

Enamel Matrix Protein (EMP)

in hard-to-heal venous leg ulcers, a controlled pilot study

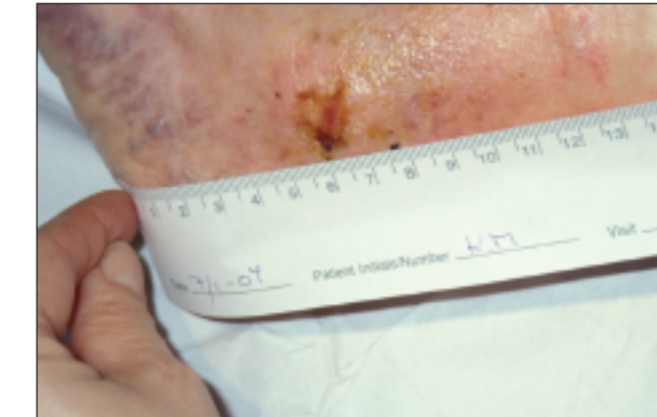
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Baseline wound size: 6 cm²
(Treatment EMP 30mg/ml, 47-year-old female,
Age of ulcer: 3 years)



Week 4 wound size: 2.5 cm²



Week 8 wound size: healed

Background

The prevalence of venous leg ulcer (VLU) is about 0.3% in western countries. A continuously increasing ageing population implicates an enhanced problem in the future. Compression therapies have been around for many years but not all venous leg ulcers heal spontaneously with compression bandaging.

This pilot study looked at a novel extracellular matrix protein and the way it effects the ulcer area and the ulcer bed. The investigation product is constituted of amelogenin proteins of different molecular weights, which assemble into large aggregates at physiological conditions. The amelogenin proteins are purified extract from the enamel matrix protein (EMP) of developing teeth of porcine origin.

Aim

The aim of this clinical investigation was to assess ulcer reduction ability of EMP in propylene glycol alginate (PGA) compared with a control, the PGA alone.

Methods

30 patients with persistent (≥ 3 months) venous leg ulcer despite compression therapy for the past month were planned to be included in this single blind, randomised three-arm investigation. The investigational products, amelogenins (3 or 30 mg/ml) or control (PGA alone) were applied weekly for a maximum of eight weeks. Compression therapy was maintained throughout the study. Ulcer size reduction was measured by tracing and assessed by digital planimetry. Wound evaluation was made by an blinded

observer, i.e. a physician unknowing of which investigation treatment each patient received.

Patients with ulcers sized between 3-25 cm² and ulcer duration of ≥ 3 months were included. Diagnosis of VLU was guaranteed by showing reflux on Doppler. Patients with highly exuding wounds, clinical signs of infection and/or patients with significant underlying diseases were excluded.

The Ethics Committee in Odense centrally approved the investigation and patients were informed both orally and in writing and a consent form was signed.

Ulcer size reduction over time was evaluated over an eight-week period or until complete healing. Wound assessment was performed every second week up to week 8. Mepilex[®] was used as a secondary dressing.

Results

Only 24 patients were included due to recruitment difficulties. 8 patients were randomised to EMP 3 mg/mL, 8 to 30 mg/ml and 8 to control treatment (PGA). 4 ulcers did not comply with protocol requirements for ulcer size, 1 allocated to EMP 3 mg/ml and 3 allocated to control. In the efficacy analysis 7 patients receiving EMP 3 mg/ml, 8 receiving EMP 30 mg/ml and 5 receiving control are included.

There were some baseline differences with regard to ulcer age and size, notable is that data are skew and therefore median values are

presented (Table 1). There were also some less important differences in demography (Table 2). No patient suffered from diabetes.

Table 1
Legend: Ulcer age and size, median values

	Age of VLU in months Median/min/max	Size of VLU in cm ² Median/min/max
EMP 3mg/ml	12 (3-72)	6.0 (3.1-14.9)
EMP 30mg/ml	6 (3-36)	3.2 (3.0-8.8)
Control (PGA)	18 (6-36)	14.0 (4.9-18.1)

Table 2
Legend: Demography, mean values

	EMP 3mg/ml	EMP 30mg/ml	Control
Gender	3 F / 4 M	5 F / 3 M	1 F / 4 M
Age	75.4y (61-88)	65.8y (32-84)	85.4y (70-97)
Use of nicotine	2 out of 7	3 out of 8	0 out of 5

The percentage change in ulcer area as measured in median values show a faster ulcer reduction in patients treated with amelogenin proteins comparing baseline to final visit (Figure 1). Four ulcers healed, two treated with EMP 3 mg/ml and two treated with EMP 30 mg/ml.

There was no difference in the outcome of safety assessments. Two adverse events were considered related to the device. An increased ulcer was reported in one patient that received 3 mg/ml EMP. The patient discontinued the investigation. In a patient treated with 30 mg/ml EMP pressure marks was reported, the patient continued the investigation. Apart from the above, eczema was

reported in five patients (9 events): two patients treated with EMP 3 mg/ml, two treated with EMP 30 mg/ml and one treated with control. Anaemia was reported for one patient in the control group.

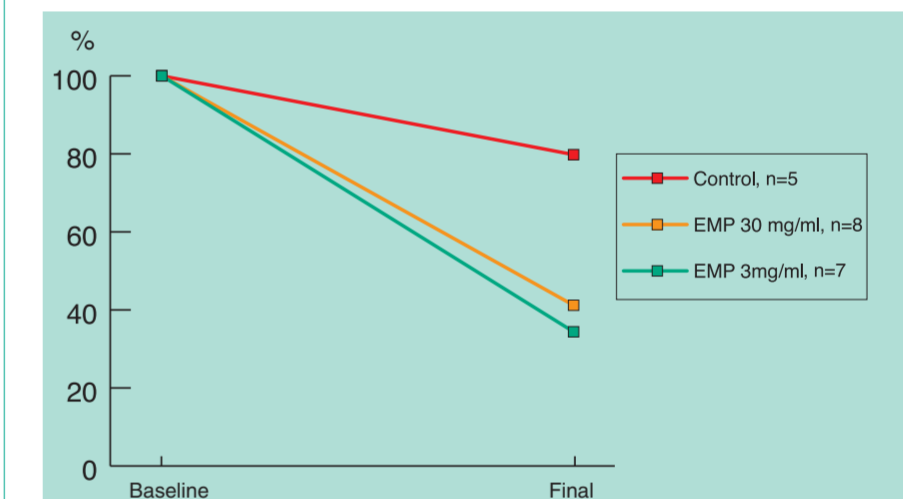


Figure 1.
Legend: Percentage change in ulcer size, baseline to final visit, median values (EMP 3mg/ml = 64.6%, EMP 30mg/ml = 58.8%, Control = 19.2%)

Conclusion

- This investigation indicates that a faster ulcer size reduction in hard to heal venous leg ulcers is obtained when treated with EMP.
- The number of patients involved is though too small to draw any conclusions. Other clinical investigations are running in order to assess the effect of EMP in hard to heal venous leg ulcers.

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