

FIVE YEARS STUDY ON IMPACT OF ANXIETY ON QUALITY OF LIFE IN PATIENTS TREATED WITH BONE MARROW TRANSPLANTATION

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SUMMARY

Objective: This longitudinal research is to follow the changes in quality of life and in anxiety level of patients treated with bone marrow transplantation (BMT).

Subjects and methods: Patients selected in period from 1990 to 2000 were treated with bone marrow transplantation and were invited to participate in the study. In ten years period 299 patients were treated with BMT. 109 patients were included in this study (58 male and 51 female) after their informed consent was obtained. 42 of 109 patients were successfully monitored during a five year period and they successfully returned completed questionnaires.

Results: The level of Karnofsky scores show statistically significant difference related to time that passed since BMT. Average value of Karnofsky scores in a group of patients 3 months after BMT was 82.22, and in group five years after BMT was 91.76. There is statistically significant difference between these values ($p=0.003$). Results of anxiety as a trait and as a state also show statistically significant decrease between measuring after leaving the hospital and five years after BMT.

Conclusions: There is statistically significant correlation between anxiety and quality of life, that is, with decrease of anxiety quality of life level increases.

Key words: anxiety - bone marrow transplantation - functional status - liaison psychiatry - quality of life

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INTRODUCTION

In recent years treating of leukaemia become more successful and bone marrow transplantation (BMT) is used in number of, up to now, life endangering diseases like leukaemia, lymphomas, aplastic anaemia and some solid tumours. As a result of these therapeutic treatments in treating malignant diseases some sequels are lagging. The procedure has become more and more sophisticated and mortality rates have decreased. Therefore, more attention is now being given to the psychosocial consequences of BMT because we can see that quality of life returns to an acceptable level for most, but not all, long term survivors (Chao et al. 1992, Baker et al. 1994, Litwins et al. 1994, Broers et al. 2000, Watson et al. 2004, Molassiotis et al. 1996, Zittoun et al. 1997). The quality of life became a great importance because

of the greater efficacy of therapeutic methods, but because of the impact that therapeutic procedures leave on a patient as well. This does not imply that patients return to the quality of life (QOL) they had before the transplantation (Andrykowski et al. 1995a, Andrykowski et al. 1995b). Because of the efficacy of therapeutic methods, question of patient's feelings, his psychological and physical status, not just the absence of disease, came to limelight.

The first attempt to analyze quality of life in a malignant disease therapy (breast cancer, colorectal cancer) started in seventies and it was followed by a number of researches in a last couple of years (Graves et al. 2003, Geiger et al. 2006).

Bone marrow transplantation (BMT) is very efficient method of treating benign and malign haematological diseases (Armitage 1994). However, treating of BMT is a very difficult and

complex procedure for patients. Intensive therapeutic methods (cytostatic treatment, radiation and its side effects), lots of complications of transplantation, complexity and lingering nature of therapeutic treatment can have significant impact on patients' physical, psychical and social status (Labar et al. 1992).

BMT involves potentially lethal doses of chemotherapy and frequently total body irradiation (TBI), followed by a prolonged period of isolation while the transplanted marrow engrafts. This isolation period is often accompanied by intercurrent infection. Following discharge from the BMT unit, there is a further period of susceptibility to infection and complications, such as graft-versus-host disease (GvHD), recurrence of leukaemia, and psychosocial occurrence of adjustment difficulties. With the associated high mortality and high morbidity, BMT is clearly a stressful treatment.

The main characteristic of psychic reactions to the transplantation procedure is anxiety, which may manifest in various degrees and which influences considerably the quality of the patient's life (Gregurek et al. 1995). Psychically unstable persons with intrapsychic or interpersonal emotional problems, with reduced tolerance of frustrations, may easily, when confronted with the illness, develop an anxious reaction with psychotic disorganization of personality. There is a strong correlation between the level of anxiety and the outcome of the transplantation therapy. For example, patients with multiple complications and worse prognosis are increasingly anxious (Gregurek et al. 1996a).

Every somatic illness, besides objective organic disturbances, causes also a change in a patient's quality of life. This is especially evident in serious, life endangering illnesses, the knowledge of which comes as a shock to the patient, requiring all his adaptation psychological

mechanisms to be mobilized in order to overcome the knowledge of endagerness, to accept the struggle for life in an entirely changed form, accompanied by many restrictions and deprivations (Gregurek et al. 1996b).

Several authors analysed quality of life in patients treated by bone marrow transplantation (Chao et al. 1992, Baker et al. 1994, Litwins et al. 1994, Broers et al. 2000, Watson et al. 2004, Molassiotis et al. 1996, Zittoun et al. 1997, Andrykowski et al. 1995a, Andrykowski et al. 1995b). The aim of this longitudinal research is to follow the changes in quality of life and in anxiety level of patients treated with autologous and allogenic bone marrow transplantation.

SUBJECTS AND METHODS

Patients

Patients were recruited from the Department of Haematology of Zagreb University Hospital Centre. All patients selected in period from 1990 to 2000 were treated with bone marrow transplantation and were invited to participate in the study. The patient's sociodemographic and clinical characteristic were collected during the admission to hospital for the bone marrow transplantation. Written informed consent was obtained from all the participants and Ethics Committee of Zagreb University Hospital Centre approved the study protocol. In ten years period 299 patients were treated with BMT, 88 patients were treated with autologous BMT, and 211 with allogeneic BMT. 109 patients were included in this study (58 male and 51 female) after their informed consent was obtained. Patients' average age was 29 (range from 19 to 53). 42 of 109 patients were successfully monitored during a five year period and they successfully returned completed questionnaires. Patients alive and responding at the consecutive measurements are displayed in Table 1.

Table 1. Number of patients that were alive and participate at the consecutive measurements

Measurements	Deceased	Alive	Responding (%)
After BMT	3	106	102 (96.2%)
3 months after BMT	11	95	67 (70.5%)
1 year after BMT	19	72	54 (75.0%)
5 years after BMT	15	57	42 (73.7%)

At fifth year after the BMT, 48 patients (44.04% of the original sample) had died. The nonrespondents at third month did not differ significantly from the respondents on any of the psychological measures. At the final measurements, respondents and nonrespondents did not differ on any of the psychological measures at third month.

Instruments

We used three self-reported instruments. All patients have completed general data questionnaire – age, gender, date of transplantation, as well as data of employment, satisfaction with their body appearance and body image, satisfaction with sexual functioning. For quality of life we used (Karnofsky Performance Scale) and for anxiety evaluation Spielberger STAI test was used. Testing was performed on the end of the hospitalisation, after third month, one year and five years after BMT. Questionnaires were mailed with return postage stamp.

The most difficult task in quality of life research is to select measures that truly reflect a person's quality of life. We decided to use Karnofsky Performance Scale (KPS) because of its brevity, simplicity and clarity (Karnofsky et al. 1948, Mor et al. 1984, Grieco & Long 1984, Wingard et al. 1991). The respondents were asked to indicate their level of physical functioning on a Karnofsky Performance Scale (KPS). The Karnofsky Performance Scale is the most widely used method of quantifying the functional status of cancer patients. The KPS is a 10-point rating scale which ranges from normal functioning (100) to dead (0). Alternate categorizations have been developed and are widely used. The KPS, or comparable measures, have been used for research purposes to stratify patient subsets exposed to various treatment interventions. It has also been used as an outcome measure to compare differences in functional abilities of patients before and after exposure to an intervention.

Patients were tested with the Spielberger State-Trait Anxiety Inventory as a measure of anxiety as a state (STAI-S) and anxiety as a trait (STAI-T) (Spielberger 1983). STAI Trait scale

consists of 20 statements to describe how the subjects generally feel. The STAI State scale also consists of 20 statements, but the instructions require subjects to indicate how they feel at a particular moment in time. The STAI was designed to be self-administering. Complete instructions are printed on the test, and the inventory has no time limits.

Statistical analysis.

The Statistical Package for the Social Sciences, version 12.0 (SPSS) (SPSS, 2002) were used to analyze the data. To test differences in a degree of anxiety explicitness in BMT patients due to time passed since transplantation ANOVA was used. *T-test* was used to examine differences in quality of life in BMT patients due to time passed since transplantation. Person's *r* was used to examine correlation between quality of life and degree of anxiety explicitness in BMT patients.

RESULTS

Questionnaires were used with patients treated with autologous and allogeneic BMT in period from 1990 to 2000. Results about occupational functioning and employment, body appearance and sexual functioning are presented in Table 2. Results show that 60.7% patients were employed after transplantation although they were at a sick-leave at the time, 1 year after BMT there were only 22.4% employed ones, and 5 years after BMT 18.6% were employed. Results of satisfaction with their body appearance increase gradually from 70.6% after leaving the hospital to 88.5% after 5 years. Patients that had transplantation show extreme discontent with their sex life, so only 11.8% patients, after leaving the hospital, were content with their sex life. This percentage increases gradually, and in fifth year after transplantation 32.7% of patients are content with their sex life.

Analyzing results of patients treated with BMT on self-report scales measuring quality of life, we can observe gradual increase of values from 82 in a first year after BMT to 91 in fifth year after BMT. Results of Karnofsky score show statistically significant difference related to time

that passed since BMT, average value of Karnofsky score in a group of patients 3 months after BMT is 82.22, and in group five years after BMT is 91.76. There is statistically significant difference between these values ($p=0.003$). Results of anxiety as a trait and as a temporary condition

also show statistically significant decrease between measuring after leaving the hospital and five years after BMT. There is also statistically significant correlation between anxiety and quality of life, that is, with decrease of anxiety level quality of life increases ($r=0.68$; $p<0.05$) (Table 3).

Table 2. Occupational functioning and employment, body appearance satisfaction and sexual functioning after bone marrow transplantation

	Discharge (N=102)	3 months (N=67)	1 year (N=54)	5 years (N=42)
Working	60.7%	59.4%	22.4%	18.6%
Satisfied with body appearance	70.6%	73.5%	83.9%	88.5%
Satisfied with sexual functioning	11.8%	23.1%	25.6%	32.7%

Table 3. Quality of life values, anxiety as a trait and anxiety as a state values in BMT patients

	Discharge (N=102)	3 months (N=67)	1 year (N=54)	5 years (N=42)
Quality of life (Karnofsky Score)	82.8 (15.26)	82.2 (21.24)	87.1 (19.27)	91.8 (7.28)
STAI - T	40.8 (12.29)	38.1 (14.03)	36.8 (8.91)	35.6 (11.36)
STAI - S	39.7 (10.31)	36.6 (13.22)	36.9 (8.07)	34.7 (10.41)

DISCUSSION

Transplantation medicine is unique clinical situation made from modern biotechnological medicine. It enables us to observe specific ways of adaptation and it gives us an opportunity to test traditional concepts of symbolization and body image.

We can see from our data that quality of life returns to an acceptable level for most, but not all, long-term survivors. This does not imply that patients return to the QOL that they had before the transplantation (Andrykowski et al. 1995a, Andrykowski et al. 1995b). Those aspects of life that are related to physical health seem to be compromised to some degree. For example, impairment in sexual functioning is common problem after BMT as we shown in our data and other investigator found significant changes in sexual life (Chao et al. 1992, Baker et al. 1994, Molassiotis et al. 1996, Andrykowski et al. 1995a, Andrykowski et al. 1995b, Mumma et al. 1992, Wingard et al. 1992, Molassiotis et al. 1995).

Body image, another aspect of self-perception, was similarly associated with quality of life and the relationship increase in significance over time.

Measurement of quality of life has been debate over the past decade as to whether self-reported (subjective), global, and disease-specific assessments are more valid than more objective assessments using standardized instruments and multidimensional assessments (Wellisch et al. 1996, Edman et al. 2001, Hoodin & Weber 2003, Wright 1999). It is our view that quality of life measures are subjective, reflecting the individual's assessment of his/her life at one time relative to his/her previous state and prior experiences. After all, it is the patient's own evaluation of his or her quality of life that is important. The patient's perception of his own quality of life may be especially poignant after BMT. Many of the patients are happy or satisfied simply with the fact that they are alive following such intensive therapy. It may be that a patient's perception of what is important for their global quality of life is simply life itself, the good and the bad.

Community reintegration problems, which included difficulty in returning to former social roles, separation from home, family, and friends, difficulty in resuming social relations, dealing with stigmatization, problems with family and children,

and financial and employment difficulties. Job discrimination was reported by a majority of our patients and it was associated with a lack of employment and loss of employment. Job discrimination was reported even among those who worked: 60.7% of the patients who reported substantial discrimination were employed. Job discrimination has been noted in other reports about experiences of survivors of cancer (Drolet et al 2005, Bradley et al. 2005, Baker et al. 1999, Spelten et al. 2002).

Most of our patients rated their quality of life above average. Although one may question the validity of the linear analogue scale, the perception of the patients' own quality of life evaluated repeatedly over time suggests strongly that, in the individual patients' own perception, his or her quality of life was above average. Finally, use of Karnofsky scale provides an objective metric for consecutive comparing patients treated with BMT through the time.

When patient first find out that he/she has a malignant disease they get more intensive emotional reaction than they would get if they found out they have any other disease. Most people relate it with certain idea they have about it which is realistic in a way, but it also have some metaphorical background. Patient's first reaction, when he finds out that he has leukaemia, is fear. It's practically greatest fear possible – fear of death, that is, fear of separation from others and themselves. These separation fears, which associate on earliest fears of separation from their first object – mother, can provoke severe anxiety conditions to the proportions of panic.

Anxiety is basic model of reaction to stress situation, and transplantation treatment is particularly suitable for it. If a person finds himself in a dangerous situation that is new for him, he reacts with anxiety that is result of previously experienced danger, instead of reacting to the present situation.

Furthermore, anxiety began to decrease within 3 months after the bone marrow transplantation, even though the degree of symptom distress did not change. This finding suggests that hopefulness and

the perception of possibilities for the future may transcend symptom distress. Findings indicate the period of greatest emotional distress and vulnerability occurred after discharge from the hospital and then decreased significantly to the baseline level 3 months after BMT and reaches normal level 1 year after transplantation. In fact, this was the time of greatest emotional distress throughout the period of hospitalization and the first year after transplantation. This finding is consistent with Andrykowski's (Andrykowski 1994) and Lesko's (Lesko 1993) descriptions of the BMT process. Also notable is that both anxiety and uncertainty dropped significantly after discharge from the hospital, similar to symptomatology. The periods of lowest emotional distress and vulnerability, including anxiety, or the periods of most positive adaptation, were 3 months and 12 months after transplantation, when the response was significantly more positive than it was at baseline, or the period before transplantation (Syrjala et al. 1993, McQuellon et al. 1998, Fife et al. 2000).

Every physical disease, together with objective organic difficulties, causes changes in psychic condition of a patient. It is particularly expressed in severe and life endangering diseases, when knowledge of life endangering overtakes the patient. That knowledge requires mobilization of all existing adaptation psychological mechanisms that enable prevalence of knowledge of life endangering, excepting a battle for life in a significantly modified form, followed by lots of limitations and renunciation. Previous experiences indicate that mentally healthy and emotionally stabile people outdo this knowledge much easier. Psychically unstable people with intrapsychic and intrapersonal emotional problems, which have reduced ability to tolerate frustrations, can easily, finding out that they are ill, develop anxious reaction with psychotic disorganization of personality.

It should be stressed out that bone marrow transplantation treatment significantly changes quality of life in leukaemia patients. By submitting to this hazardous and hardly bearable treatment,

patients have an opportunity to decrease fatal prognosis of the disease.

The limitations of this study were the heterogenic histology of the leukaemia but all patients were treated with the same BMT protocol. All patients during hospitalisation had psychiatric support and they did not have any psychiatric complications during the bone marrow transplantation. Next possible limitation of this study was usage of self-report questionnaires which were delivered to participants by mail so there was no direct communications between participants and researches. However, it seems unlikely that these factors undermine the validity of this investigation in a major way.

CONCLUSION

Quality of life returns to an acceptable level for most, but not all, long-term survivors after BMT. The patients didn't return to the QOL that they had before the transplantation and those aspects of life that are related to physical health seem to be compromised to some degree. There is statistically significant negative correlation between anxiety and quality of life. Psychiatrist in team for transplantation has a task to recognize anxiety in forehand and to prevent it if possible. Inclusion of psychiatrist in an interdisciplinary team of experts that work together on a bone marrow transplantation is the first step to achievement of liaison psychiatric approach.

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