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Research Article

Effect of Beta Glucan on Quality of Life in Women with Breast Cancer Undergoing Chemotherapy: A Randomized Double-Blind Placebo-Controlled Clinical Trial

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Abstract

Purpose: Breast cancer is the most common female malignancy in the world. Beta glucan may improve quality of life in cancer patients receiving chemotherapy. The aim of this trial was to determine the effect of Beta glucan on quality of life in women with breast cancer undergoing chemotherapy.

Methods: This study was conducted on 30 women with breast carcinoma. The eligible participants were randomly assigned to intervention (n=15) or placebo (n=15) groups using a block randomization procedure. Patients in the intervention group received two 10-mg capsules of soluble 1-3, 1-6, D-beta glucan daily and the placebo group received placebo for 21 days, in an interval between two courses of chemotherapy. Health - related quality of life (HRQL) was evaluated using the EORTC Quality of Life Questionnaire version.3.0 (EORTC QLQ-C30) at the beginning and end of the study.

Results: At the end of the study, the Global health status /QoL score for the Beta glucan group was significantly increased (P=0.023), but the difference between the two groups was not significant. After intervention, the Functional scales score showed no significant change (P=0.099) between the two groups or within the groups. At the end of the study, the Symptom scales\items score was decreased significantly in Beta glucan group comparing the placebo group (P=0.048), as well as after adjusting for baseline score. The Symptom scales\items score's change was significant (P=0.012) within the Beta glucan group, compared with the baseline score.

Conclusion: The findings suggest that Beta glucan may be useful as a complementary or adjuvant therapy for improving quality of life in breast cancer patients in combination with cancer therapies.

Introduction

Breast cancer is one of the most common cancers among females in the world.[1] Epidemiological studies indicate that the annual incidence of breast cancer is increasing and is occurring in countries with a previously low incidence rate of breast cancer. In Iran, the incidence rate of disease is rising.[2] It has been shown that women aged 40-49 years have the most prevalence of breast cancer in Iran, but; over 30% of patients were under 30 years old. The incidence rate of breast cancer in women over 30 in Iran is 22 per 100,000.[3]

Polychemotherapy treatmet was used in women with ealry breast cancer.[4] Chemotherapy has short-term and long-term side effects. Short-term effects normally occur during the course of treatment and typically subside within months after treatment.[5] However, chemotherapy is typically accompanied by severe side effects such as nausea, vomiting and alopecia. Theses complications can induce psychological side effects such as anticipatory nausea and vomiting.[6] In cancer patients, quality of life is an important consideration in treatment selection.[7] The assessment quality of life in breast cancer patients was considered after systemic adjuvant therapy.[8] Health-related quality of life is now considered an important goal in cancer clinical trials. It has been shown that assessing quality of life in cancer patients could contribute to improved treatment.[9] Many efforts have been made to promote immunotherapy strategies for the treatment of malignancies. The use of biological response modifiers for improving host defence responses against tumors is one of the most commonly

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considered efforts.[10] β-glucan derived from the yeast species cell wall such as *Saccharomyces cerevisiae* can modulate immune responses in vitro and in vivo conditions. Host resistance to various foreign antigens improves by administration of β-glucan isolated from S. cerevisiae. In addition this form of β-glucan can protect against tumors via immunostimulation.[11] BRMs have been used in combination with cytotoxic chemotherapeutic agents. Lentinan (a purified polysaccharide of β-1, 3-glucan isolated from Shiitake mushrooms) has been reported to have a life-prolonging effect in patients with unresectable or recurrent gastric cancer receiving an oral fluoropyrimidine.[12] In a meta-analysis Oba et al[13] declared that when fluorinated pyrimidines accompanied with lentinan, it could prolong the survival of patients with advanced gastric cancer.
Shimizu et al[14] reported that superfine dispersed lentinan could improve survival and quality of life status assessment in pancreatic cancer patients.
Regarding the positive immunomodulatory properties of Beta glucan on chemotherapy side effects, the present study aimed to investigate the effect of Beta glucan on quality of life in women with breast cancer undergoing chemotherapy.

Materials and Methods

Study design

This randomized, double-blind, placebo-controlled clinical trial with an allocation ratio of (1:1) was carried out in the Oncology Ghazi Tabatabayee and Sheikholrais clinics of Tabriz University of Medical Sciences, Tabriz, Iran. The study included women diagnosed as breast cancer patients by oncologists, aged 28-65 years.
The sample size was determined based on the data obtained from Demir et al.'s study[15] of lymphocytes as recorded in our unpublished data. We assumed α value equal to 0.05 and a power of 80% for calculating the sample size. The sample size was computed as 15 patients per group considering the 20% dropout rate. Inclusion criteria were women with stage II and III breast cancer, confirmed by oncologists and pathology, chemotherapy adjuvant treatment, drinking at least 100 ml of water per day, non-allergy to fungi and yeast, adequate bone marrow function, proper functioning of kidneys, absence of acute medical conditions, women aged 20 years and older, no history of gastrointestinal disease, renal or liver disorders, and no consumption prebiotics, probiotics, or antibiotics. Exclusion criteria were the patient's unwillingness to participate in the study, pregnancy, lactation, vitamin and mineral use that affected immune system and not receiving blood transfusion.

Patient and variable assessment

The eligible participants were randomly assigned to Beta glucan or placebo groups by a block randomization procedure and subject were matched in each block based on age, course of chemotherapy and menopause status. Patients were grouped into 15 triad blocks. Finally each group consisted of 15 patients. The flow chart of the study is shown in Figure 1. Patients were recruited between the second and fourth chemotherapy course. During the interval between two chemotherapy courses (21 days), patients in the intervention group received two capsules containing 10-mg of soluble 1–3, 1–6, D-beta glucan derived from *Saccharomyces cerevisiae* daily while the control group received placebo the same shape and size. In order to reduce the dropout rate and ensure the consumption of the supplements, the subjects received a phone call once per week. Participants were asked to return the Beta glucan package in order to assess the supplement consumption of each patient. All the participants were asked not to change their usual dietary intakes, recommended vitamin or minerals supplements, physical activity, medication or traditional medicine as adjuvant therapy over the course of the study. The patients were asked to inform the researcher about changes in medicine and blood transfusion during the study. Demographic data including age, course of chemotherapy, type and stage of disease and chemotherapy protocol were obtained using the questionnaire. Anthropometric indicators including body weight, height, waist circumference (WC) and hip circumference (HC) were measured at beginning and at the end of the study.
Body weight and height were measured using scales (Seca, Hamburg, Germany) with 0.1 kg accuracy weighing the patient wearing light clothing and without shoes, and by stadiometer (Seca) with 0.1 cm accuracy without shoes, respectively. Body mass index (BMI) was calculated by divided body weight in kilograms to the square of height in meters (kg/m2). Waist circumference (WC) (cm) was measured at a point of midway between the lower rib margin and the iliac crest, and hip circumference (HC) at the widest point between the iliac crest and buttock.

Health-related quality of life measure

Breast cancer patients' HRQL was evaluated using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire version.3.0 (EORTC QLQ-C30), downloaded from the EORTC website.[16] Questionnaires were filled at the beginning and at the end of the study between two courses of chemotherapy.
The EORTC QLQ-C30 contains Global Health Status\QoL, Functional scales and Symptom scale/ items. Functional scales include physical, role, emotional, cognitive, and social functioning. In QoL and Functional subclasses, high scores represent a high QoL and a high level of healthy functioning respectively. Symptom scale/ items include fatigue, nausea and vomiting, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties; higher scores indicate greater symptom

severity[17,18] The EORTC QLQ-C30 is a well-recognized HRQL questionnaire designed for use in a wide range of cancer patient populations and is considered as a reliable and valid measure of HRQL. This questionnaire was translated into Persian. Reliability and validity of the QLQ-C30 (version 3.0) questionnaire were evaluated for application to an Iranian sample of breast cancer patients.[19]

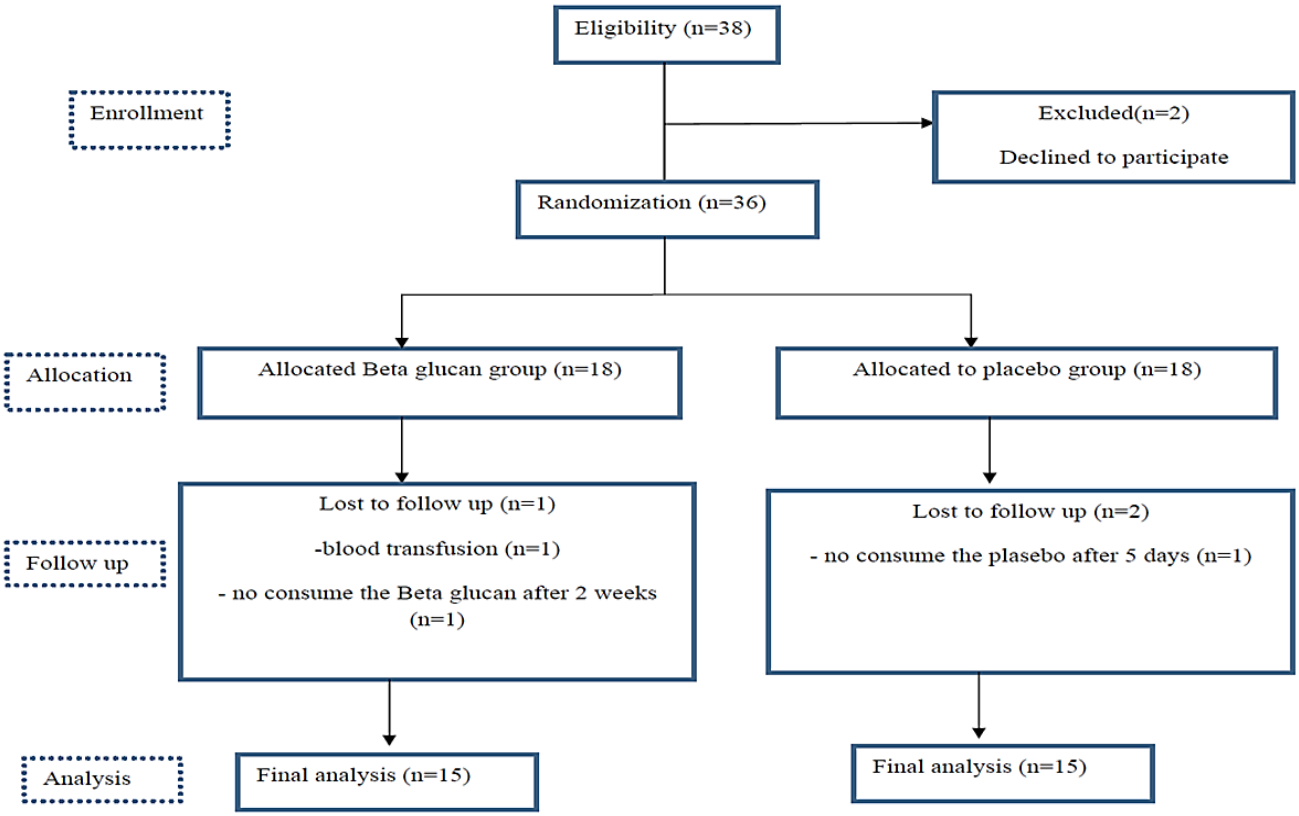

Figure 1. Flow chart of the study

Statistical analysis

EORTC QLQ-C30 changes including global health status\QoL, functional and symptom scales/items scores were calculated at the beginning and at the end of the study. The data were analyzed by SPSS ver.13 (SPSS, Inc. IL, Chicago, USA). The analyses were done by original assigned groups (Intention to treat). Normality of variables distribution was evaluated using Kolmogorov-Smirnov test. Quantitative data were stated as mean (standard deviation (SD)). The changes in anthropometric measurements and QOL scores of the participants within the beginning and end of the study in each group were compared by using paired sample t-test. The changes in anthropometric measurements and QOL scores of the participants between two groups at beginning and end of the study in the two groups were compared using independent sample t-tests. Analysis of covariance was used to identify any differences between the two groups after intervention, adjusting for baseline scores.[20]

Results

General and anthropometric characteristics of the participants are shown in Table 1. This randomized, double-blind, placebo-controlled clinical trial was conducted on 30 breast cancer patients according to inclusion and exclusion criteria. Patients did not express any adverse effects or symptoms associated with the Beta glucan supplementation. In the two groups weight, height, BMI, waist circumference and hip circumference showed no significant differences during the study. Table 2 notes the stage of disease and the treatment protocols. According to Table 2, in intervention the group 26.7, 46.6 and 26.7% of patients received the second, third and fourth chemotherapy course respectively. In the control group 33.3, 40 and 26.7% of patients received the second, third and fourth chemotherapy course, respectively. The chemotherapy protocol is illustrated for the two groups in Table 2 and both groups were matched as closely as possible.

Table 1. General and anthropometric characteristics of study participants

	Characteristics	Beta glucan Group (n=15)	Placebo Group (n=15)
	Age (years)	46.20±8.96	49.40±7.75
	Height (cm)	160.27± 4.93	159.50±3.77
Beginning of the study	Weight (kg)	67.60±12.21	66.80±10.81
	BMI (Kg\m2)	26.29±4.44	26.02±3.71
	Waist circumference (cm)	91.40±11.12	88.66±6.56
	Hip circumference (cm)	105.73±11.81	105.00±7.77
End of the study	Weight (kg)	67.73±12.04	66.26±10.66
	BMI (Kg\m2)	26.34±4.40	25.81±3.65
	Waist circumference (cm)	91.60±11.13	88.36±6.35
	Hip circumference (cm)	104.95±11.69	104.83±7.94

Table 2. Disease characteristics and chemotherapy protocols of study participants

Characteristics	Beta glucan Group (n=15)		Placebo Group (n=15)	
Chemotherapy course (%)	2	26.7	2	33.3
	3	46.6	3	40
	4	26.7	4	26.7
Chemotherapy protocol (%)	AC(Adriamycin 60 mg\m2 Cyclophosphamide 600mg\m2)		AC(Adriamycin 60 mg\m2 Cyclophosphamide 600mg\m2)	
	40		46.7	
	CMF (Cyclophosphamide 600mg\m2 , Methotrexate 40 mg\m2 , Fluorouracil (5-FU) 600 mg\m2)		CMF (Cyclophosphamide 600mg\m2 , Methotrexate 40 mg\m2 , Fluorouracil (5-FU) 600 mg\m2)	
	20		13.3	
	ECF (Epirubicin 50-100 mg\m2, cisplatin 500-600 mg\m2, fluorouracil (5-FU) 500-600mg\m2)		ECF (Epirubicin 50-100 mg\m2, cyclophosphamide 500-600 mg\m2, fluorouracil (5-FU) 500-600mg\m2)	
	40		40	
Stage of disease (%)	II:73.3		II:80	
	III:26.7		III:20	

Internal consistency

The Cronbach's alpha for the study questionnaire was 0.96, 0.86 and 0.70 for Global helth status/QoL, functional scales and symptom scales/ items respectively. The effect of Beta glucan on Quality of Life in breast cancer patients is noted in Table 3. The results are illustrated in three subclasses including Global health status/QoL, Functional scales and Symptom scales\items. According to Table 3, there were no significant differences in Global health status score at the beginning of the study between the two groups. At the end of the study, Global health status/QoL score in the Beta glucan group was increased significantly (p=0.023). The Global health status/QoL score showed no significant changes in comparison with the placebo group (P=0.936) and after adjusting for baseline score (P=0.488). At the beginning of the study, there were no significant differences in Functional scales score between two groups. At the end of the study the Functional scales score showed no significant change (P=0.099) between the two groups. Covariance analysis did not show significant changes (P= 0.07) in Functional scales score after it was adjusted for baseline score. Functional scales score changes were not significant within the groups compared with the baseline values. The third sub-group, Symptom scales\items score did not show significant differences at the beginning of the study; after intervention, the symptom scales\items sore was decreased significantly in the intervention group compared with the placebo group (P=0.048). Results of covariance analysis showed the changes in symptom scales\items score between the two groups were significant (P<0.001) when adjusted for baseline. The symptom scales\items score change was also significant (P=0.012) within the Beta glucan group compared with the baseline score.

Table 3. Effects of Beta Glucan on Quality of Life

		Beta glucan Group(n=15)	Placebo Group(n=15)	Mean Differences (95% CI, p)
Global health status/QoL	**Baseline**	35.55(19.53)	34.44(15.38)	1.11(-12.04- 14.26, 0.864)[b]
	After intervention	40.55(16.32)	37.77(11.72)	2.77(-7.85-13.40, 0.936)[b]
	Mean Differences (95% CI, p)	-5.00(-9.20- -0.79,0.023)[a]	-3.33(-10.26- 3.59, 0.032)[a]	2.02(-3.81- 7.86, 0.488)[c]
Functional scales	**Baseline**	36.29(14.29)	33.62(14.90)	2.66(-8.25-13.58,P=0.621)[b]
	After intervention	40.44(10.56)	33.03(13.06)	7.40(-1.49-16.31,P=0.099)[b]
	Mean Differences (95% CI, p)	-4.14 (-17.03- 8.74, P=0.501)[a]	0.59(-13.68- 14.87, P=0.930)[a]	9.07(3.71-14.43, P=0.07)[c]
Symptom scales\items	**Baseline**	64.27(14.72)	62.73(11.90)	1.53(-8.47-11.54, 0.755)[b]
	After intervention	56.75(9.87)	63.98(9.25)	-7.23(-14.39- -0.07, 0.048)[b]
	Mean Differences (95% CI, p)	7.52(1.90-13.13, 0.012)[a]	-1.25(-5.71- 3.20, 0.556)[a]	-8.13(-12.47- -3.79, <0.001)[c]

[a] Paired sample t-test
[b] Independent sample t-test
[c] Analysis of covariance (ANCOVA) test, adjusted for baseline scores

Discussion

The present study aimed to investigate the effect of Beta glucan on quality of life in breast cancer patients receiving chemotherapy. According to our findings in the Beta glucan group the quality of life in symptom scales\items and Global health status/QoL improved after 21 days of the intervention. Recently, health-related quality of life has come to be considered as an important outcome in cancer clinical trials. As mentioned above, it has been revealed that the assessment of quality of life in cancer patients could contribute to improved treatment and could be a prognostic factor.[9] It has also been shown[21] that lentinan (a form of Beta glucan), as an adjuvant with conventional chemotherapy enhances immunity, improves effectiveness of treatment and improves quality of life. In recent years, Beta glucan has been considered as an adjunctive therapy in cancer patients for immunomodulation properties. Investigators suggest that Beta glucans could induce secretion of INF-gamma, and IL-12.[11,22,23] To our knowledge Beta glucan was administrated in the form of superfine dispersed lentinan in some cancers. Scientific research literature shows that the effect of lentinan on quality of life has been investigated in esophageal, advanced gastrointestinal, pancreatic, colorectal and gastric cancer patients undergoing chemotherapy.[12,14,24,25] Our results showed that soluble 1–3, 1–6, D-beta glucan derived from *Saccharomyces cerevisiae* improved some aspects of quality of life in breast cancer patients undergoing chemotherapy. Our findings were consistent with other studies. Wang et al[24] showed the combination of chemotherapy regimen with lentinan improved the general condition, symptoms and signs, and quality of life in patients with esophageal carcinoma. Lentinan up-regulates pro-inflammatory cytokines and down-regulates anti-inflammatory cytokines. In one study,[26] it has been proved that LEM with the FEC 75 therapy in breast cancer patients might have prevented host immunity during the second cycle of chemotherapy. Lentinan is an immune adjuvant medicine for advanced gastric cancer used in Japan. Hazama and et al[25] investigated the efficacy of orally administered superfine dispersed lentinan (β-1,3-Glucan) in advanced colorectal cancer patients. In Hazama and et al.'s study, SDL was administered at a dose of 15 mg of LNT once daily for 12 weeks. In that time, the patients were also treated with various chemotherapy regimens. In their study, low QOL scores in 23 patients reported a significant improvement after 12 weeks of SDL administration. Ina et al[12] showed that chemo-immunotherapy with lentinan presents a principle advantage over S-1-based chemotherapy alone in terms of survival in patients with advanced gastric cancer. They suggested Lentinan should be accepted for the treatment of unresectable or recurrent advanced gastric cancer. Chemo-immunotherapy combined with lentinan and an S-1-based regimen might be a candidate for the standard treatment of advanced gastric cancer. Significant correlation between QOL scores and subsequent survivals was seen after 12 weeks of SDL treatment in advanced pancreatic cancer.[14] The researchers suggested changes in QOL scores were promising prognostic predictors in cancer patients with SDL treatment.

The limitation of this study included a short time of intervention; Thus, long term supplementation with Beta glucan in breast cancer patients should be further investigated in combination chemotherapy courses. The strength of our study is the high acceptance of Beta glucan in female breast cancer patients undergoing chemotherapy, as well as the weekly monitoring of patients by phone call.

Conclusion

The results of this study showed that Beta glucan consumption in breast cancer patients receiving chemotherapy improved Global health /QoL status and symptoms scales/ items, although changes in Global health scores were not significant in comparison with the placebo group. We did not see significant changes in Functional scales in the Beta glucan group in comparison with the placebo group. These findings suggest that Beta glucan usage may be useful as a nutrition adjuvant therapy in combination with cancer treatments. Further studies over longer intervention time and larger sample sizes are needed in order to confirm other positive aspects of Beta glucan supplementation in breast cancer patients' undergoing chemotherapy.

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Ethical Issues

This clinical trial was approved by the Regional Ethics Committee of Tabriz University of Medical Sciences. Written informed consent was obtained from all patients' at the beginning of the study. The EORTC QLQ-C30 questionnaire was used by EORTC, Quality of Life Department permission in this study. The registered number in IRCT is IR201212172017N10.

Conflict of Interest

The authors have no conflict of interest.

References

1.Coughlin SS, Ekwueme DU. Breast cancer as a global health concern. *Cancer Epidemiol* 2009;33(5):315-8.

2. Montazeri A, Vahdaninia M, Harirchi I, Harirchi AM, Sajadian A, Khaleghi F, et al. Breast cancer in Iran: need for greater women awareness of warning signs and effective screening methods. *Asia Pac Fam Med* 2008;7(1):6.

3. Mousavi SM, Montazeri A, Mohagheghi MA, Jarrahi AM, Harirchi I, Najafi M, et al. Breast cancer in Iran: an epidemiological review. *Breast J* 2007;13(4):383-91.

4. Polychemotherapy for early breast cancer: an overview of the randomised trials. Early Breast Cancer Trialists' Collaborative Group. *Lancet* 1998;352(9132):930-42.

5. Partridge AH, Burstein HJ, Winer EP. Side effects of chemotherapy and combined chemohormonal therapy in women with early-stage breast cancer. *J Natl Cancer Inst Monogr* 2001(30):135-42.

6. Payne SA. A study of quality of life in cancer patients receiving palliative chemotherapy. *Soc Sci Med* 1992;35(12):1505-9.

7. Coates A, Gebski V, Bishop JF, Jeal PN, Woods RL, Snyder R, et al. Improving the quality of life during chemotherapy for advanced breast cancer. A comparison of intermittent and continuous treatment strategies. *N Engl J Med* 1987;317(24):1490-5.

8. Lindley C, Vasa S, Sawyer WT, Winer EP. Quality of life and preferences for treatment following systemic adjuvant therapy for early-stage breast cancer. *J Clin Oncol* 1998;16(4):1380-7.

9. Montazeri A. Health-related quality of life in breast cancer patients: a bibliographic review of the literature from 1974 to 2007. *J Exp Clin Cancer Res* 2008;27:32.

10. Schepetkin IA, Faulkner CL, Nelson-Overton LK, Wiley JA, Quinn MT. Macrophage immunomodulatory activity of polysaccharides isolated from Juniperus scopolorum. *Int Immunopharmacol* 2005;5(13-14):1783-99.

11. Yoon TJ, Kim TJ, Lee H, Shin KS, Yun YP, Moon WK, et al. Anti-tumor metastatic activity of beta-glucan purified from mutated Saccharomyces cerevisiae. *Int Immunopharmacol* 2008;8(1):36-42.

12. Ina K, Furuta R, Kataoka T, Kayukawa S, Yoshida T, Miwa T, et al. Lentinan prolonged survival in patients with gastric cancer receiving S-1-based chemotherapy. *World J Clin Oncol* 2011;2(10):339-43.

13. Oba K, Kobayashi M, Matsui T, Kodera Y, Sakamoto J. Individual patient based meta-analysis of lentinan for unresectable/recurrent gastric cancer. *Anticancer Res* 2009;29(7):2739-45.

14. Shimizu K, Watanabe S, Watanabe S, Matsuda K, Suga T, Nakazawa S, et al. Efficacy of oral administered superfine dispersed lentinan for advanced pancreatic cancer. *Hepatogastroenterology* 2009;56(89):240-4.

15. Demir G, Klein HO, Mandel-Molinas N, Tuzuner N. Beta glucan induces proliferation and activation of monocytes in peripheral blood of patients with advanced breast cancer. *Int Immunopharmacol* 2007;7(1):113-6.

16. EORTC. European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30). Brussels, Belgium: EORTC Quality of life; [cited 2012 May]; Available from: http://groups.eortc.be/qol/questionnaires_qlqc30.htm.

17. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993;85(5):365-76.

18. Fayers PM, Aaronson NK, Bjordal K, Groenvold M, Curran D, Bottomley A. On behalf of the EORTC

quality of life group. The EORTC QLQ-C30 Scoring Manual. 3rd ed. Brussels: European Organisation for Research and Treatment of Cancer; 2001.
19. Safaee A, Moghim Dehkordi B. Validation study of a quality of life (QOL) questionnaire for use in Iran. *Asian Pac J Cancer Prev* 2007;8(4):543-6.
20. Asgharijafarabadi M, Mohammadi S. Statistical Series: Summarizing and Displaying Data. *J Diabetes Lipid Dis* 2013;12:83-100.
21. Yoshino S, Watanabe S, Imano M, Suga T, Nakazawa S, Hazama S, et al. Improvement of QOL and prognosis by treatment of superfine dispersed lentinan in patients with advanced gastric cancer. *Hepatogastroenterology* 2010;57(97):172-7.
22. Budak F, Goral G, Oral HB. Saccharomyces Cerevisiae Beta-Glucan Induces Interferon-Gamma Production in Human T Cells Via IL-12. *Turk J Immunol* 2008;13(1):21-6.
23. Ross GD, Vetvicka V, Yan J, Xia Y, Vetvickova J. Therapeutic intervention with complement and beta-glucan in cancer. *Immunopharmacology* 1999;42(1-3):61-74.
24. Wang JL, Bi Z, Zou JW, Gu XM. Combination therapy with lentinan improves outcomes in patients with esophageal carcinoma. *Mol Med Rep* 2012;5(3):745-8.
25. Hazama S, Watanabe S, Ohashi M, Yagi M, Suzuki M, Matsuda K, et al. Efficacy of orally administered superfine dispersed lentinan (beta-1,3-glucan) for the treatment of advanced colorectal cancer. *Anticancer Res* 2009;29(7):2611-7.
26. Nagashima Y, Sanpei N, Yamamoto S, Yoshino S, Tangoku A, Oka M. Evaluation of host immunity and side effects in breast cancer patients treated with adjuvant chemotherapy (FEC therapy). *Gan To Kagaku Ryoho* 2005;32(11):1550-2.