

Impact of autologous hematopoietic stem cell transplantation on the quality of life of patients with multiple sclerosis

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ABSTRACT

Objective: To evaluate the impact of autologous hematopoietic stem cell transplantation (autoHSCT) in the health related quality of life (HRQL) in patients with multiple sclerosis. **Method:** The sample consisted of 34 patients, over 18 years old, treated at a University Hospital in the state of São Paulo, Brazil. For data collection MOS SF-36 and EDSS scales were applied at three time points: admission of the patient, hospital discharge and 1 year posttransplantation. **Results:** 27 patients (79%) showed stabilization or neurological improvement 1 year posttransplantation. At this time point, there was statistically significant improvement in all domains of the HRQoL. When EDSS scores were correlated with the domains of the MOS SF-36 scale, statistically significant correlations were found with physical functioning at the three time points analysed. **Conclusion:** In spite of the high risk of complications of the procedure, the HSCT had positive impact in the health related quality of life.

Key words: quality of life, multiple sclerosis, bone marrow transplantation.

Impacto do transplante autólogo de células-tronco hematopoéticas na qualidade de vida de pacientes com esclerose múltipla

RESUMO

Objetivo: Avaliar o impacto do transplante de células-tronco hematopoéticas (TCTH) na qualidade de vida relacionada à saúde (QVRS) de pacientes com esclerose múltipla (EM). **Método:** A amostra foi composta por 34 sujeitos, maiores de 18 anos, atendidos em um hospital-escola do interior do Estado de São Paulo, Brasil. Para coleta de dados foram aplicados os instrumentos MOS SF-36 e EDSS. **Resultados:** 27 (79%) sujeitos apresentaram estabilização ou melhora neurológica um ano após o TCTH. Decorrido um ano do procedimento, houve melhora estatisticamente significativa em todos os domínios da QVRS. Ao relacionar os escores da EDSS com os domínios do MOS SF-36, foram encontradas diferenças estatisticamente significantes na Funcionalidade nos três momentos do TCTH. **Conclusão:** Apesar do elevado risco de complicações, pode-se afirmar que o TCTH repercutiu positivamente na apreciação que o paciente faz de sua QVRS. **Palavras-chave:** qualidade de vida, esclerose múltipla, transplante de medula óssea.

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In addition to the physical complications to which the sufferer of multiple sclerosis (MS) is subject, the psychological aspects of this disease should also be considered. The incidence of psychopathological disorders, especially depression, is high in MS and may be even higher than in other neurological and chronic disabling diseases. The results of some international studies suggest that up to one third of MS patients may have symptoms of depression¹. In the Brazilian context the prevalence of depressive symptoms in MS reaches 17.9% and anxiety symptoms, 35.7%².

Another study in 104 patients with MS showed that depression has a negative impact in all domains of the health-related quality of life (HRQoL) and anxiety has negative impact in mental domains³. Other studies show that depressive symptoms in MS correlate with fatigue⁴⁻⁶.

Another variable which influences the HRQoL in MS patients is functional disability, which is measured by the EDSS scale. In the literature, it was observed positive correlation of depression and functional impairment and negative correlation between functional impairment and HRQoL domains measured by the MOS SF-36 scale⁷.

Advances in pharmacobiological therapy for systemic autoimmune diseases (AID) have not prevented a sub-population of patients with progressive forms of these diseases, refractory to conventional therapy, having a poor prognosis. The low life quality and life expectancy of these patients justifies the use of very aggressive therapies such as high dose chemotherapy, immunotherapy and/or radiotherapy, with or without hematopoietic stem cell transplantation (HSCT)⁸.

HSCT is essentially the replacement of defective bone marrow with a healthy and efficacious one⁹. There are currently various types of HSCT, the differentiator being the source of the progenitor cells. Autologous HSCT, the object of this study, is characterized by the fact that the donor is the patient himself, who has his cells extracted during the process of remission of the disease.

Autologous HSCT appears in this scenario as a promising alternative treatment for MS. It was initially proposed as a treatment for this disease in the nineties¹⁰. Studies showed that there was a halt in the progress of the disease after three years in about 75% of cases of MS patients who underwent autologous HSCT¹¹.

However, despite the initial encouraging results, it should be noted that HSCT is not a procedure that yields full resolution. The immunosuppression induced by the preHSCT conditioning makes the patient temporarily vulnerable to many complications which impair his/her physical well being and threaten his/her life⁸.

Because it is an innovative therapy in the treatment of AID, there is an urgent need for studies that can assess not only the effectiveness of the technique, but also its impact on patients' lives. Most studies have been lim-

ited to the clinical approach, despite the wide recognition of the importance of also evaluating the emotional aspects involved when this therapy is used to treat diseases such as MS.

The assessment of the quality of life construct allows an analysis to be made, from the perspective of the patient, of the impact of a disease and of the proposed treatments. In this context, quality of life constitutes an important indicator of the ability of a chronic autoimmune disease, such as MS, to significantly affect the patient's welfare¹².

As the present study is within a biomedical field, the concept of health-related quality of life was used, which can be understood as the perceived health status. This refers to the perception of a person, with or without a disease, in relation to their state of health¹³⁻¹⁴.

Among the instruments used to assess HRQoL, the generic ones are those developed in order to reflect the impact of a disease on the lives of patients in a wide variety of populations¹⁵. Medical Outcomes Study 36-Item Short-Form Health Survey (MOS SF-36) is one of the most used questionnaires, in a health context, throughout the world.

A study of HRQoL compared the performance obtained by patients with MS in relation to the normative population and demonstrated an overall negative impact caused by the disease in all evaluated domains¹⁶. In the Brazilian context, the study compared HRQoL in MS patients with a healthy population and confirmed the hypothesis that the patients have impaired HRQoL in physical and psychosocial domains, in relation to the healthy population¹⁷.

On study performed in Brazil¹⁸ showed that autoimmune diseases by themselves lead to an intense decrease of HRQoL in patients submitted to HSCT for those diseases. In that study, pretransplant and early posttransplant results were compared in 19 patients submitted to HSCT. The evaluation indicated an improvement in the domain of physical functioning of HRQoL assessed by the MOS SF-36 scale. The improvement of some aspects of the HRQoL after transplantation, compared to the pretransplant period, was observed both in the national and international literature¹⁹⁻²⁰.

According to the literature, the variables that may influence the HRQoL in patients with MS submitted to HSCT are general mental health (anxiety and depression disorders), vitality (fatigue, tiredness, exhaustion), the EDSS score and the time from diagnosis to the procedure.

This study aims to contribute to this field of research, since, in both national and international literature, there are few studies on the quality of life of MS patients undergoing HSCT therapy, due to its high complexity and pioneering status.

The goal of the study was to evaluate the impact of the HSCT in the HRQoL of MS patients. Specifically, it

evaluated the relationship between the dependent variables time, EDSS score and HRQoL domains in MS patients submitted to HSCT.

METHOD

This is a descriptive, exploratory and clinical study, with longitudinal cross-section. The project was approved by the Ethics Committee of the Clinical Hospital, School of Medicine of Ribeirão Preto, University of São Paulo (HCFMRP No 5808/2007).

Patients

The sample consisted of 34 patients with MS, of both sexes, who had undergone autologous HSCT in the Bone Marrow Transplant Unit (BMTU) - HCFMRP-USP, between May 2003 and May 2008. The sample represents 85% of the study population. The selection criteria included having MS diagnosis; having a minimum age of 18 years; being attended on the ward and at the outpatient clinic of the BMTU during the period defined by the evaluation; presenting medical and psychological conditions; being willing to cooperate voluntarily with the research.

Instruments

[1] The Medical Outcomes Study 36-Item Short-Form Health Survey (MOS SF-36 Health Survey)²¹ is a measure of health status designed for use in clinical practice, research, health policy evaluations, and general population surveys. It is a multidimensional instrument for generic assessment of HRQoL, originally created in the English language, translated and validated for Brasil²². It consists of 36 items that assess two components: the physical health component (PHC) and the mental health component (MHC). The PHC comprises the domains: physical functioning, role limitations due to physical problems, bodily pain and general health perceptions. The MHC comprises the domains: vitality, social functioning, role limitations due to emotional problems and general mental health. The results of each domain range from 0 to 100, in which zero represents the worst state of health and 100 the best state of health²².

[2] Expanded Disability Status Scale (EDSS)²³: is a scale employed to determine functional performance in MS, translated and validated for the Portuguese language²⁴. The scale is used as a main measurement of efficacy in most clinical studies of MS, albeit it overemphasizes mobility and is less sensitive to other dimensions of the disease²⁵. EDSS values are directly proportional to the patient's neurological dysfunction.

HRQoL evaluation

Data were collected at the three critical points proposed for evaluation patient admission, hospital discharge

and 1 year after transplantation. The instruments were applied individually in a closed environment, considering the principles of comfort and privacy of the subjects of the study.

The job of scoring the MOS SF-36 data was carried out by two judges, both psychologists with expertise in psychological assessment, one of them being the researcher. They independently established the results and classified the protocols. The judges operated according to specific recommendations from the literature for correction of each instrument.

With the scored protocols, the data was tabulated using the database program *Excel for Windows*® 2007 ver-

Table 1. Numerical and percentage distribution of patients with multiple sclerosis undergoing stem cell transplantation, according to socio-demographic and clinical characteristics (n=34). Ribeirão Preto, Brazil, 2003-2008.

Socio-demographic and clinical variables	N	%
Sex		
Female	18	52.9
Age group (years)		
≤25	2	5.9
26 a 35	7	20.6
36 a 45	16	47.1
≥46	9	26.4
Conjugal status		
Without partner	13	38.2
With partner	21	61.8
Education (years)		
1 a 4	5	14.7
5 a 11	15	44.1
≥12	14	41.2
Occupational situation		
Inactive	28	82.3
Active	6	17.7
Household income (minimum wages)		
<3	7	20.6
3 a 5	14	41.2
>5	13	38.2
Religion		
Practicing	23	67.7
Non-practicing	11	32.4
Length of diagnostic (years)		
≤5	8	23.5
6 a 7	13	38.3
8 a 10	8	23.5
≥11	5	14.7
Clinical form of MS*		
RRMS	7	20.6
PPMS	5	14.7
SPMS	22	64.7

*The clinical forms of MS: RRMS-relapsing remitting multiple sclerosis, PPMS primary progressive multiple sclerosis, SPMS-secondary progressive multiple sclerosis.

sion. To achieve the objective of the study, a statistical analysis was used to evaluate the relationship of dependent variables (time of HSCT, EDSS score, vitality, general mental health, physical functioning) and independent variables (other domains of HRQoL evaluated by the MOS SF-36 scale). In order to evaluate the difference between the results obtained in the 3 time points of the study, the nonparametric Friedman test for multiple comparison was used. To evaluate the correlations between dependent and independent variables, the nonparametric Spearman correlation test was used. Significance levels used were $p \leq 0.05$ e $p \leq 0.01$.

RESULTS

Table 1 displays the social-demographic and clinical profile of the patients included in the study.

In Table 2 the results of the MOS SF-36 scores for HRQoL are shown in three periods (preHSCT, postHSCT1 and postHSCT2).

Comparing the three time points, it is observed an EDSS stabilization in 16 patients (47%), reduction of EDSS values in 11 (32%) and increase of EDSS in 5 (15%); in two patients (6%), there was progression of neurolog-

ic disability in the 2nd time point followed by improvement in the 3rd time point. In summary, in 27 out of 34 patients (79%), EDSS score established or reduced 1 year after transplantation.

Table 3 shows the correlations between EDSS values and the MOS SF-36 domains.

DISCUSSION

In relation to the clinical forms of the disease, a prevalence of progressive forms could be seen, 80.4% in total, with 64.7% of patients diagnosed with the secondary progressive form (SPMS). Relapsing remitting MS (RRMS) appeared in 20.6% of patients who comprised the sample. This result is in disagreement with the results of epidemiological studies and the clinical characterization of MS in the Brazilian context, which demonstrate a prevalence of RRMS²⁶⁻²⁸. This finding suggests that patients with more severe forms of MS are more likely and motivated to accept treatment as complex and impacting as HSCT.

Patients with long-term MS who have lived for many years with the disease have suffered sharp depreciations in their HRQoL as a result of disease progression and have tried various treatments without obtaining satisfactory re-

Table 2. Comparison between time of HSCT and the MOS SF-36 domains (n=34), Ribeirão Preto, Brazil, 2003-2008.

MOS SF-36 Domains	PreHSCT × PostHSCT1	PreHSCT1 × PostHSCT2	Post HSCT1 × PostHSCT2
	p	p	p
Physical functioning	0.09	<0.01	<0.01
Role limitations due to physical problems	0.76	<0.01	<0.01
Bodily Pain	0.50	<0.01	<0.01
General health perceptions	0.12	<0.01	<0.01
Vitality	0.28	<0.01	<0.01
Social functioning	0.99	<0.01	<0.01
Role limitations due to emotional problems	0.86	0.01	0.01
General mental health	0.48	<0.01	<0.01

HSCT: hematopoietic stem cell transplantation.

Table 3. Correlations between EDSS values and the MOS SF-36 domains (n=34), Brazil, Ribeirão Preto, 2003-2008.

MOS SF-36 Domains	preHSCT EDSS		post HSCT1 EDSS		post HSCT2 EDSS	
	p	r	p	r	p	r
Physical functioning	0.002*	-0.509	<0.001*	-0.667	0.001*	-0.534
Role limitations due to physical problems	0.464	0.130	0.344	-0.167	0.594	-0.095
Bodily pain	0.438	-0.137	0.288	-0.187	0.066	-0.318
General health perceptions	0.893	-0.24	0.314	-0.178	0.091	-0.294
Vitality	0.815	0.042	0.621	0.008	0.717	-0.065
Social functioning	0.732	-0.061	0.525	-0.113	0.187	-0.232
Role limitations due to emotional problems	0.686	-0.072	0.353	-0.164	0.518	-0.115
General mental health	0.493	0.122	0.697	-0.069	0.746	0.058

* $p \leq 0.01$

sults. Probably, these patients are tired of living with limitations, such as changes in vision, loss of balance, tremors, weakness, changes in the rhythm of speech, memory loss, among others. This makes them more motivated to undergo a radical treatment such as HSCT. Transplantation offers the possibility of a recovery of quality of life which is already highly compromised. This finding corroborates the results of other studies²⁹⁻³⁰.

In the MOS SF-36 evaluation, it is observed a significant improvement in all HRQoL domains 1 year after transplantation (period postHSCT2) but not after hospital discharge (postHSCT1).

In another Brazilian study¹⁸ comparing the results of the domains of HRQoL assessed by MOS SF-36, in patients with autoimmune diseases who received HSCT treatment, no significant differences between the pre-HSCT and post-HSCT period (30 days after the procedure) was shown. However, the authors pointed out that the patients demonstrated perception of improvement in some aspects of their HRQoL, suggesting the importance of research using a qualitative approach to identify subtle differences in the self-assessment of patients.

The perception of improvement of HRQoL in the late posttransplantation period may be related to the fact that the patients may not face the constant possibility of disease progression, translated by stabilization or improvement of neurologic function 1 year after the procedure. This result may be interpreted as a positive outcome of the HSCT for MS, measured by the evolution of the EDSS score.

Another finding of our study is a negative correlation between the EDSS score and the score of physical functioning of the MOS SF-36 scale in the three time points. This result agrees with data from the literature showing that the functional capacity estimated by the EDSS score influences the HRQoL of patients with MS³¹⁻³³.

To the extent that this stressor, so characteristic of patients with MS, is alleviated and limited by HSCT treatment, the possibility emerges to rethink work and family issues, and also to recapture some of the dreams and undertake projects that had been put aside. This shows that patients feel more excited about the chance to be able to reorganize their lives and reintegrate into society¹⁸.

One factor that must be considered when referring to the HRQoL of patients with MS, especially in its more severe forms, undergoing HSCT, is the change imposed on the way they live life. Patients recover HRQoL they had before the procedure, but not the quality of the *same life*. Perception of changes, such as greater appreciation of life, resignification of values and the seeking of closer and more satisfactory relationships being common³³. Thus, from the patients' perspective, the changes imposed by the transplantation procedure not always have negative meaning.

When affected by a progressive and disabling disease

like MS, patients feel that they have lost control of their destiny. HSCT brings relief and restores the hope of, once again, having their lives in their hands. Despite all the complications and the impact caused by this therapy, it could be argued that it reflects positively on the appreciation patients' have for their HRQoL.

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