Efficacy, safety and acceptability of a new two-layer bandage system for venous leg ulcers

- **Objective:** To evaluate the efficacy, tolerability and acceptability of a new two-bandage compression system in the local management of venous or mixed aetiology ulcers predominantly of venous origin.
- **Method:** This was a prospective non-comparative open label phase III clinical study. Forty-two patients were recruited from 12 centres. Inclusion criteria included ulcers with at least 50% granulation tissue, a surface area of 2–20cm^2, an ulcer duration of 1–24 months, an ankle circumference of less than 28cm, and no history of deep vein thrombosis in the three months before enrolment. The primary endpoint was reduction in ulcer surface area, and secondary endpoints were the evolution of leg oedema and patient comfort. During the six-week follow-up, patients underwent weekly clinical assessments and their ulcer surface area was measured by planimetry and photography every alternate week.
- **Results:** The mean ulcer surface area at inclusion was 7 ± 6cm^2. The mean surface reduction after six weeks was 58.5%, with 24% of the treated wounds healing in a mean time of 25.9 ± 9.46 days. The patients considered that the new compression system had a better effect on quality of life, evaluated by parameters such as pain, heat, itching and general comfort, than the system worn before entry into the study. Patient concordance with the new system was excellent and 86% of leg ulcers improved or healed after six weeks. Local tolerance was considered very good.
- **Conclusion:** This new two-bandage compression system is effective and well accepted by patients.
- **Declaration of interest:** This study was sponsored by Laboratoires Urgo, Chenôve, France.

multi-bandage system; compression therapy; clinical trial; venous leg ulcers

The pain and isolation caused by chronic venous leg ulcers has a major impact on patients' quality of life.[1-3] There are two complementary local treatments for these ulcers:[4]

- Topical treatment (such as zinc paste bandage) plus a primary dressing that uses the principles of moist wound healing to recover the wound bed and the surrounding skin[5,6]
- Compression therapy, which addresses the aetiological cause of the ulceration by promoting venous return and restricting venous stasis.[7,8] Compression therapy systems include elastic or non-elastic bandages, monolayer or multilayer bandaging, short-, medium- or long-stretch bandages and hosiery.[9]

A better understanding of the pathophysiology of venous disease and the advent of systems that can measure the interface pressures exerted by compression bandages have led to the development of reliable and effective compression systems.[10] Selection depends on parameters including patient preference, patient concordance and acceptability and ease of use for both the practitioner and patient.[11]

There are wide variations in venous leg ulcer management. In the US Unna's Boot is favoured, while in the UK multilayer elastic compression is widely used and in continental Europe short-stretch bandaging is standard practice.[12] However, each type of compression has disadvantages[13] that can limit patient concordance. In addition, numerous randomised clinical studies have been unable to show the superiority of one multilayer compression system over another,[14-17] while others have found no differences between short-stretch and multilayer bandages.[18-21]

Laboratoires Urgo has recently developed a two-bandage compression system, K-Two. This is the first two-bandage system in which the two layers are designed to spread the pressure evenly between them. This clinical trial set out to evaluate the therapeutic efficacy, tolerability and acceptability of this new compression system in the management of venous leg ulcers.

Materials and method

This multicentre non-comparative phase III open-label clinical trial was conducted in France by private specialist physicians (angiology-phlebology) and physicians from hospital dermatology and vascular medicine units. One physician from each of the 12 participating centres recruited adult outpatients into the six-week trial.

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Table 1. Patient demographic data (n=42)

Gender:	
• female	22 (52%)
• male	20 (48%)
Age (years)	70.5 ± 14.1 (37.5–92.9) 73.9
Weight (kg):	
• female	78.3 ± 20.9 (52–130)
• male	92.4 ± 24.9 (56–140)
Height (cm):	
• female	162 ± 10 (142–180)
• male	177 ± 7 (160–195)
Body mass index (kg/m²)	29.5 ± 6.8 (19.8–45.2) 27.7
Medical history:*	
• hypertension	18 (43%)
• heart disease	9 (21%)
• cigarette smoker	9 (21%)
• diabetes mellitus	8 (19%)
• allergy to a previous wound dressings	4 (10%)
Phlebological history:*	
• previous history of leg ulceration	36 (86%)
• phlebitis	21 (50%)
• stripping	21 (50%)
• sclerosis	12 (29%)
• family history of chronic venous disorders	28 (68%)

Data were given for more than one category
Results are given as mean ± SD (range) followed by the median unless otherwise indicated

The inclusion criteria were:
- Ulcer size of 2–20cm²
- Ulcer duration of 1–24 months
- Venous aetiology, confirmed by Doppler
- Patients who had already been treated with multilayer compression (two-, three- or four-bandage)
- Ulcers with more than 50% granulation tissue
- Patients who could be followed up by the same investigator for the six-week treatment period.

Exclusion criteria were:
- An ankle circumference over 28cm
- Dry, non-exuding, sloughy ulcers (as these would be unsuitable for the primary dressings supplied to the investigators)
- Ulcers with clinical signs of infection
- Malignant ulcers
- Progressive neoplasic lesions being treated with radiotherapy or chemotherapy, immunosuppressive drugs or high-dose corticosteroids
- Patient who had presented with deep vein thrombosis in the three months before inclusion.

The Versailles medical ethics committee approved the study, which was conducted in concordance with the principles of good clinical practice and the Declaration of Helsinki. Written informed consent was obtained from each patient before inclusion.

The new compression system

The K-Two system comprises two bandages:
- K-Tech — the primary bandage, which is composed of viscose and polyester wadding within a knitted compressive layer. According to the manufacturer, it offers good absorbency and protection and a light compression
- K-Press — a secondary, woven, cohesive, stretch bandage.

When applied with the recommended 50% overlap, the two bandages produce an average pressure of 40mmHg at the ankle.[22,23] Both bandages have elliptical patterns on them that form circles when applied (stretched) correctly — this is referred to as the 'etalonnage'. According to a paper presented at a recent conference, this simplifies application and makes it easier to ensure the correct pressure is given.[23]

K-Two is contraindicated in patients with arterial ulcers and arterial disease, and is not recommended for those with an ABPI less than 0.8.

Primary dressings

The study sponsor provided the investigators with two primary dressings — UrgoCell Non-Adhesive (Cellosorb Non-Adhesive, Laboratoires Urgo) or Urgotul (Laboratoires Urgo), with the intention of avoiding the potential for bias resulting from the use of different primary dressings. However, the physicians were free to use other primary dressings if they thought the wound required it, although in the event none did so.

The primary dressing was changed at the same time as the K-Tech bandage. The investigators, who were experienced in the use of multilayer compression therapy, all received the same training on the application of the new system. The frequency of dressing changes was determined by the physicians, based on clinical need.

Clinical assessment

The physicians measured the ulcer surface area using planimetry and photographs at entry and then every two weeks. Clinical assessments, recorded at baseline and then weekly, included:
- The condition of the surrounding skin
- Ankle brachal pressure index measurements
- The presence of oedema on the lower limb (circumference measured using a tape measure)
- Presence of trophic disorders on the contralateral lower limb
- Exudate level
- Spontaneous wound pain (that occurring between dressing changes).

References

1 Hareendran, A., Bradbury, A., Budd, J. et al. Measuring the impact of venous leg ulcers on quality of life. J Wound Care 2005; 14: 2, 53-57.
2 Smith, J.J., Guest, M.G., Greenhalgh, R.M., Davies, A.H. Measuring the quality of life in patients with venous ulcers. J Vasc Surg 2000; 31: 4, 642-649.
3 Lamping, D.L., Schroter, S., Kurz, X. et al. Evaluation of outcomes in chronic venous disorders of the leg: development of a scientifically rigorous, patient-reported measure of symptoms and quality of life. J Vasc Surg 2003; 37: 2, 410-419.
4 Phillips, T.J. Current approaches to venous ulcers and compression. Dermatol Surg 2001; 27: 7, 611-621.
5 Winter, G.D. Formation of the scab and rate of re-epithelialization of superficial wounds in the skin of the young domestic pig. Nature 1962; 193: 293-294.
6 Winter, G.D. Effect of air drying and dressings on the surface of wounds. Nature 1963; 197: 91-93.
7 Moffatt, C. Leg ulcers. In; Murray, S. (ed.). Vascular Disease: Nursing and management. John Wiley & Sons, 2001.
8 Vowden, P. The investigation and assessment of venous disease. J Wound Care 1998; 7: 3, 143-147.
9 Bello, Y.M., Phillips, T.J. Management of venous ulcers. J Cutan Med Surg 1998; 3: 1 (Suppl.), 6-12.
10 Ramelet, A.A. Compression therapy: a new demonstration of its effectiveness. Dermatology 1998; 197: 4, 309.

Endpoints

The primary endpoint was the reduction in wound surface area during the six-week follow-up period. Secondary endpoints were:

- An improvement in the clinical condition of the wound, as assessed above
- Occurrence of adverse events: clinical signs of wound infection as diagnosed by the investigators, and bleeding from the wound or damage to the surrounding skin
- Acceptability of the new system to the patient: defined as concordance and its effect on quality of life, measured as pain intensity, frequency of pain, itchiness, sensation of heat under the compression bandages, ease of wearing shoes, and general comfort both during the day and during the night.

Statistical analysis

A descriptive statistical analysis was performed on all patients included in the trial, conducted on an intention-to-treat (ITT) basis for the primary and secondary endpoints. If the patient withdrew or healed before week 6, the efficacy analysis took account of the last evaluation available (last observation carried forward, LOCF). Continuous data are described by sample size, mean, standard deviation, median and range; discrete data are described by absolute and relative frequencies.

Results

Baseline population

Forty-two outpatients were recruited from the 12 investigating centres. This was considered sufficient to determine the efficacy of the new system, as defined by the study. Patient demographic data are given in Table 1.

The gender distribution was evenly balanced, while the mean body mass index (BMI) was 'overweight' at 29.5 ± 6.8 kg/m². There was a relatively high incidence of high blood pressure (43%) and diabetes mellitus (19%).

Ulcer history

Baseline ulcer characteristics are given in Table 2. Most of the ulcers were recurrent (62%), and in only three cases (7%) was the surrounding skin 'healthy'. Spontaneous pain was moderate to intense in over 70% of the patients, even when venous origin was confirmed by Doppler (ABPI: 1.0 ± 0.1).

Twenty-nine patients (69%) presented with oedema in the lower ulcerated limb.

All but one had been wearing compression bandaging applied by the investigators — the exception being a patient who was presenting with an ulcer for the first time:

- 32% used a single bandage (long-stretch)
- 39% used a two-bandage system
- 29% used a three- to four-bandage system.

Table 2. Baseline leg ulcer characteristics (n=42)

Ulcer duration (months)	8.1 ± 10.4 (1–60)
Ulcer surface area (cm²)	6.97 ± 6.43 (0.78–27.76)
Recurrent ulcer	26 (62%)
Venous insufficiency:	
• superficial venous system	26 (62%)
• superficial and deep systems	11 (26%)
• Deep	5 (12%)
ABPI	1.0 ± 0.1 (0.8–1.3) 1.0
Ulcer location:	
• right lower limb	15 (36%)
• left lower limb	27 (64%)
Ulcer position:	
• malleolar	12 (29%)
• supramalleolar	15 (36%)
• submalleolar	4 (10%)
• other	11 (26%)
Condition of the surrounding skin:*	
• healthy	3 (7%)
• erythematous	23 (55%)
• eczematous	10 (24%)
• oedematous	18 (43%)
• irritated by the dressing(s)	7 (17%)
• macerated	6 (15%)
• other	3 (7%)
Exudate level:	
• absent	1 (3%)
• moderate	30 (79%)
• heavy	7 (18%)
• very heavy	–
Oedema in the lower limb under study	29 (69%)
Spontaneous wound pain:	
• absent	4 (10%)
• minor	8 (19%)
• moderate	16 (38%)
• intense	14 (33%)
Response to previous treatment:	
• clear improvement	5 (12%)
• moderate improvement	14 (33%)
• stagnation	11 (26%)
• worsening	12 (29%)

* More than one response could be given
Results are presented as mean ± SD (range), followed by the median unless otherwise stated
ABPI = ankle brachial pressure index

11 Dale, J.J., Ruckley, C.V., Gibson, B. et al. Multi-layer compression: comparison of four different four-layer bandage systems applied to the leg. Eur J Vasc Endovasc Surg 2004; 27: 1, 94-99.

12 Cullum, N., Nelson, E.A., Fletcher, A.W., Sheldon, T.A. Compression for venous leg ulcers. Cochrane Database Syst Rev. 2001; 2: CD000265.

13 Gardon-Mollard, C., Ramelet, A-A. La contention médicale. Collection Abrégés de Médecine, edition MASSON, 1999.

14 Vowden, K.R., Mason, A., Wilkinson, D., Vowden, P. Comparison of the healing rates and complications of three four-layer bandage regimens. J Wound Care 2000; 9: 6, 269-272.

15 Moffatt, C.J., Simon, D. A., Franks, P.J. et al. Randomized trial comparing two four-layer bandage systems in the management of chronic leg ulceration. Phlebology 1999; 14: 139-142.

16 Franks, P.J., Moffatt, C.J., Ellisson, D.A. et al. Quality of life in venous ulceration: a randomized trial of two bandage systems. Phlebology 1999; 14: 3, 95-99.

17 Moffatt, C.J., McCullagh, L., O'Connor, T. et al. Randomized trial of four-layer and two-layer bandage systems in the management of chronic venous ulceration. Wound Repair Regen 2003; 11: 3, 166-171.

18 Partsch, H., Damstra, R.J., Tazelaar, D.J. et al. Multicentre, randomised controlled trial of four-layer bandaging versus short-stretch bandaging in the treatment of venous leg ulcers. VASA 2001; 30: 2, 108-113.

19 Franks, P.J., Moody, M., Moffatt, C.J. et al. Randomized trial of cohesive short-stretch versus four-layer bandaging in the management of venous ulceration. Wound Repair Regen 2004; 12: 2, 157-162.

20 Polignano, R., Bonadeo, P., Gasbarro, S., Allegra, C. A randomised controlled study of four-layer compression versus Unna's Boot for venous ulcers. J Wound Care 2004; 13: 1, 21-24.

Table 3. Acceptability and effect on quality of life of the compression systems used at baseline and throughout the study

	Baseline	Throughout study*
	No. (%)	No. (%)
Pain under compression system?		
• Yes	33/41 (81)	115/215 (53)
• No	8/41 (20)	100/215 (47)
Intensity of pain:		
• minor	6/33 (18)	29/115 (25)
• moderate	12/33 (37)	52/115 (45)
• intense	13/33 (40)	29/115 (25)
• very intense	2/33 (6)	5/115 (4)
Frequency of pain**		
• continuous	10/31 (32)	10/115 (9)
• intermittent	21/31 (68)	105/115 (91)
Itchiness†		
• none	18/41 (44)	159/268 (59)
• moderate	17/41 (42)	87/268 (32)
• intense	6/41 (15)	21/268 (8)
• very intense	—	1/268 (0.3)
Sensation of heat†		
• none	23/41 (56)	175/268 (65)
• moderate	14/41 (34)	78/268 (29)
• intense	4/41 (10)	12/268 (5)
• very intense	—	3/268 (1)
Ease of wearing shoes†		
• very easy	7/41 (17)	59/268 (22)
• easy	24/41 (59)	166/268 (62)
• difficult	7/41 (17)	35/268 (13)
• very difficult	3/41 (7)	8/268 (3)
General comfort during the day†		
• very good	4/41 (10)	107/268 (40)
• good	28/41 (68)	147/268 (55)
• poor	9/41 (22)	14/268 (5)
• very poor	—	—
General comfort during the night‡		
• very good	4/26 (15)	92/262 (35)
• good	17/26 (65)	149/262 (57)
• poor	5/26 (19)	19/262 (7)
• very poor	—	2/262 (0)

*To give a full picture of the effects of the new two-bandage compression system on quality of life, results are given for all weekly clinical assessments conducted throughout the six-week follow-up period
** Data are missing for two of the 33 patients who experienced pain at baseline
† One patient had not been prescribed compression before inclusion
‡ The total is different to 41 for baseline general comfort during the day because some patients did not wear compression system during the night

Nearly 55% of the treated ulcers had not improved despite the compression therapy.

Effect of the prior treatment on quality of life

At the inclusion visit, the investigators evaluated the acceptability of the previous compression system used and its effect on quality of life:

- Thirty-three patients (81%) had experienced pain, which was 'intense' in 13 (40%) and 'continuous' in 10 (32%)
- Twenty-three (57%) perceived that their skin felt moderately or intensely itchy under the previous compression system
- Eighteen (44%) considered that their skin felt moderately or intensely hot under the compression system
- Ten (24%) had difficulty putting on their shoes when wearing the compression bandages
- Nine (22%) and five (19%) reported that the compression bandaging was uncomfortable during the day and at night respectively.

Full results are given in Table 3.

Efficacy

Planimetric measurements for all patients identified a mean reduction in wound surface area of 58.51% after six weeks (median value: 72.5%). Fig 1 illustrates the mean reduction that occurred during the course of the treatment.

At the end of the six-week treatment, the mean surface area was 2.42 ± 3.60cm^2 (median 1.05cm^2) $p<0.0001$), compared with 6.97 ± 6.43cm^2 (median 4.96cm^2) at baseline.

Ten ulcers (24%) healed in a mean of 25.9 ± 9.46 days (range 7–41). Their baseline mean surface area was 6.2cm^2 and the mean duration was 6.7 months. The baseline surface area reduced by more than 40% in 32 of the 42 patients in a mean of 18.8 days.

At six weeks, the investigators considered that 10 ulcers had healed, 26 had 'improved', four had stagnated and two had increased in size.

Secondary endpoints

- ***Clinical assessments*** At week 6, only five patients (12%) still had clinical oedema of their lower limb compared with 29 (70%) at baseline. Ten ulcers (30%) had a healthy surrounding skin, compared with only three (7%) at baseline.
- ***Impact on quality of life*** Patients reported that they had experienced spontaneous pain in 53% of the weekly assessments conducted throughout the course of the study. It was considered 'intense' in 25% of the study assessments, compared with 45% at baseline. When present, pain was reported as 'continuous' in 9% of the study assessments, compared with 32% at baseline.

Less itchiness was perceived underneath the new system: patients reported no itchiness in 59% of the

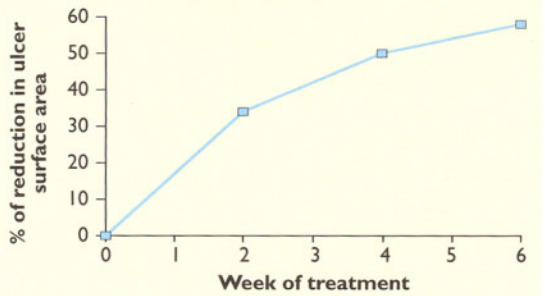
32 Hill, D.P, Poore, S., Wilson, J. et al. Initial healing rates of venous ulcers: are they useful as predictors of healing? Am J Surg 2004; 188: (1A Suppl), 22-25.

33 Prince, S., Dodds, S.R. Use of ulcer size and initial responses to treatment to predict the healing time of leg ulcers. J Wound Care 2006;15: 7, 299-303.

34 Gelfand, J.M, Hoffstad, O., Margolis, D.J. Surrogate endpoints for the treatment of venous leg ulcers. J Invest Dermatol 2002;119: 6, 1420-1425.

35 Dereure, O., Vin, F., Lazareth, I., Bohbot, S. Compression and peri-ulcer skin in outpatients' venous leg ulcers: results of a French survey. J Wound Care 2005; 14: 6, 265-271.

Fig 1. Mean percentage reduction in ulcer surface area over the six-week treatment period with the new compression system (n=42)



The improvement in the condition of the surrounding skin recorded here may be due to the use of the lipidocolloid primary dressing, which has shown similar improvements in clinical or observational leg ulcer studies.[29,35]

In terms of its impact on patients' day-to-day quality of life, patients considered that sensations of pain, heat and itchiness decreased with the new system and found it easier to put their shoes on. Furthermore, 50% and 40% reported that general comfort during the day and at night, respectively, was better than with their previous system.

In order to document the interface pressures sustained by three compression therapy systems over seven days (a four-layer bandage [Profore, Smith and Nephew] and a short stretch [Actico, Activa]), a prospective randomised study involving 24 healthy volunteers was conducted.[22] The K-Two system was able to sustain an effective interface pressure (>40 mmHg) for one week, like the four-layer bandages system. No adverse events were noted in the K-Two group, whereas 25% discontinued the four-bandage system after three days due to pain. The investigating physicians noted the new system was easy to apply in all cases, probably due to the 'etalonnage'.

This was confirmed when 32 nurses tested the same three compression systems on a healthy volunteer; the results, presented at the same conference, showed that K-Two was easier to apply and delivered effective therapeutic pressure (level superior to 40mmHg, as measured by the Kikuhime sub-bandage pressure monitor).[23]

Conclusion

Our results indicate that K-Two is effective in the management of venous leg ulcers. Compared with the compression therapy systems used before entry, clinical benefits included increased patient comfort, which was reflected by total concordance with the new system, the avoidance of dressing slippage and the reduction in bulk.

These preliminary results indicate that the two-bandage compression system represents a suitable alternative to other compression systems, enabling an improvement of the patient's quality of life. ■

Bulletin board

The editor welcomes information on resources, organisations and new products. These should be sent to the *Journal of Wound Care*, MA Healthcare, St Jude's Church, Dulwich Road, Herne Hill, London, UK. Fax: +44 (0)20-7733 2325. Email: jwc@markallengroup.com

Offloading boot available on prescription

A boot that offloads pressure away from high-risk areas of the foot and accommodates bulky dressings is now available on prescription.

Produced by Ark Therapeutics, the Kerraped All Purpose Boot is designed for people with diabetic foot ulcers and other lower limb wounds.

The manufacturer says the boot is easy to fasten and provides the appropriate level of offloading and foot support without interfering with the patient's normal walking gait.

• For more details, ring 0800 1077 107.

Research into foot ulcers and rheumatoid arthritis

A nurse conducting a PhD on the prevalence of foot ulcers in people with rheumatoid arthritis and the possible associated risk factors has won a Smith & Nephew Foundation Post-Doctoral Nursing Research Fellowship worth £120,000 to continue her work in this area.

Jill Firth, a former clinical nurse specialist at St Luke's Hospital, Bradford, will look at the impact of foot ulcers on patients with rheumatoid arthritis and the care they receive.

The Doctoral Nursing Research Studentship was awarded to a senior lecturer, Julie Santy, from the University of Hull, who is researching how best to visually identify external fixator pin-site infection. □