

MENTAL STATE AND ITS PSYCHOPHYSICAL CONDITIONS IN PATIENTS WITH ACUTE LEUKAEMIA TREATED WITH BONE MARROW TRANSPLANTATION

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SUMMARY

Background: Acute leukaemia and bone marrow transplantation (BMT) as a method of its treatment are great psychological stressors, which are responsible for anxiety and depression in the group of patients. The aim of the study was to assess the patients' mental state and its psychophysical predictors before and after BMT.

Subject and method: The study was of a longitudinal and self-descriptive character. The questionnaires: LOT-R, AIS, Mini-Mac, CECS, RSCL and HADS were filled by 60 patients with acute leukaemia before and after BMT.

Results: There were no essential statistical differences between the severity of anxiety and depression before and after BMT but the pattern and the power of various mental state predictors changed in the course of the hospitalization. Anxiety before transplantation was greater when the psychological stress and the strategy of "anxious preoccupation" were stronger and the strategy of "fighting spirit" and the level of generalized optimism were weaker. The factors explained 51% variations of anxiety before transplantation. After BMT 77% variations of anxiety were explained, which were associated with a high level of distress at the end of the hospitalization, higher level of anxiety before transplantation, weaker strategy of "fighting spirit" before transplantation and stronger strategy of "anxious preoccupation" after BMT. Before transplantation 36% variations of depression were explained and estimated as weaker "fighting spirit" and worse "global life quality". The essential predictors of depressive symptoms after transplantation, explained by 81% variations of depression, were weaker "fighting spirit" before transplantation, stronger "anxious preoccupation" after transplantation, worse "global life quality" after transplantation and higher level of anxious and depressive symptoms on admission to hospital.

Conclusion: The psychological and pharmacological interventions, which reduce anxiety, depression and "anxious preoccupation" as well as enhance "fighting spirit", should be introduced before BMT to improve the patients' mental state.

Key words: bone marrow transplantation – depression – anxiety – coping – fighting spirit

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INTRODUCTION

Bone marrow transplantation (BMT) is acknowledged as a risky but potentially satisfying therapeutic method used in many haematological disorders. Its efficacy estimated as a likelihood of 5 year remission is assessed over 50% in acute leukaemia, when allogeneic hematopoietic transplantation is used (Apperley 2012). On account of its increasing specialization and simultaneously decreasing danger, greater attention is drawn to its psychosocial consequences, mainly assessed in terms of life quality. Health-related quality of life is defined as a functional result of illness and its treatment perceived by a patient (Schipper 1996).

Leukaemia as well as bone marrow transplantation constitute a great source of distress for a patient (e.g. Fife 2000, Trask 2002). Severe physical symptoms, decreased quality of life and affective disturbances are considered to be the consequences of the distress.

Anxiety disturbances are commonly met in patients with cancer. Anxiety is diagnosed in about 20-50% patients with cancer and haematological cancers (Boyes 2011, Clinton-McHarg 2014, Linden 2012, Romito 2008, Santos 2006). The anxiety may result from uncertainty about the further course of illness, from a risk associated with bone marrow transplantation and from fears of any

future consequences of leukaemia and its treatment in all life areas. Sasaki et al. (2000) showed, that tension associated with anxiety boosted a development of mental disturbances in the course of isolation during bone marrow transplantation. Anxiety may also decrease a level of patient's immune competence (Vedhara 2005).

Depressive disturbances are diagnosed in about 15-50% patients with haematological disorders (Andrykowski 1994, Clinton-McHarg 2014, Leigh 1995, Montgomery 2003, Neitzert 1998, Trask 2002). In spite of its undoubtedly negative influence on life quality (Andrykowski 1994), depression may affect a course of illness alone and a result of bone marrow transplantation (Colon 1991, Hoodin 2004, Pulgar 2012). Chang et al. (2004) showed, that depressive symptoms increased the risk of death by 7% when a result of Beck's Depression Inventory was increased even about 1 point. The meaning of depression for survival is not yet reliably proved (Hoodin 2003). Some studies indicate, that depression affects unfavourable immunological changes negatively (Koh 1998, Vedhara 2005, Zhou 2005). Pulgar et al. (2012) showed, that depression correlated positively with a number of infections during hospitalizations associated with bone marrow transplantation. Additionally, depression influences coping strategies negatively, what leads to a further deterioration of mental state.

Coping with stress associated with illness includes many cognitive and behavioural efforts aimed at managing in a situation of danger (Lazarus 1984). Preferences in the use of the specific coping reactions may be important not only for a level of distress and for an adjustment to cancer, but as some scientists indicate (Hoodin 2003, Hoodin 2004), for survival after bone marrow transplantation. Grulke et al. (2005) showed, that strategies such as acceptance, taking control, emotional support and compensation are essentially associated with survival after bone marrow transplantation. In turn, Tschuschke et al. (2001) illustrated, that distraction and “fighting spirit” influence a 5-year survival after bone marrow transplantation in a statistically essential way. Montgomery et al. (2003) noted in reference to mental state, that patients with leukaemias and lymphomas and a greater tendency to use “fighting spirit” as a coping strategy and a smaller tendency to use “hopelessness-helplessness” as a coping strategy suffer from depression less frequently. The results are consistent with the remarks of other scientists, who noted, that avoidance strategies are combined with negative affect and worse adjustment to illness (Aarstad 2005, Constanzo 2006, Devine 2003, Fife 2000, Schoulte 2011, Shapiro 2010).

Two aspects must be taken into account in the analysis of coping with illness. The first one refers to cognitive assessment of a stressor understood as leukaemia and BMT. According to Lazarus and Folkman’s theory, the patient’s situation may be perceived as threat, harm/loss or challenge (Lazarus 1984). Many studies have shown, that the capacity to redefine illness as challenge and search for constructive aspects of the situation affected a patient’s functioning positively (Bigatti 2012, Widow 2005). The second aspect of coping with illness is linked to Hobfoll’s conservation of resources theory (Hobfoll 1998). Persons with greater amount of resources cope more efficiently with situations of danger. It is worth noting, that according to the Hobfoll’s theory resources are material and immaterial and the latter may be associated with human personality predispositions.

Generalized optimism is defined as a generalized expectation of positive events (Scheier 1992). In many studies it has been shown, that optimism is a personality resource leading to smaller severity of distress, depression and anxiety, and more adaptive strategies to life with cancer and improvement of life quality, and even to longer survival after diagnosis of cancer (Baker 1997, Carver 1993, Curbow 1993, Herzberg 2013, Rasmussen 2009, Schou 2004). However, there are reports indicating a lack of essential correlations between optimism and some dimensions of patient’s functioning (Coyne 2010, Schoen 2007). Some scientists reported a negative character of the correlation between optimism and the severity of distress, survival and mental wellbeing (Coyne 2010, Goetzman 2008). The discrepancies stimulate further studies in this area.

Acceptance of illness is frequently indicated as a predictor of life quality, mental state, life satisfaction and current health state (Bossema 2011, McCracken 2006). Finally, suppression of emotions may affect the severity of distress and physical symptoms, and thereby may be an essential predictor of a negative course of cancer (Mols 2012, Temoshok 1987).

To summarize, the authors of the article make the following assumptions: 1) mental state (anxiety and depression) affects the course of leukaemia and bone marrow transplantation; 2) mental state may be influenced by the symptoms of illness and the personality predispositions; 3) identification of the personal resources as predictors of anxiety and depression may help to understand better the dynamics of the affective state in the patients treated with bone marrow transplantations.

AIM

The aim of the study was the assessment of the patients’ mental state and estimation of the patients’ psychological resources and strategies used in managing acute leukaemia during treatment with bone marrow transplantation.

SUBJECTS AND METHODS

The study was accepted by the Committee of Bioethics at the Medical University of Silesia in Katowice. The study was of a longitudinal character.

60 patients (34 women and 26 men) at the age of 18 to 67 ($M=39.62$, $SD=12.80$) selected according to the diagnosis of acute myeloma or lymphoblastic leukaemia hospitalized in the Clinic of Hematology and Bone Marrow Transplantation in Katowice were examined. They had to satisfy the following recruitment criteria: consent to participation in the study, age from 18 to 70 absence of hallucinations and delusions, absence of cognitive disturbances, ability to fill self-report questionnaires. The characteristics of the examined patients in reference to sociodemographic and medical data are shown in the table 1.

The following self-report questionnaires were used in the study:

- The Acceptance of Illness Scale (AIS) developed by Felton et al. (1984), adapted to the Polish language by Juczyński (2001) is applied to measure the degree of acceptance of illness. It consists of 8 items, that describe negative consequences of undesirable health. A participant assumes his/her attitude to particular 5-degree items, where 1 means “strongly agree” and 5 means “strongly disagree”. The higher a scale results is, the better the patient accepts his/her illness and adapts more suitably to the illness with lower feeling of psychological discomfort. The AIS has satisfactory psychometric properties. The Cronbach’s *alpha* for the Polish version is 0.82.

Table 1. The characteristics of the participants in reference to sociodemographic and medical data

Characteristics	N	%
Gender		
Female	34	56.7
Male	26	43.3
Level of education		
Primary	2	3.3
Vocational	17	28.4
Secondary	20	33.3
University	21	35.0
Employment status		
Unemployed	5	8.3
Retired	22	36.7
Student	3	5.0
Physical work	12	20.0
White-collar work	18	30.0
Marital status		
Married	41	68.4
Widowed	2	3.3
Divorced	2	3.3
Single	15	25.0
Having children (yes)	39	65.0
Type of leukaemia		
Acute lymphoblastic leukaemia	19	31.7
Acute myeloblastic leukaemia	41	68.3
Type of transplantation		
Allogeneic	47	78.3
Allogeneic sibling	13	21.7
Risk level		
Intermediate	11	18.3
High	49	81.7
Complications (yes)	36	60.0

- The Courtald Emotional Control Scale (CECS) developed by Watson and Greer (1983), adapted to the Polish language by Juczyński (2001) consists of three 7-item subscales, which refer to various ways of anger, depression and anxiety expression. A participant assumes his/her attitude to particular items describing a frequency of use of emotional expression ways, where 1 means “almost never” and 4 means “almost always”. The tool allows to measure rates for the particular subscales as well as the general rate of emotional control, which is a sum of all subscales and reflects the participant’s own opinion about own capacity to control own reactions in a situation, when negative emotions are experienced. The higher result is achieved by the participant, the greater tendency to suppress negative emotions is shown. The Cronbach’s *alpha* coefficients are estimated as: 0.80 for the control of anger, 0.77 for the control of depression, 0.78 for the control of anxiety and 0.87 for the common coefficient of emotional control.
- The Life Orientation Test (LOT-R) developed by Scheier et al. (1994), adapted to the Polish language by Juczyński (2001) assesses generalized optimism.

The questionnaire consists of 10 items and 6 of them refers to generalized optimism. A participant assumes his/her attitude to a particular 5-degree statement. The higher result, the higher level of generalized optimism. The Cronbach’s *alpha* coefficient is estimated as 0.76.

- The Mental Adjustment to Cancer (MAC) developed by Watson et al. (1994), adapted to the Polish language by Juczyński (2001) as (Mini-Mac) is a tool, which allows to measure coping reactions in patients with cancer. The questionnaire consists of 29 items referring to various strategies of coping with cancer. A participant assumes his/her attitude to particular 4-degree statements about currently used coping strategies, where 1 means “definitely no” and 4 means “definitely yes”. The Polish version of the tool allows to measure rates for four coping reactions: “anxious preoccupation”, “fighting spirit”, “helplessness-hopelessness” and “positive redefinition”. The scale “positive redefinition” in the Polish version is an equivalent of the scale “fatalism” in the original version, and the strategy originally called “cognitive avoidance” corresponds the strategy called “fighting spirit” in the Polish version. The higher result is in each scale, the more dominating the particular strategy is. The Cronbach’s *alpha* coefficients are estimated as: 0.92 for the helplessness-hopelessness, 0.90 for the fighting spirit, 0.89 for the anxious preoccupation and 0.87 for the positive redefinition.
- The Rotterdam Symptom Checklist (RSCL) developed by de Haes et al. (2012), adapted by Majkowicz (2000) is a self-report tool to assess the quality of life in patients with cancer. The tool consists of 39 items forming 4 subscales: physical symptom distress (23 items), psychological symptom distress (7 items), activity level (8 items) and overall valuation of life (1 item). A participant assumes his/her attitude to particular 4-degree statements about severity of a particular symptom. The only exclusion is the scale called “overall valuation of life”, which is the 7-degree Likert’s scale. The higher result of physical and psychological symptoms, the worse the patient’s state. However, the high result in the scales called “activity level” and “overall valuation of life” reflects better functioning of a particular patient. The coefficients of inner consistency based on the Polish studies conducted on a group of terminal patients were estimated as: *alpha*=0.86 for physical symptoms, *alpha*=0.83 for psychological symptoms and *alpha*=0.87 for activity.
- The Hospital Anxiety and Depression Scale (HADS) developed by Zigmond and Snaith (1983), adapted by Majkowicz (2000) detects states of anxiety and depression. The questionnaire consists of 7 items for anxiety and 7 items for depression. A participant assumes his/ her attitude to particular 4-degree statements about a frequency of negative emotions. The higher result, the greater severity of anxiety or depression. The questionnaire is a commonly used

tool and the result more than 8 points in each subscale means, that the particular patient is in a risk group of the clinical anxiety or depressive disturbances. The inner consistency (Cronbach's *alpha*) measured at the stage of the first treatment is estimated as 0.79 for the scale of anxiety and 0.83 for the scale of depression.

Patients received the questionnaires of the following scales, namely AIS, CECS, LOT-R, Mini-Mac, HADS, RSCL and a survey including questions about socio-demographic data during hospitalization by admission. They assessed again their mental state fulfilling HADS, RSCL and Mini-Mac after BMT.

Statistical Analyses

The statistical analysis was conducted using SPSS Statistics version 22.0. The statistical description of data was performed using size and percent values for qualitative variables or using mean and standard deviation for quantitative variables. The comparison between the groups was made using the *t*-Student test (for the variables with a normal distribution) or the *U* Mann-Whitney test (for the variables with a distribution other than normal). The strength of association between the variables was estimated using the analysis of Pearson's correlation coefficient. To estimate the predictors of anxiety and depression was used stepwise analysis of multiple regression.

RESULTS

In the group of patients before as well as after BMT, a higher severity of anxiety than depression was observed. The statistical description of the examined variables was shown in the table 2.

40% patients before BMT got at least 8 points in the scale of anxiety, what means, that they were in a risk group of anxiety disturbances. There were 31.1% patients after BMT in the risk group of anxiety disturbances. In a case of depression, there were 13.3% patients before BMT in a risk group of depressive episode and 9.8% patients after the procedure.

There were no differences in a level of the anxiety and depression severity between subgroups differentiated in reference to sex, level of risk and a type of bone marrow transplantation.

However the changes in the severity of symptoms associated with life quality were observed in the area of physical symptoms and activities (Table 2). The severity of physical symptoms was increased after BMT and a level of activity was essentially decreased. There was no essential statistical difference between a severity of psychological distress before and after BMT.

There was observed a different distribution and strength of the mental state predictors before and after BMT (Table 3 and 4).

Anxiety before transplantation was greater when the psychological stress and the strategy of "anxious preoccupation" were stronger and the strategy of "fighting spirit" and the level of generalized optimism were weaker. The factors explained 51% variations of anxiety before transplantation. After transplantation, 77% variations of anxiety were explained, which were associated with a high level of distress at the end of the hospitalization, higher level of anxiety before transplantation, weaker "fighting spirit" before transplantation and stronger "anxious preoccupation" after transplantation.

Table 2. The psychophysical functioning before and after bone marrow transplantation

Psychophysical functioning	Before BMT		After BMT		Comparison (p)
	M	SD	M	SD	
Anxiety	6.53	4.08	6.35	4.19	0.576 ^a
Depression	3.93	3.42	4.07	3.91	0.608 ^a
Physical symptom distress	32.92	6.49	38.33	9.08	<0.001 ^b
Psychological symptom distress	11.53	3.78	11.85	3.85	0.387 ^a
Activity level	26.10	4.64	23.58	4.93	<0.001 ^b
Overall valuation of life	2.58	1.21	2.83	1.36	0.117 ^a
Strategies of coping					
Anxious preoccupation	14.33	4.54	13.73	4.01	0.106 ^b
Fighting spirit	23.50	3.02	23.98	2.97	0.102 ^a
Helplessness/hopelessness	10.78	3.35	10.55	3.56	0.512 ^a
Positive redefinition	21.80	2.54	22.20	2.58	0.146 ^a
Acceptance of illness	30.02	5.50			
Dispositional optimism	17.02	4.05			
Emotional expressiveness	48.00	13.41			
Control of anger	15.82	5.10			
Control of depression	15.80	4.64			
Control of anxiety	16.35	5.53			

Note: N=60; ^a – *U* Mann-Whitney test; ^b – *t*-Student test

Table 3. The predictors of anxiety before and after bone marrow transplantation

Predictors	Anxiety					
	Before BMT adj. R ² =0.51			After BMT adj. R ² =0.77		
	ΔR ²	β	SE	ΔR ²	β	SE
Dispositional optimism	0.10	-0.09*	0.10			
Fighting spirit (pre-BMT)	0.07	-0.20*	0.13	0.14	-0.10*	0.10
Anxious preoccupation (pre-BMT)	0.17	0.23*	0.10			
Anxious preoccupation (post-BMT)				0.19	0.05*	0.09
Psychological symptom distress (pre-BMT)	0.17	0.47***	0.11			
Psychological symptom distress (post-BMT)				0.31	0.42***	0.09
Anxiety (pre-BMT)				0.13	0.43***	0.10

Note: N=60; BMT – bone marrow transplantation; adj.R² – adjusted R²; * p<0.05; *** p<0.001

Table 4. The predictors of depression before and after bone marrow transplantation

Predictors	Depression					
	Before BMT adj. R ² =0.36			After BMT adj. R ² =0.81		
	ΔR ²	β	SE	ΔR ²	β	SE
Fighting spirit (pre-BMT)	0.14	-0.16	0.13*		0.14	-0.18*
Overall valuation of life (pre-BMT)	0.22	-0.53	0.33***			
Overall valuation of life (post-BMT)					0.12	0.31***
Anxious preoccupation (post-BMT)					0.10	0.20*
Depression (pre-BMT)					0.38	0.79***
Anxiety (pre-BMT)					0.07	-0.23**
Anxiety (pre-BMT)	0.14	-0.16	0.13*		0.14	-0.18*

Note: N=60; BMT – bone marrow transplantation; adj.R² – adjusted R²; * p<0.05; ** p<0.01; *** p<0.001

Before transplantation 36% variations of depression were explained and estimated as weaker “fighting spirit” and worse “global life quality”. The essential predictors of depressive symptoms after transplantation, explained by 81% variations of depression, were weaker “fighting spirit” before transplantation, stronger “anxious preoccupation” after transplantation, worse “global life” quality after transplantation and the higher level of depressive symptoms and lower level of anxiety on admission to hospital.

DISCUSSION

The statistical analysis used in the study allowed to explain a high percentage of anxiety variation (77%) and of depression variation (81%) after BMT and also, but to a lesser extent, before BMT (anxiety variation 51%, depression anxiety 36%). The results are congruent with other studies and confirm a high prevalence of anxiety and depressive symptoms in patients treated with BMT (Boyes 2011, Clinton-McHarg 2014, Linden 2012, Leigh 1995, Montgomery 2003, Neitzert 1998, Romito 2008, Santos 2006, Trask 2002). In contradiction to other studies (e.g. Fife 2000, Hjermstad 1999, Shirinbakhsh Masule 2014), a decrease of anxiety after BMT was not observed. The high level of anxiety after BMT may be explained by fears of recurrence of illness or impossibility to lead active life again. The last fear may be especially difficult for the patients, when the

physical symptoms, such as fatigue, still exists. An argument confirming the suggestion may be the results of regression analysis, which indicated, that “anxious preoccupation” and intense psychological distress played an essential role as the predictors of anxiety after BMT. It means, that danger in the present and future situation is exaggerated as if life was a catastrophe.

A mean level of depression did not differ before and after BMT. Moreover, there was no difference in a level of psychological distress associated with the quality of life. The results do not confirm other scientists’ observations, which indicated a decrease of depressive symptoms after BMT (Chang 2005, Fife 2000).

There were no differences in a level of anxiety and depression severity between the patients’ subgroups differentiated in reference to sex. This result is congruent with the study by Montgomery et al. (2003). We may assume, that the situation of being ill makes a risk of affective disturbances equal in men and women.

The negative relationship between level of pre-BMT anxiety and post-BMT depression is a very interesting result. It was proven in some studies analysing influence of surgical procedures on patients’ mental state, that moderate anxiety before surgical operation coexisted with better patients’ adaptation after treatment (de Bruin 2001, Heszen 2007). However, a lack of anxiety coexisted with further mental disturbances and severe physical symptoms. Perhaps, anxiety associated with leukaemia and BMT plays a similar role. The high level

of anxiety before BMT is linked to a higher level after treatment, but it may simultaneously stimulate a mechanism of relief associated with the observation, that fears before BMT turned out untrue. The mechanism protects from the decrease of mood. In turn, a lack of anxiety linked to a further confrontation with the consequences of BMT, e.g. fatigue, a decrease of activity, severe physical symptoms, may act as a frustrating factor and lead to depression.

It was proven, that optimism was an important protective factor only before BMT. Its protective role disappeared after treatment, because the circumstantial and affective factors became dominating. It seems, that optimism had a meaning for creation of an attitude to own treatment and influenced patient's adaptation to the procedure of transplantation. However, the current patients' experiences were more important after BMT than their personal predispositions. Such a conclusion is important in the context of a mode of psychotherapeutic work with patient. At the beginning of the hospitalization, it may be more productive to boost the patient's positive attitude towards treatment, whereas the solution of current troubles or reduction of anxiety and psychological distress are more essential after BMT.

The study showed a differentiated role of strategies of coping with illness for the patients' mental state. The most meaningful were "fighting spirit" and "anxious preoccupation". Interestingly, a current tendency to use the strategy of "anxious preoccupation" was a predictor of the current patient's state. Meanwhile, the severity of "spirit fighting" before BMT (and no after BMT) was a predictor of anxiety and depression before as well as after treatment. A tendency to use the strategy of fighting spirit was not an essential predictor after BMT. The observation may be linked to the fact, that fighting spirit is simultaneously a mechanism, which helps a patient to create more positive self-esteem (Johnson 2004). It is possible, that self-efficacy, determination and strength in fighting with illness, which are the elements of "fighting spirit", are truly a personal predisposition equal with general self-value. It had been proven many times, that high self-esteem was an important feature for better coping with illness and better patient's state. It is worth continuing studies over mutual associations of "fighting spirit" and self-esteem in patient, who are treated with BMT.

It is noteworthy, that the emotional expressiveness and strategies such as "hopelessness/helplessness" or "positive redefinition" had no meaning as predictors of patient's mental state. These strategies were not statistically essential in the study and the result is not congruent with other studies, which proved negative associations between hopelessness/helplessness or fatalism and adjustment to illness (Classen 1996, Kissane 2004, Montgomery 2003).

Several limitations of the study should be taken into account in the analysis of the study. The first one is associated with the fact, that answers given by discharge from the hospital might be distorted by fears associated

not with illness itself, but with the factors referred to a situation at home and life outside the hospital. The second limitation is the use of HADS, because the test as a wide screening tool does not allow to assess anxiety and depressive symptoms precisely. Finally, a relatively small group of patients makes it impossible to use the statistical methods, which allow to verify the hypothesis about curvilinear dependences between optimism or strategies of coping with illness and patients' mental state.

CONCLUSIONS

The study proved differences in a system in the predictors of anxiety and depression before and after BMT, what reflected the dynamic changes in patients' mental state during treatment with BMT. Although the results of the questionnaires filled by patients before and after BMT stayed the same, it seems, that other psychological processes took place. The other processes should influence a change in therapeutic approach during hospitalization.

The study indicated an important role of the strategies, which help to cope with illness as the predictors of patients' mental state in the course of BMT. The psychological and pharmacological interventions, which reduce anxiety, depression and "anxious preoccupation", as well as enhance "fighting spirit", should be introduced before BMT to improve the patients' mental state.

Acknowledgements:

The study took place thanks to Prof. Sławomira Kyrz-Krzemień, MD, PhD, who is a headmaster in Department of Haematology and Bone Marrow Transplantation at Medical University of Silesia in Katowice.

Conflict of interest: None to declare.

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