Combined Modality Treatment of Lymphedema using the ReidSleeve and the BioCompression/Optiflow System.

Renee Robinson, Lisa A Massa PT CLT, Jennifer Maddox, PT, Nancy Guillett, LMT, CLT-LANA, Katherine Arsenault, MPT, CLT-LANA, Deborah Daugherty, MOT, CLT-LANA, Cheri Hoskins, Stephen Morgan, Ann Hafner and Tony Reid MD, Ph.D.

Duke University School of Medicine (LM, JM), Healthtronix Lymphedema Management, Inc (NG, KA, DD, CH) and Peninsula Medical (RR, SM, AH, TR)

Abstract

35 patients (16 upper extremity/19 lower extremity) with refractory lymphedema were enrolled on a longitudinal study using the ReidSleeve in combination with the BioCompression/Optiflow system. The primary objective of this study was to evaluate the effectiveness of this combined modality therapy. Patients wore the ReidSleeve at night and used the BioCompression pump with the ReidSleeve Optiflow insert for 2 sessions of 60 minutes during the day with class II compression stocking for the remainder of the day. Among patients with upper extremity edema, the reduction in lymphedema was 24.7, 53.8 and 80.2% at 4, 12 and 28 weeks. Linear regression analysis demonstrates a highly significant ($p<0.001$) reduction in arm edema during the course of treatment. A plateau phase occurred between weeks 4 and 8 weeks. Among patients with lymphedema edema of the lower extremity, the average reduction was 296, 646, 607, 484, 305, and 884 ml at 1, 2, 4, 8, 12 and 16 weeks respectively. These patients demonstrated marked reductions in lymphedema during the first 2 to 4 weeks followed by a period of relatively stable lymphedema until week 12 with a further decrease in average volume of lymphedema of 14496 cubic centimeters by week 16. Linear regression analysis demonstrates a significant ($p<0.001$) decrease in leg edema. The ReidSleeve used in combination with the BioCompression/Optiflow system provides effective management for upper and lower extremity lymphedema.

Introduction

Lymphedema in developed countries is generally secondary to radiation induced damage or surgical resection of lymphatic vessels and nodes resulting in lymphatic obstruction and the accumulation of a protein-rich interstitial fluid. Chronic inflammation caused by the abnormal accumulation of interstitial fluid causes proliferation of fibroblasts, keratinocytes and adipocytes, disruption of normal elastic fibers and the accumulation of subcutaneous lipid deposits. The chronic responses result in the characteristic thickening, hardening and discoloration of the skin. Treatment strategies for lymphedema need to address 1) the acute accumulation of interstital fluid and 2) the chronic adaptive changes that result in thickened and abnormal skin and subcutaneous tissue.

Lymphatic vessels collect fluid from the interstitial area between cells. Lymphatic fluid is propelled forward by the arterial and muscle pumps. Lymphatic vessels are squeezed by the expansion and recoil of the arterial system contained within the same connective tissue sheath. Similarly, the compression of lymphatic vessels by expansion and contraction of muscles during movement propels lymphatic fluid forward. Retrograde flow is prevented by numerous one-way valves within the lymphatic vessels. The resilient foam construction of the ReidSleeve with high and low compression points is designed to simulate and augment the expansion and recoil of the artery and muscle on lymphatic vessels and the effects of the lymphatic gates. A protocol was developed at Duke University combining the ReidSleeve with intermittentgradient, sequential, pneumatic compression. The rationale for this combination was that the ReidSleeve Optiflow insert combined with intermittent sequential pneumatic compression could effectively modulate interstitial pressure, mimick the effects of the muscle pump and enhance the therapeutic impact of each modality. The impact of combined therapy with the ReidSleeve and the BioCompression/Optiflow system is reported.

Methods:

Design of the study:
Patients were treated by a protocol used at Duke University for the treatment of moderated to severe lymphedema. Patients were fitted for the ReidSleeve Classic and used this garment during the nightime. During the daytime the patients wore class II compression stocking except for 2 sessions of treatment with intermittent sequential pneumatic compression using a BioCompression pump with a ReidSleeve Optiflow insert. The addition of the Optiflow insert resulted in a baseline compression of 4 to 6 mmHg, approximately the level of venous pressure. Intermittent compression was provided by the sequential pneumatic pump. The maximal compression was initially set at 20mmHg and gradually increased in increments of 5mmHg over several hours. The compression was set for each patient at a point that provided comfortable compression without a sensation of congestion or discomfort. If the patient subsequently developed symptoms of discomfort, the pressure was reduced in increments of 5mmHg until the discomfort resolved. The compression of the ReidSleeve Classic was set using the Precise Compression gauge and increased in 5mmHg increments as described above until comfortable compression was obtained without the sensation of congestion or discomfort.

Sequential circumferential measurements using a gauged that provided consistent stretch force during measurements. Measurements were taken every 3 inches over the length of the extremity. The volume of the extremity was calculated with the truncated cone formula. Changes were determined, when possible, as a percentage of excess volume compared to the uninvolved extremity. Many of the patients with lower extremity edema had bilateral involvement. Among these patients the change is shown as absolute volume.

Patients were treated according to the Duke protocol and informed consent was obtained for collection and analysis of the measurements under the auspices of the Duke IRB.

Results:

16 patients with moderate to severe upper extremity edema were treated according the Duke protocol. These patients received treatment with the ReidSleeve Classic as detailed in the methods, coupled with 2 daily treatment with intermittent sequential pneumatic compression using the BioCompression pump with the Optiflow compression insert. The patients wore compression sleeves/stocking during the intervening times. The results of treatment are shown in **Fig. 1**. The patients demonstrated rapid and consistent reduction in lymphedema during the first 4 weeks of treatment, achieving a 25% reduction in lymphedema by the 4^{th} week. 50% reduction in lymphedema was observed at 16 weeks and 80% reduction was observed at 28 weeks. Between weeks 28 and 36 there is an apparent increase in lymphedema among these patients; however, nearly half of these patients achieved effective control of the lymphedema and entered the maintenance phase of treatment and were seen less frequently. As a result, patients with effectively controlled lymphedema were no longer included at these late time points. Nevertheless, patients with more severe lymphedema were responding and the reductions these patients achieved was 50 to 75% at 36 weeks.

Linear regression analysis was used to determine the significance of the reduction in lymphedema with time of treatment (**Fig. 2**). This analysis demonstrates that there is a consistent improvement in lymphedema with time after initiation of treatment with the ReidSleeve-BioCompression/Optiflow system. 50% reduction in lymphedema is seen at approximately 16 weeks. The response to treatment is highly significant ($p<0.001$). By approximately 60 days some patients had achieved reductions in excess of 90%. These patients were placed on

maintenance therapy and were taken of the study. As a result, the average improvement during subsequent times reflects the patients remaining on study and the average response is lower as the best responding patients were removed. During the initial phase some patients had worsening lymphedema. These exacerbations were transient and due to secondary causes common among patients with moderate to severe lymphedema including infections. When treated these patients were put back on treatment. By 3 to 4 months after initiation of treatment, marked improvement in lymphedema was observed in nearly all patients.

A plateau in response can be seen between weeks 4 and 8 among these patients. The initial rate of reduction was 6.2% per week (**Fig. 1**). Following a leveling off or plateau period, further reductions are observed, however, the rate of reduction is 3.1% per week.

Reductions in excess of 100% are noted in some patients. After effective control of lymphedema, the affected extremity can be smaller than the unaffected extremity. This appears to be due to atrophy of the musculature of the affected extremity.

The results of treatment of patients with lower extremity edema are shown in **Fig. 3**. Mobilization of excess edema can be seen among these patients during the first 2 weeks of therapy. These patients have moderate to severe lymphedema and the average loss of edema observed during the first two weeks is 700cc. The marked decrease in lymphedema observed among these patients was followed by a plateau phase between weeks 2 and 12. Following week 12, further reductions in lymphedema were observed among these patients.

Discussion

Lymphedema is a complex problem. In most cases in the developed countries, lymphedema arises from the disruption of lymphatic vessels and nodes due to surgery, radiation or both. Obstruction of lymphatic flow results in retention of interstitial fluid within the tissue leading to swelling. Retention of interstitial fluids and associated proteins results in chronic inflammatory process that leads to the changes characteristic of lymphedema. This includes thickening and discoloration of the skin, loss of tensile strength of elastic fibers and accumulation of adipocytes and subcutaneous fat. Effective treatment of lymphedema requires the resolution of excess of interstitial fluid and normalization of the compensatory abnormalities of the skin and subcutaneous tissue. Therefore, removal of the accessible interstitial fluid is an important first step in the treatment of lymphedema, but must be followed by reduction of the excess fibroblasts and adipocytes, removal of excess lipid, remodeling of the thickened layers of skin and restoration of the tensile strength of elastic fibers. Effective remodeling of the skin and subcutaneous tissue, requires minimization of the stress on these tissues. To achieve the optimal interstitial pressure that will facilitate removal of excess interstitial fluid and to minimize stress on recovering tissues, we have used the ReidSleeve in combination with the BioCompression/Optiflow system.

The ReidSleeve provides gentle compression using a multitude of high and low compression points. The resilient foam used in the ReidSleeve models the compression normally applied to the lymphatic system by the expansion and recoil of the arterial system and the intermittent compression of the muscle pump. To assure minimal stress on the recovering tissue, soft foam is used at the lowest pressure necessary to achieve reduction of interstitial edema. Excess pressure not only adds increased stress to the tissue but can also lead to compression and obstruction of functioning lymphatic vessels.

The ReidSleeve Optiflow insert inside of the sequential pneumatic compression chamber to achieve optimal interstitial pressure without causing obstruction. The intermittent compression of the sequential pneumatic pump can augment the massaging effects of the Optiflow insert. Furthermore, the sequential pneumatic pump can be adjusted to optimize the interstitial pressure. The system is designed to provide a baseline compression of approximately 4 to 6 mmHg pressures, a level of compression consistent with venous pressure. During inflation, the pressure exerted increases smoothly and gradually to a peak pressure that can be adjusted to the patients needs. In this protocol, the peak pressures were increased in increments of 5mmHg to achieve reduction in lymphedema without causes the sensation of congestion or discomfort in the extremity. The ReidSleeve was used nightly, the BioCompression/Optiflow system was used for 2 periods of 60 minutes during the day and level II compression sleeves were used for the remainder of daytime wear.

The results from this study demonstrated marked reduction of lymphedema of the upper and lower extremity of patients with moderate to severe lymphedema refractory to other treatments. Patients with upper extremity lymphedema demonstrated a 25% reduction at 4 weeks, 50% reduction at 16 weeks and 80% reduction at 28 weeks. The initial rate of reduction was 6.2% per week. However, this rate decreased to 3.1% per week following a brief plateau phase. The initial response most likely represents removal of excess interstitial fluid. The rate of improvement was slower in subsequent weeks consistent with the remodeling and normalization of the skin and subcutaneous tissues. The long-term treatment of lymhedema is dependent on reversing the skin and subcutaneous tissues. Proliferation of fibroblasts, keratinocytes and adipocytes occur in response to the irritation and stress of the accumulated interstitial fluid. The continued reduction in lymphedema and the improvement in skin tone and color were achieved over the course of treatment demonstrates that this combination of therapies can 1) decrease interstitial edema and 2) facilitate the healing of the skin and subcutaneous tissues.

Marked reductions in lymphedema and improvements in skin and tone and appearance were also observed among patients with lower extremity lymphedema. Many of these patients had bilateral lymphedema that precluded the precise determination of the volume of the unaffected extremity. However, significant absolute volume reductions were observed among these patients with moderate to severe lymphedema over the first 2 to 4 weeks of treatment. This was followed by a protracted plateau phase that was characterized by gradual improvement in skin tone and color. Starting at approximately 12 weeks additional reductions in lymphedema were observed. By maintaining optimal interstitial compression while avoiding unnecessary stress on the tissues during the plateau phase, the necessary tissue repair became evident and provided a basis for further reductions in the subsequent weeks and months. The results of this study demonstrate that because lymphedema is the combination of both interstitial fluid and the compensatory proliferative changes of the skin and subcutaneous tissues, the true measure of success in treating lymphedema should be determined over 4 to 12 months of treatment.

Figures

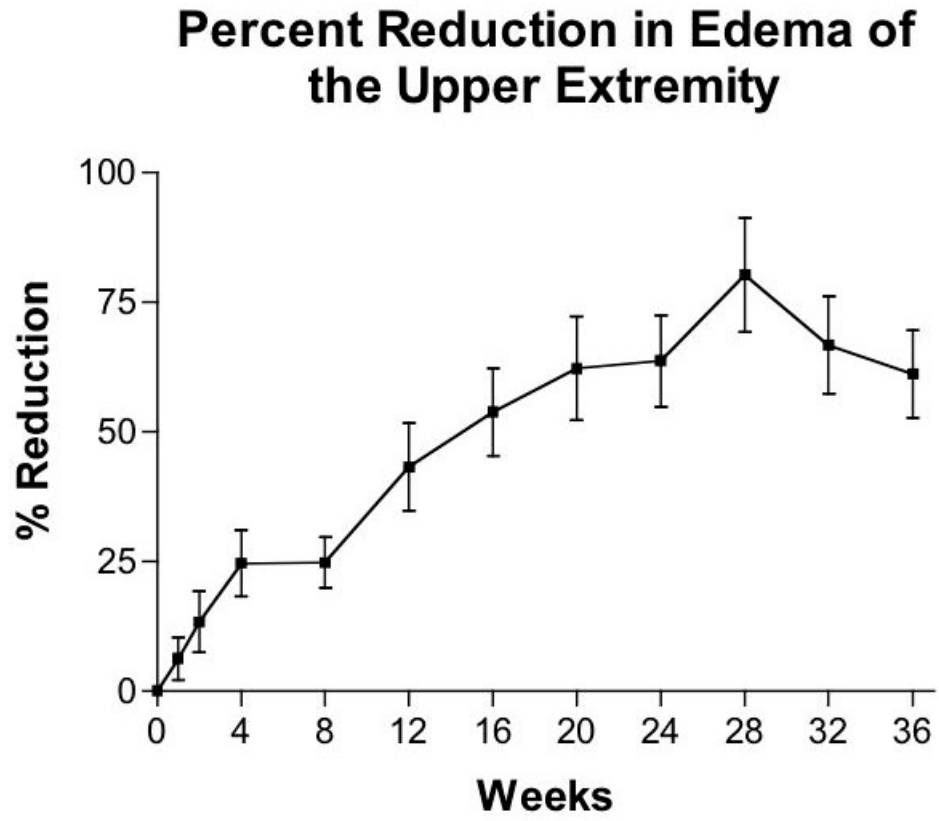

Fig. 1. Effect of Combined Treatment with ReidSleeve and BioCompression/Optiflow. 16 patients with refractory lymphedema were followed for 36 weeks following initiation of treatment using the Duke protocol. The percent reduction in lymphedema was determeined by subtracting the volume of the unaffected extremity from the volume of the affected extremity leaving the amount of excess volume. A 100% reduction would result in normalization of the volume of the affected extremity.

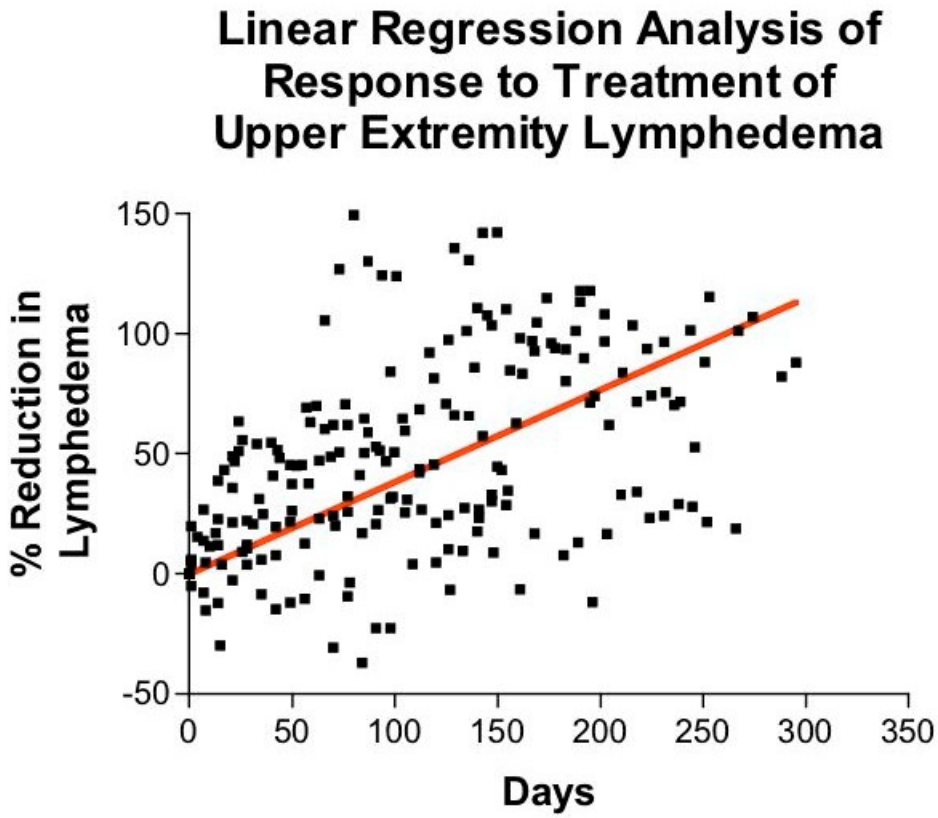

Fig. 2. Scattergram of the effect of the ReidSleeve Biocompression/Optiflow System. Linear regression analysis demonstrates progressive decrease in lymphedema with time of treatment.

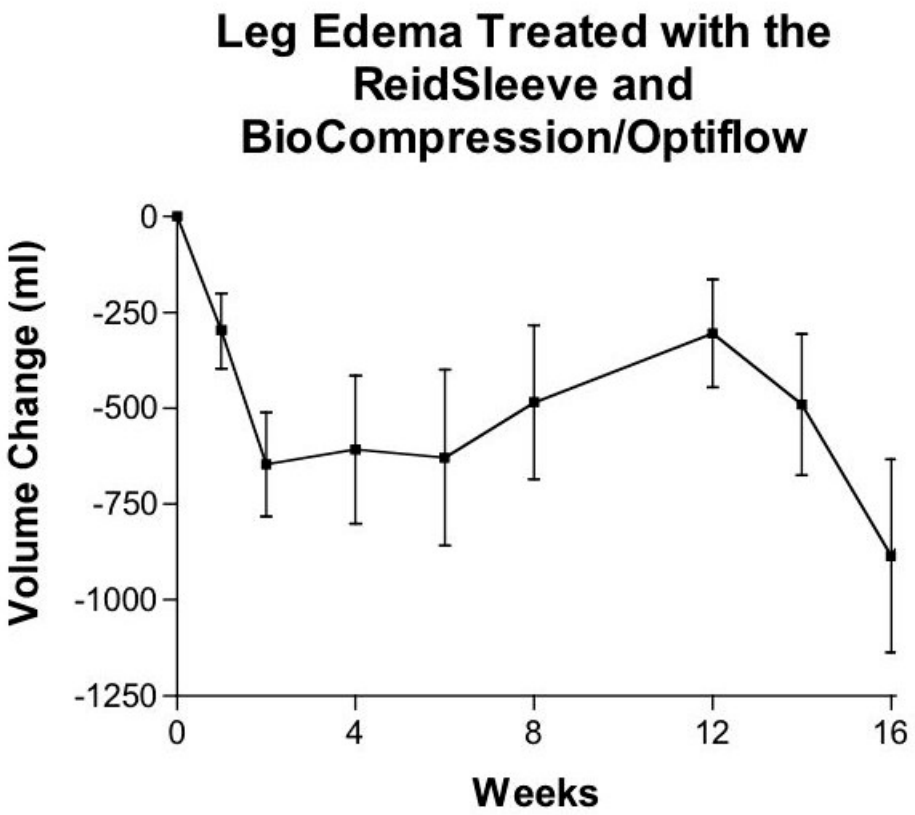

Fig. 3. Effect of Combined Treatment with ReidSleeve and BioCompression/Optiflow among patients with lower extremity lymphedema. 19 patients with refractory lymphedema were followed for 16 weeks following initiation of treatment using the Duke protocol. The reduction in tissue volume of the affected extremity is shown.