Life Prolongation and QOL Improvement Effect of Modified Arabinoxylan from Rice Bran (BioBran/MGN-3) for Progressive Cancer

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Abstract

The present study was designed to determine whether the administration of BioBran/MGN-3 could have its apothanasia effect and improve QOL for 205 progressive and partially metastasized cancer patients in late III-IV stages after surgery. BioBran/MGN-3 is a rice bran arabinoxylan derivative known to have immunomodulation activity. The participants in this clinical study were hospitalized patients in our clinic treated with complementary alternative medicines ("Non-Conventional Therapy") and anticancer drugs with lesser side effects. The 205 patients hospitalized for 6 months were placed into two groups, viz, 109 patients (control group) treated with our standard complementary alternative medicines, and 96 patients who were further given BioBran/MGN-3 (BioBran/MGN-3 group) for one year and a half.

All patients were monitored for natural killer (NK) cell activity as an indication for the variation of

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immunoparameters. Simultaneously, the QOL of the patients was also checked. The NK cell activities of the patients after surgery were low on average; however, after administration of BioBran/MGN-3, NK activity increased, as did apothanasia ratio; the higher the patient NK activity the higher the apothanasia ratio was observed to rise. These findings indicate that NK activity can be used as a pathological index in progressive cancers. QOL improvement was also observed with the administration of BioBran/MGN-3.

Introduction

We perform a complementary alternative therapy developed in our clinic on progressive cancer patients who have a metastasis or unresectable lesion after surgery to maintain high QOL and prolong survival time, and have obtained good results. This therapy consists of hospitalization and home treatment. The mean duration of hospitalization is 1 month, during which patients are treated and educated for treatment at home. After discharge, they are based on home care and periodically visit the clinic for examination and treatment. This therapy causes no large damage to patients in principle. The main aim of the therapy is to put cancer cells into a dormant state. Normally, this therapy should be used in postoperative patients without recurrence or metastasis. In the present study, however, the life prolongation effect of BioBran/MGN-3 was confirmed in 205 cancer patients in late III-IV stages, including those who had a metastasis or unresectable lesion left after surgery. The purpose of this study was to determine whether the addition of BioBran/MGN-3 to our complementary alternative therapy prolongs survival time and improves QOL by enhancing the original effects of the therapy.

Methods

1. Patients

Subjects were patients hospitalized in our clinic who were treated with a complementary alternative therapy developed here (**Table 1**) and anticancer drugs that induce less severe adverse reactions. They were 205 progressive-cancer patients in late III-IV stages, who had recurrence, unresectable lesions, or metastasis after surgery. The primary lesions were in the lung (31 patients), liver (18), uterus (7), breast (33), prostate (4), rectum (28), stomach (34), lymph node (11), or others (29).

Table 1 Details of Complementary Alternative Therapy

immuno-enhancement:	CDA-II (enzyme in urine), germanium mushroom polysaccharides, specific substance Maruyama (SSM) oriental medicines, Lymphocytes
diet therapy:	Gerson's special diet therapy, kale vegetable juice, vitamins
intra-intestinal environmental improvement:	probiotics, prebiotics
thermotherapy:	far infrared ray, thermotherapy with loquest leaves
blood catharsis:	SOD, coffee enema
psycho-therapy:	thoroughgoing of positive way of thinking by seminars/lectures

Table2 Patients participated in the clinical study, MGN-3 Group and Control Group

Cancer site	MGN-3 Group	Control Group
Lung	14	17
Liver	10	8
Uterine	7	0
Breast	18	15
Prostate	3	1
Large intestine	9	19
Stomach	15	19
Lymph nod	7	4
Others	13	26
Total	96	109
Sex	Male 55, Female 41	Male 59, Female 50
Average age	56.0	53.5

Table 3 Scoring of QOL checkpoints and levels

pain, malaise and nausea		appetite	
none:	0	no appetite:	0
scarcely:	1	scarcely:	1
fairly strong:	2	fairly:	2
strong:	3	good appetite:	3
very strong:	4	-	

2. Investigational substance

BioBran/MGN-3 is a rice bran arabinoxylan derivative obtained by hydrolyzing hemicellulose of rice bran with many glycosidase, which has an immunomodulatory[2-3], active-oxygen scavenging[4], and blood-sugar controlling effects[5], and reduces adverse reactions to anticancer drugs[6]. The brand name of BioBran/MGN-3 is Lentin Plus 1000, manufactured by Daiwa Pharmaceutical Co., Ltd. (Tokyo).

3. Methods

A total of 205 patients who visited our clinic within about 6 months were randomly divided into 2 groups (control and BioBran/MGN-3 groups). The control group was given a treatment prescribed in our clinic, and the BioBran/MGN-3 group was given BioBran/MGN-3 in addition to this therapy. The breakdown of the patients is shown in **Table 2**. BioBran/MGN-3 at 1 g was given orally 3 times a day after meals. The observation period was 18 months, and the patients visited once a month during the period to determine the activity of natural killer cells (NK activity) as an immune parameter. Patients who stopped visits without notice were excluded as dropouts from the study. Patient QOL was checked by observation and enquiry during the study. Pain, malaise, and vomiting were evaluated using 4 grades, and appetite assessed using 3 grades to compare the scores before and after treatment. **Table 3** shows the details.

Table 4 Relation among total survival rate, NK activity and survival rates in 2 groups

Group	MGN-3 Group	Control Group
Total survival rate	52/96 (54.2%)	19/56 (35.8%)
NK activity category		
Less than 19.9%	17/40 (42.5%)**	2/16 (12.5%)
20%-40%	18/35 (51.4%)*	7/25 (28.0%)
More than 40%	17/21 (81.0%)	10/15 (66.7%)

*significant to the control group **$p < 0.01$ *$p < 0.05$

Table 5 QOL amelioration

QOL	Pain			Malaise			Nausea			Appetite		
	BT	AT	%	BT	AT	%	BT	AT	%	BT	AT	%
Control group	2.9	2.5	-14.0	3.5	2.9	-17.1	2.5	2.9	-14.6	1.6	1.9	+15.6
MGN-3 group	2.2	1.9	-15.9	2.9	2.4	-17.3	2.3	2.0	-13.3	1.7	2.1	+24.2

Note; BT: Before treatment AT: After treatment

%: Amelioration degree = (Scores at initiation less scores at termination) divided by scores at initiation

(-): indicates negative factors (decrease), (+): indicates positive factors (increase).

Results

1. Subjects included in analysis

A total of 152 of 205 patients were eligible for analysis, including 96 in the BioBran/MGN-3 group and 56 in controls. The main reasons for dropping out were that the prescribed treatment became impossible due to increased pain, malaise, or vomiting, and decreased appetite due to cancer progression in some cases, or that other patients were pessimistic and gave up the prescribed treatment. There were no dropouts in the BioBran/MGN-3 group, and all patients were included in the analysis. In the control group, 53 patients, accounting for 49%, dropped out.

2. The number of surviving patients and survival rates at 18 months

The survival rate at 18 months of treatment was 54.2% for the BioBran/MGN-3 group (52 patients) and 35.8% for the control group (19). An investigation showed that no dropout survived. This means that the survival rate for the control group was 17.4% of 109 patients at the start of study.

3. Changes in NK activity

After starting the study, patients had decreased, unchanged, or increased NK activity. In the BioBran/MGN-3 group, NK activity fell in 45.9% of patients, was unchanged in 21.9%, and increased in 32.3%. In the control group, NK activity fell in 51.8%, was unchanged in 9.0%, and increased in 39.3%. There was no difference in patients with increase or decrease in NK activity between both groups, but the rate of patients with unchanged NK activity was higher in the BioBran/MGN-3 group.

4. Relation between NK activity and prolongation of survival

NK activity before completion of the study was classified into categories of ≤20%, 20%-40%, and ≥40% to compare survival rates. The survival rate was higher in patients with higher NK activity in both groups. The results are shown in **Table 4**.

5. QOL

Table 5 shows mean QOL scores and improvements (%) before and after treatment for 96 patients in the BioBran/MGN-3 group and 56 in the control group.

Improvement of QOL was observed in both control and MGN-groups, suggesting that our clinic's complementary alternative therapy is effective in improving QOL for patients with progressive cancer. In particular, the BioBran/MGN-3 group showed a marked increase in appetite.

Conclusion

The life prolonging and QOL improving effects of BioBran/MGN-3 were studied in progressive cancer patients given a clinic-prescribed therapy and those given the same therapy plus BioBran/MGN-3. As a result, clear prolongation of life expectancy and QOL improvement were observed. The mean duration of hospitalization was 1 month. Although the maintenance of patients numbers was not perfect during the study, a total of 205 participated in the study, and data were obtained from 152 of them. This is sufficient for statistical analysis. The patients' NK activity was clearly decreased, and the survival rate tended to be low in patients with decreased NK activity. The proportion of patients with unchanged or increased NK activity was higher in the BioBran/MGN-3 group than in the control group, resulting in a 1.5 times higher survival rate in the former group. There are many reports on the NK activity modulating effect of BioBran/MGN-3, and the results of the present study supported this. With respect to QOL appetite clearly increased in the BioBran/MGN-3 group. While 49% dropped out in the control group, there were no dropouts in the BioBran/MGN-3 group. This was at least in part because of the improvement of the nutritional state due to increased appetite.

The relation between NK activity and immunity against a tumor is controversial, and the role of NK cells is not completely clear. However, it is considered a good indicator of nutritional status in progressive cancer patients, because those with NK activity above a certain level are likely to survive for a longer time. Preventing NK activity from declining and maintaining it at a high level may lead to prolongation of survival.

BioBran/MGN-3, which helps the maintenance and enhancement of patient's self-curative ability, can be a useful tool for complementary alternative therapy.

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