A multicentre evaluation of a new chitosan FH02™ spray-on dressing in patients with chronic wounds in the UK

Andrew Sharpe, Joy Tickle, Sylvie Hampton, David Gray
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Chronic wounds such as venous leg ulcers and diabetic foot ulcers are increasing in prevalence and impose a significant burden on patients and the NHS alike, particularly if complications related to delayed healing occur, such as infection, cellulitis or amputation. LQD™ wound spray is a new primary dressing that contains chitosan FH02™. A multicentre evaluation was carried out across four centres in the UK to determine the efficacy of LQD in promoting wound healing in patients with long-standing venous leg ulcers and diabetic foot ulcers (n=39). The evaluation found that LQD promoted wound healing in almost half of the wounds (n=18), and 15 wounds made significant progress towards healing as measured by reduced wound dimensions and an increase in the healthy wound tissue present. Two wounds remained unchanged. Patients and clinicians reported that the use of LQD had a positive impact on wound progress.

Keywords:
- Chronic wounds
- Venous leg ulcers
- Delayed healing
- Diabetic foot ulcers
- Chitosan FH02™ spray

Chronic wounds are a significant drain on NHS resources. A recent debate in the House of Lords highlighted the need to improve wound care strategy across the UK in order to respond to the growing number of patients with chronic wounds (Browning, 2018).

Guest et al (2015) studied the number of wounds within the UK population using a 1000 patient sub-sample of the THIN database. The cost of managing wounds in the UK each year was estimated to be in the region of £5.3 billion; the same as obesity, the cost of managing which is very well publicised and in the public eye. This is a significant sum and highlights the need to create a strategy for the improved management of wounds that aims to improve healing and reduce chronicity.

The study by Guest et al (2015) also revealed that in the UK annually, 730,000 leg ulcers and 169,000 diabetic foot ulcers are treated.

VENOUS LEG ULCERS

Venous leg ulcers develop as a result of underlying venous insufficiency. Risk factors for venous disease include a history of deep vein thrombosis, obesity, pregnancy and previous venous surgery (Anderson, 2008). In the early stages, inadequate or damaged valves in the lower limb results in a backflow of blood which pools in the veins resulting in increased venous blood pressure. Proteins, blood cells and fluid begin to leak into the tissues of the legs (Timmons and Bianchi, 2008). The colouration of the skin changes as red blood cells burst and stain the surrounding skin with pigment known as haemosiderin (Anderson, 2008). With time, the limb becomes oedematous, the skin condition changes and becomes more easily damaged (Timmons and Bianchi, 2008).

Left untreated venous disease can progress to the point where it affects patient mobility and if the skin is damaged, the patient is likely to develop a leg ulcer (Vowden and Vowden, 2012). The underlying venous insufficiency has to be corrected in order to facilitate healing. Therefore the main focus of leg ulcer management is compression therapy which helps to improve venous return, reduces oedema and improves wound healing (Anderson, 2008).

In addition, local wound management should focus upon removing any local barriers to wound healing, such as devitalised and sloughy tissue and high wound bioburden and managing symptoms such as exudate, odour and pain.

DIABETIC FOOT ULCERATION

Diabetic foot ulcers also arise as a consequence of underlying systemic disease. The two key contributing factors are neuropathy and peripheral vascular disease, with other contributing factors including infection, mechanical stress, and chemical, traumatic and thermal injury that can lead to further complications (Renwick et al, 2016).

Damage to the nerves supplying the foot occurs over time in people with diabetes and is related to thrombus formation in the small vessels that supply the nerves, as well as poor glycaemic control (Ang et al, 2014).
As the nerve damage progresses the foot becomes insensate, which can lead to tissue damage as a result of mechanical trauma, e.g. tight-fitting shoes. The patient may not be aware of the tissue damage occurring until significant ulceration is present.

The impact of neuropathy on the muscles within the foot is also pronounced. Clawing deformity, a change in gait and development of callous over high-load bearing areas can develop. In some cases the change in foot shape is severe, with patients developing Charcot deformity (Jeffcoate, 2014).

In patients with diabetes, vascular disease can be present in both the macro-vessels in the leg and the micro-vessels in the foot. Problems can range in severity from chronic ischaemia where the long-term impacts include skin thinning, to dominant critical ischaemia where immediate re-perfusion is necessary (Renwick et al, 2016). Delayed healing in the diabetic foot can be caused by wound infection, macro-vessel and micro-vessel disease resulting in a reduction in oxygenation and nutrient supply, continued trauma and the continued effects of hyperglycaemia (Jeffcoate, 2014).

Treatment of patients with diabetic foot disease includes tight control of blood glucose concentration, off loading, wound bed preparation, and prevention and management of infection. As with venous leg ulcers, diabetic foot ulcers can often be slow to heal because of the underlying pathology and the presence of local barriers to wound healing. Wound care is often about managing the presenting symptoms of the wound, however, this can result in long-term wounds remaining stuck in the inflammatory phase of healing (Schultz et al, 2004).

In order to facilitate healing in any patients with long-standing chronic wounds, it is important to challenge the local wound conditions; regular debridement should be performed and wound care products used that can help to stimulate healing in the wound bed.

With chronicity, both of these patient groups are at risk of costly complications such as wound infection and cellulitis. Wound infection can have a negative impact on the healing process and also on the patient’s quality of life, with increased pain and increased exudate volume (Cutting and Harding, 2004). Cellulitis can result in costly hospital stays; in 2013–14 there were 104,598 cases of cellulitis treated in secondary care with a mean bed stay of 6.2 days (Lee and Levell, 2016).

For patients with diabetic foot ulcers, the risk of amputation is ever present. A report by NHS Diabetics (NHS Digital, 2016) showed that around 10 per cent of people with diabetes will have a diabetic foot ulcer at some point in their lives, at an estimated cost of £650 million to the NHS; equivalent to £1 in every £150 spent (NICE, 2012). Diabetic foot ulcers precede more than 80% of amputations (NICE, 2015).

Technology that can expedite the wound healing process should be embraced in these patient groups, particularly to avoid the costly complications of delayed healing.

**LQD® AND THE ROLE OF CHITOSAN IN WOUND HEALING**

LQD® wound spray is a new spray-on primary dressing that is indicated for the external, local treatment of chronic wounds (such as leg ulcers and diabetic foot ulcers), secondary wound healing disorders, acute wounds and epidermal and superficial partial thickness burns.

LQD’s main component is chitosan-FH02™, contained in an aqueous solution with a skin-neutral pH.

Chitosan is derived from a naturally occurring biopolymer, chitin. It’s positive charge is known to give chitosan its antimicrobial properties and beneficial effects on every stage of wound healing (Dai et al, 2011). Studies have shown that chitosan is a natural haemostat, and that it accelerates the wound healing process by helping to control growth factors within the wound (Foda et al, 2007; Lee et al, 2009).

Chitosan also stimulates the immune response by encouraging the migration of essential leukocytes and macrophages to the wound site (Lee et al, 2009). Chitosan has been shown to assist in the granulation and epithelializing stages of wound healing by stabilising fibroblasts and promoting keratinocyte proliferation. Furthermore, chitosan also assists in the laying down of collagen, helps with wound tensile strength and also influences scarring through interaction with TGF-β.

The unique chitosan FH02 in LQD is engineered to undergo a high degree of n-deacetylation; a process that enhances the positive charge and therefore the beneficial effects of chitosan.

**Figure 1.**
*Final wound outcome results for all patients (n=35).*
LQD wound dressing is simply sprayed onto the wound bed following cleaning, and after a two-minute drying period, the spray forms a thin, elastic, transparent film, that physically protects the wound from the environment. The dressing is removed as part of standard wound cleaning or remains on the wound until removal during natural skin renewal. If considered clinically necessary, LQD can be covered with a secondary dressing.

The spray formulation may mean the product is particularly beneficial in dressing suitable wounds that are in difficult anatomical locations that are problematic to dress with traditional dressings.

**EVALUATION**

The aim of the multi-centre evaluation was to examine the effect of LQD wound spray on promoting healing in chronic venous leg ulcers and diabetic foot ulcers. The product was evaluated in four differing clinical locations in the UK.

**METHODS**

Inclusion criteria for the evaluation included people with venous leg or diabetic foot ulceration that was static or slow to heal despite best practice. The wounds were not displaying any clinical signs or symptoms of wound infection or the presence of biofilm, such as increased exudate volume, wound stasis or deterioration in the quality of granulation tissue within the wound bed (Wolcott et al, 2017), that could have been a cause of delayed healing. In all cases, the use of LQD wound spray was added to the existing treatment regimen.

Efficacy was determined by the collection of data relating to a pre-determined set of wound parameters using the same evaluation form across the centres. Clinician and patient opinion of LQD wound spray was also recorded.

The following parameters were assessed by the clinicians at baseline, and at each dressing change.

- Duration of the wound
- Size/area of the wound
- Previous dressing regimen
- Tissue types within the wound
- Condition of the peri-wound skin.

Patients and clinicians were also asked for their opinions on the use of LQD spray with a series of open-ended questions:

1. Please state if the patient felt the use of LQD had a positive effect on his/her wound in terms of healing
2. Please state if you felt the use of LQD had a positive effect on the patients wound in terms of healing
3. Please state if you would use LQD on your patients in the future?
4. Please state if you would recommend LQD to other clinicians.

All patients gave written informed consent to be included in the evaluation.

**RESULTS**

Thirty-nine patients were recruited to the evaluation (venous leg ulcer, n=28; diabetic foot ulcer, n=11). One patient was withdrawn following a wound diagnosis of pyoderma gangrenosum.

**Wound parameters**

The total wound outcomes are presented in Figure 1. Duration of the wounds included in the evaluation ranged from 21–1071 days. The average duration of patients with diabetic foot ulcers before the study was 239 days.

Of the venous leg ulcer patients included in the evaluation (n=27), 48% healed completely (n=13); 11 patients showed a 75% area reduction and an increase in the percentage of healthy tissue (granulation and epithelial tissue) present in the wound bed. Three patients were lost to final follow-up.

**CASE STUDY 1**

This 72-year-old female presented with a history of venous disease and diverticulitis. Her ulcer had been present for 3 months before participating in the LQD® evaluation. Treatment on presentation was a hydrofibre dressing, superabsorbent and Actico 2c compression.

At the beginning of the evaluation the wound area was 48cm². The wound was covered in sloughy tissue and with moderate levels of exudate. The wound did not have signs of infection, however, there was a possibility of biofilm in the wound bed (Figure 1).

Following application of LQD spray, the clinician stopped using the secondary dressings (hydrofibre and superabsorbent). Actico short-stretch bandage was continued. The image taken on the 4th July following 2 weeks of treatment with LQD shows a significant reduction in the wound size with a corresponding increase in granulation tissue (Figure 2).

At final review (Figure 3) taken on the 11th August (7 weeks into treatment) the wound bed was almost completely covered with 80% epithelial tissue and 20% granulation tissue.

In this case when LQD was used, the clinician was able to step-down the use of two dressings. This would reduce the cost of treatment by approximately £5.00 at each dressing change. Over a period of 7 weeks this would equate to a saving of £84.00 in dressings costs alone.
In the diabetic foot ulcer group (n=11), five patients healed and four made progress towards healing. One patient who had a diabetic foot ulcer for 375 days before treatment with LQD® wound spray achieved 90% healing within 7 weeks of LQD being added to the treatment regimen. The peri-wound skin was dry and fragile with some signs of maceration. Lower limb oedema was also present (Figure 1).

Two patients with diabetic foot ulcers had wounds which were considered to be unchanged in the evaluation; one patient had an ulcer for 2 years 11 months before inclusion and presented with kidney failure which may have contributed to the lack of progress. The other patient had an ulcer for more than two years, and had a history of peripheral vascular disease. In both cases, the evaluating clinician commented that they had not expected much progress owing to the complex co-morbidities of these patients.

During the evaluation, none of the patients showed or reported any clinical signs or symptoms of infection or biofilm formation.

**Clinician/patient opinion**
The following quotes were recorded in response to question 1 (Please state if the patient felt the use of LQD had a positive effect on his/her wound in terms of healing):

‘Definitely yes’

‘I felt the wound spray definitely helped my wound to heal’

‘Fantastic’.

The following quotes were recorded in response to question 2 (Please state if you felt the use of LQD had a positive effect on the patients wound in terms of healing):

‘The patient was able to be self caring and apply the dressing on their own after instruction’

**Table 1: Results of evaluation**

<table>
<thead>
<tr>
<th>Wound type</th>
<th>No of wounds healed</th>
<th>No of wounds reduced in size and tissue type improved</th>
<th>No of wounds unchanged</th>
<th>No of wounds with signs of infection/biofilm</th>
</tr>
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<tbody>
<tr>
<td>Venous leg ulcer (n=27)</td>
<td>13</td>
<td>11*</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Diabetic foot ulcer (n=11)</td>
<td>5</td>
<td>4</td>
<td>2</td>
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</tr>
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</table>

*Three VLUs were lost to final follow-up
CASE STUDY 3

A 70-year-old male with a history of diabetes and peripheral vascular disease presented with a small troublesome ulcer of 850 days’ duration. The wound was sloughy on presentation, with some callous present and haemosiderin staining of the surrounding skin (Figure 1). Following application of LQD®, a secondary foam dressing was used. At the end of the evaluation, the wound was 100% granulating and was almost healed and the condition of the surrounding skin had improved (Figure 2).

“The LQD spray definitely improved granulation and epithelialisation within the wound”.

In response to questions 3 and 4, the evaluating clinicians reported that they would use LQD on patients in the future, and would recommend LQD to other clinicians.

COST SAVINGS

In order to determine any cost savings resulting from the use of LQD wound spray, cost comparisons with the treatments used before the evaluation were made with the costs of adding LQD to the treatment regimen for the duration of the evaluation, in both patient groups.

The total cost for the treatment of the group of patients with diabetic foot ulcers up to the point of starting the evaluation was £4835.58 (Table 2). The cost until healing occurred for the group once LQD was introduced to treatment was £1063.83; a saving of £3771.75 (consisting of dressing cost savings and clinician time). The average treatment time saved was 117 days. If we analyse the duration of the ulcers before LQD treatment, the average was 154 days and the average healing time was 37 days.

In the venous leg ulcer group, the cost of care for patients before joining the evaluation was £2488.34. The cost to healing was £996.15 (Table 3). This resulted in an overall saving of £1492.19 during the period of the evaluation. Compression bandaging regimen used before evaluation was continued throughout the LQD treatment phase, however, the clinicians were able to ‘step-down’ the dressings previously used in two of the patients, resulting in a saving per treatment.

The duration of the leg ulcers before application of LQD was 377 days (range = 44–80 days; mean = 94.25 days). The total healing time in days for all four patients in this group was 154 days (range= 14–77 days; mean healing time = 38.5 days).

This resulted in a cost saving and more importantly improved quality of the life for the patients, particularly the time spent in bandaging.

Once healed patients with venous leg ulcers can be placed into compression hosiery which helps improve mobility, self esteem and ability to self-care. It also helps to prevent leg ulcer recurrence (Wounds UK, 2016).

DISCUSSION

The cost of chronic wounds in the UK continues to grow as the number of patients with wounds increases year on year (Guest et al, 2015). The patients in this evaluation appear to be typical in that many of them have had chronic wounds for long periods despite best treatment.

The cost of an unhealed leg ulcer is estimated to be around £13500 per patient per year compared with the cost of a healed ulcer which on average is £2300 (Guest et al, 2017). This is significant given that a large number of leg ulcer patients remain unhealed after one year. In this small evaluation, the overall trend in patients with venous leg ulceration and diabetic foot ulceration was that healing was achieved in almost 50% of patients and that those who did not heal completely were showing significant improvement (>75% healing) following the addition of LQD wound spray to the treatment regimen.

In all patients with chronic wounds it is essential to question and change existing therapy at regular intervals in order to trigger the healing process if it appears stalled. Prevention of infection, in both the diabetic foot patients and venous leg ulcer patients is a key priority since infection is a significant cause of morbidity. This is particularly the case in patients with diabetic foot ulceration. Here, infection can quickly lead to amputation if appropriate treatment is not sought. Patients with diabetic foot ulceration leading to amputation have a 5-year survival rate of only 50% (Jeffcoate, 2014).

The role of chitosan in wound healing is well documented (Dai et al, 2011) and it would appear that its properties as a natural haemostat, antimicrobial, and stimulator of wound healing helped contribute to the progress of the patients in this evaluation. Although the numbers are too small to conclude that improvements in wound condition were purely a result of applying LQD, it is likely that the chitosan FH02 component of LQD wound spray stimulated the wound healing process.

CONCLUSION

The growing number of patients with chronic wounds in the UK is of major concern to the NHS. With budgets...
already stretched, there is a need to improve outcomes in order to help reduce the costs of management. Improving patient outcomes involves a more structured approach to assessing and managing wounds that use appropriate pathways of care and informed clinical decision making. In addition, innovation and new products that can bring solutions for wounds that are challenging needs to be embraced.

This evaluation of LQD spray primary dressing has demonstrated how the natural anti-microbial action and ability to stimulate wound healing of chitosan FH02 can benefit patients with chronic wounds. The results have demonstrated how LQD can be simply used as part of best practice in a cost-effective manner to effectively promote wound progress in patients at risk of complications caused by delayed healing.

**REFERENCES**


Dai T, Tanaka M Huang YY and Hamblin MR

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**Table 2. Diabetic foot ulcers**

<table>
<thead>
<tr>
<th>Dressing regimen</th>
<th>Treatment duration</th>
<th>Weekly cost of dressing(s)</th>
<th>Weekly clinical cost</th>
<th>Total weekly cost</th>
<th>LQD cost (weekly)</th>
<th>Other dressings used</th>
<th>Weekly dressing costs (excluding LQD)</th>
<th>Weekly clinical cost</th>
<th>Total weekly cost</th>
<th>Dressing cost saving per week with LQD</th>
<th>Time to healing with LQD</th>
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| LQD cost (weekly) | £148.05           | £815.31                     | £773.64              | £298.57          | £483.58          | £1063.83         |

<table>
<thead>
<tr>
<th>Dressing regimen</th>
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<th>Time to healing with LQD</th>
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<td>44 days</td>
<td>£10.06</td>
<td>£36.50</td>
<td>£46.56</td>
<td>£1.50</td>
<td>K2</td>
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| LQD cost (weekly) | £175.40           | £175.40                     | £175.40              | £175.40          | £2488.34         | £596.15          |

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*Clinician time based on Virgin Care podiatry cost of £45.00*

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**Table 3. Venous leg ulcers**

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<th>Dressing regimen</th>
<th>Treatment duration</th>
<th>Weekly cost of dressing(s)</th>
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| LQD cost (weekly) | £175.40           | £175.40                     | £175.40              | £175.40          | £2488.34         | £596.15          |

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*Clinician time based on district nurse visit lasting 30 minutes*


