



Detecting and treating Elevated Protease Activity (EPA) in chronic diabetic wounds

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BACKGROUND

Proteases have various roles in wound healing such as the migration and activation of fibroblasts, extra cellular matrix remodelling and growth factor activation. However, in some non-healing chronic wounds, protease activity remains at an elevated level which impairs wound healing and can lead to chronic inflammation. The impact of elevated protease activity (EPA) on wound healing is being discussed more frequently clinically and the need to control these proteases is being considered in the selection of treatment for chronic wounds. Chronic wounds with EPA have a 90% probability they won't heal without appropriate intervention. But approximately 28% of non-healing wounds have EPA. The aim of the study was to evaluate the role of EPA detection in diabetic ulcers and whether using a new protease activity test* could help improve clinical outcomes by targeting treatment on wounds which have EPA.

METHODS

20 diabetic foot ulcers which had been present for a minimum of 6 weeks were randomly divided into two groups: **Group A** – 10 patients, all tested for EPA. Wounds with EPA were treated with a protease modulating dressing** to lower protease activity; wounds found to have low protease activity were treated with standard care.

Group B – 10 patients, none tested for EPA, all treated with standard care.

The 2 key measures were healing (wound closed in 12 weeks of treatment) and wound improvement (wound area reduced by 50% in 12 weeks of treatment).

RESULTS & CONCLUSIONS

60% of the wounds in group A had EPA and treatment was targeted accordingly (n=10). In Group A 40% of wounds healed by week 12, compared to 10% in group B (p<0.01). 100% of the wounds that healed (4) in group A had EPA. 100% of EPA wounds either healed (4) or improved (2) by week 12 once identified with the protease activity test* and treatment was targeted appropriately with a protease modulating dressing**. We can conclude that testing for EPA using a protease activity test* can help to target appropriate treatments more effectively and therefore increase clinical and economic outcomes in chronic wounds.

Methods: Study Design

20 diabetic chronic wounds present for at least 6 weeks, IA (TU), non-infected, non-ischemic, Probe to bone neg, Microbiological examination culture neg, Tcpo2 >50mmHg

Group A: Test and Treat for EPA

All wounds tested for EPA.

EPA



treated with protease
modulating dressing*

Low protease activity



treated according to
standard of care

Group B: Standard care

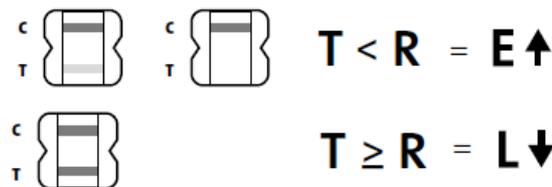
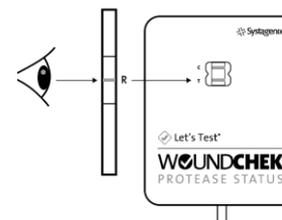
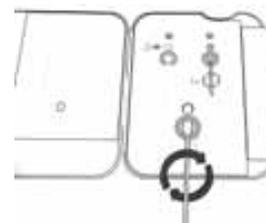
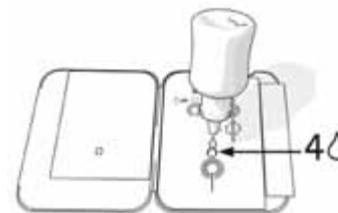
All wounds treated to
standard of care and not
subjected to any assessment
of protease activity

Wounds assessed at week 12 to determine if:

- Healed (wound closed in 12 weeks of treatment)
- Improved (wound reduced in area by 50% in 12 weeks of treatment)

Methods: Test Procedure

1. **Cleanse the wound with sterile saline**
2. Lay test card flat on the work surface and slowly add 4 drops of Reagent to the top hole.
3. **Apply additional saline to the wound area to be swabbed, such that the area is visibly moist.**
4. **Press the head of the swab flat against the base of the wound and gently roll it back and forth several times while applying pressure until fully coated and discoloured (tan/yellow) by wound fluid.**
5. Insert sample swab into the bottom hole of the test card and firmly push upwards so the swab tip is fully visible in the top hole and Rotate swab shaft 5 times, then wait 10 minutes.
6. Peel off adhesive liner from the right edge of the test card. Close and securely seal the card, then wait 5 minutes.
7. Read test result in window 5 minutes after closing the test card. If the Control Line (C) does not appear the test is **invalid**. For all valid tests, interpret the results by comparing the color intensity of the Test Line (T) to the color intensity of the Result Interpretation Reference Line (R), which is located on Result Interpretation Reference Strips provided in the kit.
 - If the color intensity of the Test Line (T) is lighter than the color intensity of the Reference Line (R), or the Test Line (T) is not visible at all, then the sample contains **elevated levels of inflammatory protease activity (E↑)**.
 - If the color intensity of the Test Line (T) is darker than or equal to the color of the Reference Line (R), then the sample contains **low levels of inflammatory protease activity (L↓)**.



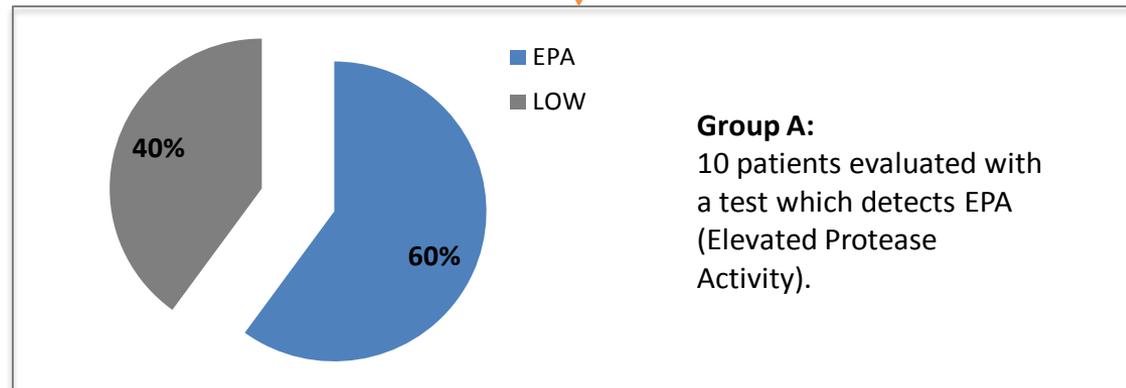
Results: Prevalence of EPA in Group A

Patient Characteristics

	Group A	Group B
Age	63±7	60±4
Duration Diabetes	15±5	12±3
HbA1c	7.2±0.9	7.4±0.5
M/F	6/4	5/5

Wound Characteristics

	Group A	Group B
Number of lesions	10	10
Probe to bone	Neg	Neg
Microbiological examination	Neg	Neg
TcPo2	>50 mmHg	>50mmHg
Texas University	1A	1A

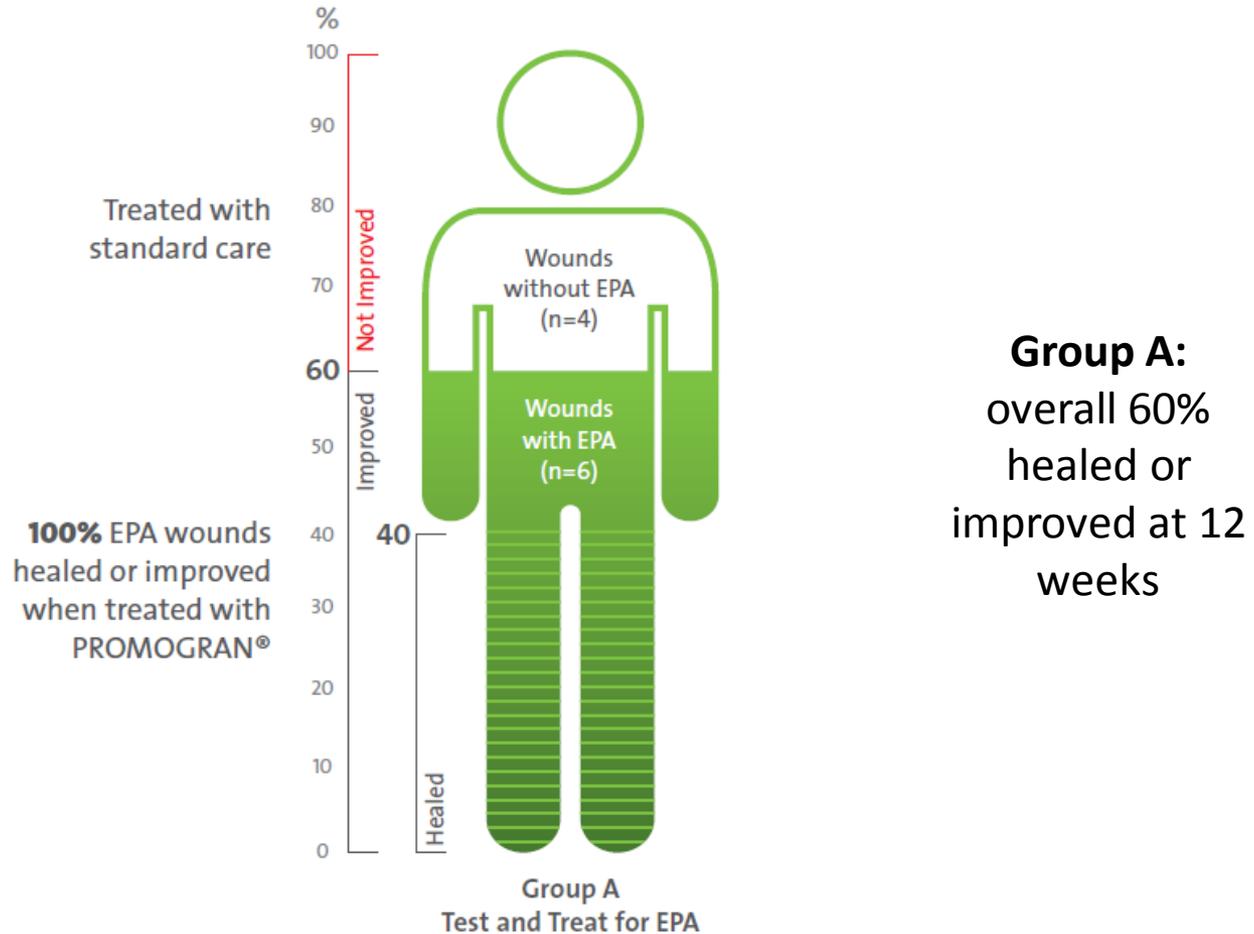


n.b. a previous study has shown that 28% of all non-healing chronic wounds have EPA¹.

1. Serena T. et al. Protease activity levels associated with healing status of chronic wounds. Poster, Wounds UK 2011.

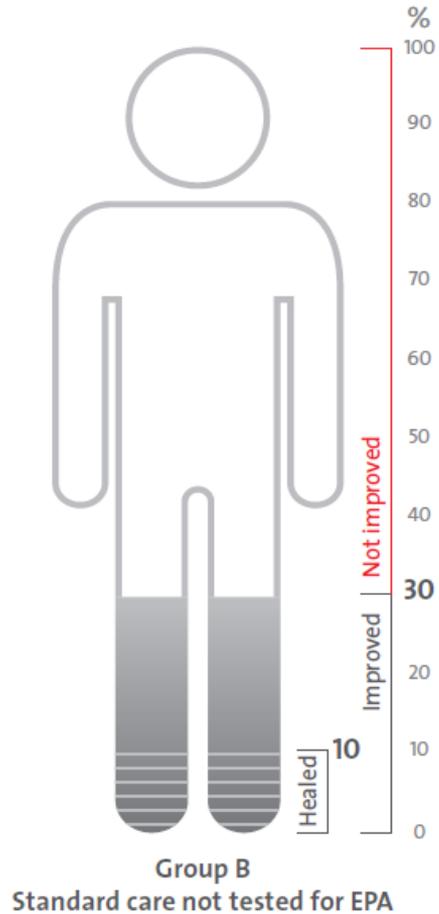
Results: Group A – Test and treat for EPA

100% of wounds with EPA healed or improved with targeted treatment with protease modulating dressing*



Results: Group B – Standard Care

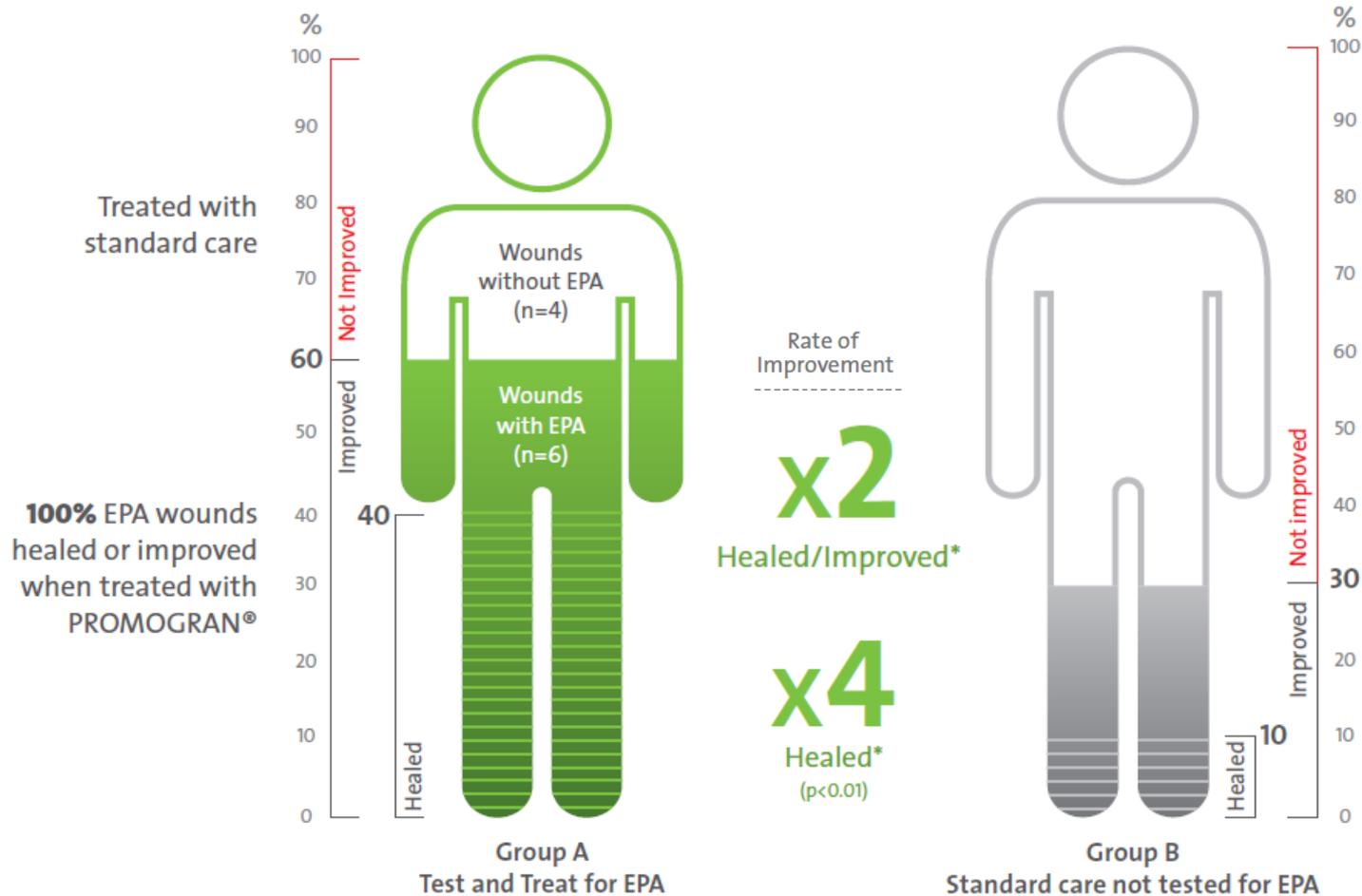
Only 30% of the wounds healed or improved at 12 weeks with standard care



12 weeks

Results: Summary

x2 improvement when testing and treating versus standard care alone



*Healing (wound closed in 12 weeks of treatment). Improvement (wound reduced in area by 50% in 12 weeks of treatment)

12 weeks

Summary of Results

- 60% (6/10) of chronic diabetic wounds had EPA in group A
- 100% (6/6) of the wounds with EPA healed or improved at week 12 when targeted with a protease modulating dressing*
- A 'test and treat' approach to care resulted in double the success rate** at 12 weeks (60%) when compared to standard care (30%)
- x4 wounds healed* in Group A than in Group B (p<0.01)

*PROMOGRAN®

**Healing (wound closed in 12 weeks of treatment). Improvement (wound reduced in area by 50% in 12 weeks of treatment)

Conclusion

- Testing for EPA can help to target therapies to modulate protease activity appropriately and can also help to avoid inappropriate use of advanced dressings
- Targeting EPA wounds with protease modulating therapies can improve healing rates in these wounds which previously had a 90% probability of not healing prior to targeted treatment¹
- A test and targeted treatment regime could help to allocate resources more cost effectively