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Multi-segment bioimpedance in the evaluation of treatment for secondary lower limb lymphedema: Gynecological cancer

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ABSTRACT

Aim: The present aimed study was to report the mobilization of body fluids after five days of intensive treatment for secondary lower limb lymphedema.

Materials and methods: A crossover clinical trial was conducted involving the analysis of changes in intracellular and extracellular fluids in all extremities and the trunk in women with lower limb lymphedema secondary to treatment for gynecological cancer. Evaluations were performed with multi-segment bio impedance analysis before and after intensive treatment using Godoy Method® eight hours per day for five days. Comparisons were made using Wilcoxon signed-ranks test.

Results: Significant changes in intracellular and extracellular fluids were found in all extremities and the trunk ($p<0.0001$ for all comparisons).

Conclusion: Intensive Godoy Method® leads to important changes in the distribution of body fluids in the treatment of lower limb lymphedema following treatment for gynecological cancer, with a significant increase in fluids in the upper limbs and trunk as well as significant reductions in the lower limb and in intracellular and extracellular water.

Keywords: bioimpedance, secondary, lymphedema, lower limbs, treatment, evaluation

INTRODUCTION

Lymphedema is one of the major complications of oncologic treatment. Resulting from a deficiency in the lymphatic system (formation and/or drainage of lymph), leading to the accumulation of macromolecules in the interstitial space and the consequent retention of fluids. The origin may be congenital or acquired; treatment for cancer is one of the main causes of secondary lymphedema in further advanced countries [1-3].

The incidence of lymphedema secondary to treatment for cancer varies widely depending on the location of cancer and treatment modalities, with estimates ranging from five to 83% with different types of cancer [3]. In a pilot study, the 12-month cumulative incidence of lymphedema resulting from treatment for gynecological cancer was 31% and the average time after treatment for the development of lymphedema was 3.2 months [4]. Biopsy of the sentinel lymph node is associated with a reduction in the risk of post-treatment lymphedema in comparison to lymphadenectomy in patients submitted to surgical staging for endometrial carcinoma [5].

The main factors associated with secondary lower limb lymphedema are gynecological cancer, age, disease stage, radiotherapy, number of lymph nodes invaded (for patients with cervical cancer), number of lymph nodes removed (for patients with cervical cancer) and obesity, the most important of which are obesity and the number of lymph nodes removed [6].

One study found that treatment for secondary lower limb lymphedema improves the quality of life of women following surgery for uterine cancer [7]. Early prevention with complex physical therapy combined with rehabilitation exercises reduced the incidence of lower limb lymphedema, improved the quality of life of the patients and reduced the occurrence of cancer-related fatigue [8]. Study randomized clinical trial was carried out with the objective of evaluating the efficacy of the modified complex decongestive physiotherapy, (self-manual lymphatic drainage) for the reduction of risk of secondary lymphedema of the lower limbs after laparoscopy radical hysterectomy with pelvic lymphadenectomy for the treatment of cervical cancer report appears to have detected 70% less lymphedema add compared to the control group [9].

Several approaches to treatment for lower limb lymphedema have been reported in the literature. However, an intensive form of treatment, denominates Godoy Method®, proposes a reduction in the volume of the limb by approximately 50% in five days and reaching normality or near

normality by the end of the first phase of treatment [10-13]. A variety of methods for limb volume evaluation are reported in the literature. Regarding diagnostic exams that measure volume, volumetry “gold standard” using the water displacement method, the measurement of circumferences and bioimpedance analysis that has emerged as a non-invasive method to measure limb volume, has been primarily studied as a diagnostic tool for lymphedema [10, 14, 15]. Multi-segment, multi-frequency bioimpedance enables a more specific evaluation of each limb. Multi-segment bioimpedance advantages to identification of early lymphedema include the potential to prevent progression to clinical lymphedema.

The present study aimed to report the mobilization of body fluids during intensive treatment for lower limb lymphedema.

MATERIALS AND METHODS

Population and Setting

The sample was composed of 96 women with secondary lower limb lymphedema submitted to intensive treatment. The mean age was 49.9±15.38 years (range: 31 to 71 years). Evaluations and treatment were performed at the Clinica Godoy, São Jose do Rio Preto, Brazil.

Design

A clinical crossover study was conducted involving the measurement of intracellular and extracellular water in all extremities and the trunk in 96 women with lower limb lymphedema following treatment for gynecological cancer. Evaluations were performed with multi-segment bioimpedance analysis before and after intensive treatment using Godoy Method® eight hours per day for five days. Comparisons were performed using Wilcoxon signed ranks test.

Inclusion Criterion

Patients with lower limb lymphedema following treatment for gynecological cancer.

Exclusion Criteria

Primary lymphedema or other causes of edema diagnosed clinically and currently with any infection.

Statistical Analysis

Descriptive statistical analysis of the data was performed, and Wilcoxon signed ranks test paired t-test was used for the comparisons, considering a 5% alpha error.

Randomization

A crossover study with inclusion of the participants consecutively upon arrival at the clinic.

Development

The patients sought the clinic with a history of lower limb edema following treatment for gynecological cancer. The patient history and physical examination confirmed lower limb lymphedema. Volumetric analysis was performed using the water displacement method, multi-segment, multi-frequency bioimpedance analysis (*InBody S10*), circumference measurements, and body weight. Other clinical abnormalities were investigated, but lymphedema was the main reason for seeking treatment. Intensive therapy, using Godoy Method® was proposed, with eight hours per day for five consecutive days (40 hours of treatment). Treatment consisted of 20 minutes per day of cervical lymphatic therapy (approximately 30 gentle surface movements of 0.5 cm in the cervical region), eight hours of mechanical lymphatic therapy using RAGodoy® device, which is an electromechanical device that performs 28 passive plantar flexion and extension movements per minute and a compression mechanism (hand-crafted stocking made of grosgrain [non-elastic] fabric that permitted adjusted to accompany the reduction in volume). On the first day, bandages (short elasticity) while the wearing hand-crafted stocking (gorgurão stocking). After treatment, the volumetric evaluations were performed again, but we only describe the bioimpedance results in the present study. The data were entered into a table of the Excel program and the Stats Direct 3 program was used for the statistical analysis.

RESULTS

Significant changes in intracellular and extracellular water were found in all extremities and the trunk after treatment ($p<0.0001$ for all evaluations, except the normal limb and intracellular water [$p<0.04$ and 0.01, respectively]).

Table 1 and **Table 2** display data from the descriptive statistics before and after treatment.

Table 3 displays the results of the statistical analysis.

Figure 1 shows the box and whisker plot of the bioimpedance analysis of extremities and trunk before and after treatment.

Figure 2 shows the box and whisker plot of the lower limbs with and without lymphedema.

Table 1. Descriptive statistics of fluids–Total body water & water in extremities & trunk

Variables	Total body water		Right arm		Left arm		Trunk		Right lower limb		Left lower limb	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Valid data	96	96	96	96	96	96	96	96	96	96	96	96
Mean	32.28	31.51	1.46	1.56	1.43	1.53	13.63	14.21	6.59	5.76	7.02	6.19
Median	33.15	32.40	1.46	1.53	1.46	1.50	13.80	13.90	5.64	5.54	5.76	5.43

Table 2. Descriptive statistics of changes in intracellular & extracellular water in lower limb with & without lymphedema

Variables	Lower limb lymphedema		Normal	
	Before	After	Before	After
Valid data	60	60	36	36
Mean	7.95	6.68	5.10	5.03
Median	7.52	6.17	5.13	5.10

Table 3. Results of Wilcoxon signed ranks test–Comparisons before & after treatment

Variables	TBW	Right arm	Left arm	Trunk	RL	LL	Lymphedema	Normal	ICW	ECW
	B/A	B/A	B/A	B/A	B/A	B/A	B/A	B/A	B/A	B/A
p-value	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0400	0.0100	0.0001

Note. TBW: Total body water; RL: Right lower limb; LL: Left lower limb; ICW: Intracellular water; ECW: Extracellular water; & B/A: Before/after;

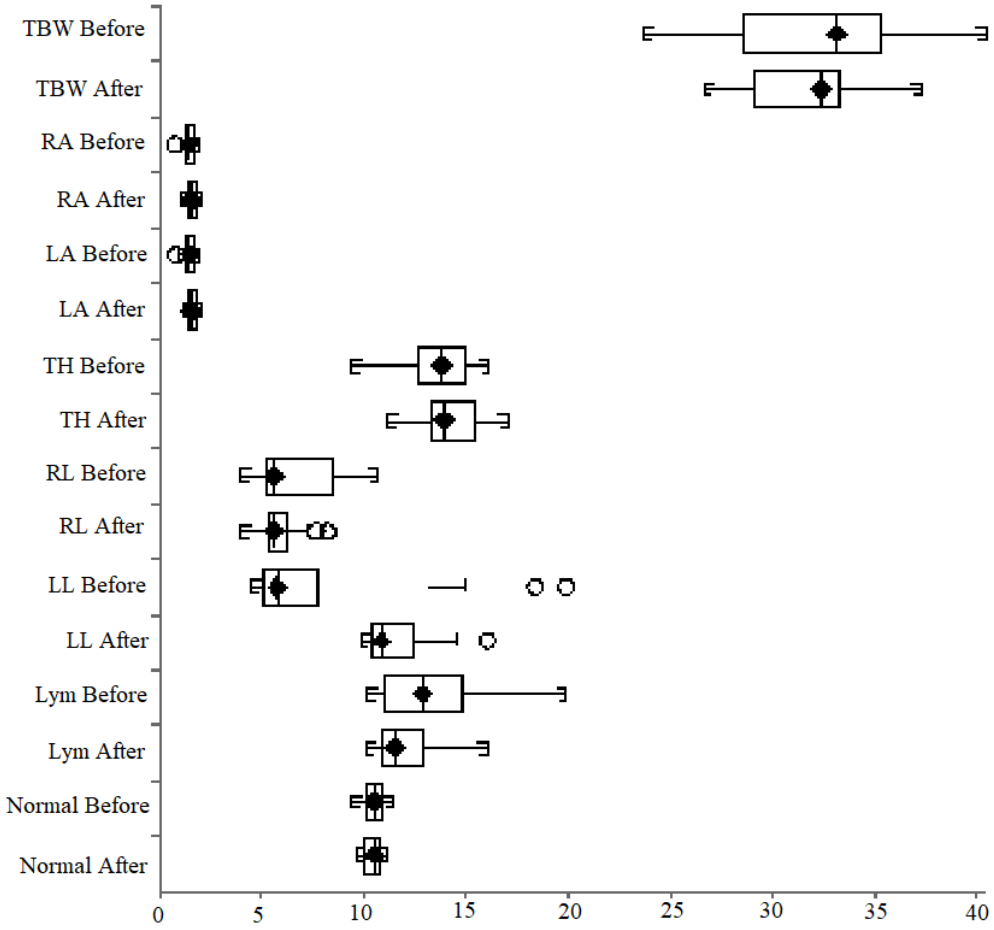

Figure 1. Comparing interquartile ranges of impedance at different frequencies before & after five days of treatment (Source: Authors' own elaboration)

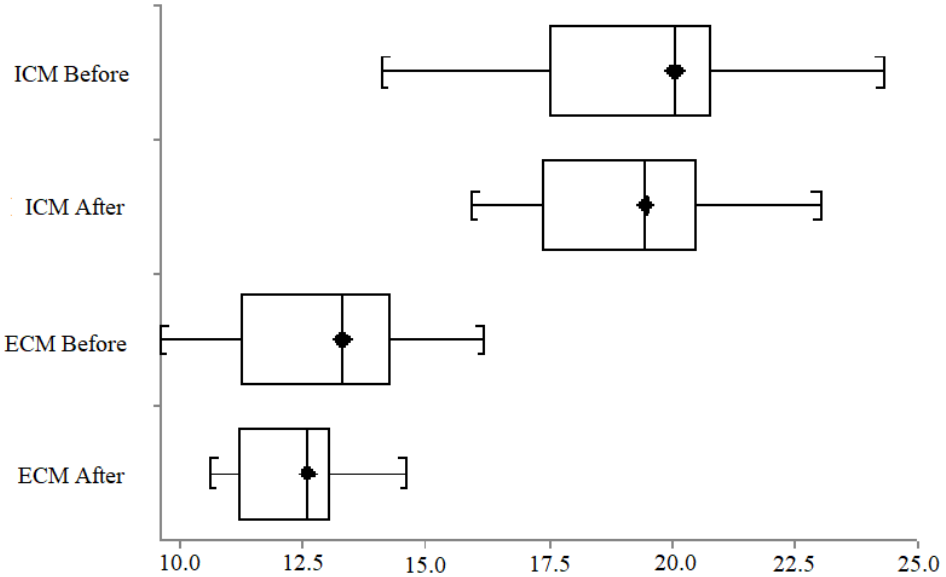

Figure 2. Comparing interquartile ranges of impedance ICW & ECW at different frequencies before & after five days of treatment (Source: Authors' own elaboration)

DISCUSSION

The present study shows the significant mobilization of body fluids after five days of intensive treatment with Godoy Method® in women with lower limb lymphedema secondary to treatment for gynecological cancer. Reductions occurred in the fluids of the lower limbs, with a more significant reduction in the limb with lymphedema and increases occurred in the upper limbs and trunk. Significant reductions were also found in extracellular and intracellular fluid. No previous studies in the literature have performed such an analysis. Therefore, the present investigation offers novel information.

Over the years, the results of multi-segment bioimpedance have highlighted certain noteworthy findings. The change in total body water was constant, although treatment was focused on the lower limbs. Intensive treatment with Godoy Method® leads to an average reduction of 50% in the volume of the limb with lymphedema in five days, reaching a reduction in weight of up to five kg in one day and 25 kg in five days. Thus, large volumes of fluid are being mobilized in this period. The first questions regard the fate of this fluid. Patients undergoing intensive treatment need to go to the toilet constantly and a large amount of this loss occurs through urination.

When we analyze physiopathology, lymphedema is associated with the accumulation of macromolecules in the interstitial space. Adequate treatment must exert a significant effect on this physiopathological process by mobilizing these macromolecules into the blood stream. The fluid is normally eliminated through urine but can be redistributed throughout the body, as suggested by the results of the present study.

An important observation regarding intensive treatment is the need to maintain compression at night. Otherwise, the limb tends to increase in volume. If the patient is not in intensive treatment, rest at night leads to a reduction in edema. The quantification of the results has confirmed this observation. These findings suggest that, during intensive therapy, the macromolecules are sent to the bloodstream and can return their place of origin. Thus, better results are achieved in these patients when compression is maintained at night.

The proposal of Godoy Method® is the normalization or near normalization of lymphedema in all clinical stages, including elephantiasis, upon the completion of treatment. In clinical evaluations, the reversal of the edema and fibrosis is undeniable, and we are currently performing biopsies before and after the clinical normalization of lymphedema.

The initial results show significant changes in type I and III collagen fibers, reticular fibers, and the epidermis, along with a novel cell type: telocytes [16, 17]. Therapeutic progress depends on novel concepts and techniques with better results. However, each novel finding in clinical practice merits a scientific evaluation. In the present study, we identified that intensive treatment for lymphedema has systemic repercussions and is not merely a localized effect.

CONCLUSION

Using Godoy Method®, the intensive treatment of lower limb lymphedema secondary to treatment for gynecological cancer results in important changes in the distribution of body fluids, with significant reductions in fluids in the lower limbs as well as intracellular and extracellular water, along with increases in the trunk and upper limbs.

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Ethical statement: Authors stated that the study received ethical approval from the Institutional Review Board of the São Jose do Rio Preto School of Medicine #2.003.952.

Declaration of interest: No conflict of interest is declared by authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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