Management of Diabetic Skin Wounds with a Natural Latex Biomembrane
Management of Diabetic Skin Wounds with a Natural Latex Biomembrane

Marco Andrey Cipriani Fradea,c, Igor Brum Cursia, Felipe Fortes Andradea, Joaquim Coutinho Nettob, Fábio Magalhães Barbettaa, Norma Tiraboschi Fossb

aServiço de Dermatologia. Hospital Universitário. Faculdade de Medicina. Universidade Federal de Juiz de Fora; bDepartamento de Bioquímica e Divisão de Dermatologia. Departamento de Clínica Médica. Faculdade de Medicina de Ribeirão Preto. USP. Brasil.

Correspondencia:
Marco Andrey Cipriani Frade
Av. Bandeirantes 3900. Monte Alegre
CP. 14049900 Ribeirão Preto. São Paulo. Brasil
Tel.: (+55) 16 602 2447 - Fax: (+55) 16 633 0236
e-mail: mandrey@fmrp.usp.br

Summary
The natural latex biomembrane (NLB) is an alternative dressing used to treat skin wounds, with activities that increase the healing process. The authors report the results obtained with the NLB dressing for chronic skin wounds of different etiologies with impaired healing affecting four diabetic patients. The NLB was found to act as an economic, easily handled and highly effective dressing, mainly because of its debriding potential and its angiogenicity, permitting a dynamic and fast healing process essential for wound healing in diabetic patients.

Key words: wound, healing, dressing, latex, diabetes mellitus.

A natural latex biomembrane (NLB) consisting of a polymer extracted from the natural latex of *Hevea brasiliensis* was developed in a project carried out at the Department of Biochemistry of the Faculty of Medicine of Ribeirão Preto, USP[1]. After its development, several reports were published about its applicability, especially for the management of leg ulcers because of its angiogenic and healing properties[2-3].

Diabetes mellitus is characterized by a clinical syndrome of chronic and degenerative evolution caused by a disorder of insulin secretion and/or action on the organism which produces a set of metabolic alterations mainly characterized by hyperglycemia[4].

Type 1 diabetes mellitus (DM) usually is an autoimmune disorder involving the production of autoantibodies against Langerhans islet β cells, with a consequent reduction in insulin[5]. Type 2 diabetes develops during chronic hyperglycemia predominantly generated by resistance of target cells (muscle, adipose and hepatic cells) to the action of circulating insulin, and may be associated with quantitatively and qualitatively deficient insulin secretion for the control of normal blood glucose levels[6].

Both types of diabetes have a chronic course involving degenerative disorders that affect the cardiovascular and nervous systems, as well as the eyes and the skin. The main pathological factor is caused by macro- and microangiopathy, although in certain tissues the pathogenesis is due to a direct effect of metabolic malfunction. Wound healing is significantly slower in affected patients[7].

We report four cases of leg ulcers in diabetic patients associated with healing difficulties, which benefited from the use of the NLB from the *Hevea brasiliensis* rubber tree.
Figure 1. Case 1: A) Initial clinical aspect of a leg ulcer. B) Clinical aspect of the same leg ulcer after 20 days. C) Clinical aspect of the leg ulcer showing a local lidocaine reaction. D) Clinical aspect of the leg ulcer after the 2nd month of biomembrane use. E) Clinical aspect of the almost totally reepithelized leg ulcer after 4 months of follow-up. F) Initial clinical aspect of the proximal stump (F1) and re-epithelization after 2 months of follow-up (F2).
Clinical cases

Four non-compensated patients with type II diabetes (mean glycosylated hemoglobin of 8.75 mg/dL) were selected at the Leg Ulcer outpatient clinic of HU-UJF and at the Neurovascular Ulcer outpatient clinic of HC-FMRP-USP after the consent term signature. The characteristics of the patients are listed in Table 1 and their ulcerated lesions are described individually. Dressings were applied on alternate days and consisted of cleaning the ulcers with 0.9% physiological saline, drying and application of the NLB to the entire bottom of the ulcer, avoiding contact with healthy skin, plus a secondary cover consisting of gauze and bandages.

Table 1. Clinical characteristics of diabetic patients with leg ulcers treated with the NLB.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Glycosylated Hemoglobin (mg/dL)</th>
<th>Time (years)</th>
<th>Associated diseases</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>54</td>
<td>F</td>
<td>8.9</td>
<td>10</td>
<td>SAH</td>
<td>OAD</td>
</tr>
<tr>
<td>2</td>
<td>53</td>
<td>M</td>
<td>9.3</td>
<td>9</td>
<td>-</td>
<td>OAD</td>
</tr>
<tr>
<td>3</td>
<td>49</td>
<td>F</td>
<td>9.5</td>
<td>10</td>
<td>SAH</td>
<td>OAD</td>
</tr>
<tr>
<td>4</td>
<td>75</td>
<td>F</td>
<td>7.3</td>
<td>15</td>
<td>SAH, CVI</td>
<td>OAD</td>
</tr>
<tr>
<td>Means</td>
<td>58</td>
<td></td>
<td>8.75</td>
<td>11</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

OAD: Oral antidiabetic drugs; SAH: systemic arterial hypertension; CVI: chronic venous insufficiency.

**Case 1**

A female patient with a painful, necrotic hypertension ulcer measuring 11 × 5 cm present in the posterior region of the left leg for 8 months (Figure 1A), associated with an ulcerated-crusty lesion of the proximal stump of the left hallux, amputated 3 months before (Figure 1F). The leg ulcer presented difficulties in distal healing due to the inadequate use of xylocaine gel by the patient in this region (Figure 1C). The gel was discontinued and reepithelization occurred within 4 months with the use of the NLB (Figure 1D). Regarding the stump, destruction of the crust and healing of the wound occurred within two months of follow-up (Figure 1E). During treatment, the patient showed lack of diabetes control (glycosylated Hb: 8.9 mg/dL) and the presence of systemic arterial hypertension (AP: 160/105 mmHg) even with the use of oral antidiabetic and antihypertensive drugs.

**Case 2**

A male patient with an ulcerated lesion in the dorsal region of the right foot caused by a chemical burn of 6 months duration measuring 4.2 x 2.0 cm caused by a car battery solution and not responding to standard treatment. The NLB provided full healing of the ulcer within 30 days, regardless of the lack of metabolic control of the patient (glycosylated Hb: 9.3 mg/dL) even with the use of oral antidiabetic drugs (Figure 2).

**Case 3**

A female patient with a painful, necrotic hypertensive leg ulcer of 6 months duration on the region of the heel tendon of the left leg, causing limitation of walking (Figure 3A). The NLB produced debridement of the lesion after the 3rd dressing (Figure 3B), reduction of pain and granulation of the entire surface within the 1st month (Figure 3C), as well as full healing during the 2nd month of follow-up (Figure 3D). The patient presented resistance to oral antidiabetic drugs (glycosylated Hb: 9.5 mg/dL) as well as lack of control of systemic arterial hypertension (AP: 170/110 mmHg) and was taking nifedipine (40 mg/day), methyldopa (1.5 g/day) and furosemide (40 mg/day).
Case 4
A female patient with a history of basal cell carcinoma in the anterior region of the right leg 3 years before (Figure 4A), had been submitted to surgery which resulted in a surgical ulcer measuring 10 x 10 cm (Figure 4B). The NLB promoted signs of granulation after the fourth dressing (Figure 4C), with rapid filling of the ulcer, which reached the epidermal level within the second month (Figure 4D). After the 4th month, the lesion presented modifications in the granulation tissue, with 1 cm of reepithelialized tissue in the margins (Figure 4E) and the patient was submitted to a skin graft (Figure 4F). The patient had uncontrolled diabetes (glycosylated Hb: 7.8 mg/dL) even with the use of an oral antidiabetic drug, whereas her systemic arterial pressure was normal with the use of methyldopa (1 g/day) and propranolol (80 mg/day).

Comment
The patients reported here had ulcerated lesions of more than six months duration that did not respond to standard therapies and that were associated with other diseases in addition to decompensated type II diabetes mellitus, such as chronic venous insufficiency and systemic arterial hypertension, and/or complications (micro- and macroangiopathy), as well as healing difficulties such as extensive ulcers or ulcers located above areas of muscular tension. Chronic ulcers affecting the lower limbs have an impact on the quality of life of the patients, with serious physical, social, psychological and financial implications, consequently impairing the control of both diabetes mellitus and of associated diseases such as systemic arterial hypertension, with a delay in the ulcer healing process.

Hyperglycemia and insulin resistance are directly involved in the chronic complications of diabetic patients both due to the difficulty in glucose utilization by the keratinocytes and to the alterations in keratinocyte growth and differentiation in vitro. It has been demonstrated that the healing of ulcers involving the dermis and epidermis of diabetic animals is slow until the introduction of insulin. Exogenous growth factors such as fibroblast growth factor (FGF) and transforming growth factor (TGF beta) have been used to treat ulcers of difficult healing in diabetic animals in order to accelerate the processes of granulation and

Figure 3. Case 3: A) Initial clinical aspect of a leg ulcer. B) Clinical aspect of the same leg ulcer after 1 week. C) Clinical aspect of the leg ulcer after 1 month. D) Clinical aspect of the leg ulcer after 2 months.
The application of platelet-derived growth factor (PDGF) has proved to be effective in the process of ulcer granulation and reepithelization in diabetic patients[10-11]. It has also been reported that diabetic patients present a reduction in cytokines and growth factors, which are important elements in the healing process, with a consequent delay in the normal granulation and healing of wounds[13].

The NLB presented a significant debriding activity by stimulating marked exudation, a fact that results in a less traumatic and painful dressing that can be easily applied at home. In parallel, the NLB behaved as a powerful stimulator of angiogenesis, significantly accelerating ulcer healing[2-3]. The real mechanism of action of the NLB is still unknown. Although its use is still limited to studies on the standardization of its indication as a therapeutic option, it has been observed that this is a low cost, effective and easy to handle product that does not pose risks of transmission of infectious agents. These effects of the NLB have been reported in studies on non-diabetic patients, with emphasis on the angiogenic effect as the main action[1-3, 14, 15], which is essential for ulcer healing, especially in diabetic patients.

**Conclusion**

The present results suggest that the natural latex biomembrane can be of help in different phases of the healing process of chronic ulcers such as removal of necrotic tissue (debridement), proliferation of granulation tissue (angiogenesis) and reepithelization even in diabetic patients with complications such as diabetic microangiopathy and arterial hypertension, and also in cases of surgical difficulties.
References


