A real world, retrospective cohort controlled, evaluation of clinical effectiveness of haemoglobin spray as adjunct therapy in chronic wounds – interim results at 12 weeks

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Introduction

Chronic wounds are a leading cause of disability and contributes to a higher burden of care than any of the common cancers in the UK. The vast majority of non-healing wounds occur in patients with one or more vascular complications such as diabetes, venous insufficiency, or atherosclerosis. Among wounds that fail to heal normally, nearly all have low or very low levels of oxygen availability in the wound bed. Correspondingly, improvement in oxygen availability is increasingly recognised as a key element for achieving healing. Facilitated diffusion using haemoglobin is a promising approach to increase oxygen availability in the wound bed, but has so far not been evaluated in a real-world care context with a representative control cohort, outside of a clinical trial setting.

Method

A controlled evaluation with two cohorts was undertaken in a primary care clinic, where a haemoglobin spray (Granulox®, infirst Healthcare) was used in a cohort of 50 patients with chronic wounds demonstrating <40% wound size reduction over the preceding 4 weeks of standard care and compared with a cohort of 50 patients selected from the same period the year prior using the same protocol, retrospectively, from the same clinic (Control). Haemoglobin spray was provided free by infirst Healthcare. No changes to care practices or dressings were made unless medically required, i.e. due to changes in exudate levels or wound size. Results were evaluated on standard wound evaluation metrics including wound surface area reduction, wound tissue type (i.e .sloughy), pain (0-10), exudate, resource utilisation, and adverse events, as well as ease of use, and patient acceptability. Wound healing at 12 weeks was set as primary (interim) outcome as part of an ongoing 6-month evaluation study.

Results

At the 12-week primary endpoint mean wound size reduction was -92%, vs -41% in the Control ($p<0.01$), and 40/50 (80%) wounds had healed vs 11/40 (28%) in the Control ($p<0.01$). A significant difference vs Control was also observed before 12 weeks. At 4 weeks 47/50 (94%) wounds in the haemoglobin spray group had demonstrated positive wound size reduction vs 20/49 (41%) in the control ($p<0.05$) and 16 had healed vs 5 in the Control ($p<0.01$). At 8 weeks the mean size reduction was more than 4 times greater in the haemoglobin group; at -87% vs -14% ($p<0.01$) and 5 times more wounds closed 40/50 (80%) vs 7/49 (14%) ($p<0.01$). Secondary outcome evaluation showed mean pain score reductions significantly greater from week one ($p<0.01$), despite being higher at baseline in the haemoglobin group. Also slough and exudate levels saw significantly faster improvements vs Control within as little as one week, with slough reduced by -25% vs -4% ($p<0.01$), and the patients with high exudate reduced from 26 to 4 vs no change in the Control (20 wounds) ($p<0.01$). At 4 weeks 100% of patients in the haemoglobin spray group were slough free vs 10/49 (20%) in the Control ($p<0.01$). At the 8-week review no patients' wounds had regressed in the haemoglobin spray group while 33/49 patients in the Control remained sloughy ($p<0.01$). Resource use analysis suggested -48% reduction in number of dressing changes, and total cost of care savings of -55% (-£1,118 cost /pt, excluding the cost of haemoglobin spray and not considering additional self-care benefits realised) over the 12-week observation period vs Control; driven by lower dressing costs (-47%, -£61/pt), lower nursing costs (-45%, -£707/pt), and fewer unplanned surgical interventions (-100%, -£350/pt). All costs based on NHS tariff prices if available. Six patients died in the Control group and one in the Haemoglobin spray group, unrelated to their wounds. There were no other adverse events in the haemoglobin spray group while there were 16 in the Control ($p<0.01$); eight surgeries, and eight infections requiring antibiotics. Patients and clinicians alike found the haemoglobin spray product acceptable and easy to use. The primary endpoint results were also robust in light of covariance (ANCOVA) to account for variations in baseline values, with the effect of haemoglobin spray on wound size reduction at 12 weeks $p<0.01$ also when controlling for baseline wound size ($p=0.59$) and prior wound persistence ($p=0.10$). Analysis for the secondary endpoints similarly showed robust results regardless of baseline variations ($p<0.05$). No adjustments for multiple analysis was made for reported p-values.

Discussion

Healing benefits at 12 weeks were highly significant and robust to covariates, with more than double the average healing speed and number of healed wounds up to 12 weeks vs Control and significant quality of life related benefits already from week one. Future research should aim to assess the effectiveness of haemoglobin spray over the longer-term, over six months – an evaluation already in progress and for which this evaluation reports the half-way outcomes.

Conclusion

Adoption of haemoglobin spray in the treatment of chronic wounds is expected to realise substantial healing benefits to patients.

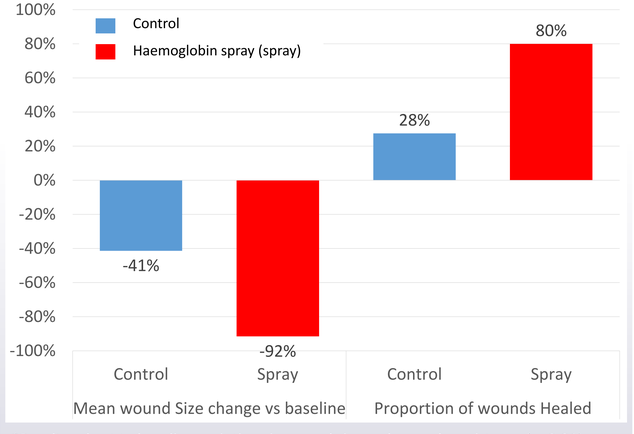
KEY POINTS

- The vast majority of non-healing wounds occur in patients with one or more vascular complications such as diabetes, venous insufficiency, or atherosclerosis contributing to low or very low levels of oxygen availability in the wound bed
- Granulox® haemoglobin spray enables increased oxygen availability in the wound bed and aids healing by aiding oxygen diffusion
- By adopting Granulox® in chronic wound care, healing times and total cost of care were reduced by half, with observed mean savings of £1,118 per patient within 12 weeks vs a retrospective control cohort.

Acknowledgements and Conflicts of interest
infirst Healthcare provided the haemoglobin spray free for the evaluation, but did not influence on 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.

More than double the average wound size reduction and number of wounds healed by week 12

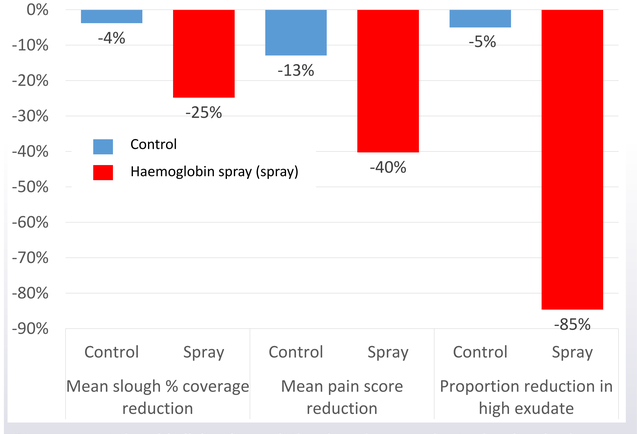
Change in wound size vs baseline, and wounds healed by week 12*



Results robust to baseline variations in wound size and wound persistency ($p<0.01$)

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

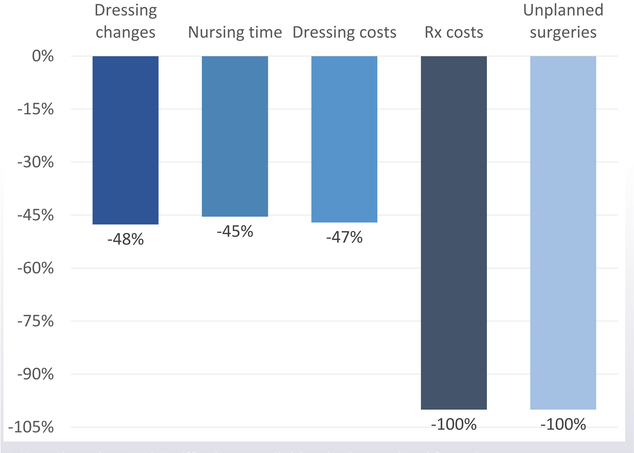
Improvements of key wound healing indicators at week 1*



Improvements in epithelial and granulation tissue in proportion to slough reduction

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

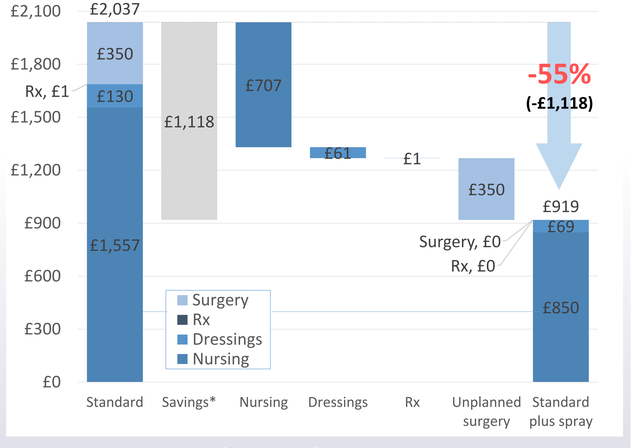
Total resources over 12 weeks, vs standard care, by cost type*



Costs based on NHS Tariff, where available, else lowest local formulary cost

Total cost of care reduced by over 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 manufacturer.

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