CASE REPORT

I|J|A|M|B https://doi.org/10.52466/ijamb.v4i2.100

INTERNATIONAL JOURNAL OF ADVANCES IN MEDICAL BIOTECHNOLOGY

Bacterial cellulose/calcium alginate hydrogels in wound's cicatricial process of diabetic foot implementation: case report

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Abstract: It is well known that Diabetes mellitus (DM) is classified as a metabolic disease and in consequence several dysfunctions are expected, such as difficulties in wound healing process. Objectives: Due to the excellent properties of the developed bacterial cellulose/alginate hydrogel (BC/ALG), this material was applied to treat a diabetic ulcer patient. Method: The treatment was carried out at the Ambulatory of Santa Casa de Misericordia de São Carlos, by applying the hydrogel twice a week during 30 days. Results: After the period of treatment, the wound showed 84% of closure reduction when compared to its initial size Conclusion: Bacterial cellulose/ alginate hydrogel presented a high potential for successful treatment of wound closure.

Keywords: Wound Healing. Wounds and Injuries. Hydrogels

Introduction

Diabetes mellitus (DM) is characterized by a metabolic disease and due to the absence or inability of insulin to perform its function, several complications may occur including a rise in glycemic levels and with the evolution of the disease, other organ dysfunctions and permanent damage [1]. According to Brazilian Diabetes Society, there are approximately 13 million people living with DM, representing 6.9% of Brazilian population[2]. It is believed that in 2040 DM can affect up to 640 million adults aged 20 –79 years worldwide[3].

Large concentrations of glucose in bloodstream can result in several metabolic complications, such as diabetic acidosis and non–ketotic hyperosmolar hyperglycemic syndrome, peripheral microangiopathy vascular disease, chronic cardiovascular disease (coronary, neurological, peripheral, renal, and retinal arterial disease) [4].

It is important to emphasize that one of the most common chronic complications caused by DM is the diabetic foot syndrome, which can be characterized by the presence of ulcers and infections, peripheral neuropathy, reduced physical mobility and in some extreme cases, the surgical limb amputation is required, which corresponds to 40 to 60% of non–traumatic amputations[5]. Despite being extremely refutable, the rate of amputations has been considered as a quality care indicator of diabetic foot complications [6].

However, Moretti et al. 2009[7] pointed out that in addition to foot ulcers leading to amputations and being considered the main causes of patient's disabilities, these factors can not be recorded as positive in relation to treatments.

According to Lima and Araujo, 2013[8] several mechanisms are identified as delay factors in healing process of diabetic patients, such as the excessive production of Reactive Oxygen Species (ROS), decreased Nitric Oxide (NO) and decreased Growth Factors (GFs) and proteins response in insulin signaling pathway. On the other hand, an ischemic microenvironment, associated with limited NO bioavailability and/or NO inactivation by ROS, leads to endothelial dysfunction characterized by the difficulty of arteries and arterioles regarding their functions in the regulation of vascular tone and adequate blood circulation. However, the presence of ROS in diabetic patients is usually the main cause that influences against to wound healing process.

In this context, Vieira et al 2017[9], emphasize the importance of new wound coverings and technologies in wound healing success. A clear and current overview of current evidence is required to facilitate decision-making regarding dressing use. Oliveira et al, 2020[10] highlighted that with the advancement of science and biotechnology the options of dressings available on the market exceeds 3000 types. In terms of composition, the most common devices are based in polymeric foam with or without silver, hydrocolloids, silver activated carbon, silver mesh, therapies based on growth factors, external tissue expanders, negative

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Received 19 February 2021; Accepted 10 April 2021; Available online 25 May 2021.
DOI: https://doi.org/ 10.52466/ijamb.v4i2.100

pressure and natural and synthetic biopolymers[10-11].

Despite of the available dressings diversity, new ones composed by natural biopolymers such as bacterial cellulose (BC) are welcome. Thus, BC obtained from Gram-negative bacteria fermentation in association with sodium alginate extracted from seaweed presented excellent properties such as less toxicity, biocompatibility and great wound healing progress when applied [12-13]. This fact could may be attributed to BC nanometer-sized fibers that mimic collagen which improves healing process resulting in reduced pain [14]. In addition, calcium alginate influences wound hemostasis by calcium ions release as the gel perform as a matrix for aggregating platelets and erythrocytes[15].

Recently Sulaeva et. al., 2020 applied BC/ Alginate membranes in wound treatment. the results showed that membranes expressed greater water retention capacity (up to 70 to 90%), kept the wound moist providing a better healing process. However, membrane dresses own some complication and disadvantages in handling during the exchange, which can cause discomfort to the patient. According to above mentioned properties, hydrogels based dressings represents the first choice and an ideal treatment of acute, chronic and diabetic wounds, minimizing infections with the bonus of easier removal [11].

Therefore, due to the excellent characteristics presented, this paper will report the use of BC/ALG hydrogel in a challenge wound closure treatment of a diabetic patient.

Methods

- **Case Report**

The Patient is a man, 63 years old, diabetic and hypertensive. His medical report revealed continuous use of specific medication supervised by frequent medical follow-up. It was also reported toe amputation in September 2019 and the presence of a diabetic ulcer in February 2020.

- **Study location**

The treatment was carried out at the Photodynamic Therapy unit of Santa Casa de Misericordia, São Carlos (Brazil).

- **Treatment**

The performed treatment protocol included asepsis of the lesion with 0.9% saline, followed by mechanical debridement by using a scalpel blade, when necessary. Thus, the wound was covered with the BC/ALG hydrogel (patent n ° BR 10 2019 021848 7), occluded with sterile gauze and bandage. This procedure was repeated twice a week, for 30 days. However, the mechanical debridement step was performed just when necessary.

Results

As mentioned before, healing process is highly complex, especially when related to a diabetic health condition, which requires special care both regarded to glycemic control, nutrition and rest, as well as direct care related to the extension of the injury. At this point, is important to consider all options available to choose the most appropriate dress that will provide better clinical performance in relation to tissue repair.

All measurements were obtained by using ImageJ software at 0, 7, 21 and 30 days, according to the pre-established time of study and converted to cm2 as shown in table 1. Each data result was carried out in triplicate and the media was calculated to each period of study. It was possible to observe a remarkable reduction of 84% of the wound area in just 30 days of treatment, when compared to the initial diameter size.

Table 1 – Data results of wound area size, measured at 0, 7, 21 and 30 days of treatment, expressed in cm^2.

Period of study	Wound size
0	2.344cm^2
7° day	2.332cm^2
21° day	0.830cm^2
30° day	0.377cm^2

Discussions

Figure 1 A shows the wound before treatment which is possible to observe hyperkeratosis at the edges of the lesion, some granulation tissue presented in wound bed, with 2,344 cm^2 of surface area. In 7th day of treatment, the wound appeared cleaner, without devitalized tissue presenting a slightly area reduction to 2,332 cm^2 (Figure 1B). Figure 1C presented the results of the 21th day of treatment, which was possible to observe a considerable wound closure that indicates that the hydrogel may be contributing to accelerate the healing process. Finally, at the and 30th day of treatment, the measurements of the wound area showed a significant reduction to 0.377cm2 (Figure 1 D).

Figure 1 – Clinical evolution of the healing process using the BC/ALG hydrogel as treatment. A) Initial; B) 7 days of treatment; C) 21 days of treatment and D) 30 days of treatment.

Some characteristics are usually involved in complex wounds, such as ischemia, necrotic tissue, excessive collagen accumulation, reduction of angiogenic factors, delay in inflammatory response which negatively influences the healing process. According to the images, clinical success in closure is an important data that indicates tissue repair. Therefore, the treatment performed with bacterial cellulose containing calcium alginate hydrogel may be a promising alternative for the treatment of complex wounds, since there was an acceleration in healing process and tissue repair of the treated diabetic wound.

Contribution to practice

It is possible to notice that the chosen treatment by using a BC/ALG hydrogel clearly promoted the closure in a challenge wound of a diabetic patient, improving the comfort and reducing the pain and injury exposure. All these factors acted into less wound contamination which probably influenced a faster wound closure. In addition, it is worth mentioning that there is no data related to this specific hydrogel used because it was recently patented by Seven Produtos Biotecnologicos – Ltda company which aims to commercialize it as soon as possible.

Conclusions

The results showed that it was possible to observe a considerable reduction of 84% in average when compared to initial wound size. This achievement may be attributed to the excellent biological properties of the applied hydrogel which highly improved the wound healing process. Despite more complementary histological data are needed to observe cellular tissue repair, it is possible to conclude that BC/ALG hydrogel configured a great option in terms of treatment of challenge diabetic wounds.

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