

Assessing cognition, depression and anxiety in hospitalized patients during pre and post-Bone Marrow Transplantation

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Objective: Bone Marrow Transplantation is considered one of the main procedures used in the treatment of both malignant and non-malignant diseases. Psychological factors after Bone Marrow Transplantation have an important role in the survival of the patients undergoing this procedure.

Method: In the present study, some parameters including depression, anxiety and cognition were assessed during both pre and post-transplantation in patients undergoing Bone Marrow Transplantation. The evaluations were performed by utilizing several questionnaires including Hospital Anxiety and Depression Scale and Wechsler Memory Scale within 72 hours after hospitalization (pre-transplantation) and one month after transplantation (post-transplantation). All patients received intensive chemotherapy during the first 72 hours after hospitalization. Paired t test was used to compare pre and post values. SPSS (version 18) was used to analysis the data. The significance level was defined as $p < 0.05$.

Results: Twenty one patients who were not receiving any antianxiety agents at least for two weeks prior to and during this study were included. It was noted that anxiety was significantly less at post-transplantation compared to its pre-transplantation level ($P = 0.008$). However, no significant difference was found between pre and post-transplantation depression. Memory function was significantly improved at post-transplantation compared to pre-transplantation ($P = 0.001$).

Conclusion: The authors suggest that the improvement of anxiety and memory status of the patients one month after the bone marrow transplantation is expected even in the absence of consumption of any antianxiety agents. However, antidepressants may be needed to help those patients who undergo bone marrow transplantation.

Keywords: Anxiety, bone marrow transplantation, cognition, depression, hospital anxiety and depression scale, Wechsler memory scale

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In recent decades, important developments have been achieved in different accepts of cancer therapy. Many cancer types may be eradicated by proper therapy and patients can even be in a cancer-free state (1).

Many patients receive BMT around the world and as a consequence, the number of survivors is increasing (2). Even though certain medications, their doses and spectrum activities are important and necessary in the treatment of a patient with different types of cancer, health professionals should also consider assessing Other means beyond just morbidity and mortality evaluations (1).

General conditions on what patients should adapt when receiving BMT have been noted in the literature; however, there are limited explanations on patient's experiences with this process (3).

Many psychometric studies have noted that psychiatric disorders and emotional distress such as anxiety and depression can follow BMT (4). The role of psychological factors in survival after BMT is supported by ongoing investigations (5). Since the number of patients who receive BMT and their life expectancy following this procedure are increasing, more attention needs to be given to those psychological factors that may affect the QOL of these individuals (6). Problems in cognitive function can interfere with daily activities, education, career and QOL of those suffering from cancer (7). Most researches have not noted any correlation between types of transplantation, conditioning regimen, usage or dosage of total body irradiation, diagnostic background and cognitive changes (8). Based on neuropsychological studies, some cancer patients have demonstrated neurological changes after hematopoietic cell transplantation (HCT) including

cortical atrophy and ventricular enlargement and shown neurotoxic side effects induced by drugs like cyclosporine and tacrolimus (9).

In 2005, Khan et al. reported that patients undergoing blood and bone marrow transplantations are at a high risk for psychiatric morbidities (10). In 2010, Maheri Azar et al. emphasized the frequent evaluation of psychological distress in BMT receivers (4). However, in 2011, Chao and colleagues noted that BMT procedure is not related to long-term morbidity in adult patients (1).

The present study was aimed to evaluate parameters such as depression, anxiety and cognition in BMT patients both during pre and post-transplantation.

Material and Methods

This prospective, cross-sectional study, held between July 2011 and May 2012, evaluated qualified candidates for receiving BMT at Valiasr BMT Center, Imam Khomeini hospital, Tehran, Iran. Participants with hematological dyscrasia who were between 18 and 55 years entered this study. Exclusion criteria included no previous history of BMT, as well as not having received antidepressants or anxiolytics or other medications with confirmed central nervous system (CNS) toxicity (such as opioids and IT methotrexate) or drugs that can induce depression and anxiety (such as theophylline, decongestants and some of cardiovascular drugs) for at least two weeks before the initiation of the study. Patients who had a history of brain cancers, major psychiatric disorders (who were not in the remission phase), or immune deficiency as well as those who did not understand Persian language were also excluded from the study. Patients were only evaluated if survived at least one month after receiving BMT.

The translations of the two scales of Hospital Anxiety and Depression Scale (HADS) (11) and Wechsler Memory Scale (WMS) (12) were utilized to evaluate anxiety and depression as well as memory, respectively. These scales are being used in studies performed for the Iranian population. The validity and reliability of the Persian version of HADS were reported to be highly acceptable. (Reliability of HADS for Anxiety: $r=0.75$, $p<0.001$; Reliability of HADS for Depression: $r=0.71$, $p<0.001$). Additionally, the validity was reported as a range of 28%-98% for the subtests of the Farsi version of WMS and reliability was reported as 72% 68% 75% 54% 73% for general memory, attention/concentration, visual memory, verbal memory and delayed memory, respectively.

HADS consists of 14 questions and assesses the severity of anxiety and depression based on patients' self-reports. The first 7 items are related to anxiety and

the second 7 items to depression. When the test is scored, a value of 0 to 3 is assigned for each answer; therefore, the maximum score of each subscale is 21. The standard cut-off points for both subscales are (0-7) for anxiety-free, (8-10) for mild anxiety, (11-14) for moderate anxiety, (15-21) for severe anxiety (4). WMS is a neuropsychological test designed to measure different memory functions in a person. Scale subtests include information, orientation, mental control, logical memory, digits forwards and visual reproduction (13). SPSS was used to analysis the data (Version 18).

Patients signed consent forms prior to entering the study. Study questionnaires were filled twice during this trial, one time before BMT procedure (within 72 hours after hospitalization) and another time 1 month after that.

Result

Twenty four patients were interviewed and entered this study. One patient expired and 2 patients did not receive BMT due to not fulfilling inclusion criteria. Twenty one patients (11 males and 10 females) entered and completed this study. Demographic characteristics are summarized in Table 1. The mean and standard deviation of the scores achieved for anxiety using HADS questionnaire in pre and post-transplantations are shown in Table 2. A significant difference was found between pre and post-BMT anxiety. Anxiety was significantly lower in post-BMT compared to pre-BMT ($P = 0.008$). No patient was found to be severely anxious at pre-BMT and post-BMT. Table 2 demonstrated the mean and standard deviation of the scores obtained for depression in pre and post-BMT patients using HADS questionnaire. Pre and post-BMT depression was not shown to be significantly different in the studied patients based on HADS. No patient was found to be severely depressed at pre-BMT and post-BMT. Table 2 shows the mean and standard deviation for pre and post transplantation of overall Memory Quotient (MQ) that was computed based on the scores of the subsets of WMS. It was shown that there was a significant difference between pre and post-BMT MQ scores; post-BMT MQ scores were significantly higher in comparison to those values at pre-BMT ($P = 0.001$).

Discussion

Hematopoietic stem-cell transplantation (HSCT) as a highly aggressive and demanding medical therapy (4) is followed by significant morbidity and mortality (8). Thus, both the underlying disease and transplantation sequels can greatly affect the daily life of the patients (14).

Table 1: Baseline demographic characteristics of patients

Variables		n [†] (percent)
Sex	Male	11(52.4%)
	Female	10(47.6%)
Marital status	Single	4(19%)
	Married	15(71.4%)
	Divorced	1(4.3%)
Education	Widow/Widower	1(4.3%)
	Being able to write	4(19.05%)
	Junior-high school	4(19.05%)
	High school diploma	8(38.1%)
Age	Academic education	5(23.8%)
	18-30	5(23.8%)
	31-43	9(42.8%)
Types of disorder	43-55	7(33.4%)
	AML	7(33.33%)
	ALL	2(9.6%)
Types of transplantation	HD	5(23.8%)
	MM	7(33.33 %)
	Allogenic	8(38.1%)
	Autologous	13(61.9%)

†: number of patients

Table 2: Comparing the score achieved for anxiety, depression and memory within 72 hours after the hospitalization and 1 month after transplantation, using Hospital Anxiety and Depression Scale (HADS) and Wechsler Memory Scale (WMS)

Time	Pre- BMT [#]	Post -BMT [§]	P* value
Anxiety			
Mean± SD [†]	6.14±3.83	3.80±3.23	0.008
Depression			
Mean± SD [†]	5.38±3.52	5.00±3.42	0.586
Memory			
Mean± SD [†]	85.52±13.81	90.66±15.57	0.001

#: Within 72 hours after the hospitalization

§: 1 month after transplantation

†: Standard Deviation

*: P-value is given for the comparison of before-after anxiety using paired-sample t test

Similar to the results observed in a study by Maheri Azar et al. (4), the present study showed that anxiety was significantly less at post-BMT in comparison to pre-BMT. Due to the fact that the subjects in our study did not receive anti-anxiety agents during the trial, it can be suggested that either the transplantation procedure by itself or the placebo effect of such a treatment may have resulted in the improvement of anxiety. However, it should be noted that none of the patients undergoing BMT were suffering from severe anxiety during both pre and post-BMT periods. Moreover, Fife et al. found that hospitalized BMT patients experienced severe psychological disorders that gradually improved within three months post-BMT (15). A prospective study by Trask et al. assessed emotional distress and anxiety in 50 potential BMT candidates and noted that approximately 50% of the patients experienced significant psychological distress at their initial BMT consultation visit. Despite the fact that the coordinators of the study underestimated the number of subjects who experienced high levels of emotional distress, there was a moderate but significant agreement between the patients and the coordinators regarding the ratings of anxiety and emotional distress.

Patients reported the psychological distress as something beyond depression anxiety whereas the coordinators noted anxiety as the primary emotional distress. (16).

The present study revealed no significant difference between pre and post-BMT mean depression scores. None of the patients suffered from severe depression during pre-BMT and at post-BMT. Based on a trial by Maheri Azar et al. none of the patients undergoing BMT were suffering major depression during both pre and post-BMT periods. However, in contrast to the results of our study, the levels of depression in their trial were significantly less during post-BMT. (4) A study by Syrjala et al. showed that physical improvement was observed earlier than psychological or work development in patients who underwent BMT. The authors of the latter study noted that the presence of depression at pre-transplantation could cause serious problems during the recovery process. Patients with GVHD and immune deficiency, poor social support as well as females were at a higher risk to experience depression after transplantation (17). Akaho et al. found an association between fatigue, depression, anger, anxiety and confusion with the rate of achieving

disease-free state at 3 months after BMT. When analyzing the data based on gender differences, the above symptoms were also shown to have associations with poor prognosis in males at 3 and 8 months after transplantation. Therefore, the results of this study indicated an association between mood status before BMT and prognosis after BMT in a gender-dependent manner (5). In a study by Khan et al. it was reported that 37.5 % of the patients who underwent blood and BMT were suffering from psychiatric disorders. The authors concluded that psychiatric interventions in these patients were of importance (10). The study of Grulke et al. indicated that 10.1% of the patients presented with severe depression (67.15%) suffered from mild depression and 22.75% from moderate depression. The average of survival rates for patients who were suffering from acute, mild and moderate depression were 418, 848 and 699 days, respectively (18).

Our study showed that the scores for MQ scores were significantly more at post-BMT when compared to pre-BMT. This can be due to the fact that patients' anxiety may have had decreased. Additionally, decreasing the side effects of intensive chemotherapy after discontinuing this treatment may have been another reason for the improvement in the patients' memory. Similarly, Syrjala et al. noted that the scores of all neuropsychological tests significantly decreased during the 80 days after BMT. Except for motor dexterity and grip strength, other tests were returned to pre BMT levels by one year. Although the recovery of memory and verbal fluency was reported to occur in one year, both of these factors were noted to be less than the normal values at all testing times (pre-BMT, 80 days and 1 year post-BMT). The above study reported that those patients who did not receive chemotherapy (subjects could receive hydroxyurea) before HCT, were not likely to have memory impairment prior to the BMT procedure. Additionally, it was pointed that treating chronic graft-versus-host disease (GVHD) could increase the risk of impairment in motor dexterity after one year; however, long-term cognitive dysfunction was probably not resulted directly by HCT (8). Also, a study by Booth-Jones et al. demonstrated that 51% of BMT patients had at least a mild dysfunction in one or more cognitive dimensions, with 28% demonstrating moderate-to-severe problem. In their study, lower IQ, being male, older age and less education were found to be risk factors for "impaired score range" in cognitive tests. Interestingly, younger patients in that study had more complaints about problems with cognition. This finding may suggest the differences between patients who complained about cognitive function and those who were suffering from actual impairments in their cognition after BMT (6). Another study by Harder et al. indicated that selective attention, verbal learning, speed of information processing, executive function, verbal and visual memory were at a higher risk to be affected in patients undergoing BMT when compared with normal

controls. Additionally, the results noted that patients scored significantly lower in the information processing speed task compared to the normal population. This study suggested educational level, fatigue and global health as predictors of impaired neuropsychological scores. Moderate to severe cognitive problems were also shown to be related to social functioning, employment status, overall mood states, physical functioning and subjective cognitive problems (19). Meyers et al. reported that cognitive and emotional functioning before transplantation are important predictors for the outcome in a long run and for the QOL in BMT patients. In addition, they reported the development of persistent short-term mood disturbance and memory problems in a few BMT patients. The level of social support, BMT type and locus of control were associated with cognitive functioning and psychological distress both during and after BMT. However, age was not a predictor for neurobehavioral symptoms during and after BMT (20). The limitations of the present study were as follows: Firstly, our sample size was relatively small in spite of enrolling patients for more than 9 months. Secondly, we did not use "structured interview" that could have resulted in the more precise evaluation of the patients in this study. Besides, one month was not a long time for evaluating psychiatric consequences of BMT. The current study provides ideas for future studies and basic information for those health professionals working at BMT wards .

Conclusion

The authors suggest that improvement of anxiety and memory status of patients one month after the bone marrow transplantation is expected even in the absence of consumption of any antianxiety agents. However, some psychosocial interventions are recommended before and after the BMT procedure in order to better prepare patients to cope with the increasing and worsening depression and anxiety during and after the time of the transplantation procedure. Further studies with larger number of patients and for a longer time are recommended to confirm the results of this study.

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