaka : On the component of ginseng. Yakugaku-Zatsi 292 : 549, 1906.
4. Yamamoto, M., Kumagai, A. and Yamamura, Y. : Metabolic actions of ginseng principles in bone marrow and testes. Proceedings of 1st International Ginseng symposium. The Research Institute, Office of Monopoly, P 129, 1974.
5. Yonezawa, M. : Restoration of radiation injury by intraperitoneal injection of ginseng extract in mice. J. Radiat. Res. 17 : 111, 1976.
6. Lee, K.Y., Kim, H.S., Cheon, H.W., Ahn, H.J. and Choi, Y.J. : The effect of Panax ginseng in the ascorbic acid and nucleic acid contents of various tissues in the Co^{60} irradiated rabbits. Korean Biochem. J. 2 : 35, 1969.
7. Philip, R. : The bone marrow organ. : The critical structure in radiation-drug interaction. Int. J. Rad. Oncol. Bio. Phy. 4 : 3, 1978.
8. Bacq. Z.M. : Chemical protection against ionizing radiation: With an introduction by Shields Warren. Spring field, III., Thomas P. 216, 1965.
9. Eldjarn, L. and Phil, A. : In mechanisms in radiology. New York Academic Press, P. 231, 1961.
10. Saito. H., Yoshida. Y. and Takagi. K. : Effect of Panax ginseng root on exhaustive exercise in mice. Jap. J. Pharmacol. 24 : 119, 1974.
11. Takagi, K., Saito, H. and Tsuchiya, M. : Effect of Panax ginseng root on spontaneous movement

and exercise in mice. Jap. J. Pharmacol. 24 : 48, 1974.

12. Oura, H., Hiai, S., Nakashima, S. and Tsukada, K. : Stimulating effect of the roots of Panax ginseng C.A. Meyer on the incorporation of labeled precursors into rat liver RNA. Chem. Pharm. Bull. 19 : 453, 1971.
13. Yokozama, T., Semo, H. and Oura, H. : Effect of ginseng extract on lipid and sugar metabolism. Chem. Pharm. Bull. 23 : 3095, 1975.
14. Kwon, Y.S., Oh, J.S. : Effect of ginseng alkaloid fraction on the lipid metabolism. Kor. J. Pharm. 5 :1, 1969.
15. Petkov. V. and Staneva, D. : The effect of an extract of ginseng on the adrenal cortex. Bull. Inst. Physiol. 10 : 39, 1969.
16. Park, C.W. : Effect of ginseng saponin fraction on the lipid metabolism in rat. Kor. Central J. Med. 17 : 41, 1969.
17. Oh, J.S., Park, C.W. and Moon, D.Y. : Action of Panax ginseng on the central nervous system. Special volume of the references on Ginseng. The Office of Monopoly, Republic of Korea, P. 5, 1971.
18. Takagi, K. : Pharmacological studies on ginseng. Korean Ginseng Studies. IL WHA Co., P. 346, 1977.
19. Popov, I.M. and Goldwag, W.J. : A review of the properties and chemical effects of ginseng. Am. J. Chinese Med. 1 : 263, 1973.
20. Han, B.H., Han, Y.N. and Woo, L.K. : Studies on the anti-inflammatory glycosides of Panax ginseng. J. of the Pharmacol. Society of Korea. 16 : 129, 1972.
21. Murata, I. and Hirono, T.,metabolism 10 : 601, 1973.
22. Oura, H., Nakashima, S., Tsukada, K. and Ohta, Y. : Effect of Radix ginseng extract on serum protein synthesis. Chem. Pharm. Bull. 20 : 980, 1972.
23. Kato, T., Taketa, A., Yonezawa, M.: Restoration of radiation injury by ginseng extract. 2. Changes of blood pictures and organs. Abstract of 20th Jap. Congress of Radiation Effect, P. 67, 1977.
24. Kato, T., Taketa, A., Yonezawa, M. : Restoration of radiation injury by ginseng extract. 4. Effect of ginseng extract on radiation after splenectomy. Abstract of 21st Jap. Congress of Radiation Effect, P. 121, 1978.
25. Chang, Y.S., Lee, J.Y. and Kim, C.W. : The effect of ginsenoside triol on the postoperative recovery in gynecological patients. Kor. J. Obstet. Gynecol. 21 : 253, 1978.