Comparative Clinical Study to show the Combined Mode of Action of Collagen/ORC/Silver in Controlling Bioburden and Modulating the Wound Microenvironment to Promote Healing

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ABSTRACT

Aim: To determine the effect of collagen/oxidised regenerated cellulose (ORC)/silver therapy on diabetic foot ulcers and to compare results with control values.

Method: Twenty-four patients were treated with collagen/ORC/silver and fifteen control patients were treated according to a standard treatment protocol. Wound area was measured weekly over a maximum of 14 weeks and outcome was determined by percentage reduction in wound area. Levels of inflammatory proteases and cytokines were measured in wound fluid samples collected at baseline and at Week 4.

Results: Levels of proteases and inflammatory cytokines were higher in non-healing wounds compared with healing wounds. There was a reduction in the level of inflammatory biomarkers after 4 weeks of treatment with collagen/ORC/silver. There was a significantly increased rate of wound healing in the collagen/ORC/silver group compared with the control group after 4 weeks of treatment (p=0.035), according to the Margolis Index. There were no withdrawals due to infection in the collagen/ORC/silver treatment group. In contrast, 33% of patients in the control group were forced to drop out of the study due to wound infection.

Conclusions: Treatment with collagen/ORC/silver can help to promote wound healing while protecting the wound from infection. This study provides evidence that non-healing wounds have high levels of inflammatory biomarkers and that collagen/ORC/silver reduces both elevated levels of inflammatory cytokines and proteases in these non-healing wounds.
In this study, treatment of diabetic foot ulcers with collagen/ORC/silver led to increased rates of healing and decreased incidence of infection.

OBJECTIVES

- To demonstrate the ability of Collagen/ORC/Silver to promote healing in diabetic foot ulcers
- To examine the effect of Collagen/ORC/Silver on reducing inflammatory mediators & inflammatory protease activity

STUDY DESIGN

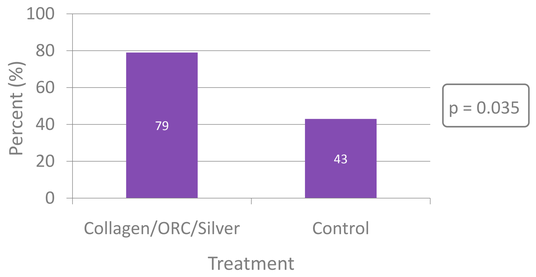
- Randomised controlled trial
- 39 patients with Diabetic Foot Ulcers, Wagner grade 2-3
- Males and females, aged between 35 and 80 years
- History of diabetes
- Initial wound area > 1cm^2
- 24 patients collagen/ORC/silver treatment, 15 control treatment
- Wound areas and wound fluid samples taken bi-weekly

INFLAMMATORY PROTEASES AND INFLAMMATORY MEDIATORS AS BIOMARKERS

- Wound fluid samples from Week 0 and Week 4 (where available) from a selection of patients were tested to determine whether there is a correlation between response to treatment and inflammation, by measuring inflammatory proteases and inflammatory mediators.
- The patients were divided into two groups; Responders (achieved >50% reduction in wound area by Week 4) and Non-responders (there was <50% reduction in wound area by Week 4).
- Patients that were forced to drop out of the study due to wound infection were included in the Non-responder group.

RESULTS: Healing at Week 4

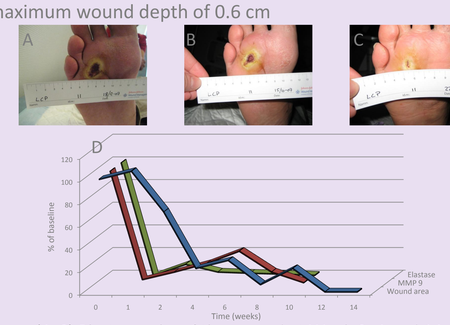
Significantly higher percentage of wounds healed and improved wounds with Collagen/ORC/Silver



(Improved defined as >50% reduction in wound size)

CASE STUDY 1

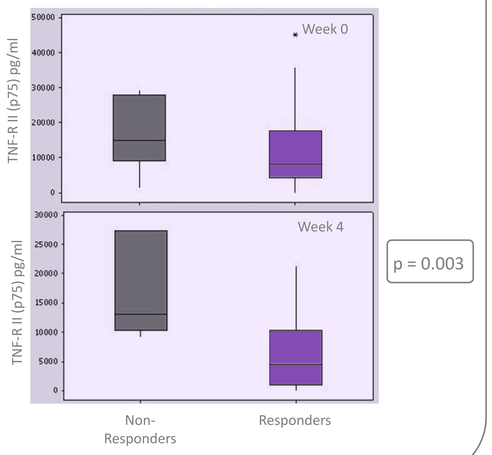
A 35 year old male with type 1 diabetes presented with a diabetic foot ulcer on the right foot (lateral). At baseline the duration of the wound was 3 years, the area was 1.4 cm ^{2} with a maximum wound depth of 0.6 cm



(A-C) Photographs of the wound at Week 0, 4 and 14 respectively. (D) The percentage reduction in wound size, MMP 9 activity and Elastase activity compared to baseline values.

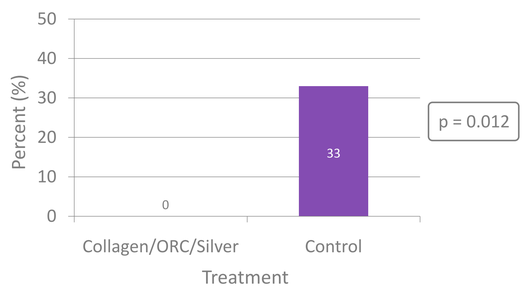
RESULTS: Inflammatory Mediators

Level of TNF-receptor II (p75) is elevated in non-healing wounds and is significantly reduced in healing wounds by week 4.



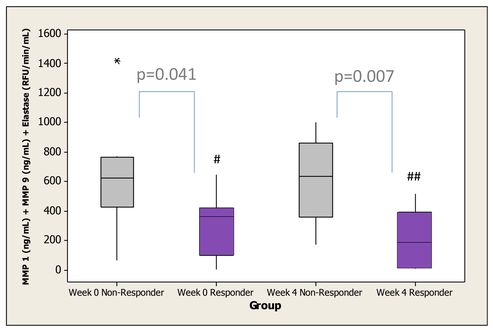
RESULTS: Infection rate over 12 weeks

Significant difference in percentage of wounds withdrawn due to infection



RESULTS: Inflammatory Protease Activity

Total inflammatory protease activity at week 0 and after 4 weeks of treatment in both responders and non-responders.

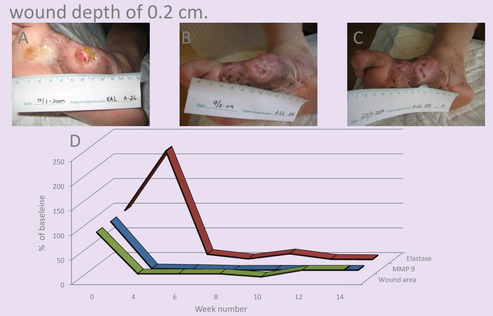


Significantly different from Week 0 Non-responders (p=0.041).

Significantly different from Week 4 Non-responders (p=0.007).

CASE STUDY 2

A 58 year old female with type 2 diabetes presented with a diabetic foot ulcer on the right foot (medial), duration 4 years. The patient had previously undergone amputation of the first toe and partial fore foot on the right foot. At baseline the wound area was 1.3 cm^2, with a maximum wound depth of 0.2 cm.



(A-C) Photographs of the wound at Week 0, 4 and 14 respectively. (D) The percentage reduction in wound size, MMP 9 activity and Elastase activity compared to baseline values.

CONCLUSIONS

This study demonstrates that collagen/ORC/silver has a combined mode of action which promotes healing in diabetic foot ulcers in two ways:

- Collagen/ORC/silver controls bioburden
  - protects wound from infection
- Collagen/ORC/silver modulates the wound microenvironment
  - reduces elevated levels of inflammatory mediators and inflammatory proteases

This dual action of collagen/ORC helps to promote healing by favourably modulating the chronic wound environment.