IJAMB
INTERNATIONAL JOURNAL OF ADVANCES IN MEDICAL BIOTECHNOLOGY

Bacterial cellulose hydrogel and calcium alginate in the cicatricial wound process from diabetic foot implementation

Gabriela A. da Silva[1]; Elissandra M. Zanchin[2]; Andressa M. da Silva[2]; Hernane da S. Barud[3]; Matheus Bertanha[4]; Antonio E. A. Junior[5]; Fernanda M. Carbinatto[6].

*Corresponding author: E-mail address: hernane.barud@gmail.com

Abstract: Objectives: Due to the excellent properties of alginate-containing bacterial cellulose hydrogel, the objective was to treat a wound that is difficult to heal in a diabetic patient. Method: The treatment was carried out at the Santa Casa de Misericordia de São Carlos Ambulatory for 30 days, with the application of bacterial cellulose hydrogel containing alginate twice a week Results: After 30 days of treatment, the wound showed an 84% reduction in its initial size Conclusion: Bacterial cellulose hydrogel containing alginate has high potential for the treatment of wounds.

Keywords: Wound Healing. Wounds and Injuries. Hydrogels.

Introduction

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

Large concentrations of glucose in the 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].

Among the chronic complications caused by DM is diabetic foot syndrome, which can involve ulcers and infections, peripheral neuropathy, decreasing physical mobility, and in some cases even surgical amputation of the affected limb, which correspond to 40 to 60% of non-traumatic amputations[5]. Despite being refutable, the rate of amputations has been considered as an indicator of the quality of care for diabetic foot complications[6].

However, Moretti and collaborators 2009 (7) point out that in addition to foot ulcers leading to amputations and being the main causes of disability for patients, they do not present a positive result in relation to treatments.

According to Lima and Araujo, 2013[8] several mechanisms are pointed out as important factors to the slowness of the healing process of the diabetic patient among them the excessive production of Reactive Oxygen Species (ROS), decrease in Nitric Oxide (NO) and in the decrease of response to Growth Factors (GFs), and proteins in the insulin signaling pathway. Endothelial dysfunction, characterized the difficulty of arteries and arterioles in exercising their functions in the regulation of vascular tone, having an appropriate stimulus, leads to an ischemic microenvironment, associated with the limitation of NO bioavailability, and decreased production by the endothelium or increased inactivation of NO by ROS. However, as the production of ROS in diabetic patients is a primary cause that favors the wound healing deficiency.

In this context, Vieira et al 2017[9], emphasize the importance of new wound coverings and technologies for the effective result and wound healing. Oliveira et al, 2020 [10] highlights that with the advancement of biotechnology the number of dressings available on the market exceeds 3000. The most commonly wound coverings used are, polymeric foam with or without silver, hydrocolloids, silver activated carbon, silver mesh, therapies based on growth; external tissue expanders; negative pressure, natural and synthetic biopolymer,

[1] Doutoranda (Ciências Fisiologicas)– Universidade Federal de São Carlos: São Carlos, São Paulo, BR.
[2] Especialização em Urgência, Emergência e UTI pela Universidade de Ribeirão Preto, Brasil.
[3] Doutorado em Quimica pela Universidade Estadual Paulista Júlio de Mesquita Filho
[4] Doutorado em Bases Gerais da Cirurgia pela Universidade Estadual Paulista Júlio de Mesquita Filho
[5] Doutorado em Programa de Pós-Graduação em Biotecnologia pela Universidade Federal de São Carlos
[6] Doutorado em Ciências Farmacêuticas pela Universidade Estadual Paulista Júlio de Mesquita Filho, Brasil

Received 15 December 2020; Accepted 20 February 2021; Available online 25 February 2021.
DOI: https://doi.org/ 10.52466/ijamb.v4i2.100

among others[10–11].

Dressings composed of biopolymers of natural origin, such as bacterial cellulose (BC) obteined of Gram–negative bacteria metabolism (genus Komagataeibacter) in association with sodium alginate from seaweed have stood out due to the properties presented, such as less toxicity, biocompatibility, and capacity of stimulating wound healing progress [12–13]. BC nanometer–sized fibers that mimic collagen fibers assist in the helping process, and reducing pain [14]. Calcium alginate can promote wound hemostasis through calcium ions released, while the gel serves as a matrix for aggregating platelets and erythrocytes [15].

Recently Sulaeva *et*., 2020 impregnated alginate in BC membranes for the treatment of wounds, resulting in membranes with greater water retention capacity, keeping the wound moist, assisting in the healing process. However, biocurative in membrane form present some difficulty in handling during the exchange, which can cause discomfort to the patient. Hydrogels have been the targets for the treatment of wound acute, chronic and diabetic wounds, as they have a hight water content of 70 to 90%, maintains the hydrated and moist wound, thus minimizing infections by pathogens, in addition, removal easier [11].

Therefore, due to the excellent properties presented, this evaluation of the use of hydrogel HC containing calcium alginate for theobjective was to treat a wound that is difficult to heal in a diabetic patient.

Methods

Case Report

Patient man, 63 years, diabetic and hypertensive, reports continuous use of the medication for pathologies cited and frequent medical follow–up. Report of toe amputation in September 2019 and wound in February 2020.

Local in Study

The treatment was carried out in the photodynamic therapy unit, located on the premises of Santa Casa de Misericordia in São Carlos.

Treatment

The wound was treated with bacterial cellulose hydrogel alginate (patent n ° BR 10 2019 021848 7), and it was cleaned with sterile saline, debridement when necessary and application of the hydrogel to the wound bed twice a week, for 30 days. The protocol performed included asepsis of the lesion with 0.9% saline, followed by mechanical debridement, when necessary with a scalpel blade, and all dressings were applied hydrogel to the wound bed and occluded with sterile gauze and bandage.

Results

The healing process in patients with this disease is highly complex, requiring special care both with regard to glycemic control, nutrition and rest, as well as direct care with the injury, involving the choice of coverage that provides an adequate environment for the epithelialization of lesion.

The wound area was evaluated using the ImageJ software and the result was converted to centimeters on days 0, 7, 21 and 30 as shown in table 1, observed with a remarkable reduction of 84% in the wound area in just 30 days of treatment.

Table 1 – Initial treatment of the wound until the 30th day of treatment with its respective measurement.

Applications	Wound size
0	2.344cm^2
7° day	2.332cm^2
21° day	0.830cm^2
30° day	0.377cm^2

Discussions

Figure 1 respectively A, B, C and D show shows the wound before treatment, presenting hyperkeratosis at the edges of the lesion, fibrin and some granulation tissue in the wound bed, with an superface area of 2,344 cm^2. In the 7th day of treatment, the wound appeared cleaner, without devitalized tissue, and a little reduction of area to 2,332 cm^2 (Figure 1B). In the 21th day of treatment, it was possible to observe that the hydrogel accelerated the healing process (Figure 1C), and in the 30th day of treatment, a significant reduction of wound area to 0.377cm^2 (Figure 1 D).

Figure 1 – Photographs of the evolution of the healing process. A. Beginning of treatment B. 7 days of treatment C. 21 day of treatment D. 30 day after treatment with CB hydrogel and alginate

Therefore, the treatment carried out revealed an

important clinical data demonstrating that the bacterial cellulose hydrogel containing calcium alginate can be a promising product for the treatment of complex wounds, since there was an acceleration in the healing process in a diabetic wound, reversing common processes for these wounds as ischemia, tissue necrotic, excessive accumulation of collagen, reduction of angiogenic factors, delay in the inflammatory response, causing delay in the healing process.

Study limitations

There is no report in the literature on the hydrogel used for the treatment of wounds as it is an innovate hydrogel.

Contribution to practice

It is succinctly contributed that treatment with alginate–containing bacterial cellulose hydrogel improved quality of life and brought greater comorbidity to the treated patient. In addition, it is worth mentioning that there is no data on the hydrogel used because it is something innovative and recently patented by the Company Seven Produtos Biotecnologicos – Ltda which will commercialize the product for its use in patients with difficult to heal wounds.

Conclusions

The results observed with the evolution of the wound healing process in 30 days of treatment with BC hydrogel alginate showed the accelerated healing process in a dificult case of diabetic wound. The follow–up with measurements prove that the wound reduces significantly the wound area, improving his quality of life. It is hoped that this case study can contribute to the development of new studies with this product.

References

[1] Lima LR. Qualidade de vida e o tempo do diagnóstico do diabetes mellitus em idosos. Rev. bras. geriatr. gerontol. 2018, **21**(2): 176–185.

[2] Sociedade Brasileira de Diabetes (SBD). O que é diabetes? – atualização 2019. Posicionamento oficial SBD – 2019. Disponível em: https://www.diabetes.org.br/publico/diabetes/oque–e–diabetes.

[3] Marques AB. Associação entre internação hospitalar por diabetes mellitus e amputação de pé diabético – Enfermaria Global, Revista Electrónica Trimestral de Enfermeria. 2018, **51**:248–256.

[4] Roberto CL, Figueiredo Nébia Maria Almeida, Meireles, Isabella Barbosa. Feridas: Fundamentos e atualizações em enfermagem. 2009, **13**(2): 295.

[5] Santana ER. A Percepção dos Pacientes acometidos por Diabetes Mellitus sobre a Complicação do Pé Diabético: Uma Revisão Integrativa. Id on Line Rev. Mult. Psic.2019, **13**: 77–88.

[6] Diniz IV. Fatores associados à amputação não traumática em pessoas com diabetes mellitus: um estudo transversal. Rev. Eletr. Enferm. 2019, **21**:52484.

[7] Moretti B. The management of neuropathic ulcers of the foot in diabetes by shock wave therapy. BMC Musculoskelet Disord. 2009; doi: 10.1186 / 1471–2474–10–54.

[8] Lima MHM, Araujo EP. Diabetes mellitus e o processo de cicatrização cutânea diabetes mellitus and the process of cutaneous healing. Cogitare Enferm. 2013, **18**(1):170–72.

[9] Vieira CPB.Tecnologias utilizadas por enfermeiros no tratamento de feridas. Rev Enferm UFPI. 2017, **6**(1):65–70.

[10] Oliveira A, Simões S, Ascenso A, Reis P. Avanços terapêuticos na cicatrização de feridas. Journal of Dermatological Treatment. 2020; 1–77. doi: 10.1080 / 09546634.2020.1730296.

[11] E Öhnstedt, H Lofton Tomenius, E Vågesjö Phillipson. A descoberta e desenvolvimento de medicamentos tópicas para cicatrização de feridas. Expert Opinion em Drug Discovery. 2019; **14**:5, 485–497. doi: 10,1080 / 17.460.441,2019. 1588879.

[12] Ahmed A, Boateng J. Curativos antimicrobianos à base de alginato de cálcio para potencial cicatrização de úlceras nos pés infectadas. Entrega Terapêutica. 2018; 185 –204. doi: 10.4155 / tde–2017–0104.

[13] Barud HS, Araújo JR, A. M, Saska S, Mestieri LB, Campos JA, Freitas RM, Ferreira NU, Nascimento AP, Miguel FG, Vaz MM, Barizon EA, Marquele OF, Gaspar Ribeiro SJ, Berretta AA. Antimicrobial Brazilian Propolis (EPP–AF) Containing Biocellulose Membranes as Promising Biomaterial for Skin Wound Healing. Evidence–Based Complementary and Alternative Medicine. 2013, 2013:1–10.

[14] Saska S, Teixeira LN, Oliveira PT, Gaspar AM, Ribeiro SJ, Messaddeq Y, Marchetto R. Bacterial cellulose–collagen nanocomposite for bonetissueengineering. J. Mater. Chem. 2012, **22**:22102–22112.

[15] Sood A, Granick MS, Tomaselli NL. Wound dressings and comparative effectiveness data. Adv.Wound Care. 2014. 511–529.