

# The Effect of Relaxation Technique on Fatigue Levels after Stem Cell Transplant

## Abstract

**Background:** Many patients undergoing hematopoietic stem cell transplant (HSCT) experience fatigue due to their disease process and its long period of treatment. Using nonpharmacological methods to help reduce their fatigue is a reasonable endeavor. The present study was conducted to investigate the effect of Benson's relaxation technique on fatigue levels in patients after HSCT. **Materials and Methods:** Thirty-seven patients were randomly selected to the intervention ( $n = 19$ ) and control group ( $n = 18$ ). In the intervention group, the participants performed Benson's relaxation exercises for 20 min twice per day over a period of 15 days. The data collection tools used included a demographic and medical information form and the Brief Fatigue Inventory, completed by both groups on three different occasions (upon admission and days 8 and 14 after the HSCT). The data obtained were analyzed in Statistical Package for the Social Sciences version-20 using statistical tests. **Results:** The results of the independent  $t$ -test showed no significant preintervention differences in fatigue levels between the two groups. On days 8 ( $t = 11.21, p < 0.001$ ) and 14 after the transplant ( $t = 15.62, p < 0.001$ ), a significant difference was observed in the mean level of fatigue between the two groups. **Conclusions:** These findings indicate that Benson's relaxation technique would improve fatigue in HSCT patients.

**Keywords:** Fatigue, Iran, relaxation, stem cell transplantation

## Introduction

Fatigue has been identified as the most prevalent and disturbing symptom of cancer patients.<sup>[1]</sup> According to the definition provided by the National Comprehensive Cancer Network (NCCN), fatigue is a subjective, unpleasant, and persistent symptom of physical, emotional, and cognitive exhaustion developed due to cancer or its treatment that disrupts the normal functioning of the individual.<sup>[2]</sup> Cancer patients undergoing stem cell transplant (SCT) experience high levels of fatigue due to the conditions of their treatment, such as receiving high doses of chemotherapy medications and total body irradiation as conditioning regimen before bone marrow transplantation.<sup>[3]</sup>

Fatigue is described as a prolonged and severe complaint in many patients receiving allogeneic and autologous hematopoietic stem cell transplant (HSCT),<sup>[4]</sup> as 35% of the patients experience severe fatigue after bone marrow transplantation.<sup>[3]</sup> Based on

previous studies, fatigue has a prevalence of 90% within 30 days from the HSCT and 81% within 100 days.<sup>[5]</sup> One study reported that most patients experience mild fatigue 3 days before the HSCT and moderate to severe fatigue 3 days after the transplant.<sup>[6]</sup> Another study showed that 41% of the patients experience severe fatigue 1–5 years after the HSCT and 32% continue to experience it 5–10 years after the transplant.<sup>[3]</sup> Moreover, the patients' physical activity reduces significantly because of their prolonged bed rest in isolated rooms due to severe aplasia and neutropenia,<sup>[7]</sup> which ultimately leads to severe and continuous fatigue in the patients.<sup>[4]</sup> Other causes of fatigue include infections, anemia, depression, pain, sleep disorders, stress, anxiety,<sup>[8]</sup> and hormonal changes.<sup>[9]</sup>

Recently, corticosteroids are used in some cases to treat fatigue in patients with progressive cancer.<sup>[10]</sup> Today, the use of complementary and alternative medicine has increased among the public all throughout the world.<sup>[11,12]</sup>

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Nonpharmacological methods are often construed as a branch of complementary medicine that the nurses as well as the patients and their family can use to reduce the fatigue caused by disease and its treatment.<sup>[13,14]</sup> Progressive muscle relaxation, guided imagery relaxation, Benson's relaxation, and deep relaxation (deep breathing) are some of the most commonly used relaxation techniques across the world.<sup>[15]</sup> The technique introduced in 1970 by Herbert Benson, however, is more desirable due to its easy instructions.<sup>[16]</sup> Relaxation technique as a kind of subjective stress management method<sup>[17]</sup> decreased the anxiety level,<sup>[18]</sup> mood disturbance,<sup>[19]</sup> body discomfort,<sup>[20]</sup> and autonomic nervous system's activity<sup>[21]</sup> and at least it might affect the quality of sleep. The time needed to fall asleep,<sup>[22]</sup> sleep-onset latency,<sup>[23]</sup> and the frequency of waking up have been reduced by relaxation therapy, as well.<sup>[22]</sup> In Benson's relaxation technique, the patient relaxes and extends each one of his muscles and learns to relax and set free his entire body. In this technique, patient inhales through the nose and exhales through the mouth. When patient breathes out, mutters the word "one." Thus, the patient reduces his/her anxiety and stress. When relaxation occurs, the stress response breaks down. Stress has a significant role in worsening the symptoms of fatigue.<sup>[15]</sup> Given that relaxation is a completely safe and easy to teach and use method that does not require the great expenditure of money or a physician's prescription, and considering that no studies have yet examined the use of Benson's relaxation technique for reducing fatigue in patients after HSCT, the present study was conducted to investigate the effect of this particular method of relaxation on fatigue levels in patients after this transplant.

## Materials and Methods

The present randomized clinical trial was conducted on 40 cancer patients undergoing HSCT at Amirkola Shafizadeh Hospital in Babol, Iran from October 2014 to August 2016 with the project code IRCT2015091624047N1. The number of participants required to conduct the research was calculated to be 17 individuals in each group using the sample size formula, with 99% confidence interval and 90% statistical power. The final sample size with anticipating 20% sample attrition was a total of 40 (20 patients in each group) participants.

The eligible patients were randomly assigned to the intervention and control groups using the random number table. Three patients were excluded from the study (one because he died and two others due to their use of narcotic). The data obtained from a total of 37 patients were ultimately analyzed [Figure 1]. The study inclusion criteria consisted of a minimum age of 18, being diagnosed with multiple myeloma, leukemia, lymphoma with indication for HSCT, and receiving HSCT for the first time. The study exclusion criteria consisted of having neuromuscular disorders, taking sedatives, previous experience with

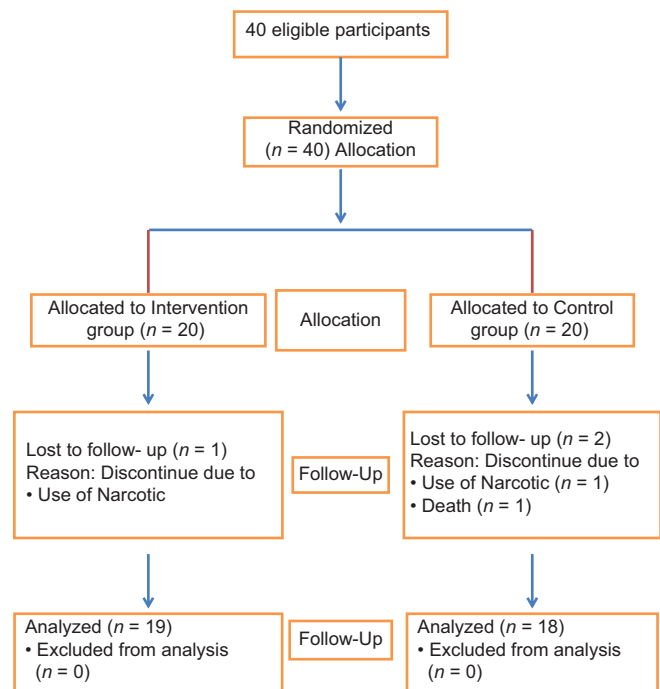


Figure 1: Consort diagram

Benson's relaxation, a history of severe mental illnesses such as depression and anxiety, serious physical health complaints such as severe infection, severe pain, acute bleeding, loss of consciousness, and graft versus host disease (GVHD) grade IV.

Data were collected using a demographic and medical information form and the Brief Fatigue Inventory (BFI) questionnaire. BFI has been used as a standard tool in numerous studies.<sup>[24,25]</sup> In line with the study objectives, the demographic form inquired about participants' age, gender, level of education, marital status, place of residence, occupation, type of disease, history of severe depression and anxiety disorders, and also about their type of transplant, GVHD type, levels of hemoglobin and hematocrit upon admission and on days 8 and 14 after the transplant.

The BFI questionnaire contains ten items. The first item determines the presence or absence of unusual fatigue in the past week with "yes" or "no" options. The other items determine current fatigue, average fatigue over the past 24 hours, the effect of fatigue over the past 24 hours on general activity, mood, the ability to walk, relations with others, and enjoyment of life. Each item is scored based on a scale from 0 to 10. A score of 0 represents the best state and the lack of fatigue and a score of 10 indicates the worst possible state of fatigue. The subjects were asked to mark their answers for each item based on their perceived severity of fatigue. Their overall level of fatigue was then measured by calculating the total score of items 2 to 10 divided by 9. A score of 0 indicates no fatigue, a score of 0.1–3.9 indicates mild fatigue, 4–6.9 moderate

fatigue, 7–9.9 severe fatigue, and 10 indicates very severe fatigue.<sup>[25]</sup>

On the day of admission, the patients filled out the demographic form and the BFI. The researcher read out the items loud to those patients who were not able to fill out the questionnaire themselves for any reason and their answers were recorded accordingly. One day after admission, the intervention group received training on Benson's relaxation by the researcher, who had taken a course in this relaxation technique under the supervision of a clinical psychologist. In addition to training the patients on the technique, a video on Benson's relaxation was also distributed among the patients to facilitate and improve their understanding of the technique and they were then asked to perform the exercises in the presence of the researcher so as to ensure the accuracy of their performance. An audiotape and an educational pamphlet were given to the patients to use in the bone marrow transplant unit. The patients were recommended to perform this technique twice per day for 20 min each time,<sup>[26]</sup> beginning on the day of receiving SCT and continuing for 15 days. The control group received no interventions. During this period, the patients were followed up by the researcher in person. Benson's relaxation technique is a stress-relief technique that provides a balanced approach to care.<sup>[27]</sup>

The patients were asked to (a) gently supine and place their hands next to the body, (b) close their eyes, (c) deeply relax their muscles from the sole to the face slowly and keep calm all the time, (d) inhale through the nose and be aware of the breathing and then, slowly breathe out through the mouth, mutter the number "one" when exhale and breathe normally and comfortably, (e) perform this procedure for 20 min and try to relax all their muscles after that slowly open their eyes but do not get up for few minutes, (f) not to worry whether they have reached a deep level of relaxation or not, (g) let relaxation happen at its own pace when distracting thoughts come to mind, try to ignore them and be indifferent toward them, (h) keep their passive attitude.

The BFI was then completed by the patients on three different occasions, upon admission (Time 1), 8 days after the transplant (Time 2), and 14 days after the transplant (Time 3). If the patients were not able to fill out the questionnaire by themselves for any reason, the researcher read out the items loud and recorded their answers in the questionnaire. The data obtained were ultimately analyzed in Statistical Package for the Social Sciences software (version 20, SPSS Inc., Chicago, IL). The Chi-square test, *t*-test, and Fisher's exact test were used to test for the homogeneity of demographic and clinical characteristics between the two groups. Normality distribution of the data was tested with the Kolmogorov–Smirnov test. To compare the mean severity of fatigue within each group, a repeated-measure analysis

of variances (ANOVA) was applied. For comparing the differences in severity of fatigue between the two groups, *T*-Test, chi-square test was used.

### Ethical considerations

This research project was approved by Mazandaran University of Medical Sciences with the code 1733. To comply with research ethics, adequate explanations were given to each of the subjects about the methods and objectives of the study. The intervention began after obtaining consent from the patients and ensuring them that this method did not hurt them or disrupt their treatment in any way.

### Results

The results showed the lack of significant differences in demographic variables and medical information between the two groups. The mean age was 43.95 (12.52) years in the intervention group and 42.33 (13.94) in the control group. Most (52.63%) of the subjects in the intervention group were male ( $n = 10$ ) and most (55.56%) in the control group were female ( $n = 10$ ). None of the subjects had a history of severe depression and anxiety [Table 1].

Before performing the relaxation technique, all the patients (100%) in the intervention group reported unusual fatigue over the past week. After performing the relaxation exercises, 57.89% of the patients reported unusual fatigue over the past week 8 days after their transplant and 26.32% had still experienced this level of fatigue over the past week 14 days after the transplant [Table 2]. The results of Chi-square test showed a significant difference between the HSCT patients who had experienced unusual fatigue over the past week 8 days after the transplant ( $p = 0.034$ ) and those who had experienced it 14 days after transplant ( $p = 0.002$ ) [Table 2].

Before performing the relaxation exercises of the patients in the intervention group, 73.68% experienced mild, 21.05% moderate, and 5.26% severe fatigue. In the intervention group, all the patients (100%) had only mild fatigue after performing the relaxation exercises and on days 8 and 14 after the transplant. In the control group, 83.33% of the patients had mild fatigue and 16.67% had moderate fatigue on the day of admission; on day 8 after the transplant, 5.56% of them had mild fatigue, 72.22% had moderate fatigue, and 22.22% had severe fatigue; on day 14 after the transplant, 72.22% had moderate fatigue and 27.78% had severe fatigue [Table 3].

The results of the repeated-measure ANOVA indicated significant differences between the severity of fatigue in the control group ( $p < 0.001$ ), but none in the intervention group ( $p = 0.069$ ) [Table 4].

The results of the independent *t*-test ANOVA showed the lack of statistically significant differences before the intervention in the mean severity of fatigue between the

**Table 1: Comparison of the demographic and medical characteristics in intervention and control groups**

Variable	All (n=37)	Intervention (n=19) n (%)	Control (n=18) n (%)	p
<b>Sex</b>				
Male	18	10 (52.63)	8 (44.44)	0.618
Female	19	9 (47.37)	10 (55.56)	
<b>Education</b>				
Below high school diploma	23	14 (73.70)	9 (50.00)	0.138
Diploma degree and higher	14	5 (26.30)	9 (50.00)	
<b>Marital status</b>				
Single	6	2 (10.53)	4 (22.22)	0.335
Married	31	17 (89.47)	14 (77.78)	
<b>Address</b>				
City	21	11 (57.89)	10 (55.55)	0.886
Village	16	8 (42.11)	8 (44.45)	
<b>Job</b>				
Employee	2	2 (10.53)	0 (0.00)	0.701
Worker	1	1 (5.26)	0 (0.00)	
Self-employed	14	6 (31.58)	8 (44.44)	
Unemployed	1	1 (5.26)	0 (0.00)	
Housewife	14	8 (42.11)	9 (50.00)	
Other	23	1 (5.26)	1 (5.56)	
<b>Diagnosis</b>				
ALL	5	3 (15.79)	2 (11.11)	0.478
AML	1	0 (0.00)	1 (5.56)	
Multiple myeloma	22	13 (68.42)	9 (50.00)	
Lymphoma	9	3 (15.79)	6 (33.33)	
<b>Type of transplantation</b>				
Autologous	30	16 (84.21)	14 (77.78)	0.693
Allogeneic	7	3 (15.79)	4 (22.22)	
<b>GVHD incidence</b>				
Skin and gastrointestinal	6	3 (15.79)	3 (16.67)	0.824
Liver, skin, and gastrointestinal	1	0 (0.00)	1 (5.56)	
<b>Mean (SD)</b>				
<b>Hemoglobin</b>				
Time 1	11.39 (1.66)	11.42 (1.98)	11.36 (1.34)	0.915
Time 2	9.37 (1.16)	9.57 (1.15)	9.18 (1.17)	0.315
Time 3	9.92 (1.06)	10.22 (1.10)	9.63 (1.03)	0.102
<b>Hematocrit</b>				
Time 1	34.67 (4.78)	34.42 (5.89)	34.93 (3.67)	0.752
Time 2	27.95 (3.76)	28.68 (3.83)	27.22 (3.69)	0.244
Time 3	29.66 (3.39)	30.38 (3.75)	28.95 (3.04)	0.212

ALL: Acute lymphoblastic leukemia; AML: Acute myelogenous leukemia; GVHD: Graft versus host disease

cancer patients undergoing HSCT in the two groups and showed the groups to be homogeneous ( $p = 0.19$ ). Eight days after the transplant, the mean severity of fatigue was 2.87 (0.73) in the intervention group and 6.90 (1.37) in the control group. Fourteen days after the transplant, the mean severity of fatigue was 2.35 (0.70) in the intervention group and 6.99 (1.07) in the control group. The results of the  $t$ -test showed a statistically significant difference between the two groups ( $p < 0.001$ ) [Table 5].

## Discussion

The present study was conducted to examine the effect of Benson's relaxation on the level of fatigue in patients

after HSCT. The review of literature revealed no studies on the effect of Benson's relaxation technique on the severity of fatigue in patients undergoing this procedure. Other studies on the use of complementary medicine on fatigue in different patients were therefore used to compare the findings of the study.

A significant difference was observed in the present study in the mean severity of unusual fatigue between the patients undergoing HSCT in the control and intervention groups after the intervention, and relaxation exercises were found to have reduced the feeling of unusual fatigue in the intervention group. In line with



the present findings, Beyk Moradi *et al.* examined the effect of acupressure on fatigue in cancer patients and showed acupressure to have reduced unusual fatigue in the intervention group.<sup>[25]</sup>

**Table 2: Comparison of the unusual fatigue upon admission and on days 8 and 14 after the transplant in intervention and control groups**

Unusual fatigue	Intervention (n=19)	Control (n=18)	$\chi^2$	df	p
Yes, n (%)	19 (100.00)	18 (100.00)			-
Time 1					
No, n (%)	0 (0.00)	0 (0.00)			
Yes, n (%)	11 (57.89)	16 (88.89)	4.502	1	0.034
Time 2					
No, n (%)	8 (42.11)	2 (11.11)			
Yes, n (%)	5 (26.32)	14 (77.78)	9.799	1	0.002
Time 3					
No, n (%)	14 (73.68)	4 (22.22)			

Time 1: Upon admission; Time 2: 8 days after the transplant; Time 3: 14 days after the transplant

This study found the level of fatigue to be significantly different on the three different occasions examined (upon admission and on days 8 and 14 after the transplant) in the control group, which may be due to the chronic nature of the disease and the long period of treatment that can have increased level of fatigue. No significant differences, however, were observed in the intervention group. Koushan *et al.* showed significant differences in the level of fatigue on the three different occasions examined (before the relaxation exercises and two and four weeks afterwards) in both the intervention and control groups. The results of Koushan study are in line with the present findings on the control group, but inconsistent with those obtained on the intervention group.<sup>[28]</sup> This inconsistency may be attributed to the different levels of fatigue in the studies' subjects before the intervention.

The results of the present study indicated that relaxation exercises can reduce fatigue in patients undergoing HSCT. Sang *et al.* examined the effect of breathing relaxation

**Table 3: Comparison of the overall severity of fatigue upon admission and on days 8 and 14 after the transplant in intervention and control groups**

Overall severity of fatigue	Intervention	Control	$\chi^2$	df	Chi-square test p
Time 1					
Mild, n (%)	14 (73.68)	15 (83.33)	1.151	3	0.562
Moderate, n (%)	4 (21.05)	3 (16.67)			
Severe, n (%)	1 (5.27)	0 (0.00)			
Very severe, n (%)	0 (0.00)	0 (0.00)			
Time 2					
Mild, n (%)	19 (100.00)	1 (5.56)	33.197	3	<0.001
Moderate, n (%)	0 (0.00)	13 (72.22)			
Severe, n (%)	0 (0.00)	4 (22.22)			
Very severe, n (%)	0 (0.00)	0 (0.00)			
Time 3					
Mild, n (%)	19 (100.00)	0 (0.00)	37	3	<0.001
Moderate, n (%)	0 (0.00)	13 (72.22)			
Severe, n (%)	0 (0.00)	5 (27.78)			
Very severe, n (%)	0 (0.00)	0			

**Table 4: A comparison of the mean severity of fatigue in intervention and control groups with repeated measures ANOVA**

Mean severity of fatigue	Mean score (standard deviation)			F	df	p (repeated-measures ANOVA)
	Time 1	Time 2	Time 3			
Intervention (n=19)	3.34 (1.67)	2.87 (0.73)	2.35 (0.70)	3.516	1.185	0.069
Control (n=18)	6.9 (1.37)	6.9 (1.37)	6.99 (1.07)	112.54	1.905	<0.001

**Table 5: A comparison of the mean severity of fatigue on the day of admission and on days 8 and 14 after the transplant between the intervention and control groups**

Mean severity of fatigue	Intervention (n=19)	Mean score (standard deviation)	Control (n=18)	t	df	p
Time 1	3.34 (1.67)	6.9 (1.37)	6.9 (1.37)	-1.34	35	0.19
Time 2	2.87 (0.73)	6.9 (1.37)	6.9 (1.37)	11.21	35	<0.001
Time 3	2.35 (0.70)	6.99 (1.07)	6.99 (1.07)	15.62	35	<0.001

exercises on fatigue in patients undergoing HSCT. In their study, the intervention group performed breathing relaxation exercises for 30 min once per day over a period of six weeks; according to the results, breathing relaxation reduced the level of fatigue in the patients.<sup>[29]</sup> Diorio *et al.* also examined the effect of yoga in 11 children aged 7–18 undergoing HSCT. In their study, the subjects practiced yoga three times per week for a period of three weeks; according to the results, complementary therapies such as yoga reduce fatigue in patients.<sup>[30]</sup> Wilson *et al.* also found that performing aerobic exercises 3–5 times per week for a period of 12 weeks increases endurance performance, reduces fatigue, and improves quality of life in patients after SCT.<sup>[7]</sup> Hadadian *et al.* examined the effect of acupuncture on fatigue in hemodialysis patients and found that acupuncture can affect the feeling of relaxation and reduce fatigue in hemodialysis patients through the release of neurotransmitters such as serotonin.<sup>[24]</sup> Koushan *et al.* also reported that Benson's relaxation exercises help reduce fatigue in hemodialysis patients.<sup>[28]</sup> The results of these studies are consistent with the results of the present study. In their study on the effect of Benson's relaxation on disease activity indices in patients with rheumatoid arthritis, Bagheri *et al.* found statistically insignificant changes in fatigue level in the intervention group,<sup>[31]</sup> which is inconsistent with the present findings. This inconsistency may be due to the differences in the statistical populations examined, the patients' conditions, and the instruments used to measure fatigue. In their study on the effect of massage therapy on patients undergoing bone marrow transplant, Ahles *et al.* found a statistically insignificant reduction in the level of fatigue in the intervention group.<sup>[32]</sup> This disparity of findings may be attributed to the differences in the complementary and alternative medicine therapies used and the different instruments used to measure fatigue.

The limitation of the present study was that the family, social, and economic problems of the subjects under study is varied, not controlled by the researcher; however, in this case, this impact was insignificant because the samples were randomly assigned to two groups.

## Conclusion

The results showed that Benson's relaxation has effects on fatigue in cancer patients undergoing HSCT. While the findings from this study are preliminary, they do provide support for continued investigation on the effect of Benson's relaxation technique on fatigue levels after HSCT.

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## Conflicts of interest

Nothing to declare.

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