

Experience with the use of an Amelogenin-Based Extracellular Matrix Substitute (Xelma®) in the Management of a Variety of Complex Hard-To-Heal Chronic Wounds

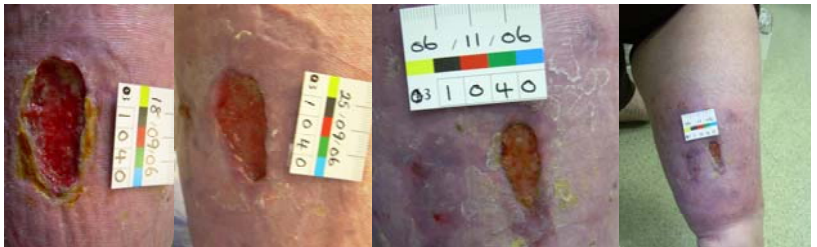
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Introduction: Wound healing involves a series of complex processes in which a number of different cell types, growth factors, enzymes, messenger molecules and the extracellular matrix (ECM) components interact. This interaction between cells and the ECM governs many cell functions and is one of the key processes in wound healing. The initial wound healing inflammatory phase involves platelet aggregation, haemostasis, neutrophil recruitment to destroy bacteria and necrotic tissue and the formation of an initial temporary ECM. Wounds next move into the proliferative phase during which activation of fibroblasts occurs and, with endothelial cells recruitment, granulation tissue is produced, a new ECM established and re-epithelialisation commenced. Failure to form an adequate temporary or new replacement ECM can therefore be seen to adversely affect healing and may be one of the causes of a wound failing to respond to treatment. Troxler et al (1) have discussed the concept of "hard-to-heal" wounds, defining them as wounds which fail to respond to "standard care" in a timely fashion and Vowden et al (2,3) have demonstrated, in two randomised controlled trials, the value of treating "hard-to-heal" venous leg ulcers with an amelogenin-based ECM substitute (Xelma®). We report here our experience using Xelma® on a variety of hard-to-heal wounds of mixed aetiologies.



Longstanding neuropathic (non-diabetic) foot ulcer previously healed with Apligraf treated with a combination of topical negative pressure therapy (to control exudate) and then two courses of topical Xelma® combined with offloading until healing.

Method: This is an ongoing product evaluation conducted to allow inclusion of a new wound care product into our formulary. The abstract details treatment of 17 wounds on 15 patients (11M, 4F), mean age 66.1 years all with longstanding chronic wounds (mean duration 34 months) that had failed to respond adequately to appropriate disease specific "standard" care. There were 2 patients with rheumatoid ulcers and 4 with rheumatoid arthritis complicating healing of other wounds, 5 with neuropathic foot ulcers (4 diabetic), 4 venous and one mixed ulcer and one pressure ulcer. All wounds were traced, photographed and documented using a standard record format and data was also collected using Teler (4). The mean wound area was 16.4 cm² (Range 1-72.4 cm²). Amelogenin proteins were applied to the wound bed according to the manufacturers instructions using the supplied applicator. For larger wounds two or more syringe applicators were used. The wounds were then dressed with an appropriate secondary dressing, the majority receiving a soft silicone foam dressing, Mepilex (Molnlycke Health Care). All patients receive their standard care as appropriate. Subsequently a further 7 patients have been treated (3 neuropathic diabetic foot ulcers and one neuroischaemic, 2 venous ulcers and one inflammatory ulcer).



Poorly controlled obese diabetic with recalcitrant venous leg ulcer with frequent episodes of cellulitis. Wound reduced from 6.5cm² to 1.7cm² after six applications of topical amelogenin. The ulcer subsequently went on to heal.

Results: In all cases there was an early reduction in both wound pain and exudates with 14 out of 17 initially treated wounds recording a reduction in pain and exudates on their Teler scores and improvement in the Health Gain Index. In two patient treatment was discontinued due to infection and wound deterioration. At the time of abstract submission 8 of the initial 17 wounds had healed (mean 8 (range 3-16) applications) and 7 of the remaining wounds had improved with over a 50% reduction in wound size. Now only 3 of the original 17 wounds remain unhealed. None of these 3 patients continues to receive amelogenin therapy. In the subsequent 7 patients treated after abstract submission 6 improved (4 healed) and one had an episode of cellulitis but has subsequently improved.

Discussion: Published randomized clinical trial results (2,3) have demonstrated statistically significant improved ulcer healing and wound size reduction rates as well as a reduction in wound exudates and wound pain when Xelma® is used as a topical wound bed application with "standard" care (compression bandaging) in the management of hard-to-heal venous leg ulceration. Experimental data has demonstrated that amelogenins, at physiological pH, assemble to form a functional extracellular matrix substitute that supports cell adhesion and growth as well as the production of essential wound growth factors (5). These properties are as relevant to the healing of all chronic wounds as they are to the healing of venous leg ulcers and hence our interest in the use of this novel form of adjunctive therapy in a variety of non-healing wounds. One striking factor that was of benefit to most patients was both a reduction in wound exudates and a reduction in wound pain. This had been noted in the earlier studies on venous leg ulcer patients (2,3) but may, on the basis of our observations, also occur with other wound types.



Diabetic patient with neuropathic heel pressure ulcer managed by debridement, initial topical negative pressure therapy and then topical Xelma® as healing failed to progress. The wound measured 9.7cm² at onset of amelogenin therapy, 6cm² at 6 weeks and 1.6cm² at 12 weeks, subsequently progressing to healing.

Conclusion: Results obtained in this varied hard-to-heal ulcer population managed in a tertiary referral wound healing unit support the use of Xelma®, an advanced wound care product, as an adjunct to standard care in this difficult to manage ulcer population. Increasing interest in therapy targeting the extracellular matrix appears justified.

References

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