The Effect of Spiritual Intervention on the Concentration of Interleukin-1\(\beta\), Interleukin-6, Interleukin-8 and Tumor Necrosis Factor Alpha Cytokines in Patients with Breast Cancer: A Pretest–Posttest Experimental Study

Abstract

Background and Aim: Breast cancer (BC) has considerable effects on the immune system by modulating various psychological and biological aspects, especially hormonal function. Given the effectiveness of various psychological interventions on the overall health status of patients, we aimed to show the effect of the spiritual intervention on the immunological structure of patients with BC.

Subjects and Methods: This was a pretest-posttest experimental study conducted from October 2017 to March 2018. There were three groups of patients with BC who referred to Shohada-e-Tajrish Hospital, Cancer Research Center, and Azar Clinic. The sample size based on Cohen’s table for each group was at least 11 and taking into account the advantages of the subjects was 15. The selection of samples in the first stage was purposeful and based on the inclusion and exclusion criteria, but they were assigned to the groups randomly. They were assigned to the experiment group and two control groups. The first group received 12 sessions of spiritual intervention, the second group received 12 sessions of nonpsychological training focused on physical care related to their illness, and the third group received no intervention. The levels of interleukin (IL)-1\(\beta\), IL-6, IL-8, and tumor necrosis factor-alpha (TNF-\(\alpha\)) were measured in all three groups by Enzyme-linked Immunosorbent Assay before, after, and 3 months after the intervention. The data were analyzed with SPSS software version 21 and the \(P < 0.05\) was considered significant.

Results: The level of cytokines was significantly changed at the time of follow-up. These changes were significant between the groups who received the spiritual intervention and nonpsychological training in comparison to the group that did not receive the intervention. Moreover, there was no significant difference between the intervention group and the training group.

Discussion/Conclusion: Our findings showed that spiritual intervention can increase the success of the treatment process and the improvement of the patients. Spiritual intervention may significantly affect the physical health of patients with special needs, especially cancer patients in both treatment and recovery states.

Keywords: Breast cancer, breast neoplasms, cytokines, immune system, nonpsychological training, spiritual intervention

Introduction

The incidence of breast cancer (BC) in Iran is increasing from 16.7 per 100,000 women in 2000 to 33.6 in 2009, and likely increases to 63 per 100,000 in 2020.[1] Development of cancers possibly is influenced by various stressors in life.[2,3] Stressors cause rapid ACTH release and subsequently, release corticosteroids from the adrenal by causing emotional changes in the organism, which these corticosteroids usually decrease the activity of the immune system and consequently, cancer progression is accelerated.[4] Negative emotions disrupt hormone secretion, while positive emotions stimulate the immune system by producing favorable hormonal changes.[5] High stress, in BC patients, disrupts white blood cell activity and disrupts body homeostasis, producing cortisol and impaired immune function; thus these adverse effects on the physiological system can affect certain parameters of the cellular immune system such as a reduction in the proliferation of T cells.[6]

Although physical alterations in cancer can affect different aspects of an individual’s emotions, attention to the effectiveness of various psychological interventions, especially strong parameters such as spirituality and religion, is increasing in the management of adverse effects of cancer.
Accordingly, more focus has been placed on the potential power of faith to heal and improve, can provide frameworks through which one can more fully understand the meaning, purpose, and values of one’s own life as a consciousness.[8] Therefore, the use of spiritual strategies is a psychological-enhancing factor and one of the most effective coping strategies that reduce mental distress and physical complaints,[9] enhance the body’s immunological ability and quality of life (QOL), and provide rest.[10]

In keeping with our model of an intimate relationship between the central nervous system and the immune system, religion serves as an example of how a pervasive cognitive system, influences interactions with one’s environment, may modulate the effects of stress on the immune system.[11,12] It was shown in a study that higher levels of religious attendance in a non-disabled population of older adults were prospectively related to lower mortality up to 12 years later and that these effects appear to be mediated by IL-6.[13] Among studies reviewed, Mindfulness-Based Stress Reduction (MBSR) interventions have been the most utilized spiritual-based interventions in BC survivors. MBSR is associated with improved inflammatory cytokine activity, improved lymphocyte function, improved or stabilization of cortisol levels, and increased or preservation of telomere activity. Findings suggest that in general, spiritual-based interventions are associated with improved neuroendocrine-immune function, particularly cortisol and cytokine activity.[14] The humoral system is weakened by reducing the production of cytokines such as tumor necrosis factor-alpha (TNF-α), which is one of the factors that induce programmed cell death in cancer cells. Hence, a reduction in the number of T cells is associated with decreased production of TNF-α, which may induce proliferation of tumor cells in the absence of such cytokines and immune cells.[15] The primary aim of therapies is to improve the immune system function, eradicate tumors, or prevent tumor recurrence through robust, specific, long-term antitumor immune responses, and focus on the function of cytokines and activation. They have been one of the most successful forms of immune-based therapeutic approaches for cancer patients to date.[16] Accordingly, more focus has been placed on the treatment of individuals based on the four physical, mental, social, and spiritual dimensions in the medical care system.[17] Therefore, given the role of mental health in human health, enhancing the immunity of patients with cancer, and preventing them from reducing their immunity, this study aimed to find a suitable solution for promoting mental health to improve the immune system in patients with BC.

**Subjects and Methods**

This was a pretest-posttest experimental designed study from October 2017 to March 2018. The study population consisted of all women with BC referred to Shohada-e-Tajrish Hospital, Shahid Beheshti University of Medical Sciences Cancer Research Center, and Azar Clinic. Inclusion criteria were the patients at clinical stage 1 and 2 of BC, aged between 25 and 65 years, having minimal reading and writing literacy to complete and sign a consent form. We selected patients with stage 1 and 2 because there were not any metastasis and recurrences in these two stages.[18] The first treatment for patients was surgery first, then chemotherapy and radiation therapy if necessary (were not neoadjuvant). By the end of their radiotherapy and chemotherapy, it had been at least 6 months and a maximum of 1 year. Exclusion criteria were advanced and metastatic cancer, neoadjuvant (those who had undergone chemotherapy and then surgery), a significant clinical disorder, psychiatric drug use for the past 3 months, participation in other therapies or their current membership, their reluctance to donate blood and to discontinue any cooperation.

The sample size of the study was determined based on Cohen’s table,[19] with an effect size of 0.5 and the power of 0.8 for each group, which was at least 11 and considering the subjects’ dropout was estimated by 15 individuals per group. For allocating the patients to the groups, after calculating the sample size, they were randomly assigned to the experiment group and two control groups in which the participants were measured three times.

The first measurement is called pretest, the second measurement is posttest and the third measurement is follow-up. The level of serum cytokines was measured in these three phases. There were eligibility criteria for performing this study. The spiritual intervention was performed by a psychologist under the supervision of a tutor. Non-psychological classes were held by specialists in each field under the supervision of the Cancer Research Center of Shahid Beheshti University of Medical Sciences. Blood samples were collected by skilled and experienced nurses of Shohada-e-Tajrish Hospital.

The experiment group was the patients with BC who underwent 12 sessions of spiritual intervention. The first control group consisted of the patients with BC who completed 12 sessions of training (except psychological content), the second control group included the patients with BC who did not receive any intervention or training. Educational and spiritual intervention sessions were held once a week for 90 min. Serum levels of IL-1β, IL-6, IL-8, and TNF-α were measured in all groups before, after, and 3 months after the last session of the intervention. In order to evaluate the serum level of cytokines, 5 ml of venous blood was taken from the patients and their serum was separated and stored at −20°C until the day of the test. Serum levels of cytokines were measured and quantified by Enzyme-linked Immunosorbent Assay (IBL Company, Germany) with the minimum detection limit of pg/ml.
The protocol of spiritual intervention

In spiritual intervention, the therapist invites the patient to explore spiritual issues and issues in order to improve and restore health along with other therapies such as medication and emphasizes spiritual issues by means of mental approaches. Spiritual intervention means considering cultural-religious beliefs and the intrinsic relationship with divine power, beyond the boundaries of religious beliefs in different religions that guide patients toward God’s divine power. Training stress management strategies with spiritual resources and attention to the meaning and QOL are useful in helping patients “personal independence and awareness in improving their treatment process. Therefore, we can use patients” spiritual beliefs and traditional ethnic values as a spiritual and supportive resource to improve the spiritual health of patients with cancer. Spiritual intervention in the present study was based on a twelve-session spiritual intervention package standardized by Vaziri et al. At Shahid Beheshti University Cancer Research Center. The contents of the package are listed in Table 1.

Ethical committee

This study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences with ethics number: IR.SBMU.RETECH.REC.1397.562.

Statistical analysis

Data were analyzed with Statistical Package for the Social Sciences (SPSS) software version 21 www.ibm.com/products/spss-statistics. The normality was assessed by the Kolmogorov–Smirnov test with P < 0.05. To compare the significance level of intergroup changes, the independent t-test was used, the ANOVA test was used to evaluate the significance level of the data in the follow-up stage, and the Bonferroni test was used for intragroup changes. In the present study, P < 0.05 was considered statistically significant.

Results

The results showed that IL-1β level was different in the intervention group between the pretest and follow-up phases (P = 0.001). The intervention group was also different in the posttest and follow-up phases (P = 0.001). There was a difference in pretest and follow-up of the training group (P = 0.001). Furthermore, there was a significant difference between the follow-up phase of the group under spiritual intervention and in the follow-up group without intervention and training (P = 0.001). There was a significant difference between the follow-up phase of the group undergoing spiritual intervention and the follow-up group without intervention and training (P = 0.001) [Figure 2].

The level of IL-8 in the pretest phase of the group undergoing spiritual intervention and follow-up was higher (P = 0.001). In the pretest phase of the training group and follow-up group, there is a difference between the two groups (P = 0.001). In the posttest phase, the intervention group did not receive any intervention, and this difference was higher in the follow-up group without intervention and training (P = 0.001). There was a significant difference between the follow-up phase of the group undergoing spiritual intervention and the follow-up group without intervention and training (P = 0.001) [Figure 3].

The level of TNF-α was significantly different in the posttest group in the spiritual intervention and follow-up group and this value was higher in the follow-up group in the spiritual intervention group (P = 0.001). Moreover, there was a significant difference between the posttest group without intervention and training and follow-up group (P = 0.001). In addition, we found a significant difference between the follow-up phase of the group under spiritual intervention and the follow-up group without intervention and training (P = 0.001) [Figure 4].

Discussion

This study aimed to evaluate the effectiveness of spiritual intervention on altering the function of cytokines in improving immune function. In other words, our hypothesis study was that spiritual intervention could help improve immune function by altering the function of cytokines. There are conflicting reports on the role of inflammatory cytokines such as IL-8, IL-6, IL-1β, and TNF-α in...
Table 1: Protocol of spiritual intervention, the twelve-session spiritual intervention package

<table>
<thead>
<tr>
<th>First session</th>
<th>Understanding and grounding the re-experience of spirituality</th>
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<tbody>
<tr>
<td><strong>Target</strong></td>
<td>Acquaintance of members with each other, knowledge of the reasons for the formation of the challenge group (awareness of the implicit and personal meaning of spirituality and its definition in terms of each member, examination of the belief in superior and sacred power in the members, and recall of perceptions and beliefs of therapists about spirituality)</td>
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<tr>
<td><strong>Second session</strong></td>
<td><strong>Introspection</strong></td>
</tr>
<tr>
<td><strong>Target</strong></td>
<td>Introspection</td>
</tr>
<tr>
<td></td>
<td>1. Overview of the first session; 2. Individual/medical examination of the group; 3. Meeting preparation; 4. Group status; 5. Introducing the subject of the second session; 8. Presenting homework and reminding the day and time of the next meeting</td>
</tr>
<tr>
<td><strong>Third session</strong></td>
<td>The sources of fear and anxiety and our resources in front of them</td>
</tr>
<tr>
<td><strong>Target</strong></td>
<td>Finding sources of fear and anxiety and resolving it</td>
</tr>
<tr>
<td></td>
<td>1. Meeting preparation; 2. Group status review; 3. Third session review; 4. Reflection on assignments; 5. Introducing a third session (sources of fear and anxiety and coping with them); 6. Reflection on assignments; Practice recognizing fear, anxiety, and relaxation. 8. Providing homework and reminding the day and time of the next meeting</td>
</tr>
<tr>
<td><strong>Fourth session</strong></td>
<td>Infinity and inheritance</td>
</tr>
<tr>
<td><strong>Target</strong></td>
<td>Understanding our endlessness and inheritance</td>
</tr>
<tr>
<td></td>
<td>1. Session preparation; 2. Group status review; 3. Third session review; 4. Reflection on assignments; Session 8. Presenting homework and reminding the day and time of the next meeting</td>
</tr>
<tr>
<td><strong>Fifth meeting</strong></td>
<td>Inheritance on the seal circuit and Inheritance on the hate circuit</td>
</tr>
<tr>
<td><strong>Target</strong></td>
<td>Understanding the results of malice and affection</td>
</tr>
<tr>
<td></td>
<td>1. Meeting preparation; 2. Prayer at the beginning; 3. Group status review; 4. Review of the fourth session; 5. Reflection on assignments; 6. Introducing the fourth session (inheritance on the seal circuit and inheritance on the Keane circuit); 7. Sealing and abstinence from the Kane; 8. Summing up the session; Meeting</td>
</tr>
<tr>
<td><strong>Sixth session</strong></td>
<td>Understanding meditation and calculation</td>
</tr>
<tr>
<td><strong>Target</strong></td>
<td>Understanding meditation and calculation</td>
</tr>
<tr>
<td></td>
<td>1. Meeting preparation; 2. Prayer at the beginning; 3. Group status review; 4. Review of the fifth session; 5. Meditation; 6. Introducing the sixth session (meditation and calculation); Meeting Session 9. Presenting Homework; Reminding the Day and Hour of the Next Meeting and Praying for the End of the Meeting</td>
</tr>
<tr>
<td><strong>Seventh session</strong></td>
<td>Meditation and calculation</td>
</tr>
<tr>
<td><strong>Target</strong></td>
<td>Performing meditation and meditation</td>
</tr>
<tr>
<td></td>
<td>1. Preparing a meeting; Initial prayer; 2. Studying group status; 3. Reviewing the sixth session; 4. Reflecting on assignments; 5. Introducing the seventh session (meditation and calculation); 6. Meditation and calculation practice; Session 8; Homework Presentation; Form Distribution; Reminder of Next Session Date and End of Prayer Meeting</td>
</tr>
<tr>
<td><strong>Eighth session</strong></td>
<td>Understanding forgiveness and resolving anger</td>
</tr>
<tr>
<td><strong>Target</strong></td>
<td>Increasing forgiveness and resolving anger toward oneself and others and the world, acceptance, patience, perseverance, responsible action, and personal and social benefit</td>
</tr>
<tr>
<td></td>
<td>1. Session Preparation; Prayer at the beginning; 2. Studying Group Status; Reviewing Seventh Session; 3. Reflecting on Tasks; 4. Introducing Seventh Session (Forgiveness and Resolution of Anger); Meeting Summary; 7. Homework Presentation; Form Distribution; Day and Hour Reminder of the Next Meeting and Prayer End of the Meeting</td>
</tr>
<tr>
<td><strong>Ninth session</strong></td>
<td>Forgiveness and resentment of anger</td>
</tr>
<tr>
<td><strong>Target</strong></td>
<td>Increasing forgiveness and resolving anger toward oneself and others and the world, acceptance, patience, perseverance, responsible action, and personal and social benefit</td>
</tr>
<tr>
<td></td>
<td>1. Meeting preparation; 2. Group status review; 3. Eighth session review; 4. Assignment; 5. Introducing the ninth session (anger forgiveness and resolving); 6. Anger forgiveness and resolving practice; Homework assignment; reminder of the day and time of the next session and prayer for the end of the session</td>
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<tr>
<td><strong>Tenth meeting</strong></td>
<td>Computation and meditation and stability</td>
</tr>
<tr>
<td><strong>Target</strong></td>
<td>Increased self-control in maintaining awareness, hope and expectation; acceptance, patience, persistence, tolerance; responsible action; and personal and social benefit</td>
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<td></td>
<td>1. Session preparation; Prayer at the beginning; 2. Group status review; 3. Ninth session review; 4. Meditation; 5. Introducing the ninth session: Computation and Meditation and Stability. 6. Computation and Meditation Practice (Self-care); 7. Meeting Summary; 8. Homework Presentation; Remembrance Day and Hours of the Next Meeting and Prayer End of the Meeting</td>
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enhancing the immune system or progressing to various stages of cancer or inducing apoptosis. Studies show that at high tumor stages, the presence of such cytokines will induce tumor growth by inducing apoptosis, but cellular studies indicate the inhibitory role of inflammatory cytokines such as TNF-α in vitro.

In this regard, there are detailed suggestions about the role of immune cells in inhibiting tumor genesis and cancer, one of which is the role of M1 macrophages. Neutrophil and macrophages these cells control and inhibit cancer cell proliferation, indicating that innate immunity plays an important role in the inhibition of cancer. It is noteworthy that the M1 macrophage phenotype is directly related to inflammatory conditions. They facilitate inflammation and a decrease in the secretion of these pro-inflammatory factors leads to a switch to other macrophage phenotypes such as M2, which leads to the growth and proliferation of tumor cells. The secretion of cytokines such as IL-1β activates innate immune cells such as natural killer (NK) cells and cellular immunity cells such as CD8+. In addition, it polarizes CD4+ cells to Th1 cells. The activation of the immune system is attenuated after a period of chemotherapy in cancer patients. However, studies have shown that the persistent presence of these cytokines in the cancerous environment stimulates the secretion of cytokines such as interferon-gamma (IFN-γ) by NK cells and cells involved in immunity and induces the expression of PD-L1 and PD-L2 molecules. IL-6 plays an important role in activation, maintenance, survival and proliferation of T cells independent of IL-2 and differentiates and maintains the balance between Th1/Th2 cells. On the other hand, IL-8 is also an inflammatory cytokine and is secreted by phagocytic cells and plays an important role in the chemotaxis of phagocytic cells such as neutrophils, and its concomitant elevation along with three other factors may indicate inflammatory cell activity.

Based on the results of this study, it seems that spiritual intervention can affect the secretion of inflammatory cytokines and consequently, the effect of these cytokines on the cellular and humoral immune system in cancer patients. Previous surgery and chemotherapy play a supporting role in the homeostasis and strengthening the immune system. On the other hand, given the different and sometimes contradictory effects of these cytokines in the metastasis of cancer and the need for continuous and unnecessary presence of these cytokines, it seems that it is better to perform effective interventions at specific intervals rather than permanent courses. It is advisable to perform effective interventions at specified intervals, rather than permanently.

Table 1: Contd...

<table>
<thead>
<tr>
<th>First session</th>
<th>Understanding and grounding the re-experience of spirituality</th>
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<tr>
<td>Eleventh session</td>
<td>Computation and Meditation and Stability</td>
</tr>
<tr>
<td>Target</td>
<td>Self-care in maintaining awareness, hope and expectation; acceptance, patience, resilience, tolerance; responsible action; and personal and social benefit</td>
</tr>
</tbody>
</table>

- 1. Meeting preparation; prayer at the beginning; studying group status; reviewing tenth session; reflecting on tasks; introducing eleventh session, calculating and meditating and stability (self-estimation); homework presentation; remembrance day and hours of next meeting and end of prayer

| Twelfth session | Together, the sustainability stabilization sessions and the announcement of course completion |
| Target | Self-care in maintaining awareness, hope and expectation; acceptance, patience, persistence, tolerance; responsible action; and personal and social benefit |

![Figure 2: Comparison of interleukin-6 levels in the experimental and control groups](image1)

![Figure 3: Comparison of interleukin-8 levels in the experimental and control groups](image2)
depending on the amount of cytokine secretion in different individuals. In other words, appropriate interventions should be optimized based on the type of cytokines and concentrations of cytokines at different stages of the disease.

Afterward, we examine the effects of cytokines in terms of their synergistic effects. For example, the only presence of transforming growth factor-beta (TGF-β) in the environment does not mean that Treg cells have increased. This may, in fact, be partially beneficial to cancer and make the environment readier for cancer progression. On the other hand, if Th17 cells are present in the environment (presence of TGF-β and IL-6), they can provide an inflammatory environment, which may augment the elimination of the tumor. Therefore, it is advisable to perform effective interventions at specified intervals, rather than permanently, depending on the amount of this cytokine secretion in different individuals and depending on the needs of individuals, which, of course, may be useful in further studies. The results showed that there was no significant difference in the levels of cytokines between the intervention and nonpsychological training groups. However, there was a significant difference between the intervention group and the group received no intervention. In relatively similar studies, the results are considerable. For example, Jim et al. (2015) in their study with the meta-analysis model showed that greater R/S is associated with better patient-reported physical health. These results underscore the importance of attending to patients’ religious and spiritual needs as part of comprehensive cancer care. Or in the study of Alexander et al. with a significant sample size of 398 people is expressed that women experience distinctly different physical well-being, social well-being, and total QOL outcomes during and after BC surgery. The genetic associations identified suggest that cytokine dysregulation influences QOL outcomes. However, specific QOL domains may be impacted by different cytokines. On the other hand Fallath et al. stated that Multivariate analysis of variance of serum levels of cytokine IFN-γ and TNF-α revealed that spiritual therapy is effective in reducing serum levels of cytokine IFN-γ and TNF-α in women with BC and has relative endurance over time. Finally we can say the level of some cytokines in tumors’ microenvironment was high and blocking these cytokines can be effective in the eradication or prevention of the recurrence of the tumor. However, in the present study, we did not encounter an inflammatory state because the tumor was removed from the patients’ bodies and inflammatory cytokines decrease after surgical intervention. Therefore, spiritual therapy might improve immune responses in terms of either cellular or humoral responses, which needs further studies to be clarified. Similar to other studies, this study showed that the gathering people and their group-participation in purposeful and reciprocal activities and learning concepts that create a sense of happiness in people and improve their overall health undoubtedly affects other aspects of their existence as well. Although spiritual intervention sessions, according to previous studies, and in particular, in this study has influenced the spiritual and psychological structure of individuals, and the nature of its function has also been shown the purpose of allocating the second group, namely the group without interfering with the spiritual and psychological content, was to neutralize the effect of the group in the study, but the elements of a group that showed the effectiveness of a group consisted of “empathy.” Empathy leads to improved mental health for those patients with BC who are experiencing higher levels of anxiety about their cancer diagnosis and subsequent treatments. After empathy, the social support that interacts with the provider and the recipient of the support may prevent unnecessary adverse effects. In addition, it has a positive effect on physical, mental, and social well-being, and ultimately enhances one’s overall performance and is effective in maintaining and enhancing hope. Leading to increased mental health, reduced distress, increased QOL, and even increased sexual self-esteem in women with BC. The originality of group efficacy has been proven in many studies, and this has attracted more research from researchers to enhance therapies based on this model. Numerous studies have been conducted to compare the different types of therapies that have shown that each approach has been effective. For example, a study by Garland et al. (2007) comparing MBSR programs and improving traumatic growth and spirituality in cancer patients showed that both programs may have positive growth after injury experiences. Improvement of life for those who participate in group therapy. But what is the effectiveness of spiritual intervention is that although the differences in the levels of cytokines in the intervention group and in the training group were not significant, the same level of effectiveness of the intervention was not neglected. In the experience of living with cancer, spirituality is considered an important and prominent aspect of a healthy life and it seems that the
threatening nature of this disease increases the spiritual needs of patients. Spirituality can lead to greater psychological adjustment by providing supportive resources for the individual and more indirectly through affecting hope.[48] Spiritual interventions in the treatment of cancer patients are, in fact, capable of utilizing their spiritual resources and resources in addressing physical and psychological problems and making life better by accepting the environment, purpose and orientation in life and make it possible to fill the semantic vacuum.[49] In addition to the effectiveness of spiritual intervention on improving the psychological and social functioning of individuals, recent studies have assessed the effectiveness of spiritual interventions on physiological dimensions.[50] Prayer and communication with God and spiritual care can reduce the symptoms of pain and improve the patient’s physical function by arousing the sympathetic nervous system.[51] For example, a study of 16 studies reported that spirituality significantly is positively related to cardiovascular functions or outcomes.[52] It has been repeatedly reported that those who were more spiritual or experienced spiritual intervention had lower blood pressure.[53] Moreover, in a study aimed at observing the relationship between cortisol levels, levels of spiritual well-being, and suicidal tendencies in Croatian war veterans suffering from Post-Traumatic Stress Disorder, the results showed that veterans with higher spiritual well-being scores have lower cortisol levels.[54] Studies on spirituality and communication or their effects on endocrine functions, positive relationships or positive effects have been reported and no studies showed any negative association or negative effects.[55] in the area of cancers, individuals who are more spiritual likely have a lower risk of experiencing cancer or a better prognosis.[56] In addition, the changes in the time-based groups were also significant because, in this study, the changes in all three groups at the time of follow-up were more significant than the pretest and posttest, and this finding confirms that besides the valuable short-term effectiveness of interventions and training, achieving therapeutic sustainability is a more important achievement. Sustainable effects are those effects that an individual experiences outside of their training and intervention experience. Thus, the emergence of psychological perception of time as a component of the neurodevelopmental process is particularly important in the social functioning and adaptive behavior of the individual. According to psychologists’ opinions, it seems that long-term estimates of survival have the highest survival value during evolution, as this process is essential for internal representations of the external environment.[57] The passage of time gradually reduces the stresses of the individual and by providing the necessary cognitive processing, leads to understanding of the reality of the event and subsequently to a new worldview and change of the dysfunctional schemas of the individual. Numerous studies have found a significant relationship between positive changes and the passage of time, even in cancer patients.[58,59]

The current study was carried out with great care. Selection of three groups of patients with BC who can evaluate both spiritual intervention and nonspiritual intervention groups and no intervention is a noteworthy feature of this study, which led many researchers to answer the question of the effectiveness of group content or function in the treatment. The next reliable item was blood sampling in three stages, which clearly indicated the issue of time without intervention in the stability of the interventions. In the end, the limitations of the study include the difficulty of finding samples and trying to keep the samples in the study for three blood sampling stages. Cytokines and complete blood count testing and lack of access to patient tissue samples are the other important limitations in this study for more accurate tissue studies.

Weaknesses and the strength of the study

Measuring psychological variables at biological level and showing these changes in the level of immune system function is one of the most strengths of the study. Studying two control groups of subjects instead of one control group and in three stages instead of two stages are also of the strongest points of the study. However, small sample size and inability to further study at the cell line level can be mentioned as its weaknesses.

Conclusion

The study revealed that the health of a cancer patient is not limited to complete medical treatment and that we showed that holistic treatment can increase the success of the treatment process and improvement of the patients. Nowadays, psychologists have realized that spiritual intervention may have significant positive effects on the physical health of patients with special needs, especially cancer patients, in both treatment and recovery states. IL-1β and TNF have antitumor activity and inhibit tumor growth. IL-6 has also inflammatory effects and controls the differentiation of T cells and balance between Th1/Th2 cells, especially Treg cells, which have negative effects on tumor inhibition; IL-8 recruits neutrophils and MDSCs into the tumor environment, which are capable of attenuating antitumor immune responses. Although the attitudes of the medical system have shifted from being one-dimensional to multi-dimensional in treating the disease, it still requires more effort to intervene in the humanities to maintain and enhance the overall health of individuals. The path of progress in the field of therapy is through the interconnection of the sciences with different perspectives and the common goal that may lead to avoidance of biased views and openness to accepting healthy and rational attitudes.

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Conflicts of interest
There are no conflicts of interest.

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