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Effects of a Structured Psychiatric Intervention on Immune Function of Cancer Patients

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The aim of the present study was to examine the influence of mood state and coping styles on the immune function in Japanese breast cancer patients who participated in a structured group intervention program. The program consisted of five-weekly 90-minute sessions, including psycho-education, psychological support, problem-solving technique and relaxation/imagery. Out of 77 breast cancer patients who participated in this program, 34 were eligible for measurement of immune functions because they received adjuvant chemotherapy. Comparison of the pre- and post-intervention scores of the Profile of Mood States (POMS) revealed significant decreases in Depression ($p < 0.05$), Lack-of-Vigor ($p < 0.01$), Tension-Anxiety ($p < 0.01$), Confusion ($p < 0.05$) and Total Mood Disturbances ($p < 0.01$), as expected. Concerning coping styles, there were tendencies to decrease the score of active-cognitive coping ($p = 0.09$), although the differences were not statistically significant.
In contrast, the pre- and post-intervention values of immune parameters such as CD3, CD4, CD8, CD4/8 and natural-killer cell activity showed no significant differences. In this report, we discuss several possibilities underlying these findings. Further studies with a larger number of subjects and controls are needed to reach conculusions.

Key words : Group intervention, Breast cancer, Coping style, Immune function, Natural-killer cell activity

INTRODUCTION

It has been shown that psychosocial interventions for cancer patient produces an improvement in clinical outcome in Western countries. For example, Spiegel *et al.* reported that breast cancer patients receiving group psychotherapy had a longer life span than the control group [1]. Richardson *et al.* showed that an educational intervention program for patients with hematological malignancies could increase their life span compared with the controls [2]. Fawzy *et al.* also reported that malignant melanoma patients who received 6 weeks of a structured group intervention showed an improvement in emotional discomfort [3]. More recently, Helgeson *et al.* demonstrated that education-based group interventions facilitated the initial adjustment to breast cancer [4].

In Japan, there have been few studies investigating effects of psychosocial interventions on emotion and quality of life (QOL) of cancer patients. We have investigated the clinical effectiveness of a structured group intervention program using a version of the structured group intervention for breast cancer patients developed by Fawzy *et al.* [3] modified for Japanese breast cancer patients. According to the pilot study, both individual-based and group-based intervention programs were effective in alleviating emotional distress among breast cancer patients [5]. Subsequent studies demonstrated a short-term effectiveness particularly in improving psychological distress for breast

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cancer patients [6], and that the effectiveness persisted for 6 months after the completion of the intervention program in the patients without adjustment disorders at the entry [7] or lymph node metastasis [8].

On the other hand, there are several studies demonstrating a relationship between stress situations and immune functions. Some studies reported that the immune function was suppressed due to acute [9] and chronic stress [10]. In contrast, the immune functions were found to be increased by relaxation, disclosure and social support [11–13]. Fawzy *et al.* also showed that malignant melanoma patients who received a 6-week structured group intervention had augmented immune functions [14], resulting in a decrease in the recurrence/mortality [15].

In Japan, it was demonstrated that the decreased immune functions of caregivers for dementia victims were improved by a structured intervention program which was developed from the program for cancer patients [16, 17].

The present study was conducted to investigate the influence of a 5-week structured group intervention on immune functions of cancer patients.

PATIENTS AND METHODS

From November, 1996, through November, 1998, a total of 77 patients with Stages I and II breast cancer were recruited to this study. All patients had undergone standard surgical treatments. All patients were fully informed by the physicians-in-charge of the methods, the aims of this study, and the rights to refuse without any disadvantages. The subjects who gave their written consent participated in the structured intervention program. This program consisted of five weekly sessions, each of which lasted 90 minutes. Each session included the following.

Psycho-education: teaching about the relationship between stress and immune function, the relationship between coping style and cancer progress, the relationship between social support and cancer progress, Type C (cancer-prone) personality and others.

Problem-solving: teaching by health professionals and/or patients themselves how to face and solve the difficulties of life in cancer patients.

Psychological support: encouraging and supporting cancer patients by health professionals and/or patients themselves.

Relaxation training: teaching relaxation techniques such as progressive muscle relaxation and autogenic training.

Guided imagery: teaching to imagine immune cells fighting with cancer cells, and eventually cancer cells be weakened and destroyed.

The number of patients assigned to one group depended upon the operation schedule, and the number ranged from 4 to 8. Once a group was formed, the intervention program was performed without changing the members.

Out of these patients, immune functions were measured from ones who did not receive adjuvant chemotherapy or radiotherapy, because these therapies might have had various effects on their immune functions.

The patients underwent the Profile of Mood States (POMS) and Dealing-with-Illness (DWI) inventory at the entry to the intervension and at the end of the fifth session. The POMS consists of 65 items and can be calculated to produce scores indicating psychological distress such as Depression, Lack-of-Vigor, Aggression-Hostility, Fatigue, Tension-Anxiety, Confusion and Total Mood Disturbances [18]. Therefore, this inventory has been frequently used to measure the changes of psychological distress caused by some kinds of psychiatric interventions. The inventory was translated into Japanese and its reliability and validity have been confirmed among Japanese subjects [19]. The DWI, which was originally developed in the U.S., is a 48-item inventory to assess cognitive and behavioral responses for coping with illness. Responses were categorized into three coping methods such as active-cognitive, active-behavioral and avoidance methods [20]. In a previous study, the DWI was administered to Japanese patients with breast cancer, and demonstrated a high Cronbach alpha coefficient available for Japanese [21].

Blood samples were collected at the beginning of the first session (pre-intervention) and at the end of the fifth session (post-intervention). The immune functions included CD3, CD4 and CD8 cell counts, the CD4/8 ratio and natural-killer (NK) cell activity. The surface marker expression was determined by flow cytometry. NK cell activ-

Table 1 Subjects

Number	34
Age (mean ± SD)	50.3 ± 8.7 (29–76)
Operative procedures	
Mastectomy only	13
Mastectomy + Reconstruction	11
Lumpectomy only	5
Lumpectomy + Radiotherapy	5
Nodal metastasis	(+) 6 (−) 28
Chemotherapy during this study	(+) 1 (oral) (−) 33
Karnofsky performance status	All > 80
Post-operative weeks	2 wks; 20, 3 wks; 11, 4 wks; 3
Marital status	Married; 30, Single; 2, Widowed; 2

ity was measured using a 51Cr release assay employing K562 erythroleukemia cell line as a target at three effector/target (E/T) ratios of 20:1, 10:1 and 5:1, then the lytic units (LU)/106 cells were calculated,with 1 LU being the number of effecter cells required to cause 30% lysis of target cells [22].

The scores of the POMS and the DWI and several measures of immune functions were compared between pre- and post-intervention. Statistical analysis was performed by Repeated measures MANOVA and multiple regression analysis using the SPSS 9.0J software (SPSS Inc, 1999).

RESULTS

Of 77 patients who participated in the intervention program, 34 who had not received adjuvant chemotherapy were eligible for measurement of immune functions. (Table 1) Their mean age was 50.3 ± 8.7 [29–76]. Six of those 34 patients had nodal metastasis but only one patient received oral anti-cancer agent. The others hesitated to receive adjuvant chemotherapy during this study. However, 5 patients eventually received monthly intra-venous chemotherapy after this study. This decision was mostly influenced by the discussion on chemotherapy among the participants.

Thirteen patients had only mastectomy, 11 had reconstructive surgery as well. Five patients had lumpectomy and another 5 had lumpectomy followed by radiotherapy.

The intervention began 2 weeks after the operation for 20 patients, 3 weeks for 11 and 4 weeks for 3. All patients had a Karnofsky performance status of over 80, which meant that no patients had any limitations to the daily life.

Table 2 shows the scores of the POMS and the DWI among 34 patients, revealing significant differences in Depression ($p < 0.05$), Lack-of-Vigor ($p < 0.01$), Tension-Anxiety ($p < 0.01$), Confusion ($p < 0.05$) and Total Mood Disturbances ($p < 0.01$) between pre- and post-intervention.

As shown in Table 2, there were no statistically significant differences in the scores of several coping styles; however, there were tendencies to decrease the score of active-cognitive coping ($p = 0.09$).

Table 3 shows the pre- and post-intervention values of immune parameters such as CD3, CD4, CD8, CD4/8 and NK cell activity. No significant difference was noted.

DISCUSSION

The main aim of the present study was to investigate the influence of our intervention program on immune functions. In contrast to Fawzy's study which demonstrated that NK cell activity was significantly improved among malignant melanoma patients [14], the present study found no improvement in NK cell activity and the other lymphocyte subsets. There are several possibilities to be discussed.

First, our intervention program might have some methodological limitations. It was reported that this intervention was effective

Table 2 Results of the Profile of Mood States (POMS) and Dealing with Illness Inventory (DWI)

	Pre-intervention		Post-intervention		F-value	P-value
	Average	S.D.	Average	S.D.		
Emotions (POMS)						
Depression	11.21	9.68	7.09	4.45	8.46	0.01
Lack-of-Vigor	30.85	4.98	26.58	5.49	19.58	0.00
Aggression-Hostility	5.18	5.57	4.12	3.81	1.12	0.30
Fatigue	6.79	4.66	5.73	4.90	0.95	0.34
Tension-Anxiety	12.52	7.32	7.48	3.83	20.70	0.00
Confusion	7.94	4.27	6.24	2.69	8.57	0.01
Total Mood Disturbances	74.48	29.98	57.24	19.59	13.53	0.00
Coping style (DWI)						
Acitive-cognitive	48.18	7.28	45.88	6.81	3.12	0.09
Active-behavioral	56.42	9.98	58.67	10.34	1.96	0.17
Avoidance	22.36	4.33	22.30	4.57	0.01	0.95

Table 3 Comparative fingings of lymphocyte subsets

	Pre-intervention		Post-intervention		F-value	P-value
	Average	S.D.	Average	S.D.		
Immunological measures						
CD3 (%)	71.75	7.08	71.45	7.88	0.07	0.79
CD4 (%)	47.94	7.74	47.43	6.39	0.24	0.63
CD8 (%)	24.74	6.60	25.38	6.23	0.54	0.47
CD4/8	2.15	0.92	2.02	0.68	1.12	0.30
NK activity ($LU/10^6$)	14.64	9.90	14.89	11.70	0.01	0.91

in improving psychological discomfort in breast cancer patients [5, 6]. This 5-week intervention program was modified to be applied for caregivers of dementia victims, and it was demonstrated that this style of intervention was effective in alleviating psychological and physical symptoms [16]. Also, NK cell activity was found to be augmented by participation in this intervention [17]. Therefore, the program used in the present study does not appear to have a methodological problem.

Second, the fact that NK cell activity was measured just after the operative procedure might be problematic. Schedlowski investigated the effects on peripheral lymphocytes numbers of a behavioral intervention similar to our program and revealed a significant increase in those vlues after the second and the tenth session [23]. Their patients had a surgical operation greater than 20 months before their study. In the present study, the duration between the surgical operation and the entry to this intervention was mostly 2weeks, ranging from 2 to 4 weeks. With respect to the effects of surgical operation on NK cell activity, a number of studies have observed post-operative suppression [24]. Although the suppression in NK cell activity is evident by the second post-operative day in most studies, Uchida *et al.* demonstrated that patients undergoing modified radical mastectomies had significantly reduced NK cell activity that continued for over two weeks following surgery [25]. Other studies observed suppression in NK cell activity that

lasted 21 or 30 days after major abdominal surgeries [24]. It is unknown how long the suppression in NK cell activity persists after mastectomy. In the present study, the intervention started 2 weeks after mastectomy and ended at the 7th week for most of the patients. Therefore, it is still possible that the study timing appropriate the changes in NK cell activity.

Third, there is a possibility that radiation therapy produced effects on immune function. Blomgren *et al*. reported that breast cancer patients showed significantly reduced NK cell activity one week after post-operative radiotherapy, followed by a return to normal levels after 3 to 4 months [26]. In the present study, 5 patients received radiotherapy after lumpectomy; however, their NK cell activities did not differ from the other subjects (data not shown). Similarly, chemotherapy might affect immune functions, but only one subject in the present study underwent oral chemotherapy during the study period. Therefore, the third possibility appears to be less likely.

This study failed to demonstrate that the structured intervention had a positive effect on immune function. However, this finding was not conclusive. Further studies with a larger number of subjects and controls are needed to clarify this potential association. Moreover, further studies should clarify the beneficial differences according to the personal factors of cancer patients [27].

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