A real world, retrospective cohort controlled, evaluation of relative effectiveness of topical haemoglobin spray as adjunct therapy in chronic diabetic foot ulcers – results after 12 weeks follow-up

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Introduction

The development and subsequent deterioration of diabetic foot ulceration (DFU) is a substantial burden to clinical resources and creates significant hardship for patients. DFU is challenging to prevent and manage due to underlying vascular and neurological impairments associated with uncontrolled diabetes that contribute to cause chronic hypoxia and corresponding healing complications. Improvement of oxygen availability is increasingly recognised as a key element for achieving healing. Facilitated diffusion using haemoglobin is a promising approach to sustainably increase oxygen availability in the wound bed but has so far not been evaluated in a real-world context with a representative control in chronic DFUs.

Method

A controlled study with two cohorts was undertaken in an acute clinical setting in North East England where a spray solution containing haemoglobin (Granulox®, infirst Healthcare) was used in 20 patients with chronic (>12 weeks) DFU and compared with 20 patients selected from the same period the year prior using the same protocol, retrospectively, from the same clinic (Control). Haemoglobin spray was provided free of charge by infirst Healthcare. Wound care was provided by the regular care team, provided by 18 health professionals, with no changes to products, devices or care practices before the evaluation. All wounds in the haemoglobin spray group were part of a previously reported cohort evaluated over 4 weeks (Bateman 2015). All patients from the evaluation opted to continue treatment and apply the product twice weekly over the 12-week period or until healed. Results were evaluated in regards to set outcomes of standard wound evaluation metrics including wound surface area (Length*Width*π/4), resource utilisation, and adverse events, as well as ease of use, and patient acceptability. Wound healing at 12 weeks was set as primary outcome.

Results

At the primary endpoint at 12 weeks, mean wound size reduction for patients that completed the evaluation was -89%, vs -37% in the Control (p<0.01), and 9/19 (47%) had healed vs 2/19 (11%) in the Control (p<0.05). A significant difference vs Control was also observed well before 12 weeks. At 4 weeks all 20 wounds in the haemoglobin spray group had demonstrated positive wound size reduction vs 15 in the control (p<0.05) and five had healed vs one in the Control (p<0.10). At 8 weeks, all patients remained improved in the haemoglobin spray group and 8 had healed, vs 5 patients non-improved and only 2 healed in the Control (p<0.10), at double the average healing speed; -78% vs -39% mean wound size reduction vs baseline (p<0.05). Secondary outcome evaluation demonstrated that all wounds commenced the evaluation with wound-bed slough present. At 4 weeks 100% of patients in the haemoglobin spray group were slough free vs 4 (20%) in the Control (p<0.01). At the 8-week review no patients' wounds had regressed in the haemoglobin spray group while 11 patients in the Control remained sloughy (p<0.01). Additionally, resource use analysis suggested a -49% reduction in overall number of dressing changes required and total cost of care savings of -65% (-£1,927 cost /pt, excluding the cost of haemoglobin spray) over the 12-week observation period vs Control; driven by lower dressing costs (-67%, -£80/pt), lower nursing costs (-51%, -£1,043/pt), fewer unplanned surgical interventions for amputation and debridement (-100%, -£804/pt, of which -£423 due to one amputation at £8,450). All costs based on NHS tariff prices if available. One patient died in each group unrelated to their wounds. There were no other adverse events in the haemoglobin spray group while there were 11 in the Control (p<0.01); one amputation, four infections, and six unplanned debridement surgeries. All patients and clinicians found the haemoglobin spray product acceptable and easy to use.

The primary endpoint results were also robust to analysis of covariance (ANCOVA) to account for variations in baseline values, with the effect of haemoglobin spray p=0.01 when controlling for baseline variations for baseline wound size (p=0.50), prior wound persistence (p=0.11), and HbA1c (p=0.31). No adjustments for multiple analysis was made for reported p-values.

Discussion

The incorporation of a haemoglobin spray solution within DFU treatment is likely to result in significantly better outcomes, with results in this study suggesting a doubling of the average wound healing rate, more than twice as many wounds healed within three months, and significant quality of life benefits gained from reduced pain and rapid wound slough elimination vs the control cohort. Future research should aim to assess the effectiveness of haemoglobin spray across a broader set of chronic wounds and clarify the extent to which these benefits are sustained longer-term, over six months – which indeed is what we are working on.

Conclusion

The incorporation of a haemoglobin spray solution within DFU treatment is likely to result in significantly better outcomes and substantial cost savings.

Acknowledgements and Conflicts of interest

infirst Healthcare provided the haemoglobin spray free for the evaluation but did not influence the design, data collection or analysis. Sharon Hunt and Fredrik Elg provide advisory and speaking services to pharmaceutical and other healthcare organisations, including but not limited to, infirst Healthcare Ltd.

KEY POINTS

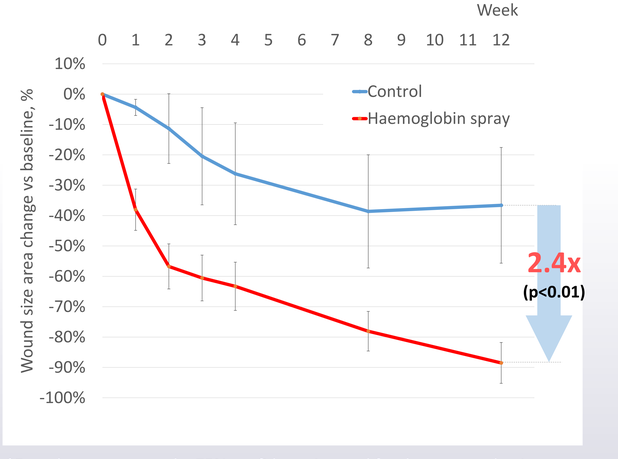
- Oxygen is essential in wound-healing, but high plasma glucose and atherosclerotic plaques associated with diabetes often lead to ischaemia due to macro and microvascular complications, reducing oxygen levels
- Granulox® haemoglobin spray enables increased oxygen availability in the wound bed and aids healing by aiding oxygen diffusion
- By adopting Granulox® as part of standard care in chronic DFUs healing times and total cost of care were reduced by half, with observed mean savings of £1,927 per patient within 12 weeks vs a retrospective control cohort.

References

Bateman (2015) Topical haemoglobin spray for diabetic foot ulceration. British Journal of Nursing, 24(12).

Significantly greater mean wound size reduction, with more than double mean size reduction by week 12

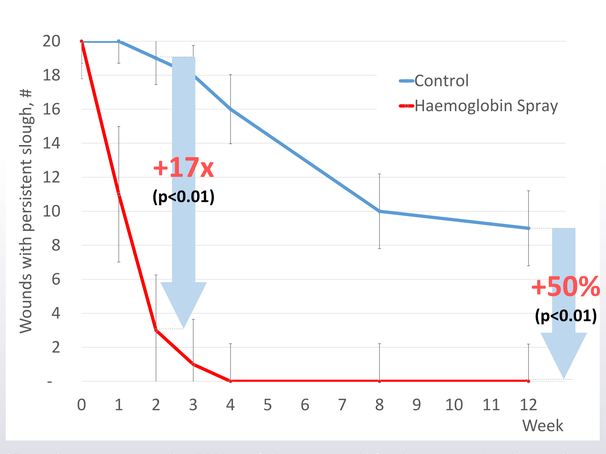
Change in wound size vs baseline, by week*



*Error-bars represent the 75% confidence interval for the mean reduction

Rapid and effective slough elimination, at substantially greater rate than standard care alone already from Week 1

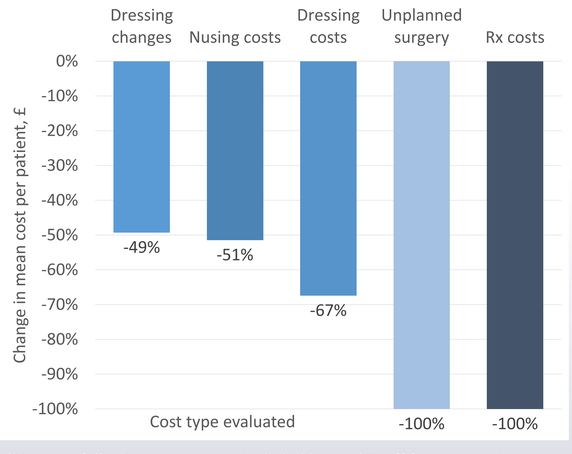
Wounds with persistent slough, by week*



*Error-bars represent the 75% confidence interval for the proportions*sample

Substantial reductions in resource demands across all major cost of care drivers within 12 weeks

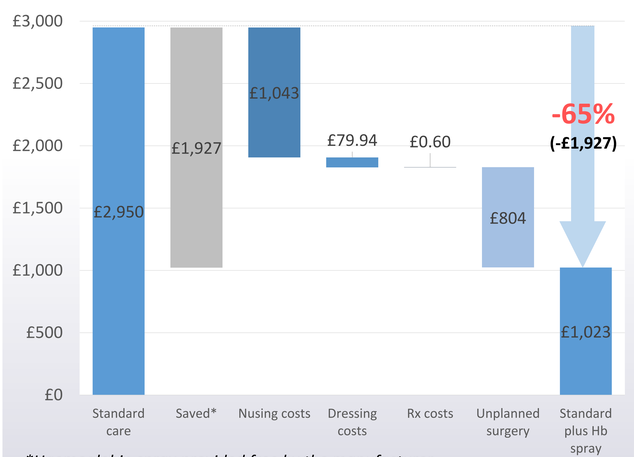
Total resource utilisation over 12 weeks, vs control, by type*



*No costs following amputation included beyond Tariff for amputation

Total cost of care reduced by half within 12 weeks of introduction of haemoglobin spray as adjunct therapy

Mean savings per patient by cost type over 12 weeks*



*Haemoglobin spray provided free by the manufacturer

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