

**BACTERIAL CELLULOSE WOUND DRESSING: A PROMISING BIOPOLYMER IN
PARTIAL-THICKNESS SKIN GRAFT DONOR SITES**

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ABSTRACT

Objective: To evaluate the use of Bacterial Cellulose (BC) dressing as a temporary wound coverage for skin autografts in comparison with the conventional. **Methods:** Twenty patients submitted to skin autografts were divided into two groups: BC group that received a BC membrane dressing and control group (CG) that received Vaseline gauze. The sociodemographic and clinical variables of the participants (age; gender; wound bed and dressing aspects, including self-adherence; pain intensity measurement by the analog scale and pruritus intensity; wound healing time; granulation and re-epithelialization wound tissue) were compared. **Results:** The patients' average age was 30.4±11.4 (BC group) and 43.9±15.1 (CG group). There was a reduction in the referred pain scale from 2.75 to 1.6 in the BC and from 3.3 to 2.4 in the CG and a decrease sensation related to pruritus was observed, especially in the BC group, with no statistical difference between groups (1st POD, $p = .658$; 7th POD, $p = .354$). A trend of decreased healing time was observed in BC group (15.8 days) compared to the CG (19.4 days), with no statistical difference ($p = .08$). The BC dressing proved to be compatible, adhered well to the wound bed and detached itself after wound re-epithelialization. **Conclusion:** The BC wound dressing adheres naturally to the wound bed, this may explain why the healing time may have been shorter in this group, and can be an effective alternative in promoting and accelerating the healing process.

KEYWORDS: Skin transplantation, Autologous, Biocompatible Materials, Wound Healing, Bandages.

1.0 INTRODUCTION

Skin grafting is one of the most indispensable procedures in plastic surgery.^[1] It is a technique used to cover skin defects resulting from a wide variety of causes, among which are burns, abrasions or injuries, skin necrosis after trauma or surgery, congenital deformities that have undergone surgical corrections, among others.^[2]

Among the burn treatment measures, the wound closure to reduce loss and prevent infection is the most important aspect, regardless of the extent and depth of the injury.^[3] Initially, temporary dressings are used to stabilize the skin graft site with permanent skin restoration^[4]. The skin donor sites in partial homologous grafts are controlled lesions, since they are performed in a surgical environment and with a previously planned thickness^[5]. Some studies indicate that occlusive dressings in this region, in addition to providing greater comfort to the patient, reduce the incidence of local complications, and allow an early discharge.^[6-8]

There are several options for covering wounds, including those from donor sites, but there is still no consensus on the ideal dressing.^[9] The ideal dressing should promote and accelerate epithelialization, reducing pain and discomfort, in addition to having an affordable cost to specialized health services.^[10,11]

The bacterial cellulose (BC) dressing was developed by Polisa LTD at the Carpina Sugarcane Experimental Station (EECAC/UFRPE) from sugarcane molasses in a fermentation-based system to produce a biopolymer matrix^[12]. BC dressing has been applied in different clinical studies^[13,14] showing characteristics that benefit the healing process, in addition to having an affordable production cost. Previous studies, including *in vitro* and *in vivo* analyses, showed an absence of toxicity^[15], and proved to be effective as a graft substitute in myringoplasty,^[16] in the treatment of urinary incontinence^[17] and for the treatment of vesico-urethral reflux.^[18]

The current study aims to evaluate the use of BC dressing as a temporary wound coverage for skin autografts in comparison with the conventional treatment used at the Burn Treatment Center of the Hospital da Restauração in Recife, Pernambuco, Brazil.

2.0 MATERIAL AND METHODS

2.1 Research Design

This is a clinical intervention study, carried out at the Burn Treatment Unit (BTU) of Hospital da Restauração (HR), Recife, Pernambuco, Brazil, performed from August 2017 to January 2018.

Among the inclusion criteria were considered: Patients admitted to the BTU, aged 12 years or over, and submitted to skin graft. Patients under the age of 12 years, with comorbidities or with active infectious processes were excluded.

Research participants were randomly divided into two groups, with 10 patients allocated to the group that received the conventional dressing (Control Group, CG) and 10 in the group that received the BC dressing (BC Group, BC).

2.2 The Bacterial Cellulose

Bacterial cellulose (BC) is an exopolysaccharide obtained from sugarcane molasses by flotation as a gelatinous matrix,^[12] biocompatible and non-toxic^[15,19]. The BC wound dressings used in this research were produced and donated by Polisa LTD, a startup incubated at the Federal Rural University of Pernambuco (UFRPE), headquartered at the Carpina Sugarcane Experimental Station (EECAC/UFRPE). Wound dressings with a size of 15 x 8 cm were used.

2.3 Technical Procedures

Participants included in the study were followed up in the baths under narcosis on alternate days until the clinical decision to perform the surgical procedure for excision of the skin autograft.

Skin excision followed the standard procedure using an electric dermatome or Blair's knife, after local infiltration of 0.9% saline solution plus 1:200,000 adrenaline concentration. All procedures were performed by the same surgical team and anesthetist.

The control group received the vaseline gauze dressing, while the experimental group (BC group) received the bacterial cellulose dressing. The BC dressing consists of a bacterial cellulose film, a biopolymer, soaked in saline. In both groups, a secondary dressing was applied, consisting of a surgical dressing (sterile compress) and wrapped in a crepe bandage. Secondary dressings were opened after 7 days and the primary dressings, if they remained in the donor site, were followed up until the wound healing process was completed and the primary dressing naturally detached. The BC dressing has the characteristic of adhering naturally to the wound bed and

detaching itself when the healing process is complete. The vaseline gauze dressing was changed on the seventh day.

The wound dressings were performed under narcosis during the hospitalization period and without sedation during outpatient follow-up, always using a 2% chlorhexidine solution and liquid vaseline.

Clinical evaluations were performed on the first post-op day (POD), on the 1st day after the dressing was opened (7th POD), and until the donor site healed. A form was used to monitor the sociodemographic and clinical variables of the participants: age; gender; wound bed and dressing aspects, including self-adherence; pain intensity measurement by analog scale from 0 to 5 (being 0, "none" and 5, "unbearable"), and pruritus intensity, by pruritus grading scale, categorized into none (0), light (1), moderate (2) and severe (3); wound healing time; granulation and re-epithelialization wound tissue.

2.4 Statistical Analysis

The Student *t* test for independent samples was used, after confirmation of normal distribution by the Kolmogorov-Smirnov test. Fisher's exact test was used for the qualitative variables. A correlation analysis using Pearson correlation test (*R*) was applied for "wound healing time *versus* age" and "wound healing time *versus* gender". All analyzes were performed using the SPSS program (IBM® SPSS Statistics for Windows, Version 24.0., 2016), with a significance level of 5%.

2.5 Ethical Aspects

This study was approved by the Institutional Research Ethics Committee (No. CAAE: 23402513.9.0000.5208), following the principles of the Declaration of Helsinki for research in human subjects. Participants were invited to participate in the study during their hospitalization stay at the Burn Treatment Unit, and inclusion in the protocol was only allowed after signing a consent form.

3.0 RESULTS

The patients' average age was 30.4±11.4 (BC group) and 43.9±15.1 (CG). Although age showed a significant difference between groups (*p*= .037), without correlation with the wound healing time (*p*= .188).

In the BC group there was a predominance of females (80%), while in the CG it was male (60%), however without significant differences between groups (*p*= .170). In both CG and BC group, the wound healing time was shorter for women (CG, 18 days; BC, 15 days) than for men (CG, 21 days; BC, 20 days), with statistically significant correlation (*R* = -.500, *p*= .025).

Regarding the complaint of pain, a progressive decrease between 1st and 7th POD was observed in both groups (Fig. 1, A and B). There was a reduction in the referred pain scale from 2.8 to 1.6 in the BC group (-1.2 points of difference) and from 3.3 to 2.4 in the CG (-0.9 point of difference).

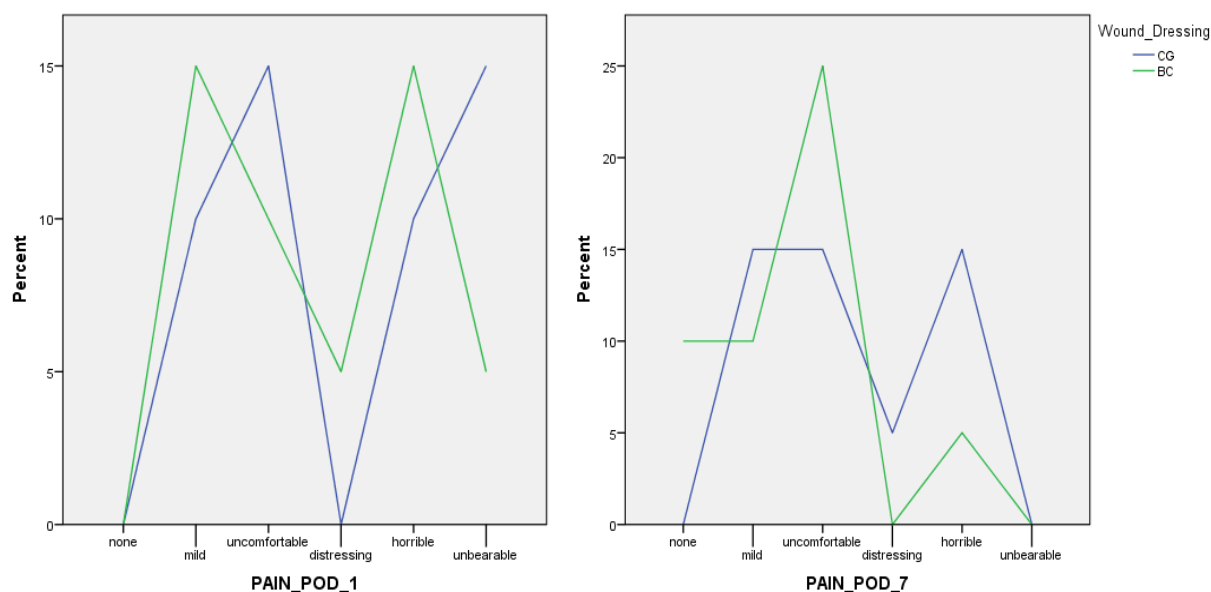


Fig. 1: A. Pain intensity measurement using an analog scale between BC group and CG on the first post-op day; B. Pain intensity measurement using an analog scale between BC group and CG on the seventh post-op day.

Note: PAIN_POD_1, means the pain intensity measurement on the first post-op day; PAIN_POD_7, means the pain intensity measurement on the seventh post-op day; CG, control group; BC, Bacterial Cellulose group.

There were 3 cases of moderate pruritus, two in the BC group (1st POD) and one in the CG (7th POD). No case of severe pruritus was observed. In general, was observed a decreased sensation related to pruritus, especially in the

BC group, with no statistical difference between groups (1st POD, $p = .658$; 7th POD, $p = .354$).

Regarding wound healing time, no statistical difference was observed between patients who used BC and conventional dressings. The average healing time was 15.8 ± 3.7 days in the group treated with BC dressing and 19.4 ± 5.0 days in the control group ($p = .083$).

Table 1 summarizes all data.

Table 1: Clinical aspects related to the control and BC groups.

Parameters		Groups		p-value
		BC (N=10)	CG (N=10)	
Age mean \pm SD		30.4 \pm 11.4	43.9 \pm 15.1	.037 ^a
Gender N (%)	Male	2 (20.0)	6 (60.0)	.170 ^b
	Female	8 (80.0)	4 (40.0)	
Pain Intensity mean \pm SD	1 st POD	2.8 \pm 1.5	3.3 \pm 1.9	.579
	7 th POD	1.6 \pm 1.2	2.4 \pm 1.3	.160
Mean difference between POD	7 th POD - 1 st POD	-1.2	-0.9	-
Pruritus Intensity N (%)	1 st POD	Absent	4 (40.0)	.658
		Light	4 (40.0)	
		Moderate	2 (20.0)	
	7 th POD	Absent	5 (50.0)	.354
		Light	5 (50.0)	
		Moderate	0 (0.0)	
Wound Healing Time (days) média \pm DP		15.8 \pm 3.7	19.4 \pm 5.0	.083 ^{a b}

Note: Data presented as absolute number (N) or mean and standard deviation (mean \pm SD) or percentage (%). BC, Bacterial Cellulose; CG, Control Group; POD, Post-Op Day. ^aif $p < .05$. ^aWhen performing the Pearson correlation test between wound healing time and age ($R = .307$, $p = .188$). ^bWhen performing the Pearson correlation test between wound healing time and gender ($R = -.500$, $p = .025$).

There were no differences in the wound healing process between groups, and the aspects related to re-epithelialization and granulation tissue were similar.

The BC dressing was previously moistened with 0.9% saline, increasing its flexibility and adjusting better to the surgical wound bed, showing good adherence and drainage (Fig. 2, A-B).

After opening the BC dressing on the 7th POD, the presence of some bloody areas was observed, and after 15 days the donor sites were completely healed (re-epithelialization) a/or with superficial crusts (Fig. 2, C).

Edge epithelization was also observed, a large amount of granulation tissue and remnants of the healing process with a BC dressing adhered to the center of the wound.



Fig. 2. Bacterial cellulose as a material for wound treatment.

A. Autograft excision. **B.** Application of the BC Membrane. **C.** Aspect on the 7th. POD, showing BC dressing partially adhered and donor site healed, with small areas showing superficial crusts.

4.0 DISCUSSION

Even with advances in biotechnology looking for skin substitutes, skin grafts remain an essential part of wound care. The regions that donate these tissues need care for effective wound healing. Often, attention is directed to the graft recipient area, underestimating the importance of adequate care for the donor site.^[20]

This study was conducted as a clinical evaluation to monitor the wound healing process in the graft donor site, between 1st POD and the 7th POD, comparing the BC dressing with the conventional dressing (vaseline gauze). For this, the following parameters were evaluated: age; gender; wound bed and wound dressing aspects, including self-adherence; intensity of pain and intensity of pruritus; wound healing time; and the wound healing process characteristics.

There was a significant difference in the age of the participants between groups, probably by the deviation in the average age due to the presence of a 71-year-old participant in the CG. In general, excluding this participant, the average age would be 35.37 ± 12.75 years old (minimum = 15 y/o and maximum = 57 y/o), in this case, without significant difference between groups. However, there was no correlation between age and wound healing time ($p = .188$), although the patient's age being a limiting factor.^[20]

The healing time depends mainly on the depth of the wound, the extent of post-op bleeding and the patient's age^[21]. In this context, there is a considerable anatomical difference related to the wound type in older patients. Skin aging in elderly patients leads to a severe decrease in epidermal and dermal thickness, as well as vascular plexuses and adnexal structures^[22]. Although in this study there was no correlation between patients' age and wound healing time, partial thick skin grafts in elderly patients can reach deeper dermal layers, causing more

bleeding and a longer healing time for the donor sites. Davidson *et al.*,^[23] also observed a slower rate of epithelialization in patients over 50 years old compared to younger patients.

A significant correlation was found in this study between wound healing time and gender ($p = .025$), where women had a shorter healing time than men. This finding corroborates with the literature, which says that wounds heal more slowly in men than women and the response is different in both sexes, probably due to the impact of hormones on cellular and tissue responses, resulting from increased inflammation, impaired cytokine signal transduction and altered balance of protein production and degradation.^[24]

Several factors can affect the wound healing process in some way, including some comorbidities (diabetes mellitus, for example), vitamin deficiencies, age range, severe trauma, burns, sepsis, smoking, use of corticosteroids, among others.^[25]

In the current study, no complications related to pruritus, infections or exudation after using the BC dressing in the donor sites of partial skin grafts were observed. The sensation of pain was not significant when BC dressing was compared to the conventional dressing. However, it seems that this absence of difference between conventional and BC dressings may have occurred mainly because the donor sites are different in both size and graft location.

In general, regardless of age or gender, there was no difference between conventional and BC dressings, however, the group that received the BC membrane had a shorter wound healing time (mean = 15.8 days). A similar result was observed in the study of Konstantinow *et al.*,^[26] using oxidized cellulose dressings plus collagen in the treatment of skin graft donor sites in 25 patients.

However, according to the current findings, after the skin graft donor site was re-epithelialized, the BC dressing detached naturally from the donor site without any reported discomfort.

The property of detaching itself from the wound, after re-epithelialization of the donor site was also considered an important factor in the choice of dressing. Dressings that provide re-epithelialization without wound handling are generally well tolerated and chosen by patients and doctors. This property has been reported in studies using a nanofibrillar cellulose (NFC)^[27] and oxidized cellulose plus collagen.^[26]

The BC wound dressing tested, has the same structure of sugar molecules as a NFC, biosynthesized by bacteria. Clinical trials among severely burned patients have found that the BC dressing allowed for rapid wound healing and showed a high level of adherence to the wound bed, especially due to the comfort provided.^[28,29] In addition, the BC dressing can be penetrated by the epithelial cells and can, therefore, integrate with the skin tissue.^[30] Recently, a randomized clinical trial with 25 patients analyzed the efficacy of the treatment of varicose ulcers of the lower limbs and observed a reduction in pain and less use of analgesics when using the BC membrane^[14] however, the number of exchanges was not analysed.

Furthermore, due to its chemical composition and physical properties, BC membrane shows to be a promising biomaterial^[31] In previous studies, BC has been shown to be a conductor and cell inducer in the healing process.^[32-35] Due to the versatility of this biopolymer, BC has been used in different areas of surgery, such as the urethral reconstruction^[7] the bio-sling for the treatment of urinary incontinence^[8,9] and as a bulking agent in orthopedics,^[10] ophthalmology^[11] and urology^[12]. Recently, BC, in film and gel, has been tested for the treatment of different types of wounds,^[14,18,36-37] with positive results.

4.1 Study Limitations

Some limitations were detected in the current study. The number of participants in the survey needs to be expanded to more accurately assess the data. No evaluations were performed on the size of the wound grafts and the regenerated area (wound healing). The number of wound dressing changes was also not evaluated. Factors intervening in the research (comorbidities, use of medications and age range, for example) need to be controlled more rigorously.

On the other hand, it should be considered that part of the limitations detected occurred due to the difficulty of accessing the participants' data or even to structural-administrative issues related to the service where the research was carried out.

Nonetheless, these aspects are being considered for a future study, where it is also intended to make a comparative evaluation of the costs of some dressings that are available for sale and the BC dressing.

5.0 CONCLUSION

The BC dressing was shown to be similar to the conventional dressing, the difference is that the BC dressing adheres naturally to the wound bed, this may explain why the healing time may have been shorter in this group, in addition to the sensation of pain and pruritus having been reduced.

The use of bacterial cellulose dressing to cover the donor area of partial skin autograft can be an effective alternative in promoting and accelerating the healing process.

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