Online ISSN: 2581-3935
Print ISSN: 2589-7837

International Journal of Medical Science and Diagnosis Research (IJMSDR)

Available Online at www.ijmsdr.com

Volume 2, Issue 6; November-December: 2018; Page No. 11-18

Lymphedema in patients in different BMI ranges and therapeutic response to intensive treatment

Jose Maria Pereira de Godoy, MD, PhD[1], Henrique Jose Pereira de Godoy[2], Ana Carolina Pereira de Godoy, MD[3], Maria de Fatima Guerreiro Godoy, OT, PhD[4]

[1]Cardiology and Cardiovascular Surgery Department of the Medicine School in São José do Rio Preto (FAMERP), CNPq (National Council for Research and Development)-Brazil

[2]Student of Medicine School of Universidade Federal do Mato Grosso-Cuiabá-UFMT and Research Group in the Clínica Godoy, Sao Jose do Rio Preto, Brazil

[3]Resident of the Pediatrics Unit Intensive Therapy of Santa Casa de São Paulo, Brazil and Research Group of Clínica Godoy, São Jose do Rio Preto, Brazil

[4]Occupational Therapist professor of the Post-Graduate *Strictu Sensu in*, Medicine School in São José do Rio Preto (FAMERP) and Research Group in the Clínica Godoy, Sao Jose do Rio Preto, Brazil

ABSTRACT:

The aim of the present study was to evaluate the therapeutic response to intensive treatment for lymphedema in different body mass index (BMI) ranges (25 to 30, 30 to 40 and > 40 kg/m^2). A cross-sectional study was conducted involving 59 patients with grade III lower limb lymphedema (elephantiasis) who arrived consecutively at the Godoy Clinic in São Jose do Rio Preto, Brazil. The diagnosis was based on the clinical history, physical examination as well as intracellular and extracellular volumes, which were determined using electrical bioimpedance analysis (InBody S10 device). Statistical analysis involved the paired t-test and Kruskal-Wallis test with the Conover-Inman post hoc test, considering an alpha error of 5%. **Results:** Significant increases in intracellular and extracellular water were detected with the increase in BMI range. Intensive treatment led to significant reductions in intracellular and extracellular water in all BMI ranges, with the exception of intracellular water in the 25-to-30 kg/m^2 range.

Key words: Lymphedema, obesity, body mass index, bioimpedance, treatment.

Introduction

The buildup of macromolecules in the interstitial space results in the accumulation of fluids, which leads to a specific type of edema denominated lymphedema. Primary and secondary alterations of the lymphatic system are described. The former denotes an abnormal lymphatic system present from birth and the latter emerges throughout the course of one's life.[1,2]

A clinical history and physical examination are generally sufficient for the diagnosis, but complementary exams may be requested in cases of doubt. Lymphoscintigraphy enables a functional and anatomic analysis, but volumetric analyses are needed to confirm clinical lymphedema. For such, volumetry, perimeter measurements and electrical bioimpedance are used.[2,3]

Among the therapeutic options, a combination of different therapies enables faster results. However, isolated forms may be indicated according to each case. Intensive outpatient therapy can lead to an approximately 50%

Corresponding author: Jose Maria Pereira de Godoy

reduction in edema in five days.[2] Therapy may involve manual and mechanical lymphatic drainage, compression mechanisms, exercise and lymphomyokinetic activities.[4-9]

The body mass index (BMI) is the most commonly used diagnostic measure of obesity. This index is calculated by dividing weight by height squared (kg/m^2). According to the World Health Organization, the ideal range for BMI is 18.5 to 24.9.[8] Electrical bioimpedance analysis (BIA) is a body composition assessment method that enables the determination of intracellular and extracellular fluids as well as fluids of the limbs and thorax.[9]

The aim of the present study was to evaluate the therapeutic response to treatment for lymphedema in different BMI ranges (25 to 30, 30 to 40 and > 40 kg/m^2).

Methods

Patients

Fifty-nine patients with clinical stage III lower limb lymphedema were evaluated for changes in intracellular and extracellular water volume after five days of intensive treatment at the Godoy Clinic in São Jose do Rio Preto, Brazil, in 2015 and 2016.

Design

A clinical trial was conducted involving 59 patients with clinical stage III lower limb lymphedema. Changes in intracellular and extracellular water volume were determined using electrical bioimpedance analysis (InBody S10 device) before and after intensive treatment using the Godoy method for five days. The participants were divided into different groups according to BMI range (25 to 30, 30 to 40 and > 40 kg/m^2).

Inclusion criteria

Patients with clinical stage III lower limb lymphedema were consecutively included in the study independently of the cause.

Exclusion criteria

Patients with a BMI lower than 25 kg/m^2 and those with other causes of edema, (heart disease, kidney disease or hypoproteinemia) were excluded from the study.

Treatment

The participants were submitted to intensive treatment for lymphedema using the Godoy method, which consisted of manual lymphatic therapy, cervical lymphatic therapy, mechanical lymphatic therapy and the use of stockings, made of handmade with eyelets and drawstrings for close. The treatment is approximately eight hours a day for five days. In this period, the patients were submitted to eight hours of mechanical lymphatic therapy using an electromechanical device that performs plantar flexion and extension, combined with 15 minutes of cervical lymphatic therapy, one hour of manual lymphatic therapy (Godoy method-treatment) and the use of compression stockings, made of handmade.

Statistical analysis

The paired t-test and Mann-Whitney U test were used for the statistical analysis, considering a 5% alpha error.

Ethical aspects

This study received approval from the human research ethics committee of Medicine School of Sao Jose do Rio Preto-FAMERP number 2.051.078, CAAE: 65260517.8.0000.5415.

Results

Fifty-nine patients (44 women and 15 men) were analyzed (mean age: 48.1 years; range: 21 to 71.7 years). Fifteen patients were in the BMI range of 25 to 30 kg/m^2, 24 were in the range of 31 to 40 kg/m^2 and 20 had BMI higher than 40 kg/m^2. Tables 1, 2 and 3 display data on age, weight, BMI, intracellular water and extracellular water before and after treatment in the different BMI ranges. Table 4 displays the mean changes in volume of intracellular and extracellular water in the different BMI ranges.

Table 5 shows the statistical analysis using the paired t-test comparing the changes in volume after treatment for lymphedema. Significant reductions in both intracellular and extracellular water were found in the two higher BMI ranges

($p < 0.000$, paired t-test). In the 25-to-30 kg/m^2 range, however, a significant reduction in extracellular water was found ($p < 0.0001$), but the difference in intracellular water was non-significant ($p = 0.32$). Greater reductions in extracellular water compared to intracellular water were found in all groups (25-to-30 kg/m^2: $p = 0.001$; 31-to-40 kg/m^2: $p = 0.01$; > 40 kg/m^2: $p = 0.04$) (Table 5).

In the inter-group analysis, no significant differences were found in the reduction of extracellular water between 25-to-30 kg/m^2 range and either the 31-to-40 kg/m^2 range ($p = 0.48$, Mann-Whitney U test) or > 40 kg/m^2 range ($p = 0.20$, unpaired t-test) or between the 31-to-40 kg/m^2 range and > 40 kg/m^2 range ($p = 0.41$). Likewise, no significant differences were found in the reduction of intracellular water between 25-to-30 kg/m^2 range and either the 31-to-40 kg/m^2 range ($p = 0.9$, Mann-Whitney U test) or > 40 kg/m^2 range ($p = 0.9$, unpaired t-test) or between the 31-to-40 kg/m^2 range and > 40 kg/m^2 range ($p = 0.67$) (Table 6).

Table 1: Age, weight, BMI, extra-cellular water and intracellular water before and after treatment in group of patients in 25-to-30 kg/m^2 range

Age	Weight	BMI	Extra-before	Extra-after	Extra-Reduction	Intra-before	Intra-after	Intra-Reduction
27	74.2	28.6	12.8	12.8	0	21.8	21.2	-0.6
56	76.6	27.2	13.1	13.1	0	21.1	21.8	+0.7
64	68.5	27.1	11.9	11.6	-0.3	18.5	18.5	0
37	82.5	27.2	17.4	16.4	-1.0	28.4	28.7	+0.3
63	70.5	26.9	13.3	11.9	-1.4	20.2	19.9	-0.3
71	67.4	28.4	13.4	12.6	-0.8	17.8	17.4	-0.4
42	66	27.1	14.5	12.6	-1.9	20.3	19.1	-1.2
23	80.9	26.7	17.2	16.5	-0.7	25.1	25.5	+0.4
35	72.4	28.1	14.4	12.4	-2.0	20.4	19.4	-1.0
67	71.2	30	11.6	10.6	-1.0	16.7	16.3	-0.4
38	83.2	26.3	20.4	19.9	-0.5	28.6	29.3	+1.3
40	68.1	27.6	13.2	11.5	-1.7	19.1	17.7	-1.4
69	79.4	30	14.1	13.4	-0.7	20.6	20.7	+0.1
49	78.3	27.7	12.8	12.5	-0.3	19.9	20.2	+0.3
25	88.5	29.1	16.8	16.2	-0.6	26.3	26.5	+0.2

Table 2: Age, weight, BMI, extra-cellular water and intracellular water before and after treatment in group of patients in 31-to-40 kg/m^2 range

Age	Weight	BMI	Extra-before	Extra-after	Extra-Reduction	Intra-before	Intra-after	Intra-Reduction
36	84.2	34.2	12.2	12.0	-0.2	20.2	20.2	0
43	118.9	35.9	26.9	23.7	-3.2	37.3	35.5	-1.8
37	117.7	36.7	20.0	18.6	-1.4	30.4	29.6	-0.8
66	87.2	31.6	16.0	15.6	-0.4	25.5	24.9	-0.5
46	108.4	33.1	22.8	20.8	-2.0	33.6	32.3	-1.3
31	83.7	31.9	15.7	14.2	-1.5	22.1	21.3	0.8
65	80.9	34.6	12.0	11.6	-0.4	17.2	17.0	-0.2
46	80.8	32.4	15.2	15.2	0	21.1	20.9	-0.2
69	79.4	31.0	14.1	13.4	-0.7	20.6	20.7	+0.1
65	130.5	36.1	27.1	25.6	-1.5	39.7	39.4	-0.3
78	76.3	34.8	10.7	10.7	0	15.6	15.6	0
59	88.8	33.8	14.1	13.0	-1.1	22.3	21.7	-0.6
73	86.4	36.4	14.3	12.7	-1.6	19.4	17.9	-1.5
82	95.5	34.7	16.2	15.4	-0.8	23.4	22.5	-0.9
61	84.3	35.3	15.0	13.1	-1.9	20.3	18.7	-1.6
30	165.0	37.4	32.9	34.4	+1.5	54.6	53.4	-1.2
76	92.5	35.2	15.2	14.3	-0.9	21.7	21.7	0
26	79.1	30.5	13.6	12.8	-0.8	20.8	20.6	-0.2
58	79.5	30.9	13.2	12.9	-0.3	20.4	20.3	-0.1
31	99.0	36.8	16.2	14.3	-1.9	24.3	23.0	-1.3
60	103.5	37.1	14.9	14.4	-0.5	21.8	22.2	+0.4
76	107.5	38.3	18.0	16.6	-1.4	24.2	23.6	-0.6
53	106.7	39.7	15.1	14.3	-1.2	23.4	23.0	-0.4
35	101.1	39.5	15.2	13.2	-2.0	22.3	21.8	-0.5

Table 3: Age, weight, BMI, extra-cellular water and intracellular water before and after treatment in group of patients in > 40 kg/m^2 range

Age	Weight	BMI	Extra-before	Extra-after	Extra-Reduction	Intra-before	Intra-after	Intra-Reduction
47	117.0	45.1	17.0	15.9	-1.1	25.7	25.1	-0.6
41	131.1	45.4	31.4	29.6	-1.8	21.7	21.6	-0.1
58	105.0	36.8	15.8	15.4	-0.4	24.6	24.1	-0.5
36	156.0	58.4	25.1	21.6	-4.5	35.0	32.5	-2.5
50	120.4	45.3	17.4	17.3	-0.1	25.8	26.0	+0.2
47	133.0	43.2	28.8	24.8	-4.0	39.5	35.2	-4.3
41	138.9	51.0-	17.4	17.6	+0.2	27.0	27.9	+0.9
41	131.3	43.2	23.6	20.7	-2.6	34.7	32.8	-1.9
32	103.5	40.4	18.6	16.8	-1.8	28.5	28.8	+0.3
43	130.3	49.6	16.9	16.1	0.8	25.8	25.8	0
39	99.8	41.0	14.2	13.4	-0.8	20.7	20.8	+0.1
60	129.2	53.1	18.5	17.6	-0.9	25.5	26.5	+1.0
44	153.0	62.5	19.4	17.8	-1.6	31.1	29.7	-1.4
67	106.1	49.1	17.9	14.4	-3.5	23.3	19.8	-3.5
76	119.5	52.4	15.3	15.0	-0.3	22.6	22.0	-0.6
46	108.8	40.5	18.3	16.1	-2.2	25.7	23.5	-2.2
55	93.2	40.3	14.4	12.7	-1.7	21.6	20.3	-1.3
59	97.3	41.6	13.7	12.8	-0.9	20.6	20.4	-0.2
63	152.0	48.5	24.1	23.0	-1.1	37.1	36.4	-0.7
75	95.5	45.7	14.1	13.5	-0.6	19.2	19.1	-0.1

Table 4: Changes in intracellular and extracellular water in different BMI ranges after five days of intensive treatment for lymphedema using Godoy method of treatment

Variables	Extra-reduction BMI 25-30	Intra-reduction BMI 25-30	Extra-reduction BMI 31-40	Intra-reduction BMI 31-40	Extra-reduction BMI > 40	Intra-reduction BMI > 40
Valid data	15	15	24	24	20	20
Mean	-0.86	-0.13	-1.00	-0.52	-1.44	-0.87
Standard deviation	0.642317	0.730623	1.381256	2.484457	1.381256	2.484457

Table 5: Paired test t results comparing reductions in intracellular and extracellular water in different BMI ranges following treatment of lower limb lymphedema using intensive Godoy method treatment for five days

BMI range	Extracellular water	Intracellular water	Extracellular water X Intracellular water
25-30	p = 0.0001	p = 0.32	p = 0.0001
31-40	p = 0.0001	p = 0.0001	p = 0.01
> 40	p = 0.0001	p = 0.01	p = 0.03

Table 6: Mann-Whitney U test results comparing reductions in intracellular and extracellular water between different BMI ranges following treatment of lower limb lymphedema using intensive Godoy method treatment for five days

BMI range	BMI range	p-value
25-30 extracellular	31-40	p = 0.48
25-30 extracellular	> 40	p = 0.20
31-37 extracellular	> 40	p = 0.41
25-30 intracellular	31-40	p = 0.09
25-30 intracellular	> 40	p = 0.26
31-40 intracellular	> 40	p = 0.7

Discussion

The present study demonstrates important changes in the mobilization of intracellular and extracellular water following intensive five-day treatment for lower limb lymphedema using the Godoy method. This form of treatment enables an average of a 50% reduction in edema volume in the limb in five days due to the significant reduction in fluids.[2,3] No previous studies using this type of analysis were found in the literature.

Among the patients in the BMI range 25-to-30 kg/m^2, only the change in extracellular water was significant, whereas the change in intracellular water was non-significant. In all patients with BMI > 30 kg/m^2, however, significant reductions were found in both intracellular and extracellular water. These findings suggest that there is an aggravating factor of lymphedema in patients with a higher BMI. These changes are evident mainly with regard to intracellular fluid, which was not altered significantly in the individuals with BMI < 30 kg/m^2.

Animal studies have demonstrated the negative impact of obesity on the lymphatic system, affecting both the pumping mechanism and capillary permeability.[10-16] From the functional standpoint, the drainage of lymph is affected by the both the change in lymphatic pumping and the greater lymph production due to the increase in capillary permeability. These mechanical and functional changes related to greater lymph production is what we denominate subclinical systemic lymphedema.[17]

The changes in extracellular fluid were greater than the changes in intracellular fluid. This confirms the physiopathology of lymphedema, which leads to the accumulation of macromolecules in the interstitial space and the retention of fluids. However, the significant increase in intracellular fluid was not expected.

Another interesting the finding was that the amount of fluid reduced after treatment was similar in the three BMI ranges. This suggests that the stimulus of lymphatic drainage employed has a uniform response in both obese and non-obese patients.

Conclusion

Five days of intensive lymphedema treatment using the Godoy method enabled a significant reduction in intracellular and extracellular fluids among patients in different BMI ranges. An important finding was that obesity can aggravate edema in these patients, leading to a new concept of lymphedema that we denominate subclinical systemic lymphedema.

References

1. Lee BB, Antignani PL, Baroncelli TA, Boccardo FM, Ibrorson H, Campisi C, Damstra RJ, Flour M, Giannoukas A, Laredo J, Liu NF, Michelini S, Piller N, Rockson SG, Scuderi A, Szolnoky G, Yamamoto T. Iua-Isvi consensus for diagnosis guideline of chronic lymphedema of the limbs. Int Angiol. 2015 Aug;34(4):311-32. Epub 2014 Mar 19.
2. Pereira De Godoy JM, Amador Franco Brigidio P, Buzato E, Fátima Guerreiro De Godoy M. Intensive outpatient treatment of elephantiasis. Int Angiol. 2012 Oct;31(5):494-9.
3. Pereira De Godoy JM, Franco Brigidio PA, Salles Cunha SX, Batigália F, De Fatima Guerreiro Godoy M. Mobilization of fluids in large volumetric reductions during intensive treatment of leg lymphedema. Int Angiol. 2013 Oct;32(5):479-82.
4. Lamprou DA, Damstra RJ, Partsch H. Prospective, randomized, controlled trial comparing a new two-component compression system with inelastic multicomponent compression bandages in the treatment of leg lymphedema. Dermatol Surg. 2011 Jul;37(7):985-91. doi: 10.1111/j.1524-4725.2011.02002.x.
5. Pereira de Godoy JM, Pereira de Godoy HJ, Pereira de Godoy LM, Guerreiro Godoy M de F. Prevalence of Idiopathic Cyclic Edema in Women with Lower Limb Lymphedema. Journal of Clinical Medicine 2018;7(1):2. doi:10.3390/jcm7010002.
6. Belczak CE, de Godoy JM, Ramos RN, de Oliveira MA, Belczak SQ, Caffaro RA. Is the wearing of elastic stockings for half a day as

effective as wearing them for the entire day? Br J Dermatol. 2010 Jan;162(1):42-5.

7. Godoy José Maria Pereira de, Godoy Ana Carolina Pereira de, Godoy Maria de Fatima Guerreiro. Godoy & Godoy Compression Sleeve in the Treatment of Arm Lymphedema: New Concepts for Materials. Braz. Arch. Biol. Technol. 2015 Dec [cited 2017 Mar 01] ; 58(6): 864-868. http://dx.doi.org/10.1590/S1516-89132015060286.
8. Nuttall FQ. Body Mass Index: Obesity, BMI, and Health: A Critical Review. Nutr Today. 2015 May;50(3):117-128.
9. Gupta D, Lis CG, Dahlk SL, Vashi PG, Grutsch JF, Lammersfeld CA. Bioelectrical impedance phase angle as a prognostic indicator in advanced pancreatic cancer. British Journal of Nutrition 2004 b; 92(6): 957-962.
10. Nitti MD, Hespe GE, Kataru RP, García Nores GD, Savetsky IL, Torrisi JS, Mehrara BJ. Obesity-induced lymphatic dysfunction is reversible with weight loss. The Journal of Physiology 2016; 594(23):7073-7087. doi:10.1113/JP273061.
11. GD García Nores , DA Cuzzone , NJ Albano, GE Hespe, RP Kataru, JS Torrisi, JC Gardenier, IL Savetsky, SZ Aschen, MD Nitti and BJ Mehrara. Obesity but not high-fat diet impairs lymphatic function. International Journal of Obesity 2016; 40:1582-1590. doi:10.1038/ijo.2016.96
12. Hespe GE, Kataru RP, Savetsky IL, García Nores GD, Torrisi JS, Nitti MD, Gardenier JC, Zhou J, Yu JZ, Jones LW, Mehrara BJ.. Exercise training improves obesity-related lymphatic dysfunction. J Physiol 2016, 594(15):4267-4282. DOI: 10.1113/JP271757.
13. Torrisi JS, Hespe GE, Cuzzone DA, et al. Inhibition of Inflammation and iNOS Improves Lymphatic Function in Obesity. Scientific Reports 2016;6:19817. doi:10.1038/srep19817.
14. Weitman ES, Aschen SZ, Farias-Eisner G, Albano N, Cuzzone DA, Ghanta S, Zampell JC, Thorek D, Mehrara BJ. Obesity impairs lymphatic fluid transport and dendritic cell migration to lymph nodes. PLoS One. 2013 Aug 12;8(8):e70703. doi: 10.1371/journal.pone.0070703. eCollection 2013.
15. Blum KS, Karaman S, Proulx ST, Ochsenbein AM, Luciani P, Leroux JC, Wolfrum C, Detmar M. Chronic High-Fat Diet Impairs Collecting Lymphatic Vessel Function in Mice. Hogan B, ed. PLoS ONE. 2014;9(4):e94713. doi:10.1371/journal.pone.0094713.
16. Sawane M, Kajiya K, Kidoya H, Takagi M, Muramatsu F, Takakura N. Apelin Inhibits Diet-Induced Obesity by Enhancing Lymphatic and Blood Vessel Integrity. Diabetes. 2013;62(6):1970-1980. doi:10.2337/db12-0604
17. José Maria Pereira de Godoy, Henrique Jose Pereira de Godoy, Maria de Fatima Guerreiro Godoy. Subclinical systemic lymphedema manifesting early in patients with clinical lymphedema. International Journal of Development Research 2018; 8(9): 23041-23044.