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ORIGINAL ARTICLE

Foam Sclerotherapy of Incompetent Perforators with Compression Versus Compression alone for Treatment of Chronic Venous Leg Ulcers

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ABSTRACT

Introduction: Venous Leg Ulcers (VLUs) account for 69% of all leg ulcers and estimates 1% of the population with a prevalence that increases with age according Edinburgh study, which was a cross-sectional study of a random sample

Objective: To compare the efficacy of compression +duplex guided injection sclerotherapy of incompetent perforators opposite compression alone in management of chronic VLUs.

Methods: Patients (older than 18 years) attending at outpatient clinic of Vascular Surgery Department, Faculty of Medicine-Zagazig University, were invited to participate in our study.

Conclusion: The compression therapy is important line in management of venous ulcers. This synergistic approach can improve quality of life through shortening time needed for compression therapy and rapid recovery for normal daily activity. Duplex-guided sclerotherapy is a minimal invasive procedure, compared to surgery, it avoids the need for general anesthesia, hospital admission and long recovery times and may be done in outpatients clinic.

As absence of serious complications and its evident success, make this the first line management for venous ulcer beside compression but we need larger number of patient and longer time for follow up to obtain good result

Key words;

Duplex Guided Foam Sclerotherapy, Incompetent Perforators Combined Compression, VLUS, Ankle brachial pressure index, Chronic venous insufficiency (CVD), Insulin-like growth factor-1

INTRODUCTION

Scottish Guideline defined the chronic (VLU) “as an open wound between knee and ankle joint that still unhealed for at least four weeks in the presence of venous disease” [1].

Chronic VLUs account for 69% of all leg ulcers and estimates 1% of the population with a

prevalence that increases with age according Edinburgh study, which was a cross-sectional study of a random sample [1].

Venous ulcer is one of the complications of chronic venous disorders (CVD) and is considered the most common cause of lower limb ulceration. Venous ulcers account for approximately 69% of all lower extremity

ulcers, with an overall prevalence of 1–2% CVD has large adverse effect on quality of life of the patient, and is associated with expensive health care costs. Surgery is relatively invasive. Recurrence rate of venous ulcer after treatment account for 20% to 80% [2,3].

Methods such as laser and radiofrequency ablation and foam injection have been increasingly used in these patients [4].

Duplex guided foam injection is less invasive and can be repeated as required. Moreover, it is less costly and able for achieving good functional and cosmetic results. Duplex guided foam injection has been considered particularly attractive as no anesthesia, no hospitalization and can be done in outpatient clinic [5].

PATIENTS AND METHODS

Study Population

Patients (older than 18 years) attending at outpatient clinic of Vascular Surgery Department, Faculty of Medicine-Zagazig University, were invited to participate in our study.

Written informed consent was obtained from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria include:

Post phlebotic venous ulcers.

Venous ulcers with significant incompetent perforators.

Able to understand and deal with the steps of the intervention.

Exclusion Criteria Include:

Chronic illness like severe hepatic disease, cardiac problem, DM or lung disease.

Medical condition need systemic corticosteroids during procedures.

Recent deep vein thrombosis

Pregnancy.

Known allergy to sclerosant material.

ABPI < 0.8

concurrent arterial disease.

Ulcers that were found to have alternative etiology as basal cell carcinoma, Squamous cell carcinoma or vasculitis.

Infected ulcers.

Study design:

The study was Randomized Control Trial, conducted on 22 patients with chronic lower limb venous ulcer subdivided in two groups by control randomization, each group 11 patients (11 ulcers): Group A: - (compression only) this group was conservatively managed by four-layer compression bandage after ulcer debridement and irrigation by saline solution for 6 sessions with one week interval between sessions. Group B: - (compression + foam injection) this group was managed by foam sclerotherapy of incompetent perforators then four-layer compression bandage after ulcer debridement and irrigation by saline solution also for 6 sessions with one-week interval between sessions.

Sample size:

Assuming that the effectiveness of ultrasound guided foam injection opposite compression alone in treatment of chronic VLU were 96% versus 30% ulcer healing.

The sample size was calculated using open epi to be 22 using power of test 80% confidence level 95% divided into two groups.

Study procedures: -

a- History:

A detailed history taking from each patient regarding the general

Demographic data including age, sex and special habits of medical importance, history of ulcer, treatment taken previously for the ulcer.

The presenting complaint of the patient.

Past history of previous operations and postoperative events (e.g. wound infection and respiratory complications), chronic disease (e.g. cardiac diseases, liver diseases and diabetes mellitus).

b- General assessment:

General physical examination of patient was done at first visit only for both groups with concentration on:

Vital sign measurement.

Vascular assessment regarding signs of CVI, any sign of lower limb ischemia and measuring of ankle brachial index.

Ankle joint mobility, any sign of infection.

Physical examination for anemia or blood disorders

c- Local examination:

Ulcer Assessment: The ulcer was assessed carefully (**at first visit & every 2weeks**) in the following aspect:

Ulcer measurement were taken in greatest length and width then calculation of ulcer size done by use of formula for an ellipse: Length \times width \times 0.7854.

Taken digital photos from the ulcer.

Assessment of surrounding skin for sign of inflammation or infection.

Investigation:

All patients had duplex scan for assessment venous system of both lower limbs to identify type of CVI and if there was indication for surgical intervention.

Ulcer management protocol for group A patient

At first visit ulcer was sharply debrided and cleaned by saline solution to remove any discharge. Sterile gauze was used to cover the ulcer and fixed in position by sterile roller bandage. In further visits each 2 weeks no more debridement performed just cleaned by saline.

Compression therapy by four-layer bandaging system (as described below) was applied and changed after two weeks.

Ulcer management protocol for group B patients

At first visit ulcer was sharply debrided and cleaned by saline solution to remove any discharge then in operation room duplex guided foam sclerotherapy of incompetent perforators combined with compression therapy.

After ulcer has healed (complete epithelization)

patient given advice for use class II below knee graded compression stocking to prevent further breakdown and outpatient clinic follow up every month.

Also if there is indication for surgical interventions to correct CVI, appointment given.

STATISTICAL ANALYSIS

Continuous variables were presented as the mean \pm SD if normally distributed or median(range) if not normally distributed. Normality was checked by Kolmogorov-Smirnov test. Homogeneity of variance was checked by Levene's test.

Categorical variables were presented by the count (percentage).

Fisher's Exact Test.

Independent-samples t-test.

Mann-Whitney U test .

Threshold for significance.

RESULTS

Table (1) Comparison between the studied groups regarding demographic characteristics: There is statistically non-significant difference between the studied groups regarding age or gender

Table (2) Comparison between the studied groups regarding past history and risk factors: There is statistically non-significant difference between the studied groups regarding comorbidities, history of previous vascular operation, smoking or type of CVI.

Table (3) Comparison between the studied groups regarding ulcer characteristics: There is statistically significant difference between the studied groups regarding duration of ulcer in weeks (which was significantly higher among combined compression and injection group). On the other hand, there is non-significant difference between them regarding ulcer side, site, length, width or surface area.

Table (4) Comparison between the studied groups regarding outcome of management approaches: There is statistically significant difference between the studied groups regarding outcome. The largest percentage of patients within both groups had complete healing by the end

Table (5) comparison between the studied groups regarding change in ulcer surface areas over time: There is statistically non-significant

difference between the studied groups regarding surface area of ulcer at first, fourth, and fifth week. There is significant difference between them at second, third and sixth week.

Table (6) Comparison between the studied groups regarding tolerability to treatment approach There is statistically non-significant difference between the studied groups regarding their tolerability to compression. In combined groups, the largest percentage tolerated gel foam infection

Table (7) linear regression of variables correlated with duration of complete healing among the studied patients: On linear regression analysis of factors significantly correlated with duration of complete healing, only ulcer surface area at start of treatment was significantly associated with it ($\beta=1.031$, $p<0.001^{**}$). Increase ulcer surface area at start of treatment by 1 cm² increase duration of healing by about 1 week.

Table (1): Comparison between the studied groups regarding demographic characteristics:

	Compression group	Combined compression and foam injection group	Test of significance	p
	N (%)	N (%)		
Gender:				
Male	9 (81.8)	11 (100)	Fisher	0.476
Female	2 (18.2)	0 (0)		
Age:				
Mean ± SD	42 ± 7.8	35.18 ± 9.74	t(1.812)	0.085
Range	28 - 53	18 – 50		

Table (2): Comparison between the studied groups regarding past history and risk factors:

	Compression group	Combined compression and gel foam injection group	X ²	p
	N (%)	N (%)		
Comorbidity:				
No	9 (81.8)	9 (81.8)	0	1
Yes	2 (18.2)	2 (18.2)		
Previous vascular operation:				
No	9 (81.8)	7 (63.6)	Fisher	0.635
Yes	2 (18.2)	4 (36.4)		
Smoking:				
No	7 (63.6)	9 (81.8)	Fisher	0.635
Yes	4 (36.4)	2 (18.2)		
CVI type:				
Primary	7 (63.6)	6 (54.5)	Fisher	1
Secondary	4 (36.4)	5 (45.5)		

Table (3): Comparison between the studied groups regarding ulcer characteristics:

	Compression group	Combined compression and foam injection group	Test	p
	N (%)	N (%)		
Site:				

	Compression group	Combined compression and foam injection group	Test	p
Left leg	7 (63.6)	6 (54.5)	Fisher	1
Right leg	4 (36.4)	5 (45.5)		
Side:			Fisher	0.635
Lateral	4 (36.4)	2 (18.2)		
Medial	6 (63.6)	9 (81.8)		
Ulcer length (cm):			Z	0.134
Mean ± SD	2.14 ± 0.74	2.48 ± 0.9		
Median	2	2.5		
Range	1 – 3	1 – 4		
Ulcer width (cm):			Z	0.313
Mean ± SD	1.73 ± 0.68	2.02 ± 0.51		
Median	1.5	2		
Range	1 – 3.5	1.2 – 2.5		
Ulcer surface area (cm²):			Z	0.05
Mean ± SD	2.14 ± 1.28	4.07 ± 2.33		
Median	2.25	5		
Range	0.5 – 5	1 – 8		
Duration of ulcer (weeks):			Z	0.007*
Mean ± SD	12.64 ± 9.99	33.82 ± 25.23		
Median	8	26		
Range	4 – 30	12 – 90		

Table (4): Comparison between the studied groups regarding outcome of management approaches:

	Compression group	Combined compression and foam injection group	X2	p
	N=11 (%)	N=11 (%)		
Outcome:			Fisher	1
Non-healing	2 (18.2)	1 (9.1)		
Complete healing	9 (81.8)	10 (90.9)		
	N = 9	N = 10	T	
Duration to complete healing:			-4.333	<0.001**
Mean ± SD	6.44 ± 1.33	10 ± 2.1		
Range (min – max)	4 – 8	8 – 12		

Table (5): comparison between the studied groups regarding change in ulcer surface areas over time:

Ulcer surface area (cm ²)	Compression group		Combined compression and foam injection group		Z	p
	Mean ± SD	Median	Mean ± SD	Median		
At 1st week	2.14 ± 1.28	2.25	4.07 ± 2.33	5	-1.961	0.05
At 2nd week	0.97 ± 0.93	0.75	3.26 ± 2.21	3	-2.28	0.023*

Ulcer surface area (cm ²)	Compression group		Combined compression and foam injection group		Z	p
At 3 rd week	0.51 ± 0.72	0.13	1.94 ± 1.45	1.5	-2.66	0.01*
At 4 th week	0.5 ± 0.72	0	1.36 ± 1.15	1.5	-1.537	0.124
At 5 th week	0.88 ± 0.88	0.88	0.84 ± 0.61	0.5	-0.280	0.780
At 6 th week	0.63 ± 0.53	0.63	0.06 ± 0.18	0	-2.294	0.025*
p(Friedman test)	0.089		<0.001**			

Table (6): Comparison between the studied groups regarding tolerability to treatment approach

Tolerability to	Compression group	Combined compression and foam injection group	X ²	P
	N (%)	N (%)		
Compression:				
Comfortable	8 (72.7)	10 (90.9)	Fisher	0.586
Non-comfortable	3 (27.3)	1 (9.1)		
Gel foam injection:				
Comfortable		10 (90.9)		
Non-comfortable		1 (9.1)		

Table (7): linear regression of variables correlated with duration of complete healing among the studied patients:

	Unstandardized coefficient		Standardized coefficients	T	p	95%CI
	β	Standard error	β			
Ulcer surface area(cm²) at start of treatment	1.031	0.197	0.785	5.228	<0.001**	3.92 – 6.77

DISCUSSION

Chronic(VLUs) are the most common cause of chronic leg ulcers with large adverse effect on quality of life of the patient and loss of productivity. Although VLUs are not usually lead to limb loss but the chronicity & refractory nature of these type of ulcers need frequent visits to medical care provider and require to use bulky dressing for long duration that usually malodorous due to excessive oozing [6].

Approximately 1% of Europeans will develop chronic venous ulcer during their life. the point

prevalence of open ulceration is estimated at 0.1%. CVI has a large adverse effect on quality of life and the condition needs high health care costs [5].

The management depend on reversing the ambulatory venous hypertension which is the essential pathological factor behind the VLUs. Local care of the wound, including debridement, is mandatory for venous ulcers. There are severe different ways for debridement of wound, including autolytic, enzymatic and biologic debridement [7].

Ultrasound imaging has increasingly been used in the procedure to assess competence and patency of the deep veins, detect the incompetent perforator for cannulation, guide cannulation, monitor the injection and flow of foam to decrease the risk of foam diffusion to the deep system. Ultrasound is usually useful in the follow up period to detect the results of management and detect the need for further injections [8].

In our study duration of ulcer in weeks in combined group longer than in compression group so healing delayed in combined group but The largest percentage of patients within both groups had complete healing by the end.

Eweda and Zaytoun[9] evaluated the using of duplex guided foam injection of incompetent perforators to treat chronic venous ulcer in 40 patients of age ranging from 20 to 62 years (mean age of 43.4 years) and in our study The patients' ages in group A ranged from 28 to 53 years with a mean age of 42 ± 7.8 years while in group B ranged from 18-50 years with a mean age of 35.18 ± 9.74 .

There is statistically non-significant difference between the studied groups regarding age or gender.

In **Pinto et al.** [10] study, the thirty-two VLUs subdivided into 17 small size ulcers ≤ 10 cm² (mean initial surface area 4.9 cm² S.D. 2.9 cm²) and 15 large size >10 cm² (mean initial surface area 27.9 cm² S.D. 18.2 cm²). The mean initial surface area in this current study for group A = 4.75cm² S.D.1.4 cm²and for group B = 5.19 cm² S.D. 2.4 cm², we include range for largest diameter of ulcer to be not excess 10 cm in inclusion criteria of this study to avoid over scattering of data between both groups.

In **Mine et al.** [11] a trial of foam injection opposite radio frequency and laser ablation would be possible but may be unnecessary.

Our study nearly agreed with results of **Pinto et al.** study as all cases of of small initial surface area group (≤ 10 cm²) completely healed but need longer duration as mean time for complete healing of all cases 6.3 weeks. The large initial

surface area group 67% of cases completely healed in mean duration of 12.6 weeks.

In a multivariate analysis, **Gohel et al.** [12] found that both long ulcer duration and deep venous reflux were bad prognostic factors; the latter appears to be the case in the present series too. Beyond 6 months, follow-up rates were really too low to take good analysis of longer time healing and recurrence rates; and repeated post-procedures ultrasound image to determine the success of management would be unnecessary However, they reasonably concluded on the basis of their short term results that foam injection of ulcers was promising.

Kulkarni et al. [13] reported that residual superficial venous reflux after surgery isn't the most important predictor of recurrence of VLU, although the hazard ratio of ulcer recurrence by 3 years was 2.5 in those with residual GSV reflux below the knee, this is not achieving statistical significance.

In **Darvall and Bradbury** [5] study, 27 patients (28 ulcers) of median age 69 years undergoing duplex guided foam injection plus compression in the management of VLUs were prospectively studied. Prior to and at 1, 3, 6 months after management. Median volume of foam used was 8 (range 2–14) mL. At 1, 3 and 6 months after foam injection, 22 (79%), 27 (96%) and 27 (96%) venous ulcers had healed. 2 (7%) ulcers had recurred, one patient died from carcinomatosis. The main finding is as follows: following foam injection with compression, 27 of 28 (96%) venous ulcers healed within 3 months and only 2 ulcers had recurred later on.

Pang et al. [14] study was performed on 130 consecutive patients (132 limbs) of median age 70 years who underwent foam injection as a part of management for venous ulcers. The main finding is that when combined with compression, elimination of superficial reflux by foam injection leads to 81% healing rate at 6 months and 5% recurrence rate at 2 years.

Gamal et al. [15] compared foam injection with surgery in management of patients with

lry chronic venous disorders. They concluded that foam injection is effective in eliminating saphenous trunks. Follow-up management foam injection and surgery accomplished similar refinements in the VCSS. The anatomical success rate was similar for both modalities.

Many of the patients in our study would have been unsuitable for catheter directed techniques and most would have required adjuvant techniques (foam injection). Patients with chronic VLU have poor healing, making incisions through diseased skin is problematic. Therefore, it seems reasonable to suggest that where possible, such patients should be treated by minimally invasive alternative.

CONCLUSION

The compression therapy is important line in management of venous ulcers. This synergistic approach can improve quality of life through shortening time needed for compression therapy and rapid recovery for normal daily activity. Duplex-guided foam injection is a minimal invasive procedure, compared to surgery, it avoids the need for general anesthesia, hospital admission and long recovery times and may be done in outpatient clinic. As absence of serious complications and its evident success, make this the first line management for venous ulcer beside compression but we need larger number of patient and longer time for follow up to obtain good result.

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