THE EFFECT OF GINSENG ON THE POSTOPERATIVE NUTRITIONAL STATUS AND IMMUNE FUNCTIONS OF GASTRIC CARCINOMA PATIENTS

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ABSTRACT

To find out the mechanisms of anticancer effect of ginseng, we performed prospective randomized study for the 39 patients with stomach cancer who had undergone radical subtotal or total gastrectomy and postoperative immunochemotherapy with PMF from July 1991 to November 1991 at Department of Surgery, Seoul National University Hospital.

The patients were randomly divided into study and control group : the study group was administered with powdered red ginseng of 5400mg daily dose for 12 months postoperatively, the control group was simply followed - up.

There were no significant differences between study and control group in twelve months postoperative body weights, triceps skin fold, hemoglobin, albumin, total protein, PNI, total WBC and lymphocyte count, and T - cell percentage ($p>0.05$). The results of preoperative DNCB skin test of study group was (0) for 8 patients and (+) for 12 patiens, but after operation, it showed the tendency of decreasing (0) and (+) ratio and increasing tendency of (++) ratio ($p<0.05$), but those of control group showed no increasing tendency of the degree of positive DNCB skin test.

From the above results, we could conclude that ginseng had anti - cancer effect by the way of immune mechanism and could be an adjunct to the patients with stomach cancer postoperatively.

INTRODUCTION

Ginseng has been used as herb medicine and vital - additive drug for long time and analysis of compositions of ginseng is under study recently[4, 26]. Some people are in favor of anti - cancer effect of ginseng, but the effect may not be constant and negligible. Furthermore, other people do not agree with that ginseng has anti - cancer effect. Many different result about the ginseng may be due to different methodology, technique and different composition of ginseng. But the anti - tumor growth effect is now acceptable to many oncologists.

The anticancer effect of ginseng is explainable by two mechanisms. The one is direct cancer cell killing effect of some composition of ginseng[3, 11, 13, 22] and the other mechanism is reinforcement of immune fuction of host, especially immune surveillance mechanism[7, 23, 27]. Other mechanisms include increasement of BMR[24], hydrocortisone - like action[15], influence on total protein[21], the change of the composition of the serum protein[18] increasement of blood cell[17], and alteration of tumorigenesis induced by MMNG(N - methyl - N' - nitro - N - nitrosoguanidine)[28].

So, this study systematically confirmed the anti - cancer effect of longterm administration of ginseng to gastric cancer patients on postoperative nutritional and immune status. We used red ginseng as adjuvant therapy for gastric cancer and studied the anti - cancer machanism of ginseng.

MATERIALS AND METHODS

The patients were diagnosed as gastric cancer through fluoroscopy, endoscopy, and biopsy from July 1991 to November 1991. They all underwent radical subtotal gastrectomy or total gastrectomy by same operator in the Department of Surgery, Seoul National University Hospital.

They all received adjuvant immunochemotherapy with Picibanil, Mitomycin, 5 - Fluorouracil. And they were divided into study and control groups by random sampling. Ginseng powder was administered by oral route to the study group and the control group was not. The red ginseng powder was prepared from 6 - year old red gingeng root and 5400 mg(54 capsules) was given daily by oral route to the study group for 12 months.

We also examined changes of weight, triceps skin fold, appetite, serum albumin, serum total protein, hemoglobin, skin hypersensitivity to 2, 4 - dinitrochlorobenzene (DNCB). We also examined T - cell percentage, total lymphocyte count as immunologic parameters. We used Mann - Whitney U test as statistical analysis.

1. Prognostic Nutritional Index (PNI)

There are many ways to represent nutritional status, we used prognostic nutritional index (PNI) as representing the nutritional status.

PNI(%) = 158 - 16.6(ALB) - 0.78(TSF) - 0.20(TFN) - 5.8(DH)
PNI = risk(percent) of a complication occurring in an individual patient
ALB = serum albumin level(grams per 100 mililiters)
TSF = triceps skinfold(milimeters)
TFN = serum transferrin level(miligrams per 100 mililiters)
DH = cutaneous delayed hypersensitivity

2. Cutaneous hypersensitivity to DNCB

We used the method of Eilber and Morton for measurement of cutaneous hypersensitivity. After cleasing of volar side of upper arm of the patients, 1cc of acetone solution which contained

2000 μg of DNCB was painted as large as 2.2cm. Seven to 14 days after painting, we judged as following criteria.

O : No response or less than 5 mm
1+ : 5 - 10 mm
2+ : Above 10 mm, presence of blister

3. Measurement of triceps skin fold

We used Lange skinfold caliper for measurement of triceps skin fold. And we repeated three times and get the mean of those.

RESULTS AND DISCUSSION

1. Results.(Table 1. - 11.)

Tbale 1. Comparison of pre - operative status for the study and control group

	Hemoglobin	Total lymphocyte count	Serum protein	Serum albumin
Study group	13.0± 1.5	2135± 693	6.9± 0.4	3.6± 0.3
Control group	12.7± 1.3	1906± 677	6.7± 0.6	3.6± 0.4
p value	>0.05	>0.05	>0.05	>0.05

Table 2. Comparison of pre - operative status for the study and control group

	Weight (kg)	Triceps skin fold (mm)	PNI*
Study group	60.3± 9	15.5± 8.4	27.7± 15.5
Control group	58.9± 9	15.0± 7.1	30.0± 10.1
p value	>0.05	>0.05	>0.05

* PNI : Prognostic Nutritional Index

Table 3. Comparison of body weight of post - operative status for the study and control group(kg)

	post - op.3mo.	post - op.6mo.	post - op.12mo.
Study group	56.1	55.3	55.7
Control group	54.3	53.5	52.4
p value	>0.05	>0.05	>0.05

Table 4. Comparison of triceps skin fold of post - operative status for the study and control group(cm)

	post - op.3mo.	post - op.6mo.	post - op.12mo.
Study group	12.9	12.2	12.0
Control group	12.5	10.6	9.9
p value	>0.05	>0.05	>0.05

Table 5. Comparison of hemoglobin of post - operative status for the study and control group(g%)

	post - op.3mo.	post - op.6mo.	post - op.12mo.
Study group	12.2	12.6	12.2
Control group	12.0	11.6	11.6
p value	>0.05	>0.05	>0.05

Table 6. Comparison of serum protein of post - operative status for the study and control group(g%)

	post - op.3mo.	post - op.6mo.	post - op.12mo.
Study group	7.1	7.1	7.0
Control group	6.9	7.0	7.2
p value	>0.05	>0.05	>0.05

Table 7. Comparison of serum albumin of post - operative status for the study and control group(g%)

	post - op.3mo.	post - op.6mo.	post - op.12mo.
Study group	3.8	4.0	4.0
Control group	3.6	3.8	3.7
p value	>0.05	>0.05	>0.05

Table 8. Comparison of transferrin of post - operative status for the study and control group(g%)

	post - op.3mo.	post - op.6mo.	post - op.12mo.
Study group	303.9	329.9	350.9
Control group	330.9	324.7	315.5
p value	>0.05	>0.05	>0.05

Table 9. Comparison of PNI of post - operative status for the study and control group(%)

	post - op.3mo.	post - op.6mo.	post - op.12mo.
Study group	12.7	9.9	10.8
Control group	8.1	14.6	13.5
p value	>0.05	>0.05	>0.05

Table 10. Comparison of total WBC count and lymphocyte fraction of post - operative status for the study and control group(cells/mm^3)

	post - op.3mo.	post - op.6mo.	post - op.12mo.
Study group	5862(34.0%)	5878(33.8%)	6010(35.5%)
Control group	5392(34.3%)	6243(30.0%)	6420(36.0%)
p value	>0.05	>0.05	>0.05

Table 11. Comparison of T-cell percent of post-operative status for the study and control group(%)

	post-op.3mo.	post-op.6mo.	post-op.12mo.
Study group	72.1	70.5	68.8
Control group	67.8	62.8	64.4
p value	>0.05	>0.05	>0.05

1) There were 20 patients(11 male and 9 female) from 28 to 67 in age in the study group and their average age was 53.3 -years. There were 19 patients (10 male and 9 female) from 33 to 66 in age in the study group and their average age was 53.3-years. There were 19 patients (10 male and 9 female) from 33 to 66 in age in the study group and their average age was 54.8-years. Total gastrectomy was performed in 4 cases of each cases the remainder were subtotal gastrectomized patients. Postoperative immunochemotherapy was performed in 17 cases of study group and 16 cases of control group. One patient died from recurrence of gastric carcinoma in each group respectively and one patient of control group was confirmed of recurrence of the disease.

2) The followings are nutritional and immunologic parameters of preoperative status.

(1) The average weight of study group was 60.3± 9.0kg, that of control group 58.9± 9.0kg. The average triceps skin fold was 15.5± 8.4 mm, that of control group 15.0± 7.1 mm.

(2) The average level of hemoglobin of study group was 13.0± 1.5kg, that of control group 12.7± 1.3kg. The average level of albumin of study group was 3.6± 0.4 g%, that of control group 15.0± 7.1 mg%. The average level of transferrin of study group was 284.2± 0.4 mg%, that of control group 237.8± 43.7 mg %.

(3) The PNI of study group was 27.7± 15.5, that of control group 30.0± 10.1.

(4) The average total count of WBC of study group was 7004± 2275.8, that of control group 7062± 3087.5. The average fraction of lymphocyte of study group was 30.6± 7.9, that of control group 26.8± 9.7%. The average fraction of T-cell of study group was 66.5± 8.6%, that of control group 63.9± 10.5%.

3) The followings are nutritional and immunologic parameters of preoperative status.

(1) The average weight of study group was 60.3± 9.0kg, that of control group 58.9± 9.0kg. The average triceps skin fold was 15.5± 8.4 mm, that of control group 15.0± 7.1 mm.

(2) The average level of hemoglobin of study group was 13.0± 1.5kg, that of control group 12.7± 1.3kg. The average level of albumin of study group was 3.6± 0.4 g%, that of control gorup 15.0± 7.1 mg%. The average level of transferrin of study group was 284.2± 0.4 mg%, that of control group 237.8± 43.7 mg %.

(3) The PNI of study group was 27.7± 15.5, that of control group 30.0± 10.1.

(4) The average total count of WBC of study group was 7004± 2275.8, that of control group 7062± 3087.5. The average fraction of lymphocyte of study group was 30.6± 7.9, that of control group 26.8± 9.7%. The average fraction of T-cell of study group was 66.5± 8.6%, that of control group 63.9± 10.5%.

3) The followings are nutritional and immunologic parameters of 3 months-postoperative status.

(1) The average weight of study group was 56.1± 9.1kg, that of control group 54.3± 11.0kg. The average triceps skin fold was 12.9± 8.3 mm, thar of control group 12.5± 5.8 mm.

(2) The average level of hemoglobin of study group was 12.6± 1.4 g%, that of control group 11.6± 1.7 g%. The average level of albumin of study group was 4.0± 0.4 g%, that of control group 3.7± 0.3 mg%. The average level of transferrin of study group was 329.9± 61.2 mg%, that of control group 324.7± 108.0 mg%.

(3) The PNI of study group was 9.9± 8.7, that of control group 14.6± 26.8.

(4) The average total count of WBC of study group was 5878± 2076, that of control group 6423± 2303. The average fraction of lymphocyte of study group was 33.8± 10.1, that of control group 30.0± 12.7%. The average fraction of T-cell of study group was 70.5± 9.2%, that of control group 62.8± 6.7%.

5) The followings are nutritional and immunologic parameters of 12 month-postoperative status.

(1) The average weight of study group was 55.7± 8.4kg, that of control group 52.4± 6.9kg. The average triceps skin fold was 12.0± 6.1 mm, that of control group 9.9 ±3.8 mm.

(2) The average level of hemoglobin of study group was 12.2± 1.5 g%, that of control group 11.6 ± 1.5 g%. The average level of albumin of study group was 4.0± 0.3 g%, that of control group 3.8± 0.3 g%. The average level of transferrin of study group was 350.9± 68.8 mg%, that of control group 315.5± 72.6 mg%.

(3) The PNI of study group was 10.8± 7.6, that of control group 13.5± 5.5.

(4) The average total count of WBC of study group was 6010± 1028, that of control group 6420± 1820. The average fraction of lymphocyte of study group was 35.5± 8.5, that of control group 36.0± 7.1%. The average fraction of T-cell of study group was 68.8± 15.0%, that of control group 64.4± 5.6%.

6) There were no statistical differences between the values of the two groups at same period (p>0.05). In study group, 8 patients revealed (0) of DNCB delayed cutaneous hypersensitivity, 12 patients (+) preoperatively, but 12 months after operation, there were 6 of (+), 13 of (++). In control group, 10 patients revealed (0) of DNCB delayed cutaneous hypersensitivity, 9 patients (+) preoperatively, but 12 months after operation, there were 3 of (0), 12 of (+) and 3 of (++). So, there were more increasement of positivity in the study group than in the control group.

From above results of immunologic and nutritional data, we could conclude that ginseng might reinforce the immunologic mechanism of the patients with gastric carcinoma and might

be a partial adjuvant therapeutic agent for gastric cancer.

3. Discussion

Ginseng has been used as herb medicine and vital - additive drug for long time and analysis of compositions of ginseng is under study recently. Some people are in favor of anti - cancer effect of ginseng[1, 7, 10, 14, 16, 23], but the effect may not be constant and negligible. Furthermore, other people do not agree with that ginseng has anti - cancer effect. Many different result about the ginseng may be due to different methodology, technique and different composition of ginseng. But the anti - tumor growth effect is now acceptable to many oncologists. But report from Cancer Chemotherapy National Service Center and reports from other similar center or research except that of Abbott[1] are consistent with the effectiveness of ginseng for anti - tumor growth to a considerable degree[7, 8].

The anticancer effect of ginseng is explainable by two mechanisms. The one is direct cancer cell killing effect of some composition of ginseng[3, 11, 13] and the other mechanism is reinforcement of immune function of host, especially immune surveillance mechanism[7, 23, 27]. The latter mechanism is associated with the function of NK cell, LAK cell, MIF(Macrophage migration inhibition factor), and increased migration of leukocyte[28].

So, this study systematically confirmed the anti - cancer effect of longterm administration of ginseng to gastric cancer patients on postoperative nutritional and immune status. We used red ginseng as adjuvant therapy for gastric cancer and studied the anti - cancer mechanism of ginseng.

The authors studied T - cell percentage, total lymphocyte count, hypersensitivity to DNCB to evaluate the tumor immunity by cell mediated immune response. And to evaluate the nutritional status, we studied triceps skin fold, hemoglobin, hematocrit, serum transferrin, and prognostic nutritional index. The following is formula for PNI.

"PNI = 158 - 16.6(Albumin gm/dl) - 0.78(Triceps skin fold mm) - 0.02(serum transferrin mg/dl) - 5.8(delayed cutaneous hypersensitivity)"

Delayed cutaneous hypersensitivity is response to the antigen of mumps, streptokinase - streptodonase, candina. The response is categorized as 0(no response), 1 (diameter<5mm), and 2(diameter>5mm).

All the patients received adjuvant immunochemotherapy with Picibanil, Mitomycin, 5 - Fluorouracil. And they were divided into study and control groups by random sampling. Ginseng powder was administered by oral route to the study group and the control group was not. The red ginseng powder was prepared from 6 - year old red ginseng root and 5400 mg(54 capsules) was given daily by oral route to the study group for 12 months. But the control group could not be administered with placebo because the agreement with the study might not be obtainable.

We confirmed improvement of immune function of the patient who received ginseng. We also confirmed that the ginseng was also effective for the improvement of nutritional status of patient. But the study must be extended to obtain the exact mechanism of anti - tumor effect of the ginseng and long - term effect.

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