

Implementation of a Physiotherapeutic Protocol in Hemato-Oncological Patients

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Implementação de um Protocolo Fisioterapêutico em Pacientes Hemato-Oncológicos

Implementación de un Protocolo de Fisioterapia en Pacientes Hemato-Oncológicos

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Abstract

Introduction: Hematological cancers affect the organism with several dysfunctions and physiotherapy aims to support the prevention and treatment, providing a better quality of life. **Objective:** To verify the effects of a physical therapy protocol in individuals with hematological cancer. **Method:** This is a quasi-experimental study with participants from 18 to 50 years old, of both genders, carried out at the Hospital Compound of Santa Casa de Misericórdia in Porto Alegre. A physiotherapeutic protocol was applied for four weeks according to the individual hematological stage, which was evaluated for strength, general well-being and performance, in addition to fatigue, with the following scales respectively: Medical Research Council (MRC), Karnofsky, Eastern Cooperative Oncology Group Performance Status (ECOG) and Multidimensional Fatigue Inventory (MFI) 20 - Brazilian version. **Results:** Eleven individuals were included. A significant increase of the muscle strength ($p=0.024$) was observed. The assessment of general well-being and performance revealed no significant difference ($p=0.192$) and ($p=0.368$), as well as in blood tests ($p>0.05$). In the analysis of vital signs, only the respiratory rate showed a significant increase before and after the protocol ($p=0.04$). There were significant correlations between the Karnofsky and ECOG scales ($r=-0.81$), MFI and ECOG ($r=0.64$) and MFI and Borg ($r=0.67$) with $p<0.05$. **Conclusion:** The results showed that it is possible to use a physiotherapeutic protocol that matches the hematological profile and the clinical conditions of the patient, showing correlations between several functional variables evaluated, nevertheless, more studies are needed.

Key words: Leukemia; Lymphoma; Fatigue; Physical Therapy Modalities; Exercise Therapy.

Resumo

Introdução: Os cânceres hematológicos afetam o organismo com diversas disfunções, e a fisioterapia tem o intuito de auxiliar na prevenção e no tratamento, proporcionando uma melhor qualidade de vida. **Objetivo:** Verificar os efeitos de um protocolo fisioterapêutico em indivíduos com câncer hematológico. **Método:** Trata-se de um estudo quase-experimental, com participantes de 18 a 50 anos de idade, de ambos os sexos, realizado no Complexo Hospitalar da Santa Casa de Misericórdia de Porto Alegre. Aplicou-se um protocolo fisioterapêutico por quatro semanas, conforme o estágio hematológico individual, no qual foram avaliados força, bem-estar geral e performance, além de fadiga, respectivamente, com as escalas: *Medical Research Council (MRC)*, *Karnofsky*, *Eastern Cooperative Oncology Group Performance Status (ECOG)* e *Multidimensional Fatigue Inventory (MFI) 20 - versão brasileira*. **Resultados:** Foram incluídos 11 indivíduos. Verificou-se um aumento significativo da força muscular ($p=0,024$). Na avaliação do bem-estar geral e performance, não houve diferença significativa ($p=0,192$) e ($p=0,368$), assim como nos exames sanguíneos ($p>0,05$). Na análise dos sinais vitais, apenas a frequência respiratória apresentou aumento significativo no pré e pós-protocolo ($p=0,04$). Houve correlações significativas entre as escalas de Karnofsky e ECOG ($r=-0,81$), MFI e ECOG ($r=0,64$) e MFI e de Borg ($r=0,67$), com $p<0,05$. **Conclusão:** Os resultados mostraram que é possível utilizar um protocolo fisioterapêutico que se adapte ao perfil hematológico e às condições clínicas do paciente nessa área, existindo correlações entre diversas variáveis funcionais avaliadas, contudo mais estudos são necessários.

Palavras-chave: Leucemia; Linfoma; Fadiga; Modalidades de Fisioterapia; Terapia por Exercício.

Resumen

Introducción: Los cánceres hematológicos afectan al organismo con diversas disfunciones y la fisioterapia tiene como objetivo ayudar en la prevención y el tratamiento, proporcionando una mejor calidad de vida. **Objetivo:** Verificar los efectos de un protocolo de fisioterapia en personas con cáncer hematológico. **Método:** Se trata de un estudio quasi-experimental, con participantes de 18 a 50 años, de ambos sexos, realizado en el Complejo Hospitalario de la Santa Casa de Misericórdia de Porto Alegre. Se aplicó un protocolo de fisioterapia durante cuatro semanas según la etapa hematológica individual, que se evaluó en cuanto a fuerza, bienestar general y rendimiento, además de la fatiga, respectivamente, con las siguientes escalas: *Medical Research Council (MRC)*, *Karnofsky*, *Eastern Cooperative Oncology Group Performance Status (ECOG)* e *Inventario de Fatiga Multidimensional (MFI) 20 - versión brasileña*. **Resultados:** Se incluyeron 11 individuos, en los que hubo un aumento significativo de la fuerza muscular ($p=0,024$). En la valoración del bienestar general y el rendimiento se encontraron sin diferencia significativa ($p=0,192$) y ($p=0,368$), así como en los análisis de sangre ($p>0,05$). En el análisis de constantes vitales, solo la frecuencia respiratoria mostró un aumento significativo antes y después del protocolo ($p=0,04$). Hubo correlaciones significativas entre las escalas de Karnofsky y ECOG ($r=-0,81$), MFI y ECOG ($r=0,64$) y MFI y Borg ($r=0,67$) con $p<0,05$. **Conclusión:** Los resultados mostraron que es posible utilizar un protocolo fisioterapêutico que se adapte al perfil hematológico y a las condiciones clínicas del paciente en esta área, mostrando correlaciones entre varias variables funcionales evaluadas, sin embargo son necesarios más estudios.

Palabras clave: Leucemia; Linfoma; Fatiga; Modalidades de Fisioterapia; Terapia de Ejercicio.

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INTRODUCTION

Hematopoietic and lymphoid tissues suffer changes in hematologic cancers¹. Overall, an abnormal production of blood and defense cells occurs, causing neutropenia or pancytopenia. These changes impact the organism with several symptoms as weakness, fatigue, fever, weight loss, respiratory infections, spontaneous bruises and bleeding^{2,3}. The current treatment consists in fighting the malignant cells to minimize them but adverse effects occur in healthy cells, making the individual prone to develop disease-related comorbidities, aggravated by side effects resulting from chemotherapy, radiotherapy, hormone therapy or autologous stem-cells transplantation⁴.

It is known that fatigue is one of the symptoms the individuals report at the most, it is severe and prolonged, disproportional to the type of activity performed and does not diminishes with rest. The disease or the effects of the treatment cause this symptom, some studies concluded it tends to increase as the duration of the treatment prolongs⁵⁻⁸. Another motive for fatigue is the reduction of daily physical activity⁹. Those who experience this lifestyle undergo psychosocial symptoms as anguish, anxiety, depressive mood and sleeping disorders¹⁰.

Cancer symptoms and treatment side effects jointly with prolonged hospitalization cause immobilism. Consequently, the functioning capacity and tolerance to daily life activities diminishes^{9,11}. Therefore, the inter-disciplinary follow up has the objective of helping the prevention and treatment since these changes affect the quality of life during and after admission mostly. Among the objectives of physiotherapy, the following proposals can be found: keep the respiratory and musculoskeletal system unharmed, improve the quality of life and reclaim possible functional limitations and impairments appeared during this phase^{12,13}. In the case of hematological patients, the main change affecting physiotherapy directly is pancytopenia. Due to this clinical alteration, the consultation of this specialty must be conducted carefully, it is paramount to verify the patient's lab tests levels and based in this analysis, elaborate proper treatment.

Because of these circumstances, the ideal exercises programs for this patient profile are still unknown¹⁴. In addition, until now, studies utilizing blood count as base for the consultation were not encountered. For this reason, in order to determine effective and safe care protocols, the study has the objective to verify the effects of a physiotherapeutic protocol in individuals with hematologic cancer.

METHOD

Quasi-experimental study approved by the Institutional Review Board of “*Irmandade Santa Casa de Misericórdia*” of Porto Alegre and “*Centro Universitário Metodista IPA*” numbers CAAE 98819018.3.0000.5335 and 98819018.3.3001.5308, respectively in compliance with Resolutions 466/12 and 510/16.

The study was developed by convenience sample at the Admission Unit of Hospital Santa Rita, within the Hospital Complex of “*Santa Casa de Misericórdia*” of Porto Alegre with individuals between 18 and 50 years old of both genders with confirmed clinical diagnosis of hematologic cancer. All the individuals with confirmed clinical diagnosis of bone fracture, neural compression, central nervous systems disorders (Parkinson disease, Alzheimer disease, multiple sclerosis), stroke, neuropathic and/or rheumatologic diseases, musculoskeletal alterations (cachexia, sarcopenia) and inability to respond to questionnaires were excluded.

The protocol of physiotherapeutic consultation was applied for a period of four weeks with weekly frequency of five consultations and duration of 30 minutes each, reaching 20 consultations. In the first moment, a complete evaluation with application of four scales was carried out: Medical Research Council (MRC) to measure the grading of strength of the main muscle groups^{15,16}; Karnofsky (EK) and Eastern Cooperative Oncology Group Performance Status (ECOG) to evaluate the general well-being and performance^{17,18}; and, finally, the Multidimensional Fatigue Inventory (MFI) 20 (Brazilian version), multidimensional scale of fatigue in different dimensions (general, physical, mental, reduced activity and reduction of motivation)^{19,20}. During the other follow up, heart rate, respiratory rate, oxygen peripheral saturation, artery rate were monitored in pre-consultation and in the end, all these variables added to Borg scale of perceived exertion²¹. All the consultations were conducted in the room or corridor of the hospital.

The protocol of exercises was based in the hematologic condition of the patient. Due to this, before the consultation, the blood count was checked and verified the values/levels of hemoglobin (Hb), hematocrit (Ht) and platelets. According to the values presented, four stages of exercises were used:

STAGE I (PLATELETS BELOW 20 THOUSAND/MM³ OR HB BELOW 8 G/DL OR HT BELOW 25%. THE APPROVAL OF THE PHYSICIAN IN CHARGE WAS REQUESTED)

In supine, ten repetitions of active exercise of plantarflexion, active exercise of knee extension, active exercise of wrist flexion and extension and sedestation at the bedside.

STAGE II (PLATELETS FROM 21 TO 30 THOUSAND/MM³ OR HB FROM 8.1 TO 10 G/DL OR HT FROM 25% TO 35%)

In sedestation, ten repetitions of active exercise of plantarflexion, active extension of knees, active exercise of hips flexion, active exercise of shoulders flexion until 90°, active exercise of elbows flexion, active diagonal extension exercise of shoulders, active exercise of flexion extension of wrists, active exercise of flexion extension of wrists and ambulation in marked 80 meters corridor.

STAGE III (PLATELETS FROM 31 TO 50 THOUSAND/MM³ OR HB ABOVE 10 G/DL OR HT ABOVE 35%)

In orthostasis, 15 repetitions of active exercise of plantar flexion, active exercise of triple hips flexion, active exercise of hips abduction, active exercise of knees flexion, active exercise of shoulder up to 90°, active exercise of shoulder abduction up to 90°, active exercise of elbows flexion, climbing one flight of stairs and ambulation in the demarcated corridor with covered distance of 160 meters.

In stages I and II, free active exercises were conducted with gravitational resistance only.

STAGE IV (PLATELETS ABOVE 51 THOUSAND/MM³)

In orthostasis, 15 repetitions with shin guard of 0.5kg in upper and lower limbs of active exercise of plantarflexion, triple flexion hip active exercise, active exercise of hips abduction, active exercise of knee flexion, semi-squatting, active exercise of shoulder flexion up to 90°, active exercise of shoulder abduction up to 90°, active exercise of elbow flexion, climb up two flights of stairs and ambulation in the demarcated corridor with a covered distance of 200 meters.

The values of the variables distributed normally based in the data were presented as mean and standard-deviation or median and interquartile range for the results that did not meet this hypothesis. The normality was verified through the Shapiro-Wilk test. Results of the qualitative variables were expressed by frequency and percent. The evolution of the parameters in the end of the treatment in comparison with the beginning was determined by test t for paired samples, Wilcoxon test and McNemar test according to the nature and distribution of variables. Results were considered significant when $p < 0.05$. Test of Cohen was used to analyze the effect size, below 0.3 was considered small value and above 0.7, large effect size. The correlations among the evolutions of scales were evaluated by the Spearman correlation coefficient. Values of R above 0.7 were considered strong associations and below 0.5, weak association. SPSS version 25 was utilized for the analyzes.

RESULTS

38 individuals with diagnosis of hematologic cancer were hospitalized during the period of data collection, but 16 did not meet the inclusion criteria. During the application of the protocol, four were transferred to the intensive care unit, three did not join the study and four were discharged from hospital, resulting in 11 patients as described in Table 1.

Table 1. Sample characterization (n=11)

Characteristics	Mean ± SD
Age (years)	33.2 ± 9.9
Weight (kg)	71.3 ± 14.5
Characteristics	N (%)
Gender	
Female	5 (45.5)
Male	6 (54.5)
Type of Cancer	
Acute myeloid leukemia	3 (27.3)
Acute lymphoid leukemia	3 (27.3)
Acute promyelocytic leukemia	1 (9.1)
T-lymphoblastic lymphoma	1 (9.1)
Chronic myeloid leukemia	1 (9.1)
Diffuse large B cells lymphoma	1 (9.1)
Lymphocytic lymphoma	1 (9.1)

Caption: SD: Standard deviation.

The results shown in Table 2 revealed muscle strength, Borg-scale of perceived exertion and pre and post intervention protocol multidimensional scale variables. For muscle strength results, the effect size was moderate ($d=0.78$), like general fatigue ($d=0.6$), despite this variable had no statistical significance ($p > 0.05$).

According to EK evaluation of general well-being, the values moved from 86.4 ± 6.7 to 89.1 ± 7.0 in the end of the intervention protocol, but without significant difference ($p=0.19$). On the ECOG scale, evaluating the performance initially, there were eight (72.3%) participants with strict restriction of physical activities (ECOG 1); of these, three (37.5%) continued within this classification, two (25%) started to be fully active (ECOG 0) and the other three (37.5%) evolved to unable to perform any labor activity (ECOG 2). The other three (27.7%), who were ECOG 2 initially, changed to ECOG 1, however, the alterations had no statistical significance ($p=0.36$).

Blood results did not present statistically significant changes, increase of Hb and reduction of Ht, platelets and leukocytes occurred as shown in Table 3.

While analyzing the vital signs, respiratory frequency had significant increase at rest (11.8 ± 1.0 vs 12.8 ± 1.2 , $p=0.04$) and post-protocol evaluation (15.2 ± 1.8 vs 16.5 ± 1.5 , $p=0.04$). Diastolic blood pressure at rest (11.0 ± 12.6 vs 11.5 ± 8.2 , $p=0.16$) and post-protocol (12.0 ± 11.0 vs 12.9 ± 7.0 , $p=0.72$) did not change like the systolic (71.8 ± 7.5 vs 76.4 ± 11.2 , $p=0.21$) and (79.1 ± 7.0 vs 83.6 ± 9.2 , $p=0.09$). Heart frequency at rest (95.7 ± 15.9 vs 83.7 ± 10.2 , $p=0.08$) and post-protocol (101.6 ± 17.6 vs 97.7 ± 12.7 , $p=0.57$) did not present significant alterations either.

In Table 4, the correlations of performance per EK, ECOG, MFI and Borg are found.

DISCUSSION

It was attempted in this study to verify the effects of hospital care protocol in individuals with hematologic cancer. It is known that in this format is a pioneer study where it is possible to find relevant data in some aspects as the increase of muscle strength and correlations between the several functioning variables evaluating the well-being, different fatigue dimensions and perceived exertion through scales utilized in the area.

The sample consisted of males mainly with mean age of 33.2 years with acute myeloid leukemia and acute

Table 2. Pre and post of muscle strength comparison, perceived exertion, and multidimensional scale

Scales	Initial (Mean \pm SD)	End (Mean \pm SD)	p-value
MRC	52.8 \pm 5.4	56.5 \pm 2.2	0.024*
Borg	1 (0 – 3)#	0.5 (0 – 3)#	0.734
MFI 20			
General fatigue	11.3 \pm 1.4	10.7 \pm 2	0.432
Physical fatigue	13.1 \pm 0.9	13.8 \pm 2.4	0.356
Reduced activity	11.3 \pm 2.6	12.4 \pm 1.4	0.227
Reduced motivation	12.0 \pm 1.7	11.6 \pm 1.4	0.650
Mental fatigue	10.9 \pm 2	11.2 \pm 2.2	0.635

Captions: SD: Standard deviation; MRC: Muscle Strength Scale; Borg: Perceived exertion; MFI 20: Multidimensional Fatigue Inventory; # Quartile * $p<0.05$.

Table 3. Pre and post-intervention of blood test comparison

	Beginning Median (1 st and 3 rd quartile)	End Median (1 st and 3 rd quartile)	p-value
Hematocrit	24.9 (20.8 - 33.1)	23.5 (22.4 - 25.1)	0.657
Hemoglobin	7.7 (6.7 - 11)	7.9 (7.7 - 8.2)	0.110
Platelets	136 (26 - 330)	133 (30 - 226)	0.423
Leukocytes	5.5 (2.1 - 18.8)	4.0 (1.4 - 5.7)	0.374

Table 4. Correlations between the performance of the scales (correlation coefficient r_s)

	KS	ECOG	GF	PF	RA	RM	MF	Borg
MRC	-0.42	-0.04	-0.05	-0.19	-0.33	0.52	-0.12	0.09
KS		-0.81*	0.34	-0.00	-0.18	-0.45	-0.32	0.06
ECOG			-0.23	0.28	0.29	0.09	0.64*	0.13
GF				-0.17	0.11	-0.28	0.14	0.67*
PF					-0.11	0.17	0.27	-0.11
RA						0.20	0.35	-0.22
RM							0.07	-0.45
MF								0.28

Captions: KS: Karnofsky scale; ECOG: Eastern Cooperative Oncology Group Performance Status; MRC: Muscle strength scale; Borg: Perceived exertion; GF: General fatigue; PF: Physical Fatigue; RA: Reduced Activity; RM: Reduced Motivation; MF: Mental fatigue; * $p<0.05$ (Spearman correlation coefficient).

lymphoid leukemia as major cancer types. A similar study was found with 17-individuals sample, mostly males with acute myeloid and lymphoid leukemia²².

Cancer causes physiological changes as weight loss, body modifications and reduction of body lean mass. A 12-week randomized controlled study, physical exercises focused in muscle reinforcement were performed with beneficial outcomes to the patients²³. This result concurs with the present study where MRC increase was found and moderate effect size after the end of the protocol, since all the exercises were targeted to the main muscle groups, using body weight or 0.5 kg weights.

In counterpart, while analyzing the gain of muscle strength with the individual's well-being, an inversely proportional correlation was found because while muscle strength increased, the well-being did not show significant alteration. It is possible to justify this result with the physical changes the participants experienced during the hospitalization, together with the anguish they feel along the course of the treatment, their adverse reactions, and the expectation of reaching its goal of cure. In a study conducted after stem-cells transplantation, results corroborating the present study were found, whose interventions of exercises associated to stress management and groups that performed only exercises or only management and significant changes in well-being were not found. Further to the anguish of the treatment, the motives are associated to the short time the patient has to recover from transplantation generated symptoms and by the fact of the intervention is not customized to the individual profile, which reduces the adherence of the activity²⁴.

Klepin et al.²⁵ also suggest in their study that strategies to improve the adherence of the participants to the exercises should be used as the conditions change frequently. The present study was developed with the purpose of matching to the current status of the individual and try to improve the adherence to the treatment, since they experience several symptoms and side effects. Due to this, a safe and flexible protocol was applied with daily consultations, alternating shifts with program of activities that could be performed in the room or corridor of the hospital.

In addition, the symptoms contribute to extend the period in bed and reduce the daily activities performed; therefore, it is believed that said results obtained can explain the non-significance in the dimensions of fatigue evaluated with the scale MFI, because there are results whose individuals report that side effects are obstacles that hinder the performance of activities, including exercises²⁶.

Fatigue is one of the symptoms patients report at the most, affecting the quality of life and reducing the rhythm

of physical activity. In this study, no statistically significant improvement was found in general fatigue, despite the clinically moderate reduction reached by the effect size. This result was reinforced with the significant, moderate positive correlation found between general fatigue and perceived exertion evaluated through Borg scale. These results concur with the study's which noticed that exercise could improve fatigue, but further investigation is required²⁷. There is a systematic review addressing the analysis of 18 studies and demonstrates that exercise brings moderate benefits to improve fatigue and quality of life²⁸.

Regarding blood tests, significant alterations were not found, as opposed to the results of Jönsson et al.²⁹, who showed significant increases in leukocytes, granulocytes, and lymphocytes in blood draws. Nevertheless, the individuals were submitted to effort test in an electronic cycloergometer at 60rpm and progressive increase of workload. This test was interrupted at maximum exhaustion and blood sample was drawn at different moments pre and post-tests, possibly explaining this alteration in blood values, which was not observed in the present study. May be this finding has occurred due the different nature of the exercises that, in the study, were limited to kinesiotherapy and lower aerobic demand.

Finally, a positive, strong, and significant correlation was obtained among the scales evaluating the well-being and performance. They are utilized often in oncology and ECOG was already used at the service, reason for which it was used in this study to verify its compatibility. In 1982, in the study that brought the ECOG standardized criteria it was reported that, for general evaluation of the patient status, it is used the performance status and, therefore, both scales are compatible regarding the definitions, confirming the findings of the current study¹⁸. Still, the dimension of the mental fatigue of MFI had positive moderate and significant correlation with ECOG, whose participants with low well-being were more fatigued. However, studies which carried out this correlation to compare findings of this study were not found. More studies should be conducted as the scarce number of participants and lack of controlled randomized study do not allow a wide generalization of the results.

CONCLUSION

The physiotherapeutic protocol with the regularity of exercises in individuals with hematologic cancer during the period of hospitalization brought favorable results to the increase of muscle strength and correlations among several functioning variables through scales utilized in this health area. Therefore, it was concluded that it is possible to utilize a protocol that matches the hematologic

profile and to the patient's clinical conditions; however, robust studies are necessary to confirm and generalize these findings.

CONTRIBUTIONS

All the authors contributed for study conception and/or design, collection, analysis and interpretation of data, wording, critical review and approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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