Lymphology 34 (2001) 135-141

EFFECT OF SEQUENTIAL INTERMITTENT PNEUMATIC COMPRESSION ON BOTH LEG LYMPHEDEMA VOLUME AND ON LYMPH TRANSPORT AS SEMI-QUANTITATIVELY EVALUATED BY LYMPHOSCINTIGRAPHY

F. Miranda, Jr., M. del C.J. Perez, M.L.V. Castiglioni, Y. Juliano, J.E. Amorim, L.C.U. Nakano, N. de Barros, Jr., W.G. Lustre, E. Burihan

Vascular Surgery Division (FM,Mde1CJP,JEA,LCUN,NdeB,WGL,EB), Nuclear Medicine Sector (MLVC), and Epidemiology (YJ), Federal University of São Paulo, Paulista School of Medicine, São Paulo, Brazil

ABSTRACT

Sequential Intermittent Pneumatic Compression (SIPC) is an accepted method for treatment of peripheral lymphedema. This prospective study evaluated the effect in 11 patients of a single session of SIPC on both lymphedema volume of the leg and isotope lymphography (99Tc dextran) before SIPC (control) and 48 hours later after a 3 hour session of SIPC. Qualitative analysis of the 2 lymphoscintigrams (LS) was done by image interpretation by 3 physicians on a blind study protocol. The LS protocol attributed an index score based on the following variables: appearance, density and number of lymphatics, dermal backflow and collateral lymphatics in leg and thigh, visualization and intensity of popliteal and inguinal lymph nodes. Volume of the leg edema was evaluated by measuring limb circumference before and after SIPC at 6 designated sites.

Whereas there was a significant reduction of circumference in the leg after SIPC ($p<0.05$),there was no significant difference in the index scores of the LS before and after treatment. This acute or single session SIPC suggests that compression increased transport of lymph fluid (i.e., water) without comparable transport of macromolecules (i.e., protein). Alternatively, SIPC reduced lymphedema by decreasing blood capillary filtration (lymph formation) rather than by accelerating lymph return thereby restoring the balance in lymph kinetics responsible for edema in the first place.

Sequential Intermittent Pneumatic Compression (SIPC) is commonly used for treatment of peripheral lymphedema with 90% good results (1). Lymphoscintigraphy (LS) to examine the effects of SIPC is controversial but LS techniques have not as yet been standardized (2-4). The objective of this study was to evaluate the effect of SIPC on peripheral lymphedema volume and on transport of intradermal radiotracer (technetium labeled 99m-dextran or ^{99m}Tc-Dx) in patients with leg lymphedema.

MATERIALS AND METHODS

Twelve patients with lymphedema of the lower limbs were included prospectively in an 11 month period. Each patient gave informed consent as approved by the Ethics Committee of the Federal University of São Paulo.

One patient developed an infection in the leg during the study and was accordingly excluded. Of the remaining 11 patients, 8

TABLE 1
Semi-Quantitative Evaluation Protocol of Lymphoscintigraphy

Leg (R or L) Lower or Upper (Thigh)	Features: Lymphatics (appearance)	Lymphatics (number)	Regional (nodes)	Dermal Backflow	Collaterals
	1 - linear	1 - none	1 - yes	1 - absent	1 - yes
	2 - tortuous	2 - single	2 - no	2 - moderate	2 - no
	3 - absent		3 - multiple	3 - intense	

R = right; L = left

were females and 3 males. Ages ranged from 25 to 75 years (mean 44.6 years). Eleven legs were studied. Three were in lymphedema phase I, 5 in phase II, and 3 in phase III according to Mowlem's classification (5). The duration of disease varied from 1.5 to 29 years (mean 12.9 years). Three patients were classified as primary and 8 as secondary lymphedema. In 5 patients, the lymphedema was unilateral and in 6 bilateral. The studies were carried out in just one leg of each patient by randomization when the lymphedema was bilateral.

Lymphoscintigraphy was performed after an intradermal injection of 185 MBq (5mCi) of ^{99m}Tc-Dx in the first interdigital space of both feet (6). Images of the legs and abdomen were performed with a gamma-camera (SPX-4HR, Elscint®), with a low energy and high resolution parallel hole collimator, and the energy centered at 140 Kev and a 20% window.

Two lymphoscintigrams were performed in each patient on two different days (48 hours apart), and images recorded at 45 minutes and 3 hours after the ^{99m}Tc-Dx injection. The first study was before compression (control). The second occurred during a session of three hours of SIPC started just after instillation of ^{99m}Tc-Dx.

We measured the circumference of the lower legs at six standard sites previously marked with permanent ink. The measurements were taken before injection of ^{99m}Tc-Dx and after pneumatic compression. An edema index was created to analyze the difference between data (in cm) collected before (pre) and after (post) compression: [Δ%=[((pre-post)/(pre))x100].

The LS scans were printed on radiographic film and interpretation of the images in lower legs and thighs was determined based on the course and number of lymphatics, presence of dermal backflow, depiction of popliteal lymph nodes and collateral circulation. The appearance and intensity of inguinal lymph nodes were also evaluated. These data were modified from other qualitative studies (6-8) and a scoring system was designed to highlight each independent variable *(Table 1)*.

Three independent observers made the semi-quantitative analysis including two nuclear medicine specialists and a vascular surgeon. The scintiscans were evaluated without patient identification and without knowledge at which time the LS was obtained (e.g., 45 minutes or at three hours), or if it was done before or after SIPC, or which leg was treated with compression.

Statistical nonparametric tests were used to analyze the results. Friedman variance analysis (9) complemented by test of multiples comparisons (10) when the results showed

TABLE 2
Mean Results of Semi-Quantitative Evaluation of Lymphoscintigraphy Before and After Sequential Intermittent Pneumatic Compression by Three Blinded Observers (A,B,C) According to Protocol Shown in Table 1

	A		B		C		X^2 calculated	
Variables	Before	After	Before	After	Before	After	Before	After
Lymphatics (appearance) in the lower leg	2.2	2.0	2.1	2.0	2.3	2.1	3.00	0.50
Lymphatic appearance in the upper leg (thigh)	2.1	2.2	2.1	1.9	2.0	2.3	0.40	2.00
Lymphatic number in the lower leg	2.1	2.3	2.2	2.4	2.0	2.4	1.00	2.00
Lymphatic number in the upper leg (thigh)	2.1	2.2	2.0	1.9	1.9	2.4	0.40	4.80
Dermal backflow in the lower leg	1.8	1.8	1.7	1.8	1.6	1.8	4.67	0.00
Dermal backflow in the upper leg (thigh)	1.8	1.8	1.1	1.2	1.1	1.4	2.00	2.00

Friedman variance analysis: X^2 critical = 5.99

TABLE 3
Presence or Absence of Popliteal Lymph Nodes in Lower Leg With Lymphedema Before and After Three Hours of Compression (SIPC)

Observer	Compression (SIPC)	Presence Yes	Presence No	Total	Ratio (%) (Yes/No)
A	Before	1	10	11	9.09
	After	2	9	11	18.18
	Total	3	19	22	13.64
B	Before	2	9	11	18.18
	After	3	8	11	27.27
	Total	5	17	22	22.73
C	Before	2	9	11	18.18
	After	3	8	11	27.27
	Total	5	17	22	22.73

Fisher's exact test; p = 0.5

significant difference: 1 - to compare the percentile difference of the measurement of the circumference before and after compression [Δ%(post - pre/post)x l00]; 2 - to compare the LS scores of the observers for each leg and to compare inter-observer scores.

Cochran G test (9) and Chi-square test (9) were used to analyze 2x2 tables. Fisher's exact test was applied in some cases taking into account Cochran's G test restrictions. The level for the rejection of the null hypothesis was 0.05 or 5%.

TABLE 4
Presence or Absence of Inguinal Nodes in Upper Leg (Thigh)
With Lymphedema Before and After Three Hours of Compression (SIPC)

Observer	Compression (SIPC)	Presence Yes	Presence No	Total	Ratio (%) (Yes/No)
A	Before	4	7	11	36.36
	After	5	6	11	45.45
	Total	9	13	22	40.91
B	Before	4	7	11	36.36
	After	4	7	11	36.36
	Total	8	14	22	36.36
C	Before	6	5	11	54.55
	After	7	4	11	63.64
	Total	13	9	22	59.09

Fisher's exact test; p = 0.5

TABLE 5
Presence or Absence of Collateral Circulation in Lower Leg
With Lymphedema Before and After Three Hours of Compression (SIPC)

Observer	Compression (SIPC)	Presence Yes	Presence No	Total	Ratio (%) (Yes/No)
A	Before	7	4	11	63.64
	After	8	3	11	72.73
	Total	15	7	22	68.18
B	Before	5	6	11	45.45
	After	7	4	11	63.64
	Total	12	10	22	54.55
C	Before	6	5	11	54.55
	After	7	4	11	63.64
	Total	13	9	22	59.09

Fisher's exact test; p = 0.5

TABLE 6
Presence or Absence of Collateral Circulation in Upper Leg (Thigh) With Lymphedema Before and After Three Hours of Compression (SIPC)

Observer	Compression (SIPC)	Presence Yes	Presence No	Total	Ratio (%) (Yes/No)
A	Before	0	11	11	0.00
	After	1	10	11	9.09
	Total	1	21	22	4.55
B	Before	1	10	11	9.09
	After	2	9	11	18.18
	Total	3	19	22	13.64
C	Before	3	8	11	27.27
	After	4	7	11	36.36
	Total	7	15	22	31.82

Fisher's exact test; p = 0.5

TABLE 7
Total of "Yes" in Response in Semi-Quantitative Variables (see Table 1) Assessed on Lymphoscintigraphy of Lower Extremities with Lymphedema Before and After Three Hours Compression (SIPC) According to Observers A, B, and C

Variables		Compression Before A	B	C	Compression After A	B	C	Compression Before G calculated	Compression After G calculated
Popliteal nodes	Yes	1	2	2	2	3	3	0.67	0.67
	(%)	9	18	18	18	27	27		
Collateral circulation (lower leg)	Yes	7	5	5	8	7	7	3.0	2.0
	(%)	64	45	45	73	64	64		
Collateral circulation upper leg (thigh)	Yes	1	1	3	1	2	4	2.0	3.50
	(%)	9	9	27	9	18	36		
Inguinal nodes	Yes	4	4	6	5	4	7	4.00	4.67
	(%)	36	36	54	4	36	64		

G-Cochran test: critical = 5.99

TABLE 8
Percentile Difference in Leg Circumference Pre- and Post-Intermittent Pneumatic Compression at Six Peripheral Sites
[Δ% = (post - pre / post) x 100]

Patient	Forefoot	Ankle	Lower Leg	Lower Thigh	Mid-Thigh	Upper Thigh
1	0	0	-2.9	-1.1	1.0	-0.9
2	0	-1.4	-1.8	-5.1	-1.5	2.9
3	0	-2.3	-3.3	-1.7	-3.7	0
4	-2.1	-4.1	-3.1	0	0	0
5	0	-4.2	-2.5	-4.8	-1.9	0
6	-2.1	-2.1	-2.7	0	-1.0	-1.8
7	0	-2.0	0	-2.2	-7.4	0
8	0	-3.7	-1.4	1.3	-4.2	0
9	0	-11.6	-10.2	1.5	0	0
10	0	-1.9	-1.2	-1.1	-1.8	-1.7
11	-3.8	-3.6	-5.0	0	-0.9	0
Mean	-0.7	-3.3	-3.1	-1.2	-1.9	0.2

Friedman variance analysis: X^2 calc = 16.57* X^2 crit = 11.07
Test of multiple comparisons: ankle and proximal leg < proximal thigh

RESULTS

The semi-quantitative results showed no significant difference among the three observers in relation to data (Fisher test) and inter-observer results (Friedman test and G Cochran test) *(Tables 2-7)*.

The leg circumference measurements taken before and after three hours of SIPC showed a significant decrease only in the ankle and lower leg *(Table 8)*.

DISCUSSION

These results showed that SIPC was effective acutely in decreasing peripheral lymphedema in agreement with prior studies (1). Edema of the thigh did not decrease probably because fluid of the lower leg was transported more proximally during compression treatment. Three hour SIPC was effective, but a greater decrease in leg volume was recorded when more prolonged compression was applied (11,12).

Lymphoscintigraphy is now considered the method of choice to document lymphvascular dysfunction and also to evaluate operative and non-operative treatment (13,14). Several LS patterns have been described for qualitative evaluation of lymphatic (dys)function (14) which are similar to our protocol. We divided the lower limb into lower leg and upper leg (thigh) including the inguinal area and designed LS parameters to be analyzed at each site before and after compression to determine whether there was altered transport of ^{99m}Tc-Dx by SIPC. No significant difference in the LS results before and after compression were observed including when independent

analysis among three blinded observers was done. The decrease of leg circumference after SIPC was not related to improved radiotracer transport as previously suggested by others (4,15). We agree with Partsch et al (3) who showed after LS (^{131}I-albumin) that compression mobilized water from the interstitium but not protein. Baulieu et al (2) also evaluated the effect of SIPC on LS (rhenium sulfide) and observed no lymphatic transport in places where functional residual lymphatics were absent. An alternative possibility is that compression therapy reduces lymphedema by opposing further blood capillary filtration (i.e., lymph formation) instead of by accelerating lymph return thereby restoring the balance in lymph kinetics responsible for edema in the first place.

REFERENCES

1. Rooke, TW, P Gloviczki: Nonoperative management of chronic lymphedema. In: *Vascular Surgery*, 4th Edition. Rutherford, R (Ed.), Philadelphia, WB Saunders Co, 1994.
2. Baulieu, F, JL Baulieu, L Vaillant, et al. Factorial analysis in radionuclide lymphography: Assessment of the effects of sequential pneumatic compression. Lymphology 22 (1989), 178.
3. Partsch, H, A Mostbeck, G Leitner: Experimentelle Unterssuchungen zur Wirkung einer Druckwellenmassage (Lymphapress) beim Lymphödem. Phlebologie u Proktologie 80 (1980), 124.
4. Leduc, A, R Bastin, P Bourgeois: Lymphatic reabsorption of proteins and pressotherapies. In: *Progress in Lymphology XL*. Partsch, H. (Ed.), Elsevier Science Publishers BV 1988.
5. Mowlem, R. The treatment of lymphoedema. Brit. J. Plast. Surg. 1 (1948), 48.
6. Cestari, SCP, V Petri, MLV Castiglioni, et al: Linfedemas dos membros inferiores: Estudo linfocintilográfico. Rev. Assoc. Med. Bras. 40 (1994), 93.
7. Gomes, SCN: Linfocintigrafia superficial de membros inferiores corn Dextran 500 Tc99m. Estudo em pacientes portadores de filariose e de linfopatias nao fllarióticas. Recife, Brazil, 1990 [Thesis - Pernambuco Federal University].
8. Nawaz, MIK, MM Hamad, S Sadek, et al: Dynamic lymph flow imaging in lymphedema normal and abnormal patterns. Clin. Nucl. Med. 11 (1986), 653.
9. Siegel, S, NJ Castellan Jr: *Nonparametric Statistics*. 2nd edition, McGraw-Hill Int. Ed., New York, 1988.
10. Hollander, M, DA Wolfe: *Nonparametric Statistical Methods*. John Wiley & Sons, New York, 1973.
11. Raines, JK, TF O'Donnell Jr, L Kalisher, et al: Selection of patients with lymphedema for compression therapy. Am. J. Surg. 133 (1977), 430.
12. Pappas, CJ, TF O'Donnell Jr: Long-term results of compression treatment for lymphedema. J. Vasc. Surg. 16 (1992), 555.
13. Mavili, ME, S Naldoken, T Safak: Modified Charles operation for primary fibrosclerotic lymphedema. Lymphology 27 (1994), 14.
14. Vaqueiro, M, P Gloviczki, J Fisher, et al: Lymphoscintigraphy in lymphedema: An aid to microsurgery. J. Nucl. Med. 27 (1986), 1125.
15. Földi, E, M Földi, H Weissleder: Conservative treatment of lymphoedema of the limbs. Angiology 36 (1985), 171.

Fausto Miranda, Jr., MD
Rua Estela, 515 bloco G conj. 81
04011-904 - São Paulo - SP - Brazil
Telephone/Fax: 55-11-5575-6955
E-mail: fmirandajr.dcir@epm.br