原 著

The Hematoimmunologic Effect of AHCC for Korean Patients with Various Cancers

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Summary

Active hexose correlated compound (AHCC) is an extract obtained from several kinds of mushroom (basidiomycetes) which are cultured in a liquid medium. This study attempted to assess the hematologic change and the cellular immunity effect of AHCC in 12 different cancer patients. The dosage of AHCC was 3 to 6 g per day orally. Peripheral blood examination, including total leukocytes, peripheral lymphocytes, hemoglobin, and hematocrit, was performed before initiation of AHCC administration and then every 3 months for a total of 3 times. Multiplying the lymphocyte % in the leukocyte count yielded the number of lymphocytes. Assessment of immune parameters, such as CD4, CD8, CD4 : CD8 ratio, and natural killer cells, was done before intake of AHCC and then every 3 months for 2 times after intake. The chemotherapy protocol was conducted as usual, and it was not related to the administration of AHCC. There was no clear change in white blood cells (WBC), hemoglobin, hematocrit, or thrombocyte number after taking AHCC, even though the patients were undergoing chemotherapy or radiotherapy. The ratio of natural killer cells to total lymphocytes, which was 21.67% before taking AHCC, increased to 26.21% and 26.0% 3 and 6 months after taking AHCC, respectively. However, the ratio of natural killer cells to total lymphocytes was in the normal range in some patients, so more large-scale randomized studies are required. This study suggests that AHCC can be used for the prevention of bone marrow depression from chemotherapy. Also, from the hematoimmunologic point of view, AHCC treatment seems to be safe and good for Korean cancer patients, acting as a biological response modifier.

Key words: Hematoimmunologic effect, AHCC, Cellular immunity, CD4, CD8

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Introduction

Interest in complementary medicine is an international phenomenon. The continuing rise in public interest suggests that previously overlooked practices are experiencing a renaissance and newer therapies are emerging. Complementary medicine has been defined as treatment and prevention measures that complement mainstream medicine by contributing to a common whole in terms of satisfying unmet demands, thereby diversifying the conceptual framework of medicine. Despite the widespread use and availability of complementary therapies, information on efficacy and toxicity remains anecdotal and efforts to facilitate research are underway internationally.

Active hexose correlated compound (AHCC) is a mixture of polysaccharides, amino acids, and minerals derived from fungi. It is obtained from hot water extraction after culturing mycelia of several basidiomycetes in a liquid culture tank and treating them with several enzymes[1]. The main active component of AHCC is a mixture of oligosaccharides with average molecular weights of approximately 5,000 kDa[1,2]. Chemical analysis has revealed that polysaccharides are the major components of AHCC, comprising approximately 74%. Nearly 20% of the polysaccharides are α-1, 4-glucan, and their acetylated forms, which are thought to be active components[1]. AHCC also contains some other polysaccharides including β-glucans. Both α- and β-glucans are shown to be responsible for the anti-tumor effects of basidiomycetes[3]. It has been reported that this extraction has various beneficial effects on both human and experimental animals, acting either as a biological responsor modifier (BRM) or an antioxidant.

AHCC is usually used as one of the complementary treatment agents for cancer patients, with an immunomodulatory property[4]. The possible effects of AHCC in cancer therapy are suppression of the cancer growth, improvement of general condition, and enhanced survival rate[4]. However, the mechanism of its anti-tumor effect in cancer patients is not clear. My particular concern is whether or not AHCC enhances defense mechanisms against tumor growth. Therefore, this study attempted to assess the hematologic change and cellular immunity effect of AHCC in various cancer patients. The specific aims for this study are as follows.

1) Does AHCC treatment change hematologic contents in various cancer patients?

① WBC count
② Hemoglobin
③ Hematocrit

2) Does AHCC treatment enhance the patient's own immune system?

① Peripheral blood lymphocytes (number, subsets)
② Natural killer cell assay
③ $CD4^+ : CD8^+$ ratio

I. Materials and Methods

1. Subjects

Patients were selected who have solid cancers confirmed histologically or surgically. Among a total of 20 patients, 8 patients were excluded from this study because of death or violation of the visit schedule. Cancers in this patient group consisted of 4 stomach cancers, 3 colorectal cancers, 2 lung cancers, 1 breast cancer, 1 ovarian cancer and 1 melanoma.

The performance status of all patients was below 2 and most of them could function in everyday life.

The patients' characteristics are as shown in Table 1.

2. Material

Table 1 Patient characteristics

No. of patients		12
Age	≦49	6
	50~59	1
	60≦	5
Sex	Male	7
	Female	5
Perfomance status (ECOG)*	0-1	8
	2	4
	3	0
	4	0
Kind of cancer	Stomach	4
	Colorectal	3
	Lung	2
	Breast	1
	Ovarian	1
	Melanoma	1

* ECOG : Eastern Cooperative Oncology Group

A freezing drying agent obtained from Amino Up Chemical, Co., Japan.

3. Medication method

AHCC was administrated principally to outpatients. The dosage of AHCC was 3~6 g per day combined with other BRM's.

4. Measurement of hematologic content

Peripheral blood examination, including total leukocytes, peripheral lymphocytes, hemoglobin, and hematocrit, was performed before initiation of AHCC administration and then every 3 months for a total of 3 times. Multiplying the lymphocyte % in the leukocyte count yielded the number of lymphocytes.

Assessment of immune parameters, such as CD4, CD8, CD4 : CD8 ratio, and natural killer cells, was performed before intake of AHCC and then every 3 months for 2 times after intake.

II. Result

1. Change in number of leukocytes

After intake of AHCC for 3 months, the number of leukocytes was reduced 6.1%, on average from 5,458 to 5,125, and 0.8% and 4.9% after 6 and 9 months (Table 2).

Table 2 Change in number of leukocytes

	Months after treatment			
	0	3	6	9
Mean WBC (number/mm^3)	5,458	5,125	5,415	5,187
Mean decrease (%)		6.1	0.8	4.9

Table 3 Change in hemoglobin

	Months after treatment			
	0	3	6	9
Mean Hb (g/dl)	12.1	12.2	11.7	14.9
Mean decrease or increase (%)		+0.8	−3.3	+23.1

Table 4 Change in hematocrit

	Months after treatment			
	0	3	6	9
Mean Hct (%)	36.9	34.8	35.7	35.6
Mean decrease (%)		5.7	3.3	3.5

2. Change in hemoglobin

After intake of AHCC for 3 months, hemoglobin increased 0.8%, from 12.1 to 12.2, then decreased 3.3% after 6 months and increased 23.1% after 9 months (Table 3).

3. Change in hematocrit

After intake of AHCC for 3 months, hematocrit was reduced by 5.7%, from 36.9 to 34.8, and by 3.3% and 3.5 % after 6 and 9 months, respectively (Table 4).

4. Change in platelets

After intake of AHCC for 3 months, the number of platelets increased by 0.5%, on average from 215,000 to 216,000, and increased by 20.5% and 6% after 6 and 9 months, respectively (Table 5).

The immune function of the human body can be divided into two, humoral immunity in which B lymphocytes take charge and cellular

Table 5 Change in platelets

	Months after treatment			
	0	3	6	9
Mean platelet (number/mm^3)	215,000	216,000	259,000	228,000
Mean increase (%)		0.5	20.5	6

Table 6 Change in the number of lymphocytes

	Months after treatment			
	0	3	6	9
Mean lymphocyte (number/mm^3)	1,608	1,987	1,584	1,850
Mean increase or decrease (%)		+23.6	−1.5	15

immunity in which T lymphocytes take charge[5].

The function of cellular immunity is decreased further below normal than the function of humoral immunity in cancer patients, and as the cancer progresses the function of cellular immunity decreases more. Because the function of cellular immunity is related to metastasis and recurrence of cancer, it is an element that has a direct effect on a patient's survival[6].

Therefore, to determine a cancer patient's immunocompetence, the function of cellular immunity must be measured. To determine the function of cellular immunity, the measurements of total lymphocyte count, helper T lymphocyte, suppressor T lymphocyte and natural killer cell number are used[7].

However, when comparing patient's immunity parameter with that of a healthy person, a change in helper T lymphocyte or suppressor T lymphocyte is not obvious. One cannot know the definite change in the function of immunity by this. Therefore, immunity is compared by the helper T lymphocyte and suppressor T lymphocyte ratio; that is, the CD4/CD8 ratio. The ratio of CD4 to CD8 is more than 1.0 in healthy persons. In autoimmune disease, the CD4/CD8 ratio increases because of a decrease in the number of suppressor T lymphocytes. In AIDS (acquired immune deficiency syndrome) and various cancer patients, the CD4/CD8 ratio decreases because of a decrease in the number of helper T lymphocytes.

Table 7 Change in NK cells

	Months after treatment		
	0	3	6
Mean NK cell (%)	21.67	26.21	26.0
Mean increase (%)		21	20

Normal NK cell: 7~35%

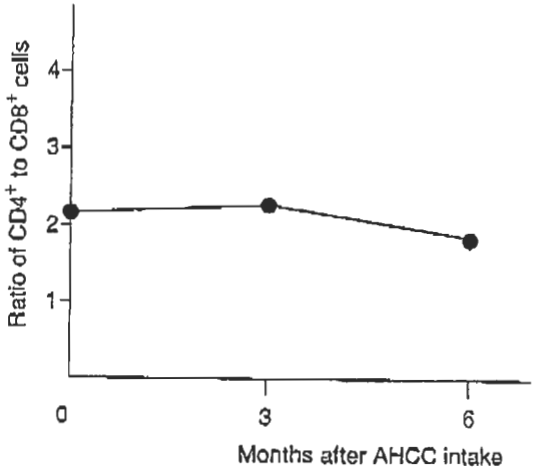

Fig. 1 Change in $CD4^+$/ $CD8^+$ ratio

5. Change in the number of lymphocytes

After intake of AHCC for 3 months, lymphocyte count increased by 23.6%, on average from 1,608 to 1,987. It decreased 1.5% after 6 months, and increased 15% after 9 months (Table 6).

6. Change in NK cells

NK cell count increased about 21% and 20% after intake of AHCC for 3 and 6 months, respectively (Table 7).

7. Change in $CD4^+/CD8^+$ ratio

There was a small change of 2.25 at 3 months after intake of AHCC in the ratio of $CD4^+/CD8^+$, and a decrease of 1.8 after 6 months (Fig. 1).

III. Discussion

Active hexose correlated compound (AHCC) is used clinically as an agent of complementary therapy for cancer patients. AHCC treatment after surgical operation may improve the quality of life (QOL) of cancer patients and increase the survival rate by inhibiting tumor metastasis[8]. The hematological change and the celluar immunity effect of AHCC to 12 cancer patients are as follows.

1) There was no clear change in white blood cell (WBC), hemoglobin, hematocrit and thrombocyte number after taking AHCC, even though the patients were undergoing radiotherapy or chemotherapy. From the hematologic point of view, AHCC treatment seems to be safe and good for cancer patients. This study therefore suggests that AHCC can be used for the prevention of bone marrow depression from chemotherapy.

2) To determine the function of celluar immunity, the measurement of peripheral blood lymphocytes is used. It shows a tendency to decrease as cancer progresses. In this study, there was a slight increase or no change after taking AHCC.

3) Natural killer cells play an important role in elimination of tumor cells in tumor immunosurveillance. The ratio of natural killer cells to total lymphocytes, which was 21.67% before taking AHCC, increased to 26.21% and 26.0% after 3 and 6 months of taking AHCC, respectively. Immunotherapy is needed to maintain the function of NK cells because anticancer drugs decrease the function of NK cells. However, the ratio of natural killer cells to total lymphocytes was in the normal range in some patients, so more large-scale randomized studies are required.

4) There was no clear change in the ratio of $CD4^+/CD8^+$ until the first 3 months, but it decreased a little after 6 months. Long-term data are needed to justify the claim that AHCC enhances the patient's own immune system.

5) From the hematoimmunologic point of view, AHCC treatment seems to be safe and good for Korean cancer patients, acting as a biological response modifier.

References

1) Kosuna, K.: Recent progress of research on AHCC. *New Food Industry* 41 : 17-23, 1999.
2) Matsushita, K., Kuramitsu, Y., Ohiro, Y. *et al.*: Combination therapy of Active Hexose Correlated Compound plus UFT significantly reduces the metastasis of rat mammary adenocarcinoma. *Anticancer Drugs* 9 : 343-350, 1998.
3) Mizuno, T. and Kawai, M.: Chemistry and Biochemistry of Mushroom, Japan Science Society Press, Tokyo, 1995, pp. 35-45.
4) Matsui, Y., Kawaguchi, Y. and Kamiyama, Y.: Effects of AHCC as a complementary therapy on prognosis of postoperative hepatocellular carcinoma patients (Abstr.), AHCC Research Association 7th symposium, 1999, p. 16.
5) Klaus, D. and Elgert, K.D : Cellular Interactions: Development of Effector Functions, Immunology, Wiley-Liss, Inc., New York, 1996, pp. 218-219.
6) Roth, C., Rochitz, C. and Kourisky, P.: Immune response against tumors, *Adv. Immunol.* 57 : 281-349, 1994.
7) Schmidit-Wolf, G.D. and Schmidit, I.G.G.: Cytokines and gene therapy. *Immunol. Today* 16 : 173-175, 1995.
8) Matsui, Y., Uhara, J., Satoi, S. *et al.*: Improved prognosis of postoperative hepatocellular carcinoma patients when treated with functional foods: a prospective cohort study. *J. Hepatol.* 37 : 78-86, 2002.