Detoxification of Venous Ulcers With a Novel Hydroconductive Wound Dressing That Absorbs and Transports Chronic Wound Fluid Away From the Wound

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The chronicity of venous ulcers (VUs) can be defined clinically by excessive granulation tissue, increased fibrosis, hyperkeratotic wound margins and increased lipodermatosclerosis.[1,2] Biochemically, chronicity can be defined by significant increases in pro-inflammatory cytokines, proteases, and neutrophil elastase.[3–6] Excessive inflammation caused by hyperstimulated neutrophil response has also been suggested as a potential cause for a wound's chronicity.[7,8] It is this protease activity, primarily caused by a specific group of proteases, called matrix metalloproteinases (MMPs), that is believed to be responsible for the destruction of the provisional matrix (fibronectin, necessary for keratinocyte migration) and other extracellular matrix components negatively affecting chemotaxis and cellular migration.[8–10]

Wound fluid (exudates) from chronic VUs contains excessive levels of MMP-2 and MMP-9. Furthermore, it has been reported that these gelatinases need to be down-regulated to permit healing to take place.[11] Down-regulation of inflammatory cytokines and MMPs 2 and 9 occurs naturally (albeit slowly) when VUs are treated with adequate compression.[12,13] It is important to lower the levels of MMP-9 in chronic VUs because it breaks down basement membrane collagens more than other MMPs do.[14,15]

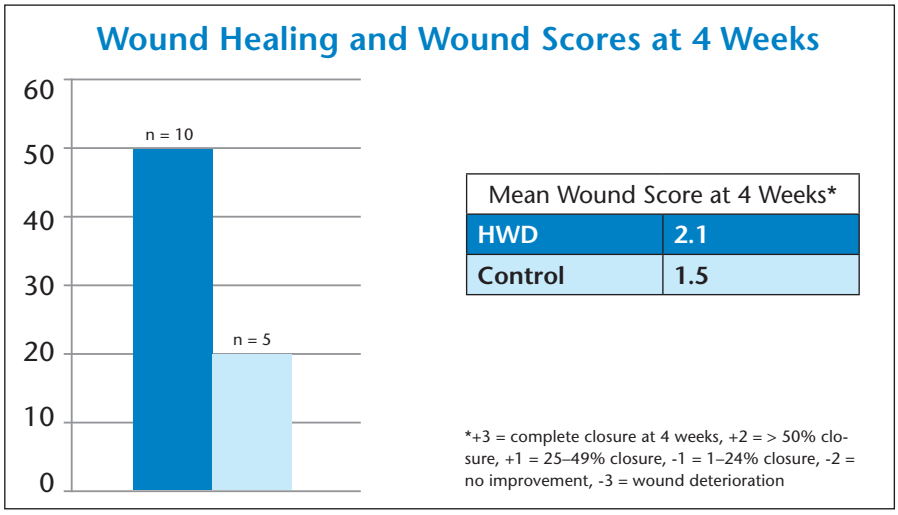

Figure 1. Proportion of wounds healed at 4 weeks.

It would seem logical that, if a device could transport chronic wound fluid from the ulcer so that it is not trapped within the primary dressing and in constant contact with the wound bed, less proteolytic breakdown of the provisional matrix would take place and, thus, improve keratinocyte migration and subsequent healing. The objective in this study was to evaluate a hydroconductive wound dressing (HWD) as a transport medium to detoxify chronic VUs by assisting the displacement of chronic wound fluid away from the wound bed.

Study Design

This was a prospective, randomized, single-center pilot study involving 15

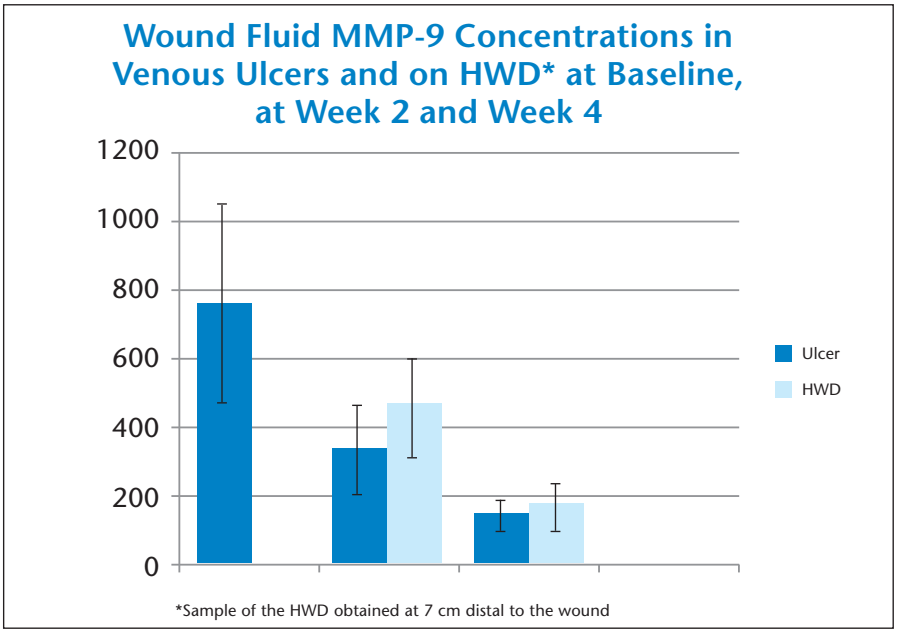

Figure 2. Wound fluid matrix metalloproteinase-9 concentrations in venous ulcers and on hydroconductive wound dressings at baseline, at week 2, and at week 4.

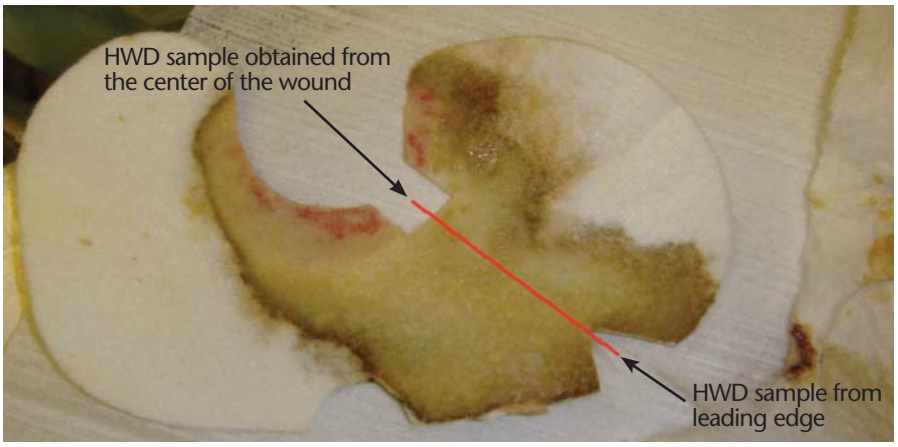

Figure 3. Absorption characteristics of hydroconductive wound dressing (HWD) and sampling of matrix metalloproteinase-9.

subjects in an outpatient wound care center setting. Each subject with a venous ulcer was randomized (2:1) to receive HWD plus compression therapy or standard care (non-adherent dressing plus compression therapy). Wound healing outcomes were graded using photo-digital planimetry software and a numerical scale of +3 to -3 (+3 = complete closure at 4 weeks, +2 = >50% closure at 4 weeks, +1 = 25–49% closure at 4 weeks, -1 = 1–24% closure at 4 weeks, -2 = no improvement, -3 = wound deterioration). In addition, wound fluid MMP-9 levels were measured in both the wound bed and HWD both proximal and distal to the ulcer. Subjects were followed until healing or for 8 weeks, and the primary endpoint was the proportion of subjects reaching 50% healing within 4 weeks.

Study Participation Criteria

The inclusion criteria were ages 18–90 years; ability to provide informed consent; open VU for at least 1 year with a surface area > to 1.5 cm^2; and an ABI > 0.70. The exclusion criteria were: target ulcer not a VU; ABI < 0.7; intermittent claudication, wound infection, cellulitis, or osteomyelitis; known hypersensitivity to cellulose, xylose, cotton, or wool, or any of the study dressings or compression bandages; a subject's receiving corticosteroids, immunosuppressive agents, radiation therapy, or chemotherapy that might interfere with wound healing; uncontrolled diabetes mellitus; immunodeficiency disorders that interfere with wound healing; a history of sickle cell anemia, thalassemia, vasculitis, rheumatoid arthritis, lupus scleroderma, or any hematological, connective tissue, or collagen vascular disorder; and wounds that had been treated with an investigational product within the previous 30 days.

Methods

Standard of care compression therapy was applied once weekly using either a four-layer bandage system (Profore Smith and Nephew, Largo FL) or a modified Unna's boot (Unna's paste boot, Viscopaste, Smith and Nephew, Largo FL, and Coban Cohesive Bandage, 3M, St. Paul, MN). The primary wound dressings were the test agent HWD (Drawtex, SteadMed Medical, Ft. Worth, TX) and Profore WCL, Smith and Nephew, Largo FL). Wounds were measured using PictZar Photodigital Planimetry Software (BioVisual Technologies, Elmwood Park, NJ).[16] Wound assessment was performed using a numerical composite scale of +3 to -3 (+3 = complete closure at 4 weeks, +2 = >50% closure at 4 weeks, +1 = 25–49% closure at 4 weeks, -1 = 1–24% closure at 4 weeks, -2 = no improvement, -3 = wound deterioration). Wound fluid MMP-9 was measured in both the wound and HWD using a direct enzyme-linked immunosorbant assay (ELISA) as described by Rayment et al.[17] Assays were performed at baseline, week 2, and week 4 on four subjects.

Results

The proportion of wounds healed and composite wound score for both treatment groups are presented in **Figure 1**. In the HWD group, the mean wound score was 40% greater than in the standard care group. The proportion of subjects reaching 50% healing at 4 weeks was 5 of 10 (50%) for the HWD group and 1 of 5 (20%) for the standard care group. Wound MMP-9 levels decreased throughout healing in the HWD group (**Figure 2**). Upon MMP analysis of HWD, MMP-9 was detected in HWD at wound interface and distal (up to 7 cm) from the wound (**Figure 3**). The absorption characteristics of HWD are illustrated in **Figure 4**. HWD is 70% more efficient in absorbing and transferring wound fluid when the absorption takes place from an edge of the dressing. This edge effect is characteristic of the hydroconductive viscose fibers. To maximize the edge effect and minimize contact

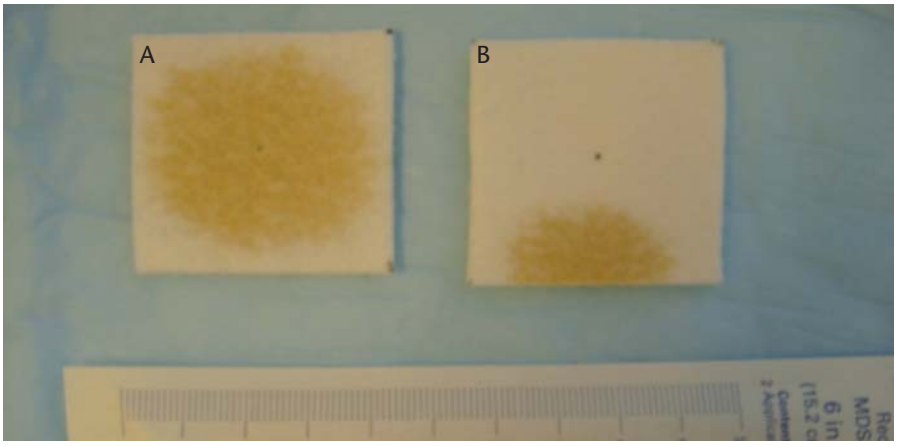

Figure 4. Absorption characteristics of a hydroconductive wound dressing (HWD). Wound fluid applied to center (A) or edge (B) of HWD. HWD is more efficient when absorption takes place from the edge. Note when 1 ml of wound fluid is applied to the center, it saturates 86% of the dressing, but when 1 ml of wound fluid is absorbed from the edge, it saturates only 25% of the dressing.

Figure 5. Method illustrating the use of a hydroconductive wound dressing (HWD). Note that, to maximize absorption from the edges (edge effect) and to minimize contact of the saturated HWD with the wound bed, the HWD was cut in a way so that only the edges came in contact with the wound.

with the saturated HWD and the wound bed, the dressings were cut so only the edge of HWD came in contact with the wound margins (**Figure 5**).

Discussion

HWD effectively transfers chronic wound fluid away from VUs by a natural vacuum created via the hydroconductive viscose fibers. This detoxification process resulted in faster healing for VUs in this feasibility study. To our knowledge, this is the first time that a primary wound dressing has been shown to sequester and transport elements of chronic wound fluid and isolate them away from the VU.

Reynolds et al conducted a randomized, multi-center, controlled study to compare HWD to standard wound dressings in chronic wounds of several etiologies. The authors reported wound improvement of 12.7% based on subjective interpretation (nurse perception); however, upon blinded assessment (based on evaluation of digital images), standard dressings were better by 6.6%.[18] These authors placed the HWD directly over the wounds. We realize the use of HWD as a primary wound dressing may be counterintuitive, because we avoid covering the wound and use it as a transport medium to evacuate harmful chronic wound fluid away from the ulcer itself.

In this small pilot study, MMP-9 levels were lower in the group treated with HWD at week 2 and at week 4. The viscosity of the wound fluid does impact the absorptive capacity and subsequent transfer of HWD. We found the hydroconductive capacity of HWD is limited by viscous or serosanguinous wound fluid.

We recommend wound bed preparation (consisting of thorough selective debridement to remove all devitalized tissues) before treating the wound with HWD. In our experience, a clean wound consisting of 90–100% granulation tissue produced a less viscous discharge that contained less necrotic cells and solid debris. More studies are needed in a variety of inflammatory chronic wounds to investigate the mechanism and effect of this wound fluid transfer phenomenon. ■

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