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Quality of life

Psychological distress of patients undergoing intensified conditioning with radioimmunotherapy prior to allogeneic stem cell transplantation

N Grulke[1], H Bailer[1], H Kächele[1] and D Bunjes[2]

[1]*University Clinic for Psychosomatic Medicine and Psychotherapy, Ulm, Germany; and* [2]*Department of Internal Medicine III (Hematology/Oncology), University Hospital Ulm, Germany*

Summary:

This is a pilot study comparing the emotional distress of patients receiving an intensified conditioning regimen (radioimmunotherapy = RIT) with patients receiving conventional conditioning for allogeneic stem cell transplantation. In total, 53 patients (18 received RIT) were given two questionnaires designed to measure emotional distress (HADS, POMS) before starting conditioning (t1) and at discharge (t2). During the in-patient period, patients answered questions daily relating to physical distress, psychological distress, and how they were 'coping with the situation'. At t2, the transplant team assessed the manner in which the patients were coping. The data displayed no relevant differences with regard to emotional distress between the two groups, both at t1 and t2. For both groups, anxiety and vigor decreased and fatigue increased between t1 and t2. On average, perceived distress was higher for those patients being treated with RIT during the in-patient time, but the differences between both groups were significant only regarding physical distress during the recovery period. No difference was found for the transplant team's assessment. We hypothesize that an intensified conditioning regimen with RIT *per se* has only a small distressing effect on the patients' psyche during their stay at the hospital. Differences between both groups probably result from independent factors such as, for example, the patients' pre-existing health conditions.
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Hematopoietic stem cell transplantation (SCT) can potentially cure several malignancies and could be considered one of the real advances in modern day medicine.[1,2] However, about 2/3 of all high-risk patients treated with SCT will die as a result of a relapse of the disease or from transplantation-related complications.[3] Increasing the TBI dose used during the conditioning regimen for SCT can reduce relapse-related deaths for leukemia patients, but it increases transplantation-related mortality, resulting in an unchanged overall survival rate.[4,5] Targeted bone marrow irradiation by using radioimmunotherapy (RIT) in addition to conventional TBI may offer a solution to this problem. This intensified treatment makes it possible to considerably increase the bone marrow dosage, while still having acceptable extramedullary toxicity to minimize the relapse risk.

Undergoing SCT is a demanding procedure involving a high level of emotional distress for the patients. In addition to dealing with a life-threatening disease, they also have to face transplantation-related complications and possible death. They suffer from adverse effects of the treatment and the possibility of a relapse after successfully having survived the initial treatment.[6–10] Clinically, it seems that patients accept and tolerate RIT rather well. On the other hand, however, increased emotional distress levels can be caused by, for example, the knowledge of being a patient with high risk for relapse and thereby a poorer prognosis for total recovery; the additional strain of total isolation on a nuclear medicine ward; irrational beliefs about incorporated radioactivity; and the necessity of a longer stay in the hospital. Until now, there has not been any kind of research on the topic of potentially increased psychological distress caused by RIT. In the context of a broader psychosocial investigation in the two transplantation centers of the Universities of Tübingen and Ulm, Germany, we were able to compare prospectively the emotional distress after transplantation of patients undergoing intensified conditioning regimen and of patients conditioned by conventional strategies. The experimental conditioning regimen is only available in Ulm, so we had to restrict our data basis to patients treated in Ulm. Our evaluation has to be seen as an exploratory, not as a hypothesis testing approach.

Patients and methods

Between October 1999 and December 2001, all in-patients on the transplantation unit of the Ulm University Hospital scheduled for their first allogeneic SCT were asked to participate in a psychosocial study (approved by the

Correspondence: Dr N Grulke, Universitätsklinik für Psychosomatische Medizin und Psychotherapie, Frauensteige 14a, D-89075 Ulm, Germany.
E-mail: norbert.grulke@medizin.uni-ulm.de
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University's Ethics Committee). In order to participate, the patients had to be at least 18 years of age and fluent in German. At the time they were hospitalized, the patients were informed that participation in the study was voluntary, and that nonparticipation would have no impact on their treatment in the unit. Patients who agreed to participate were asked to sign an informed consent form. We then interviewed the patients and gave them widely used questionnaires to be filled out before the start of the conditioning regimen (t1) and when they were being discharged (t2). At discharge, we asked the transplant team (physicians and nurses) to assess each patient's coping skills. In addition, during the in-patient period, the patients were asked to assess the distress they experienced on a daily basis.

Patients

During the recruiting period, 101 patients were hospitalized in the transplantation unit. Eight patients did not meet the inclusion criteria, and one patient was not recruited due to organizational problems. Of the remaining 92 patients, 22 patients (11 being scheduled for RIT) did not want to participate. Thus, 70 patients became part of the study. Finally, one patient had to be excluded because he did not supply the necessary data on the questionnaires, and 16 patients dropped out after t1, that is, no questionnaires are available at t2 (Four, all receiving RIT, died during in-patient time; six, of whom one received RIT, refused further participation before discharge; and the last six, of whom two received RIT, did not return their questionnaires after discharge). As a result, a total of 53 patients were evaluated. In total, 35 of these patients received conventional conditioning and 18 received RIT conditioning (for sample characteristics, see Table 1). Both groups were treated on the same ward of the transplantation unit (other than the 3–5 days in the nuclear medicine ward for the RIT patients), and received the same care from the doctors and nursing staff.

There were no significant differences between the two groups regarding age, sex, HLA identity, source of stem cells, and donors (t-test for age, χ^2-tests for other variables), but there were some differences regarding diagnosis ($P<0.005$, only leukemia were treated with RIT) and TBI ($P=0.005$, less patients with RIT received additional TBI).

Table 1 Sample characteristics

	No RIT (n = 35)		*RIT (n = 18)*		*Total (n = 53)*	
Age (years)						
Mean	40.6		39.9		40.3	
s.d.	11.9		9.4		11.1	
	Count	*%*	*Count*	*%*	*Count*	*%*
Sex						
Female	11	31.4	6	33.3	17	32.1
Male	24	68.6	12	66.7	36	67.9
Diagnosis						
Acute leukemia	11	31.4	16	88.9	27	50.9
CML	12	34.3	2	11.1	14	26.4
Others	12	34.3			12	22.6
Source of stem cells						
BM	9	25.7	2	11.1	11	20.8
PBSC	26	74.3	16	88.9	42	79.2
HLA						
Mismatch	3	8.6	3	16.7	6	11.3
Ident	32	91.4	15	83.3	47	88.7
TBI						
No TBI	5	14.3	9	50.0	14	26.4
TBI	30	85.7	9	50.0	39	73.6
Donor						
Unrelated	18	51.4	10	55.6	28	52.8
Sibling	16	45.7	7	38.9	23	43.4
Other relative	1	2.9	1	5.6	2	3.8

BM = bone marrow; PBSC = peripheral blood stem cells; RIT = radioimmunotherapy.

Assessment instruments

To assess emotional distress (anxiety, depression, and overall mood), we used two of the most common assessment instruments:

(1) *The Hospital Anxiety and Depression Scale*[11] *(HADS)*: This questionnaire consists of 14 items, assessing the patients' anxiety and depression levels (seven items each) with regard to the last 7 days. The advantage of this instrument is that it does not take somatic symptoms (eg weight loss, fatigue), which are often associated with psychopathology, into consideration. In cancer cases, these symptoms are normally confounded with the disease and treatment. The items were designed in a Likert-type style with a range of 0–3 for each item. The scores for each scale are obtained by adding the individual scores for each item. Both scales range from 0 to 21, higher scores reflecting higher depression or anxiety levels.

(2) *Profile of Mood States*[12] *(POMS)*: The POMS assesses the patients' mood. We used the German short-form, which asks for Likert-type responses (range 0–6) to 35 adjectives (eg 'angry', 'sad', 'energetic') during the past 24 h. The items are added up to build scores for four subscales: depression (14 items), fatigue (7), vigor (7), and anger (7), resulting in ranges for scales from 0 to 42 in the case of seven items per scale, and from 0 to 84 for 'depression'.

The two HADS scales and the three scales depression, fatigue, and anger of the POMS represent the measurement of the patients' emotional distress, while vigor would indicate a positive state of mind.

During their time in the hospital, the participants were asked to assess their perceived distress each evening while looking back on their day. They evaluated their 'physical state', their 'psychological state', and how they were 'coping with the situation' by using a six-point Likert scale that follows the well-known German grading system at school (1 'very good' to 6 'very poor'). These 'diaries' were collected once a week. To simplify, we computed a score for each item and for three time periods: (i) 'pre SCT': the days before SCT, that is day −5 to day −1; (ii) 'isolation': the days of isolation from SCT until engraftment and the end of the reversed isolation period, that is, day 'zero' to day

+14 (we chose this day because 75% of the patients in our study could leave isolation between days +9 and +14); and (iii) 'recovery': the days from leaving isolation until discharge, that is, day +15 to day +29 (at day +29, 75% of the patients had been discharged). Each score was calculated as the arithmetic mean of all available daily ratings in the respective period. Correspondingly, the score for the total period is defined as the arithmetic mean of all valid ratings during day −5 to day +29.

At t2, the transplant team was asked 'Looking back at the in-patient time, in general, how did the patient cope with the situation?' The assessments followed the already mentioned six-point Likert-scale.

Statistical procedures

Statistical evaluation was performed by using the SPSS for Windows software program.[13] Differences in the mean between two independent or dependent groups were evaluated by using the appropriate *t*-test, and the χ^2 test was used for four-fold tables.

We evaluated the effects by applying a mixed analysis of variance with treatment group (RIT *vs* conventional conditioning) as the between-subject factor, and time (measurement before SCT and at discharge) as the within-subject factor.

Results

Table 2 shows the mean scores for the HADS and POMS scales at t1 and t2. The results for the ANOVAs can be summarized as follows (no other trends or significant results for main or interaction effects resulted if not stated): HADS-depression ($P=0.048$) and POMS-fatigue ($P<0.01$) increased over time while HADS-anxiety decreased ($P<0.01$). For POMS-depression and POMS-anger, there is a trend ($P<0.06$) regarding the interaction of time and treatment group, in both instances showing, over time, increasing distress for the RIT group, and decreasing distress for the conventional conditioning group. For POMS-vigor, both main effects are significant, showing decreasing vigor over time ($P=0.028$) and lower scores for the RIT group ($P<0.012$).

Figure 1 compares perceived distress during the in-patient time period for both treatment groups. For all researched subject areas and all periods concerned, the mean distress is higher for the RIT group. There are significant differences between the two groups regarding 'physical distress' during the 'recovery period' (<0.01).

With respect to coping with the situation, the transplant team did not see any relevant differences between conventional conditioning and RIT: mean (s.d.) 2.14 (0.77) *vs* 2.39 (0.78) for physicians, and 2.40 (0.95) *vs* 2.78 (1.06) for nurses.

Table 2 Mean, standard deviation (s.d.), and number of cases (*N*) for HADS and POMS scales at t1 and t2 compared by conditioning regimen

	t1			*t2*		
	Mean	*s.d.*	*N*	*Mean*	*s.d.*	*N*
Anxiety (HADS)						
No RIT	5.91	3.74	35	5.03	3.47	34
RIT	5.80	3.00	18	4.00	3.09	18
Total	5.87	3.48	53	4.67	3.35	52
Depression (HADS)						
No RIT	4.26	3.61	35	4.74	4.43	35
RIT	4.50	2.96	18	5.91	4.29	18
Total	4.34	3.37	53	5.14	4.38	53
Depression (POMS)						
No RIT	15.43	16.24	35	12.83	14.99	35
RIT	10.50	8.38	18	14.50	16.95	18
Total	13.75	14.18	53	13.40	15.54	53
Fatigue (POMS)						
No RIT	10.02	8.85	35	14.66	9.28	35
RIT	11.02	7.37	18	16.94	7.40	18
Total	10.36	8.32	53	15.43	8.68	53
Anger (POMS)						
No RIT	7.34	9.59	35	5.71	6.66	35
RIT	3.11	3.83	18	5.61	7.77	18
Total	5.91	8.31	53	5.68	6.98	53
Vigor (POMS)						
No RIT	24.03	7.58	35	22.08	7.96	35
RIT	20.00	8.17	18	16.47	6.10	18
Total	22.66	7.94	53	20.17	7.80	53

Discussion

We compared data from 18 patients who underwent SCT and were receiving new, nonstandard, intensified conditioning with data from 35 patients receiving the conventional myeloablative conditioning regimen. Patients were assessed with regard to their emotional distress by way of questionnaires while being admitted to the hospital and while being discharged after SCT. During the in-patient time period, they assessed their daily distress by way of three simple criteria.

Although it seems likely that anticipating an additional strain by the intensified treatment and being aware of a poorer prognosis should lead to increased emotional distress for the RIT group at t1, our data does not support this assumption. The only notable difference seems to be the decreased vigor of the RIT patients, a difference that holds over time. It may just be a coincidence, but could perhaps also be a reflection on the severity of the disease.

Figure 1 reflects our general clinical impression that patients were most distressed during the isolation period. Clear relief is notable thereafter and reflected in our data. Physical distress affects the patient more than anything else. On both psychological scales, the patients rate their distress as quite low. Comparing the bars between the treatment groups, the time at the hospital was slightly more difficult for the RIT patients, predominantly regarding physical distress (showing the only statistically significant difference as well). This may be an effect of RIT. However, as already mentioned, it could also reflect the severity of the disease or just be a coincidence.

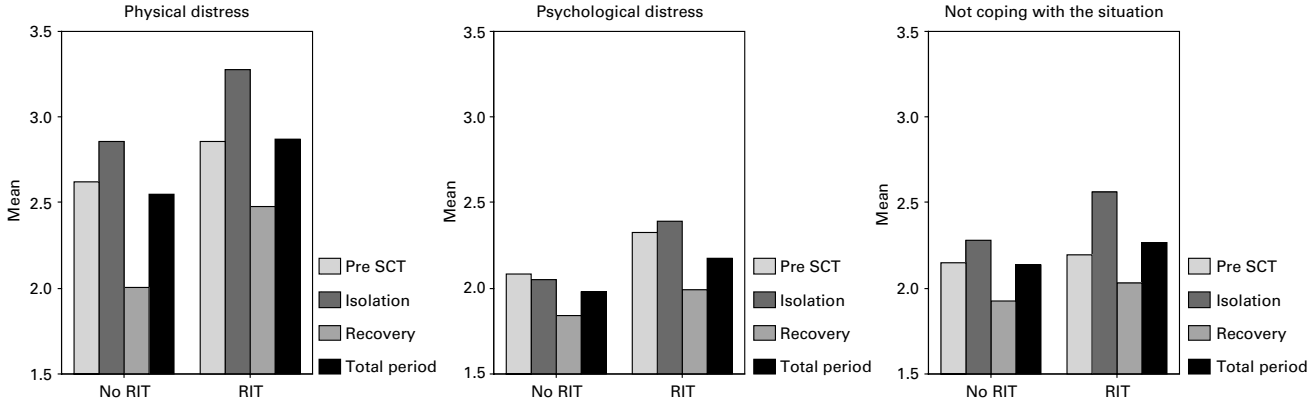

Figure 1 Mean scores for perceived distress during the in-patient period (days −5 to +29) comparing conventional conditioning regimen with RIT.

We did not find any relevant differences between both groups at t2 besides the pre-existing difference on the POMS-vigor scale. Both groups show a decreasing anxiety level from t1 to t2, a trend that is not surprising because filling in a questionnaire at t2 means that the patient had survived the acute treatment and was facing discharge. A decrease in vigor and an increase of fatigue can be expected as well as a normal side effect of the myeloablative procedure.

In total, 50% of the eligible patients who did not consent to participate in our psychosocial study received RIT. In addition, all four participants who died before t2 were receiving RIT. Their average scores on all the HADS and POMS scales at t1 showed higher distress than of those patients that dropped out for other reasons, and the scores of the last mentioned patients were higher than those answering at t2 (results not reported). This suggests that our RIT sample initially represents the healthier subjects among those who received RIT during the study period. If this assumption is correct, we would expect that several of the nonparticipating patients would have died during the transplantation period (as all four deceased study patients during this period received RIT). We checked records for these patients and found that, in fact, all of the 11 nonparticipating RIT patients were registered as having left the hospital alive.

This finding supports the interpretation of the differences between the RIT and the non-RIT group as resulting from the physical status of the patient and not as an effect of the treatment with RIT *per se*. Even though RIT has an effect on the perceived distress, it would be a small one. This view is supported by the fact that the transplant team did not report a significant difference between both treatment groups with respect to coping with the situation. The nurses on the ward and the physicians expressed that, in general, patients undergoing RIT do well. Also, the hospital's psychosomatic consultation liaison service reports that it does not have to be more involved with these patients than with others on the transplantation unit.

In summary, we hypothesize that RIT *per se* has only minor distressing effects on the psyche of the patients during the transplantation period. Differences between both groups probably result from independent factors, for example, the patients' pre-existing health status.

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