Accelerate wound healing of acute and chronic wounds in patients with Diabetes: Experience from Mexico using supplementary haemoglobin spray.

Obdulia Lopez Lopez¹, Fredrik Elg² Peter Engels³, ¹Universidad Juarez Autonomo de Tabasco, Tabasco, Mexico, ²infirstHEALTHCARE Ltd, London, UK, ³Bergisch Gladbach, Germany.

Introduction: Patients with diabetes frequently develop chronic wounds with a common problem in of insufficient supply of nutrients and oxygen to the affected tissue. But oxygen is an essential component of the wound-healing process. Overall body function at the cellular level, including the prevention of bacterial activity, can use up to 90% of consumed oxygen in the body. Several approaches are available to provide additional oxygen topically to the wound. One of the most recent developments is to facilitate oxygen diffusion at the wound by applying purified haemoglobin. Several reports treating different types of chronic wounds described an enhanced wound healing using topically applied haemoglobin.

Aim was to evaluate the usefulness of implementing haemoglobin spray in the treatment of severe wounds of patients with diabetes. Here we present 15 cases of patients with diabetes mellitus presenting either severe acute (trauma) or chronic wounds, all treated at a wound care centre in Tabasco, Mexico.

Wound treatment: All cases were treated at the same wound care centre. All patients suffer from diabetes mellitus as primary disease.
- Wounds were thoroughly debrided (if required) and rinsed with an antimicrobial electrolyzed acid solution.
- Thereafter, the haemoglobin spray was administered as thin layer.
- A sterile paraffin gauze served as dressing.
- Frequency of dressing changes was initially three times per week or twice per week while reduced later to once weekly.
Results: In total 15 patients (19 wounds) were analysed;

- Average baseline wound size was 46 cm²/41 cm³, and average treatment period was 91 days (14 weeks);
- Average of wound dressing changes was 16 (median 16), and 15 haemoglobin applications (median 14);
- Wound closure of 19 (out of 19) wounds in 15 patients;
- In 7 cases amputation was prevented;
- Average cost of material per patient and dressing change including haemoglobin spray was at €9.30;
- No adverse events related to the treatment with the haemoglobin spray were reported;
- Frequency of treatment was initially two to three times per week during the first days or weeks, and could be reduced to once weekly at later stage of wound healing.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Gender</th>
<th>Wound type</th>
<th>Wound No.</th>
<th>Wound Age</th>
<th>Wound size</th>
<th>Treatment period</th>
<th>No. of dressing changes</th>
<th>Haemoglobin spray</th>
<th>Risk of amputation</th>
<th>Wound closure</th>
<th>Costs per treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Days</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Euro</td>
</tr>
<tr>
<td>1</td>
<td>67</td>
<td>F</td>
<td>Acute abscess/Pressure ulcer, left</td>
<td>1</td>
<td>7</td>
<td>80</td>
<td>80</td>
<td>177</td>
<td>29</td>
<td>28</td>
<td>n</td>
<td>yes*</td>
</tr>
<tr>
<td>2</td>
<td>43</td>
<td>M</td>
<td>Pressure ulcer</td>
<td>2</td>
<td>26</td>
<td>26</td>
<td>30</td>
<td>8</td>
<td>7</td>
<td>n</td>
<td>yes</td>
<td>n.d.</td>
</tr>
<tr>
<td>3</td>
<td>51</td>
<td>M</td>
<td>Pressure ulcer</td>
<td>3</td>
<td>12,5</td>
<td>12,5</td>
<td>77</td>
<td>8</td>
<td>8</td>
<td>n</td>
<td>yes</td>
<td>n.d.</td>
</tr>
<tr>
<td>4</td>
<td>50</td>
<td>M</td>
<td>Acute trauma, right foot</td>
<td>1</td>
<td>8</td>
<td>71</td>
<td>34</td>
<td>91</td>
<td>17</td>
<td>16</td>
<td>y</td>
<td>yes</td>
</tr>
<tr>
<td>5</td>
<td>50</td>
<td>M</td>
<td>Chronic venous leg ulcers, left leg</td>
<td>1</td>
<td>730</td>
<td>257</td>
<td>257</td>
<td>269</td>
<td>39</td>
<td>37</td>
<td>y</td>
<td>yes</td>
</tr>
<tr>
<td>6</td>
<td>62</td>
<td>M</td>
<td>Abscess, right leg</td>
<td>1</td>
<td>5</td>
<td>23</td>
<td>18,4</td>
<td>77</td>
<td>15</td>
<td>14</td>
<td>n</td>
<td>yes</td>
</tr>
<tr>
<td>7</td>
<td>50</td>
<td>M</td>
<td>Acute Trauma, left foot</td>
<td>1</td>
<td>15</td>
<td>42</td>
<td>42</td>
<td>112</td>
<td>22</td>
<td>21</td>
<td>y</td>
<td>yes</td>
</tr>
<tr>
<td>8</td>
<td>66</td>
<td>M</td>
<td>Wound after amputation of finger F-V, right hand</td>
<td>1</td>
<td>3</td>
<td>115</td>
<td>69</td>
<td>98</td>
<td>22</td>
<td>21</td>
<td>y</td>
<td>yes</td>
</tr>
<tr>
<td>9</td>
<td>43</td>
<td>F</td>
<td>Acute trauma, right leg</td>
<td>1</td>
<td>20</td>
<td>10</td>
<td>3</td>
<td>112</td>
<td>18</td>
<td>18</td>
<td>n</td>
<td>yes</td>
</tr>
<tr>
<td>10</td>
<td>56</td>
<td>M</td>
<td>Acute trauma, toe of right foot</td>
<td>1</td>
<td>30</td>
<td>6</td>
<td>18</td>
<td>42</td>
<td>10</td>
<td>9</td>
<td>y</td>
<td>yes</td>
</tr>
<tr>
<td>11</td>
<td>80</td>
<td>M</td>
<td>DFU/after amputation, left foot</td>
<td>1</td>
<td>30</td>
<td>36</td>
<td>3,6</td>
<td>72</td>
<td>14</td>
<td>13</td>
<td>n</td>
<td>yes</td>
</tr>
<tr>
<td>12</td>
<td>78</td>
<td>M</td>
<td>Abscess, right buttoc</td>
<td>1</td>
<td>26</td>
<td>22,5</td>
<td>4,5</td>
<td>87</td>
<td>18</td>
<td>17</td>
<td>n</td>
<td>yes</td>
</tr>
<tr>
<td>13</td>
<td>50</td>
<td>F</td>
<td>DFU, right foot</td>
<td>1</td>
<td>25</td>
<td>45,5</td>
<td>22,7</td>
<td>89</td>
<td>16</td>
<td>13</td>
<td>y</td>
<td>yes</td>
</tr>
<tr>
<td>14</td>
<td>50</td>
<td>F</td>
<td>Wound healing disturbance, right buttoc</td>
<td>1</td>
<td>39</td>
<td>43,7</td>
<td>13,1</td>
<td>49</td>
<td>9</td>
<td>9</td>
<td>n</td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Days</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>n.d.</td>
</tr>
<tr>
<td>2</td>
<td>39</td>
<td>F</td>
<td>Abscess, right butoc</td>
<td>1</td>
<td>9</td>
<td>25</td>
<td>125</td>
<td>54</td>
<td>12</td>
<td>11</td>
<td>n</td>
<td>yes</td>
</tr>
<tr>
<td>Median</td>
<td>51</td>
<td>5/10</td>
<td>(F/M)</td>
<td>20,00</td>
<td>26,30</td>
<td>19,00</td>
<td>87,00</td>
<td>16,00</td>
<td>14,00</td>
<td></td>
<td></td>
<td>7,52</td>
</tr>
<tr>
<td>Average</td>
<td>58</td>
<td></td>
<td></td>
<td>60,7</td>
<td>46,2</td>
<td>41,6</td>
<td>91,2</td>
<td>16,3</td>
<td>15,4</td>
<td></td>
<td></td>
<td>9,26</td>
</tr>
<tr>
<td>50</td>
<td>12</td>
<td></td>
<td></td>
<td>167,8</td>
<td>56,8</td>
<td>59,4</td>
<td>59,7</td>
<td>8,8</td>
<td>8,4</td>
<td></td>
<td></td>
<td>3,41</td>
</tr>
</tbody>
</table>
Case No. 3 & 5

51 years old male patient
Amputation prevented

Diagnosis: Diabetic foot. Wound caused by an injury was located on the dorsal dorsal and plantar surface of the first metatarsophalangeal joint of the right foot
Patient Care: A comprehensive treatment protocol was applied, based on the result of the patient's overall assessment. Double antibiotic therapy prescribed to combat the infection, followed by prophylactic monotherapy, subject to kidney function values. Walking completely avoided for three weeks, then only relatively.
Wound Care: Following surgical debridement, the wound was washed with diluted neutral soap, and rinsed with an antimicrobial solution (electrolysed acid solution). Haemoglobin spray was added first time at the second dressing change after rinsing. The wound was covered with sterile paraffin gauze to protect the granulation tissue. During the first two weeks the treatment including haemoglobin spray application was performed every three days, thereafter the dressing change including application of the haemoglobin spray was performed every eight days until the patient was discharged.

Results: Complete wound healing was achieved within 149 days after 24 wound treatments and 23 applications of haemoglobin spray. Amputation could be avoided. In addition type 2 Diabetes Mellitus, chronic hypertension, and obesity were treated adequately.

Fig. 1: Wound at A-C. Wound after cleansing & first application of Granulox, D - H: Wound after 16, 23, 37, 51, and 93 days; I: end of treatment (Day 149).

50 years old female patient
Planned amputation prevented

Diagnosis: Extensive contaminated, complicated chronic venous ulcer affecting the outer and inner sides of the left leg from below the knee to above the ankle which developed over the last two years
Underlying Conditions: Uncontrolled type 2 Diabetes Mellitus, chronic hypertension, peripheral venous insufficiency, obesity and depression.
Patient Care: A comprehensive treatment protocol was applied, based on the result of the patient’s overall assessment. Double antibiotic therapy prescribed to combat the infection, followed by prophylactic monotherapy, subject to kidney function values.
Wound Care: After surgical debridement, the wound was washed with diluted neutral soap, and rinsed with an antimicrobial solution (electrolysed acid solution). Haemoglobin spray was added first time at the second dressing change after rinsing. The wound was covered with sterile paraffin gauze to protect the granulation tissue. During the first two months the treatment was performed every three days, thereafter the application of the haemoglobin spray was performed every eight days while twice a week dressings were changed by her family at home.

Results: Complete wound closure of the more than 2 year old large lower leg wound could be achieved within 9 months. A planned amputation of the leg could be prevented.

Fig. 3: Wound at A & B) Wound before and after debridement, C) application of Granulox, D - G: Wound after 10, 45, 97, and 174 days; H: end of treatment (Day 279).
Case No. 8 & 13

64 years old male patient
Amputation prevented

Diagnosis: Wound on the palmar and dorsal surfaces of the right hand with amputation of the fifth finger subsequent to drainage, surgical debridement and amputation caused by an abscess resulting from a splinter injury.

Underlying Conditions: Five-year history of uncontrolled type 2 Diabetes Mellitus and untreated Peripheral Venous Insufficiency.

Patient Care: A comprehensive treatment protocol was applied, based on the result of the patient’s overall assessment. Double antibiotic therapy prescribed to combat the infection, followed by prophylactic monotherapy, subject to kidney function values.

Wound Care: Surgical debridement was performed at day one and again two days later to remove the remaining affected tissue from the wound. After debridement and/or cleansing, the wound was washed with diluted neutral soap, and rinsed with an antimicrobial rinsing solution. Haemoglobin spray was applied at the third dressing change (Day 3 of treatment). The wound was covered with sterile paraffin gauze to protect the granulation tissue, applying surgical dressings and a bandage without compression. The patient had daily dressing changes for the first three days, until the surgical debridement was completed and haemoglobin spray was applied for the first time. Next two weeks it was applied twice a week, then once per week.

Results: After 22 treatments and 21 applications of haemoglobin spray the wound was almost healed within 5 months.

Fig. 2: Wound at A & B: Start after amputation and debridement before haemoglobin spray application C & D: day 5 (second application of haemoglobin spray), E & F: Day 28; G & H: Day 135 (21 applications of haemoglobin spray);

50 years old female patient
Planned amputation prevented

Diagnosis: Diabetic foot. Necrotic wound located on the dorsal surface of the right foot (secondary to atopic dermatitis).

Underlying Conditions: Fifteen-year history of type 2 Diabetes Mellitus and systemic hypertension, obesity (metabolic syndrome), and untreated peripheral venous insufficiency.

Patient Care: A comprehensive treatment protocol was applied, based on the result of the patient’s assessment. Treatment of associated metabolic diseases (type 2 Diabetes Mellitus, Chronic Hypertension) was modified, treatment was added for Peripheral Venous Insufficiency and Obesity. Double antibiotic therapy prescribed to combat the infection, followed by prophylactic monotherapy, subject to kidney function values. Patient had to avoid walking as much as possible.

Wound Care: After surgical debridement, the wound was washed with diluted neutral soap, and rinsed with an antimicrobial rinsing solution (electrolysed acid solution). Haemoglobin spray was applied from the second dressing change after wound rinsing. The wound was covered with a sterile paraffin gauze to protect the granulation tissue and an adhesive protective dressing was applied.

Results: Healing is complete within 2 months and 27 days, after 16 wound treatments and 15 applications of the haemoglobin spray.

Fig. 4: Wound at A) Start of treatment after surgical debridement, B) second dressing change before application of haemoglobin spray, C) & D) tenth and eleventh dressing change (Day 47/ 54) E) Day 75 (fourteenth dressing change) and F) end of treatment;
Discussion

Haemoglobin spray is an effective adjunctive therapy option for acute and chronic wounds in patients with diabetes, based on:

- Excellent tolerability: In all cases, the haemoglobin spray was well tolerated and no adverse effects were reported.
- Effective facilitation of healing at all stages: Can be applied during all wound healing phases in combination with most of the wound rinsing solutions and dressings.
- Cost effective: Total costs for materials used per patients were €9.30 per dressing change (€7.50 median).
- Early implementation of the haemoglobin spray in ulceration in diabetics may help prevent development of chronic wounds and/or amputation.
- Further studies are desirable to further evidence the beneficial effect of the haemoglobin spray in wounds at risk to develop a wound healing disturbance.

Conclusion: Haemoglobin spray is an effective adjunctive therapy option for acute and chronic wounds in patients with diabetes to accelerate wound healing.