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CLINICAL RESEARCH ARTICLE

Clinical effectiveness of hemoglobin spray (Granulox®) as adjunctive therapy in the treatment of chronic diabetic foot ulcers

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Introduction: Hemoglobin spray (Granulox®) comprises purified hemoglobin and is a novel approach for increasing oxygen availability in the wound bed in diabetic foot ulcer patients. Its mode of action is to bind oxygen from the atmosphere and diffuse it into the wound bed to accelerate wound healing in slow-healing wounds.

Patients and methods: Wound healing outcomes, that is, wound size, pain, percentage of slough, and exudate levels, were compared retrospectively to a similar cohort of patients treated over the same period the previous year. The same inclusion and exclusion criteria applied to both groups.

Results: All 20 (100%) hemoglobin spray-treated patients and 15 (75%) control patients experienced some wound healing by week 4, with 5 (25%) and 1 (5%), respectively, achieving complete wound closure. At week 4, mean wound size reduction was 63% in the hemoglobin spray group versus 26% for controls, increasing to 95% reduction at week 28 in the hemoglobin spray group versus 63% for controls ($p < 0.05$ at all timepoints). Hemoglobin spray was associated with substantially lower pain scores using a 10-cm visual analogue scale, with 19/19 patients (100%) being pain-free from week 12 onwards, compared to 6/18 patients (33%) in the control group. At week 28, 2/18 patients (11%) in the control group still had pain. Both groups had similar baseline slough levels, but hemoglobin spray-treated wounds had slough completely eliminated after 4 weeks versus 10% mean reduction in the control group ($p < 0.001$). Hemoglobin spray was associated with markedly reduced exudate levels; within 4 weeks, no patients had high exudate levels in the hemoglobin spray group versus 5 in the control group.

Conclusion: Standard wound care plus hemoglobin spray results in improvements in wound closure, wound size reduction, pain, slough, and exudate levels compared to control patients for chronic diabetic foot ulcer treatment.

Keywords: *diabetes-related complications*; *diabetic foot ulcer*; *hemoglobin*; *topical oxygen therapy*; *wound healing*

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It was estimated in 2000 that 2.8% of the worldwide population had diabetes, and this is projected to reach 4.4% of the population by 2030 (1). Diabetes is a life-long condition, and sufferers may have to deal with a range of associated short- or long-term complications (2); furthermore, diabetic patients are at higher risk of overall mortality (3). In an 11-year retrospective audit by Chammas et al., results showed that patients with a diabetic foot ulcer (DFU) have a greater than two-fold increase in mortality compared with non-DFU diabetic patients (3).

DFU is multifactorial and notoriously difficult to heal. If left untreated, it can result in infection, extensive tissue damage, amputation, and long-term disability (4). It is estimated that around 10% of people with diabetes will develop at least one DFU over their lifetime (5), and it represents one of the most common reasons for admission of a diabetic patient to a healthcare setting in the United Kingdom (6). A report published by the NHS Diabetes states that £650 million is spent in the United Kingdom alone on treatment of DFU and associated amputations each year (7).

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Oxygen is an essential component in the wound healing process (8) and without it, wounds fail to heal. There is an increased demand for oxygen in the healing of damaged tissue, thereby enabling wound healing to progress effectively; however, in patients with diabetes, the capacity for vascular supply of oxygen is often greatly reduced due to macro- and micro-angiopathy. Temporary hypoxia after injury triggers wound healing by stimulating the release of growth factors and angiogenesis, but persistent hypoxia delays wound healing by increasing the levels of oxygen free-radicals (9, 10). The resulting chronically oxygen-depleted cells in these patients have devastating effects on vulnerable tissue, often resulting in infection, wound deterioration, disfigurement, and disability (11).

A topical hemoglobin contact spray (Granulox®, infirst Healthcare Ltd, London, UK) is a novel treatment that accelerates healing in slow-healing wounds, including DFU, and it was first approved for use in chronic wounds in 2012. The active ingredient is purified hemoglobin, and its mode of action is to bind oxygen from the atmosphere and then release it into the wound bed by facilitating diffusion (12–16).

The safety and efficacy of this hemoglobin spray added to standard wound care was initially evaluated in a wound care clinic in a group of 20 patients presenting with chronic (>12 weeks) DFU. Patients received the standard wound care regimen that they had received prior to entering the evaluation, with the only variable being the addition of hemoglobin spray. A preliminary analysis that was published after 4 weeks showed that all wounds had positive wound reduction, 25% had complete wound closure, and no adverse events were reported (17). We now present the wound healing outcomes for the same 20 DFU patients after an extended 28-week period for the first time, and the results have also been compared with a retrospective patient cohort treated the previous year with standard wound care alone, that is, before the introduction of hemoglobin spray into the clinic.

Patients and methods

This evaluation was conducted in a single wound care clinic in a large UK general hospital, with patients recruited in February 2015 and followed for a 6-month period (i.e. 28 weeks); control patients were retrospectively selected from the same clinic and period in February 2014. The evaluation was not conducted as a formal clinical study, but data on the use of the hemoglobin spray and the outcome of the wounds were collected by the wound care nursing team as part of standard care and then compared retrospectively to a similar cohort of patients, using the same inclusion and exclusion criteria, over the same period the previous year before the introduction of the hemoglobin spray in the clinic. Ethics committee approval was not required in line with the NHS Trust's policy on clinical evaluations of CE marked products used within their licensed indications without randomisation. Patients were required to give verbal consent following an explanation and review of the product and information leaflet prior to receiving the hemoglobin spray. This procedure was documented by the clinician in the patient notes.

The same inclusion and exclusion criteria applied to both patient cohorts. Inclusion criteria comprised patients aged >18 years with DFU that had failed to heal substantially, defined as $<40\%$ reduction, in the last 12 weeks. The DFU had to be located below the ankle and have a Site, Ischemia, Neuropathy, Bacterial Infection, Area and Depth (SINBAD) score of a maximum of 2 (Table 1). The SINBAD classification system encompasses variables that are recognised to contribute to ulcer outcome. The maximum SINBAD score of 2 was selected for this evaluation since patients scoring ≥ 3 usually have vascular insufficiency and other wound healing issues that would impair the effectiveness of any wound healing product. Patients were excluded if they presented with infected ulcers, were receiving systemic antibiotic therapy or corticosteroids, were pregnant or lactating, had an ankle-brachial pressure index <0.5 or toe pressure <70 mmHg, or a hemoglobin A1c (HbA1c) measurement $>10\%$ (13.3 mmol/L), in line with the recommendations for use in the product label where underlying conditions should be treated and all alternative options for revascularisation of arterial insufficiency should have been exhausted.

A total of 20 patients who presented at the department with chronic DFU for ≥ 12 weeks who met the inclusion criteria and who verbally consented to participation were

Table 1. The SINBAD system for classifying and scoring foot ulcers

Category	Definition	SINBAD score
*S*ite	Forefoot	0
	Midfoot and hindfoot	1
*I*schemia	Pedal blood flow intact, one pulse palpable	0
	Clinical evidence reduced pedal blood flow	1
*N*europathy	Protective sensation intact	0
	Protective sensation lost	1
*B*acterial infection	None	0
	Present	1
*A*rea	Ulcer <1 cm^2	0
	Ulcer >1 cm^2	1
*D*epth	Ulcer confined to skin and subcutaneous tissue	0
	Ulcer reaching muscle, tendon, or deeper	1
Total possible score		0–6

Source: Adapted from Ince et al. (31).

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treated with standard wound care plus hemoglobin spray and were monitored over 28 weeks. Each patient group (i.e. both the hemoglobin spray group and the retrospective control group) was cared for in the same clinical setting by the same medical team. The patients in the hemoglobin spray group were also maintained on the same dressing type they were using prior to the evaluation. Patients were permitted to continue using off-loading devices, such as surgical shoes or foam boots. Debridement was carried out in both groups based on medical need. The hemoglobin spray was applied in the clinic by the wound care nurse twice a week until complete wound closure, with dressings changed each time the hemoglobin spray was applied. If required for appropriate wound management, additional dressing changes and spray applications were permitted.

Data regarding wound size and wound healing attributes, including exudate levels, percentage of slough, and pain levels, were collected by the same wound care team at each dressing change using a standard data collection sheet based on the applied wound management assessment documentation, which is the standard wound care documentation used in the NHS Trust (18). Wound size was measured using a disposable paper ruler. Pain levels were evaluated using the McGill Pain Index for all patients who reported suffering pain at baseline, with the pain levels scored on a 10-cm visual analogue scale from 0 = 'No pain' to 10 = 'Pain as bad as possible'. Data for the control cohort were collected retrospectively from patient notes from the same clinic during the same period the previous year using the same inclusion and exclusion criteria and using the same data collection form. The control group were selected sequentially over the same time period the previous year to ensure minimisation of sampling bias.

Statistical analysis

Statistics are reported using chi-square test for group-level (nominal) data and unpaired two-tailed *t*-test for numeric (parametric) values. Statistical significance was defined as $p < 0.05$. No adjustment for multiple statistical analyses was made. The primary outcome was defined as wound healing over 28 weeks.

Results

Patient disposition

A total of 40 patients were included in this evaluation: 20 patients in the hemoglobin spray group, and 20 in the retrospective control group. Preliminary data up to week 4 from the 20 patients in the hemoglobin spray group were reported previously (17). Small deviations from the previously published information are possible as all analyses were re-conducted from current patient notes.

The mean age of the patients was 55.0 years in the hemoglobin spray group and 54.4 years in the control group (range from 18 to 89 years overall). In the hemoglobin spray group, 50% of the patients were male, and in the control group, 55% were male. The mean HbA1c was 7.0%/8.6 mmol/L in the hemoglobin spray group and 6.9%/8.4 mmol/L in the control group (Table 2). Anatomical sites for the DFU represented the common sites (19) for these ulcers to occur, with the most common location being plantar (hemoglobin spray group 40%; control group 50%) (Table 3). The mean time for wounds being present prior to the application of hemoglobin spray was 5.8 months compared with 5.4 months in the control group. The mean baseline wound size was slightly larger in the control group at 6.6 cm^2 versus 5.1 cm^2 in the hemoglobin spray group ($p = 0.45$) (Table 2). Eleven patients (55%) in each group used a variety of off-loading devices to aid pressure reduction, with the most common being a surgical shoe (hemoglobin spray group 30%; control group 35%) (Table 3). Overall there were no statistically significant differences between the two groups at baseline for any of these parameters (Table 2).

Table 2. Baseline data

	Hemoglobin spray group (*N* = 20)	Control group (*N* = 20)	*p*[a]
Mean age (range), years	55.0 (18–89)	54.4 (26–85)	0.92
Gender (male/female), *n*	10/10	11/9	0.75
Mean hemoglobin A1c at week 0,%/mmol/L	7.0%/8.6 mmol/L	6.9%/8.4 mmol/L	0.84
Mean wound size at week 0, cm^{2b}	5.1	6.6	0.45
SINBAD score (score 1/score 2)	8/12	8/12	1.0
Duration of wound at week 0 (range), months[b]	5.8 (3–18)	5.4 (3–12)	0.72
Neuropathy present (Yes/No)	10/10	9/11	0.75
Ischemia[c] present (Yes/No)	9/11	8/12	0.75

[a]*p* values for difference between the two groups, using chi-square for group-level data and independent two-tail *t*-test for numeric variables. [b]Based on oval of L*W. [c]Vascular deficiency to foot.

Table 3. Wound location and off-loading devices

	Hemoglobin spray group ($N = 20$) *n* (%)	Control group ($N = 20$) *n* (%)
Wound location		
Plantar	8 (40)	10 (50)
Calcaneus	4 (20)	4 (20)
Hallux	4 (20)	3 (15)
Pedal	3 (15)	3 (15)
Phalanges	1 (5)	0
Total	20	20
Off-loading device (number of patients)		
None	9 (45)	9 (45)
Surgical shoe	6 (30)	7 (35)
Airboot	3 (15)	4 (20)
Foam boot	1 (5)	0
Heel cast	1 (5)	0
Total	20	20

Wound healing

All of the patients in the hemoglobin spray group had some degree of wound healing by week 4, ranging from a reduction of 18 to 100%, with a mean reduction of 63%, and five patients (25%) had complete wound healing by week 4. In the control group, 15 patients (75%) had some degree of wound healing by week 4, with wound size reduction ranging from 4 to 100%, with a mean reduction of 26%, but only one patient achieved complete healing at this timepoint, and five patients actually had an increase in wound size (increase ranging from 10 to 108%). All of the healed wounds in the hemoglobin spray-treated group at week 4 were of the smallest wound size category (0–2 cm^2). These patients also had a shorter duration of wound pre-evaluation, were in a lower age range (except for one patient), were free of neuropathy and vascular deficiency, and had an HbA1c of 8% (10.1 mmol/L) or lower. Similarly, the patient in the control group whose wound healed within 4 weeks was non-neuropathic, had no ischemia, was young (age 28), the wound had been present for only 3 months and was of the smallest wound size category (2 cm^2) at baseline. None of the wounds that were healed by week 4 recurred over the course of the 28-week evaluation period.

After 28 weeks' treatment, a total of 15 patients had their wounds completely healed in the hemoglobin spray group. Of the remaining five patients whose wounds had not healed at this point, one patient had died due to a non-wound-related cause, and three of the remaining four patients had stopped the hemoglobin spray treatment prematurely and then became static or worsening again after achieving reductions in wound size of 68, 79, and 91%, respectively, with the hemoglobin spray treatment. The remaining patient, a 76-year old with poorly controlled diabetes, had achieved 95% wound size reduction at 28 weeks despite a relatively large foot ulcer measuring 3.8 × 1.5 cm at baseline and suffering from both neuropathy and limb ischemia. In the control group at week 28, a total of eight patients had their wounds completely healed. One patient in this group also died due to a non-wound-related cause, one patient underwent an amputation, six patients had notably reduced wound sizes (65, 98, 96, 90, 56, and 37%), one patient's wound had not changed, and three patients had an increase in wound size (50, 33, and 33%).

A rapid reduction in overall wound size was seen in the hemoglobin spray group compared with the control group. By week 4, there was an average wound size reduction of 63% in the hemoglobin spray group versus 26% in the control group ($p = 0.03$). By week 16, this had increased to 91% in the hemoglobin spray group compared with 43% in the control group ($p = 0.01$), and this increased further to a 95% reduction in wound size at week 28 in the hemoglobin spray group compared with a 63% reduction in the control group ($p = 0.02$) (Fig. 1).

The number of wounds that had not healed by completion of the evaluation, that is, had not achieved full epithelialisation by week 28, is shown in Fig. 2. A significant difference was seen between the two groups at week 9 (12 patients in the hemoglobin spray group with a wound that had not healed (on intent-to-treat basis) compared with 18 patients in the control group) ($p = 0.04$), and by week 16 there was a 50% difference between the groups in favour of hemoglobin spray (9 patients in the hemoglobin spray group with a wound that had not healed compared with 18 patients in the control group) ($p < 0.01$). By week 28, only five wounds in patients treated with hemoglobin spray had not fully healed (one of whom had died) compared with 12 in the control group (including one death and one amputation) ($p = 0.04$) (Fig. 2).

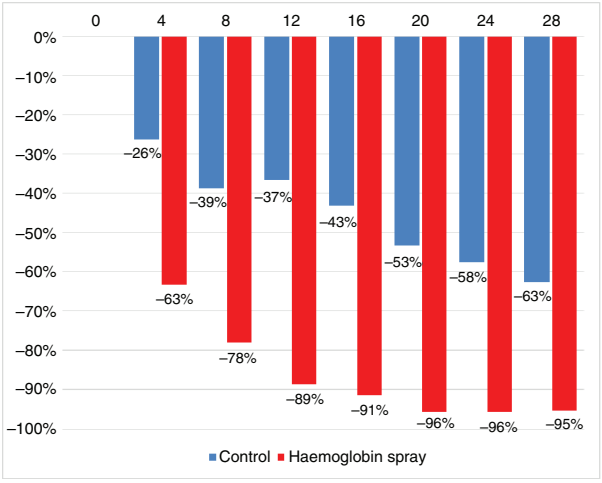

Fig. 1. Percent wound size change versus baseline by week.

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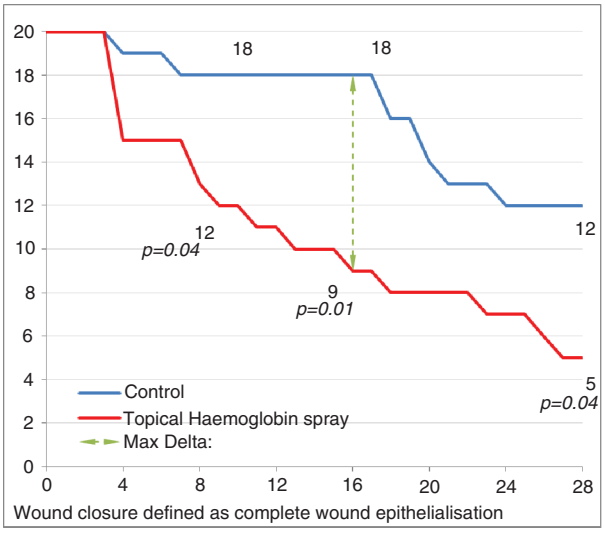

Fig. 2. Number of wounds not healed by week.

Pain assessment

Pain levels were evaluated for all patients who reported suffering pain at baseline (16 patients in hemoglobin spray group, 14 control patients). As some patients were unable to feel any pain at all due to loss of sensation in the feet, patients without any pain at baseline were not included in the pain evaluation. Mean pain scores were similar between the two groups at baseline (5.1 for both groups). Hemoglobin spray treatment was associated with substantially lower pain scores throughout the evaluation period. By week 4, mean pain score in the hemoglobin spray group was 0.3, and all patients were completely pain-free from week 12 through to week 28. In the control group, mean pain score was 3.5 at 4 weeks ($p < 0.001$ compared to the hemoglobin spray group), at week 12, six patients still suffered from pain and these six patients had a mean pain score of 3.7, and by week 28, two patients still had a mean pain score of 4.0 (see Fig. 3 for mean pain scores by group).

Slough levels

All wounds in both groups had a similar degree of slough present at baseline, with an average level of slough coverage of 50% in both groups ($p = 0.99$). Wounds in the hemoglobin spray group rapidly achieved slough elimination over the course of treatment. After 4 weeks, all patients treated with hemoglobin spray achieved complete slough elimination, compared with only a 10% reduction in the control group ($p < 0.001$). After 24 weeks of treatment, one patient in the hemoglobin spray group had recurrence of slough in the wound, however this patient had stopped using hemoglobin spray prematurely which may have contributed to the slough recurrence, while in the control group, presence of slough was still evident in four wounds, with an average remaining slough coverage of 43% (see Fig. 4 for mean slough coverage). As a result of the superior wound healing, there was no debridement required in the hemoglobin spray group, with only basic wound cleaning with saline needed, versus the requirement for three cases of theatre surgery and three cases of bedside debridement in the control group.

Exudate levels

At baseline, 12 patients had a high level, 8 patients had a moderate level, and 0 patients had a low level of exudate in the hemoglobin spray group, whereas 9 patients had a high level, 5 patients had a moderate level, and 6 patients had a low level of exudate in the control group. By week 4, exudate levels demonstrated a significant reduction across all patients in the hemoglobin spray group, with all

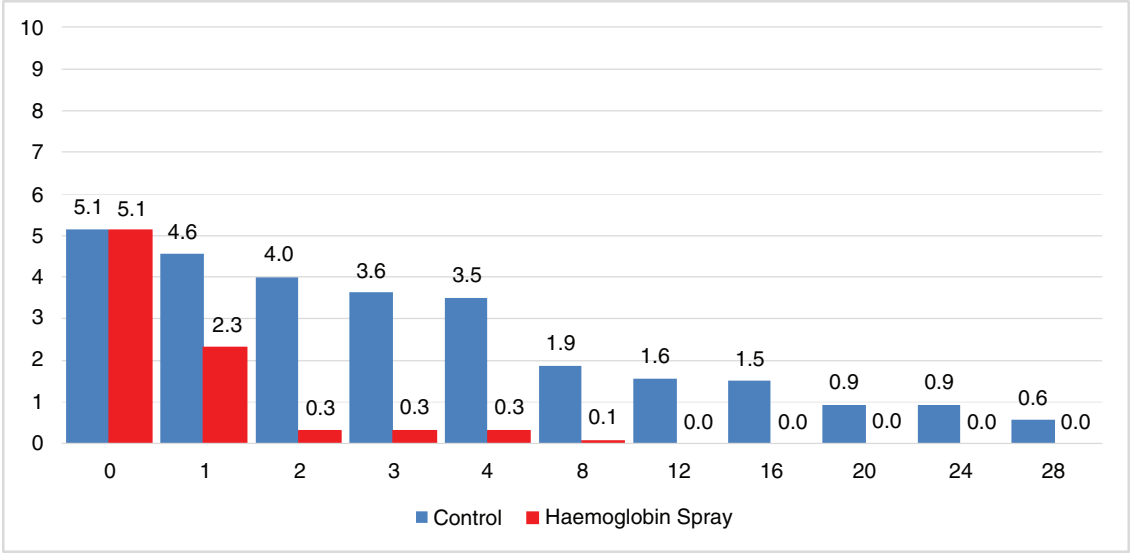

Fig. 3. Average reported pain scores using a 10-cm visual analogue scale (VAS) by week.

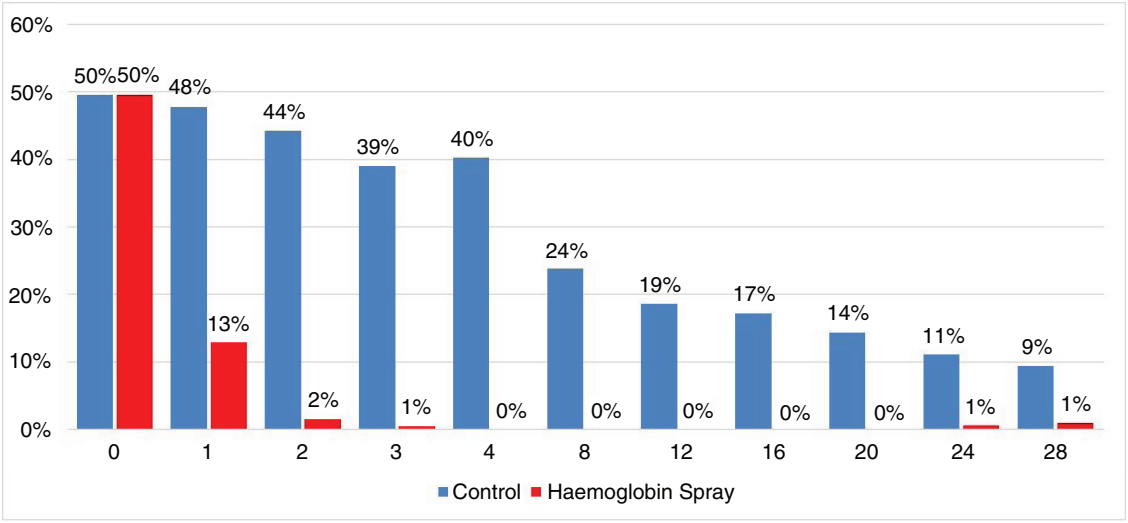

Fig. 4. Average percent wound coverage with slough by week.

12 patients with high levels of exudate at baseline being reduced (100%), versus 4 out of 9 patients (44%) in the control group. After 28 weeks of treatment, 0 patients had high levels, 2 patients had moderate levels, 1 patient had low levels, and 16 patients had no exudate or were healed in the hemoglobin spray group, whereas in the control group, 1 patient had persistent high exudate levels, 5 had moderate and 4 had low levels, and 8 patients had no exudate or were healed (Fig. 5).

Safety

One patient in each group died; however, neither of the deaths was related to the wounds or to use of hemoglobin spray. There were an additional nine events in the control group, but no further events in the hemoglobin spray group. The events in the control group comprised one amputation, three unplanned surgeries for wound debridement requiring treatment in a surgical theatre, and five cases of wounds that were infected and required antibiotic treatment (in four of the patients).

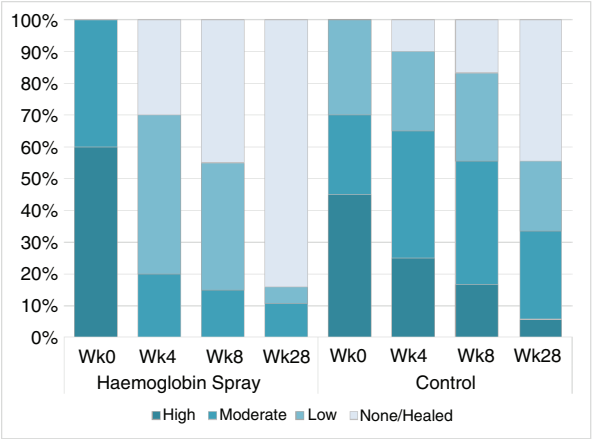

Fig. 5. Level of wound exudate by week.

Discussion

DFUs are extremely debilitating for patients and are difficult to treat for clinicians (20). DFUs are a worldwide problem and a major cause of morbidity in diabetic patients, in particular, ulcerations and amputations (21, 22). Standard care generally comprises a multidisciplinary approach, but more recently, adjunctive therapies, such as aided oxygenation, represent new treatment modalities, although there has been criticism that many lack significant high-powered studies to support their use as standard of care (20).

Local oxygen delivery is a crucial element in wound healing, and it is widely recognised that limited oxygenation can lead to a chronic non-healing ulcer (23). Wound tissue requires a constant supply of oxygen to meet the increased metabolic demands of the wound healing process (24, 25). Hypoxic tissue cannot regenerate and is unable to move along the wound healing stages of inflammation, proliferation, and maturation (24), so it remains in the inflammatory stage, thereby increasing the risk of bacterial infection and tissue disfiguration (26). However, the body's tissues have no capacity for retaining oxygen molecules and, therefore, require a consistent oxygen delivery if wound healing is to occur effectively (27). Topical oxygenation can be delivered as pure oxygen, either under pressurised or ambient conditions, through chemical release via an enzymatic reaction, or by facilitated diffusion using oxygen binding and releasing molecules, for example, using hemoglobin (12). Topical hemoglobin treatment permits hemoglobin-mediated oxygen diffusion within the aqueous medium naturally present within the wound bed (13).

A novel adjunctive therapy developed to accelerate healing in slow-healing wounds by improving oxygenation is a topical hemoglobin spray (Granulox®) that acts as an oxygen transporter from surrounding air to

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improve oxygen availability in the wound bed. However, the studies to date have not been aimed specifically at DFUs, and this lack of wound-specific data is considered by some to be insufficient to evaluate improvements in wound healing (28). In an attempt to address this point, this controlled evaluation was conducted to investigate the use of a topical hemoglobin spray when added to standard wound care regimens in an acute setting in patients who presented specifically with chronic DFU, despite having previously received best practice wound care according to NICE NG19 guidelines (5). A retrospective control group was selected from the same clinical setting over the same period in the previous year to provide a comparison. This ensured all other elements of care remained constant so that the clinician could observe any difference after the introduction of hemoglobin spray as an adjunctive therapy to the usual care regimen. Baseline characteristics were similar between the two groups, and it is noted that all patients were assessed at baseline using the SINBAD foot ulcer classification system, which is considered a valuable universal tool for predicting ulcer outcome.

Throughout the evaluation, a rapid reduction in wound size was seen in the hemoglobin spray group compared with the control group. This was evident as early as the first week, and by week 4 where there was an average wound size reduction of 63% in the hemoglobin spray group versus 26% in the control group. This increased further to a mean 95% reduction in wound size at week 28 in the hemoglobin spray group compared with a mean wound healing reduction of 63% for control. By week 28, only five wounds in patients treated with hemoglobin spray had not fully healed, compared with 12 in the control group ($p = 0.04$). As expected, those patients with a shorter duration of wound pre-evaluation, small wounds, in the younger age bracket, and free from neuropathy and vascular deficiency saw the most rapid wound healing benefits. It is of note that there were more small wounds $< 2\ cm^2$ in the hemoglobin spray group, however, the average size and distribution of wound sizes at baseline between the two groups were not statistically significantly different.

Mean pain scores also decreased to a greater extent in the hemoglobin spray patients compared with the control patients, and there was also a notable reduction in slough levels. The number of patients with a significant reduction in exudate levels was also greater in the hemoglobin spray group, thus indicating that all measured wound healing parameters were improved with the use of the topical hemoglobin spray. The long-term data reported here after 28 weeks follow-up support the initial 4-week data previously published (17) and indicates substantially improved healing outcomes with hemoglobin spray compared to standard care alone. Furthermore, the results of this evaluation support the findings from other controlled studies using hemoglobin spray on lower limb wounds (13, 14). A number of recent UK case series evaluations investigating chronic ulcers have also shown the effectiveness of hemoglobin spray in promoting healing (15, 16, 29). Also in the author's experience, the results from this evaluation are representative of the overall picture seen in the clinic with the continued use of the hemoglobin spray, with repetitive themes of pain reduction in approximately 80% of patients, and slough and exudate reduction in most patients by week 4. Patients find the hemoglobin spray easy to use, and the positive effects are seen regardless of the wound presentation or the type of dressing used.

The results of our evaluation and other investigations into DFU management, thus, demonstrate that when hemoglobin spray is added to standard wound care, it confers significant benefits in terms of wound closure, wound size reduction, pain reduction, improvements in visible presence of slough and exudate levels. However, it is very important that hemoglobin spray treatment is continued until full wound closure is achieved as premature discontinuation can result in relapse, as indicated by the patients in this evaluation who stopped treatment with hemoglobin spray prematurely and subsequently stagnated or worsened. Also, despite its obvious benefits, there are some limiting factors associated with the use of hemoglobin spray, and it is important that best possible conditions should be met prior to its use (23). For example, it is deemed unsuitable for use with certain disinfectants, such as octenidine, as these may impair its effectiveness, and it should not be used in those patients who are pregnant or lactating. Also the underlying disease conditions, notably diabetes and peripheral vascular disease should be treated appropriately.

In addition, there are a number of limitations that should be addressed in future research in this field. This evaluation was not conducted as a formal randomised clinical study, since data on the use of the hemoglobin spray and the outcome of the wounds was collected by the wound care nursing team as part of standard care and then compared retrospectively to a similar cohort of patients treated over the same period the previous year. A formal randomised clinical study may provide more robust results and may reduce any potential bias caused by a Hawthorne effect, that is, where the participation in the evaluation itself has a positive impact on the outcome. Also the patients included in this evaluation represented only a small subset of patients who require treatment for chronic DFU. Furthermore, there was no investigation into whether these wounds would have healed even faster if the hemoglobin spray had been applied more frequently.

In conclusion, the results of this 28-week evaluation of DFU patients are positive and support the addition of hemoglobin spray to standard DFU wound care regimens.

This conclusion concurs with the consensus recommendations developed by Chadwick et al. in which a working group of key opinion leaders met in 2015 to determine the potential role of topical hemoglobin in non-healing wounds and to develop a clear decision-making pathway for clinical practice (30). The guidelines state that topical hemoglobin should be considered after 2–4 weeks of standard care in patients with a non-healing wound, and potentially earlier for patients at high risk of delayed wound healing (30). However, it should be recognised that DFU prevention and management must be individualised and conducted using a multidisciplinary approach that includes effective patient education, accurate assessment, and diagnosis of underlying conditions, as well as effective management, planning, and re-evaluation (19). Development of user-friendly innovative wound management therapies is important for effective future treatment, and the results of this investigation could be used to inform the design of other methodologically robust studies in the wider field of wound management in real-world practice.

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Conflict of interest and funding

Sharon Hunt and Fredrik Elg provide advisory and speaking services to pharmaceutical and other healthcare organisations, including but not limited to, infirst Healthcare Ltd. infirst Healthcare provided the hemoglobin spray free of charge to the study centre but did not have any influence on the design of the evaluation or the collection of the data. infirst Healthcare also provided financial support for data management, statistical analysis, and medical writing to help the authors publish the results of this evaluation.

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