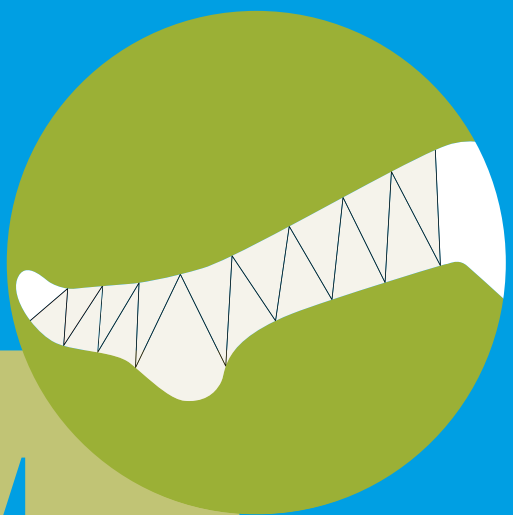
LOWER LEG ULCER DIAGNOSIS
AND PRINCIPLES OF TREATMENT

INCLUDING RECOMMENDATIONS FOR COMPREHENSIVE ASSESSMENT AND REFERRAL PATHWAYS



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9. Local treatment of lower leg ulcers

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This chapter discusses the local treatment of lower leg ulcers. Local treatment involves a series of procedures including dressing selection and monitoring. There is big variety in methods of local treatment of lower leg ulcers available. This is due not only to the many different aetiologies of such lower leg ulcers but also to the widely varying preferences of physicians and nurses, and to the lack of strong evidence and relevant guidelines regarding the most appropriate form of local wound treatment. For healable wounds, local wound treatment interventions can range anywhere along the spectrum from maintaining a moist environment to sharp debridement (166). On the other hand, treatment of maintenance and non-healable wounds is focused on selective debridement or manage infection, exudate or odour (166). In the following section, a synthesis of systematic reviews discussing the local treatment of lower leg ulcers is outlined. Excluded was compression therapy (see Chapter 8).

Wound cleansing and debridement in lower leg ulcers

Only two systematic reviews were identified addressing the topics of wound cleansing and debridement of lower leg ulcers. McLain and colleagues assess in their work the effects of wound cleansing, wound cleansing solutions and techniques for treating VLUs (167). The results show that it is uncertain whether aqueous oxygen peroxide makes any difference to change in ulcer size after 8 weeks (MD –1.38cm^2, 95% CI –4.35 to 1.59 cm^2) or 12 months (RR 1.88, 95% CI 1.10 to 3.20) when compared with sterile water. No difference in wound size reduction was also observed comparing propyl betaine and polyhexanide. The same results are shown when comparing octanedione dihydrochloride/phenoxyethanol with Ringer's solution (RR 0.96, 95% CI 0.53 to 1.72). The authors concluded that there is insufficient evidence to demonstrate whether the above-mentioned solutions make any difference in the treatment of VLUs.

A similar conclusion was drawn by Gethin, Cowman and Kolbach (168). They were determining the effects of different debriding methods on the rate of debridement and wound healing in VLUs which included 10 RCTs with 715 participants. The review shows that 80% of the ulcers treated with dextranomer beads and 14% treated with Edinburgh University Solution of Lime (EUSOL) achieved complete debridement (RR 5.71, 95% CI 2.84 to 11.52). Using hydrogel (76%) was also effective compared to the use of paraffin gauze (45%) (RR 0.67, 95% CI 0.45 to 0.99). One study (n=48) reported that by 12 weeks, 15/18 (84%) ulcers treated with biocellulose wound dressing had achieved a 75% to 100% clean, granulating wound bed versus 4/15 (26%) treated with non-adherent petrolatum emulsion-impregnated gauze. A reduction in wound size was assessed comparing cadexomer iodine with paraffin gauze (MD 24.9cm^2, 95% CI 7.27 to 42.53, P value 0.006) and hydrocolloid compared to paraffin gauze (MD 23.8cm^2, 95% CI 5.48 to 42.12, P value 0.01).

Wound dressings in lower leg ulcers

Wound dressings support the healing process while promoting an optimal environment. To select the optimal wound dressing a holistic approach is needed. Several systematic reviews were identified focused on different wound dressings. One systematic review included five RCTs including 295 participants aiming to compare alginate dressing in combination with compression compared with other dressings (169). One RCT included 20 participants comparing different alginate dressings, three RCTs included 215 participants comparing

alginate and hydrocolloid dressings, and one RCT with 60 participants compared alginate and plain non-adherent dressings. All studies show that there is no statistical significance between the alginate group with the comparison (169). A meta-analysis was feasible for one comparison (alginate and hydrocolloid dressings), with data from two RCTs (n=84) pooled for complete healing at 6 weeks (RR 0.42 (95% CI 0.14 to 1.21) (170). The authors conclude that alginate dressings are more or less effective in the healing of VLUs than hydrocolloid or plain non-adherent dressings, and there is no evidence to indicate a difference between different proprietary alginate dressings.

The effects of topical hydrogel wound dressings on the healing of VLU were studied by Ribeiro and colleagues (171). The systematic review included four RCTs (272 participants) comparing hydrogels to a wide variety of wound dressings including gauze and saline, alginate dressing, manuka honey and hydrocolloid. The authors conclude that there is inconclusive evidence to determine the effectiveness of hydrogel dressings compared with gauze and saline, alginate dressing, manuka honey or hydrocolloid on VLU healing. One of the limitations is that different dressing categories were compared with hydrogel. Similar conclusions were made when reviewing the use and effects of topical honey dressing on VLU healing (172); they were not able to determine any significant effect of use due to the small number of papers, all of which were of low-quality evidence. The evaluation of the impact of foam dressings on VLU healing was also unable to find evidence of effect, reporting that there was no difference in healing outcome when hydrocellular foam dressings and polyurethane foam dressings were used compared to a variety of wound dressings (paraffin gauze, knitted viscose, hydrocapillary dressings or protease modulating matrix (PMM) dressings). Pooled data across five RCTs (418 participants) showed no statistically significant difference between foam dressings and hydrocolloid dressings in the proportion of ulcers healed at 12 to 16 weeks (RR 1.00, 95% CI 0.81 to 1.22).

The use of antimicrobials in lower leg ulcerations was studied in four systematic reviews. Norman and colleagues (170) included 78 RCTs with 7014 participants assessing the effects of dressings and topical agents for healing of VLUs in any care setting. They show that the included evidence was of low certainty. The authors argue that this low certainty was continued when the results were considered by ranking the treatments in terms of the probability that they were the most effective for lower leg ulcer healing, with many treatments having similar, low, probabilities of being the best treatment. The two most highly ranked treatments (with a 50% probability) were sucralfate and silver dressings. It has to be taken in consideration that the sucralfate study was small. If sucralfate and silver dressings were compared with other dressings, there was some evidence that silver dressings may increase the probability of VLU healing, compared with non-adherent dressings (RR 2.43, 95% CI 1.58 to 3.74). Otherwise, the literature is unclear whether the intervention (antimicrobial dressing) increased the probability of healing. A systematic review assessing the evidence supporting the use of dialkylcarbamoyl chloride (DACC)-coated dressings in the clinical environment was performed (173). The authors show data from a pilot-RCT comparing the effects of DACC-coated dressings and silver impregnated dressings in chronically infected or heavily colonised leg ulcers of vascular origin and a cohort study including 19 patients (20 wounds) with chronically infected vascular ulcers. Both studies demonstrate a statistically significant reduction ($p<0.01$) of bacterial load and a positive outcome in relation to wound size reduction.

Another systematic review assessing the effects of the use of systemic antibiotics, topical antibiotics and antibiotics on VLU healing reported by 45 RCTs using 53 comparisons (n=4486) show that more participants were healed when they were prescribed levamisole (systemic antibiotics) compared with placebo: RR 1.31 (95% CI 1.06 to 1.62) (174). No between-group differences were detected in terms of complete healing for other comparisons (other antibiotics). However, the same systematic review highlighted that more participants were healed when given

cadexomer iodine compared with standard care. The pooled estimate from four RCTs for complete healing at 4 to 12 weeks was RR 2.17 (95% CI 1.30 to 3.60). No between-group differences in complete healing were detected when cadexomer iodine was compared with hydrocolloid dressing, paraffin gauze dressing, dextranomer, and silver-impregnated dressings. The same systematic review demonstrates there were no between-group differences in complete healing detected comparing the use of povidone-iodine compared with hydrocolloid, moist or foam dressings or growth factors. Additionally, it was shown that the use of peroxide-based preparations when compared with usual care for surrogate healing outcomes (change in ulcer area). Using honey-based products compared with usual care showed no difference in time to healing or complete healing. Moreover, there were no between-group differences in complete healing observed when using 1% silver sulphadiazine ointment compared with standard care/placebo or tripeptide copper complex or different brands of silver-impregnated dressings or when silver-impregnated dressings were compared with non-antimicrobial dressings. O'Meara et al. showed further that more participants healed at 4 weeks when treated with an enzymatic cleanser (a non-antibiotic preparation) compared with a chloramphenicol-containing ointment (additional active ingredients also included in the ointment): RR 0.13 (95% CI 0.02 to 0.99) (174). The use of an antiseptic ointment (ethacridine lactate) was responsive (defined as >20% reduction in area) at 4 weeks when compared with placebo: RR 1.45 (95% CI 1.21 to 1.73). ***However, the authors concluded that there is no evidence available to support the routine use of systemic antibiotics in promoting healing of VLUs***. A systematic review by Broderick and colleagues (175) determined whether topical agents and wound dressings affect healing in arterial ulcers. It compared healing rates and patient-centred outcomes between wound dressings and topical agents. The results show that there is an accelerated wound healing in the 2% ketanserin ointment in polyethylene glycol group. Another topical agent studied was the application of blood-derived concentrated growth factor compared with polyurethane film or foam. Two studies were found and in both studies the sample size was small, the reported results were inadequate, and the methodological quality was rated low. However, the results show that 66.6% of patients with a diabetic arterial ulcer (6/9) receiving blood-derived concentrated growth factor showed more than a 50% decrease in ulcer size compared to 6.7% (2/30) of patients with non-healing ulcers treated with standard dressing.

Topical agents or wound dressings to manage wound-associated pain

The use of topical agents or wound dressings for the management of patients' pain from VLU was explored in a systematic review by Briggs et al. (176). The review found six studies (involving 343 participants) evaluating the use of local lidocaine cream (EMLA: Eutectic Mixture of local anaesthetic [Lidocaine/Prilocaine]) to help manage procedural pain (debridement). They found a statistical difference in pain score in favour of EMLA cream (MD –20.65, 95% CI –12.19 to –29.11). Additionally, they reviewed two studies (470 participants) assessing the use of ibuprofen slow-release foam dressings for persistent VLU pain. Compared to local best practice, one paper reported significant benefits in total maximum pain relief scores, but the second paper reported no significant difference between the two groups. The conclusion of this systematic review was that EMLA cream provides effective pain relief during debridement and that there was some evidence to suggest that ibuprofen dressings may offer pain relief to people with painful VLUs, but further research was needed to assess the true impact.

Autologous platelet-rich plasma (PRP) in lower leg ulcerations

The use of autologous platelet-rich plasma (PRP) promoting wound healing was assessed by Martinez-Zapata et al. (177). The results reported on wounds of the lower leg (VLU) show that it is unclear if autologous PRP affects healing (RR 1.02, 95% CI 0.81 to 1.27).

Ultrasound therapy

The impact of local ultrasound therapy on VLU

healing was reviewed by Cullum and Liu (178); their systematic review identified 11 research papers (10 of which were judged as being at an unclear or high risk of bias). There were nine trials which evaluated high-frequency ultrasound, seven provided data for ulcer healing, and two showed data on ulcer change size with two trials which evaluated low frequency ultrasound; both reported ulcer healing. They concluded that it was uncertain whether therapeutic ultrasound (either high or low frequency) improves the healing of VLUs due to low and very low-quality evidence.

Electromagnetic therapy (EMT)

One systematic review was identified investigating the impact of electromagnetic therapy (EMT) on the healing of VLUs (179). There were three RCTs identified, and all compared the use of EMT with sham-EMT. Two trials reported ulcer healing rates; one small trial (n=44) reported that significantly more ulcers healed in the EMT group than the sham-EMT group; however, this result was not robust due to the assumptions made about the outcomes of participants who were lost to follow-up. The second trial that reported numbers of ulcers healed found no significant difference in healing. The third trial was also small (n=31) and reported significantly greater reductions in ulcer size in the EMT group but did not report overall healing data. It remains unclear whether EMT influences the rate of healing of VLUs.

Protease modulating matrix (PMM) treatments

A systematic review by Westby et al. (180) aimed to determine the effect of PMM treatments on the healing of VLU; it included 12 studies (784 participants). Nine of the included studies compared PMM treatments with other treatments and reported healing as primary outcomes, seven of which recruited participants described as having 'non-responsive' or 'hard-to-heal' ulcers. Comparators were other types of wound dressings, and in all studies PMM was used as an adjunct to standard compression therapy. They reported that there was uncertainty whether PMM dressing regimens heal VLUs quicker than non-PMM dressing regimens (low-certainty evidence from one trial with 100 participants) (HR 1.21, 95% CI 0.74 to 1.97) and it was unclear whether PMM dressing regimens influence venous ulcer healing in comparison with to dressing regimens without PMM activity.

Summary

The synthesis of the systematic reviews (1A) shows that there is not enough evidence that one wound dressing would be superior to another neutral dressing when chosen according to wound bed and exudation. However, when consulting PROSPERO and clinical trials.gov there are promising ongoing publications, systematic reviews and clinical trials, to manage exudate in lower leg ulcerations (181, 182). Nevertheless, more methodologically robust clinical trials are needed to close this gap. The authors therefore conclude that the characteristics of the wound (for example, exudate, odour and/or pain) should be the deciding factor in choosing the most appropriate dressing for treating a lower leg ulceration (1A).

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