Volume 19 Issue 40
Originally issued as J5



Global Journal of Medical Research: J
Dentistry & Otolaryngology
Volume 19 Issue 5 Version 1.0 Year 2019
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

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Abstract- Oral mucositis is a common and debilitating consequence of cancer patients undergoing antineoplastic treatment. There is no consensus on the most appropriate treatment for this condition. The best protocol to use should. consider each patient's specific needs and cost-effectiveness of treatment. Copaiba oil is a low-cost herbal medicine with scientifically proven anti-inflammatory, bactericidal, antitumor, and healing action.

Keywords: *copaiba, dentistry, oncology, oral care, oral mucositis.*

GJMR-J Classification: *NLMC Code: WU 600*



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Copaiba Oral Hydrogel for Oral Mucositis Control - Search Note

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Abstract- Oral mucositis is a common and debilitating consequence of cancer patients undergoing antineoplastic treatment. There is no consensus on the most appropriate treatment for this condition. The best protocol to use should consider each patient's specific needs and cost-effectiveness of treatment. Copaiba oil is a low-cost herbal medicine with scientifically proven anti-inflammatory, bactericidal, antitumor, and healing action. So, from this reality, this unpublished study set out to create and verify the efficacy of a Copaiba-based Oral Hydrogel in the control of chemo and radio induced oral mucositis, compared with the use of Low Power Laser and the Standard Operating Protocol of Oral Care. The study was developed at a referral center for cancer treatment, where it was possible to identify the good acceptance of the three methods used. The data obtained are under analysis. This previous note intends to report a clinical case in which the positive relationship between good oral hygiene and reduction of acute complications of head and neck radiotherapy in the stomatognathic system was verified when the patient is under specialized dental care.

Keywords: copaiba, dentistry, oncology, oral care, oral mucositis.

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I. Introduction

The use of medicinal plants and their extracts has been studied and used for medicinal purposes and can be said to have been born with humanity. Evidence of this use has been found in older civilizations and is considered one of the most remote practices used by humans to cure, prevent and treat diseases, serving as an important source of biologically active compounds[1,2].

A increased interest in the use of medicinal plants and their extracts in therapy has been observed and, under certain circumstances, constitutes an aid in primary health care and a therapeutic complement, compatible with conventional medicine[2]. Among the medicinal plants, we can highlight the Copaiba that has been arousing the interest of the scientific community because of its therapeutic possibilities.

The copaiba is a common tree in Latin America and West Africa, which can be found in Brazil in the Southeast, Midwest, and Amazon. Such plants come to live about 400 years, reach a height between 25 and 40 meters. From the tree of copaiba, an oil-resin is extracted, of color that varies from golden yellow to brown, depending on the species. This oil-resin is used since the arrival of the Portuguese to Brazil in traditional folk and forestry medicine for various purposes, and

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today is one of the most relevant Amazonian natural products marketed and exported to the United States, France, Germany and England[3].

The chemical structure of the oil-resin constituents, as well as the oil obtained from the seeds, is formed by various diterpenes, sesquiterpenes and polylactic acid responsible for the analgesic, anti-inflammatory, antiseptic and healing effect[4]. According to the literature, a variety of therapeutic properties associated with the use of copaiba oil-resin are related in addition to those already mentioned, such as antiseptic, antibacterial, germicidal, antitumor, analgesic, diuretic and expectorant action[3].

Oral mucositis (OM), characterized by acute inflammation of the oral mucosa seen in immune compromised patients, is a common and debilitating consequence of cancer patients undergoing high doses of chemotherapy or radiotherapy in the head and neck region. Radiation is a very effective therapy and can be an alternative to surgical treatment or a valuable adjunctive modality for surgery and chemotherapy in loco regional treatment and control of head and neck cancer. However, besides acting on tumor cells, radiation-induced tissue ionization is capable of causing very harmful damage to the stomatognathic system[5,6].

These patients may have decreased oral functions such as swallowing, speaking, and chewing, which impairs their quality of life. Also, oral mucositis is a gateway to opportunistic microorganisms, increasing the risk of morbidity and mortality in these patients[5]. Several disadvantages may result in increased length of stay or hospitalization, as well as burdening treatment costs[6].

Although therapy in the treatment of OM has shown to be supportive and palliative, there is still no consensus on the most appropriate treatment[7-9].The use of low power laser (LPL) has a preventive and curative nature to treat injuries caused by OM, and several studies show its benefits for the treatment of these injuries[6]. Its effect is related to tissue biomodulation that results in decreased damage, repair, and analgesic effect[5].

Despite the various therapeutic possibilities available, the best protocol to be used should consider the specific needs of each patient and the cost-benefit ratio[8-10]. So, from this reality, this unpublished study proposed to create and test the Copaíba-based Oral Hydrogel, after approval of the project by the Research Ethics Committee (Approval Protocol: 2.143.119) whose partial result is exemplified below in this case report.

II. Case Description

The Copaiba Oral Hydrogel with bacterial cellulose membranes (MCB) ground with a magnetic stirrer in aqueous medium is a innovative product. The prepare of formulations included mixing the reagents by a mechanical stirrer. We cannot describe the reagents as the formula is under patent. The final product has the consistency of hydrogel for oral use with a production of 50g and 100g. (Figure 1)

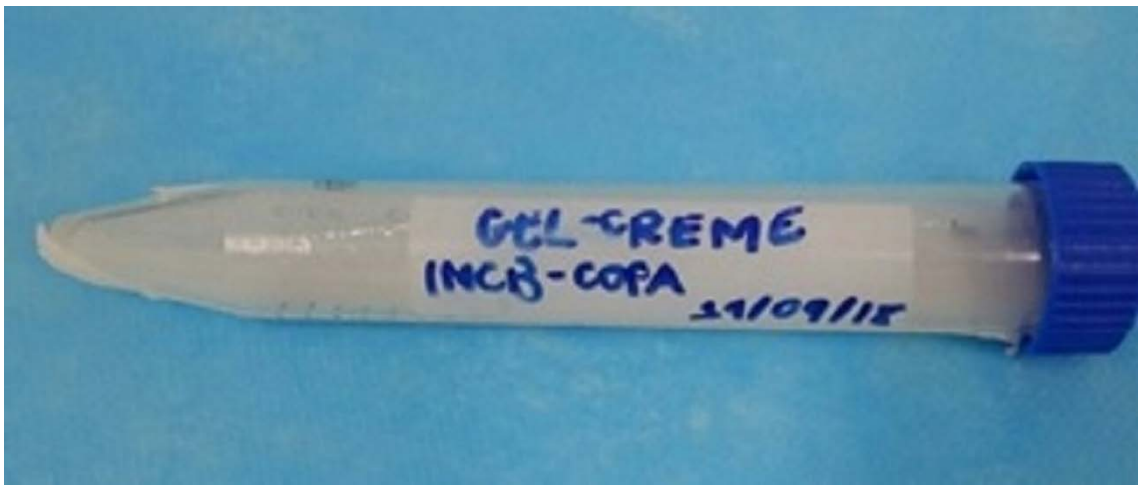


Figure 1: Presentation of Copaiba-based Oral Hydrogel.

The study is a randomized clinical trial[11]. The sample consisted of 60 individuals (male and female), aged at 18 years or older, diagnosed with solid or hematological malignant neoplasia and under chemotherapy and/or radiotherapy treatment, the latter in the head and neck region. The study took place at a referral center for cancer treatment. All participants signed the Informed Consent Form, thus allowing the use, after random drawing, of one of the three methods used in this study: a) Standard Operating Protocol of Oral Care (POP –Oral); b) POP-Oral + LPL; c) POP-Oral + Copaiba Oral Hydrogel for prevention and treatment of OM. The data obtained are under analysis.

Since there are no objective, practical methods of pain measurement, this information was obtained through scales[12]. Thus, the Numerical Pain Scale (0-10)

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consisting of a ruler divided into eleven equal parts, successively numbered from 0 to 10, was applied. The patient had to identify the correlation between the intensity of his pain and a numerical score, where 0 corresponds to "no pain" and 10 to "maximum pain" [13].

The World Health Organization (WHO) Classification was used to record OM, where grade 0 means no mucositis; grade I presence of erythema; grade II presence of erythema, edema, and painful ulcer; grade III severe oral ulceration; and grade IV patients require enteral or parenteral nutritional support[6,14-16].

Aiming to anticipate and share the findings of this unpublished study, we described in the following case report the use of POP-Oral and the topical application of Copaiba-based Oral Hydrogel used to control radio-induced grade II MO presented by the patient. The participant signed the Informed Consent Form, consenting to the disclosure of her case for academic purposes.

BMJ, female, 77 years old, illiterate, stable union, mother of 8 children, farmer. She smoked for about 70 years, ten cigarettes a day, and quit smoking in March 2018 after the diagnosis of oral cancer. She sought the Head and Neck service of the Oncology Center, presenting ulcerated lesion on the left border of the tongue for about one year. After the biopsy and histopathological analysis (AP 191438), the diagnosis concluded for moderately differentiated invasive squamous cell carcinoma (histological grade 2), pathological staging ptT3, T2N0M0.

The treatment proposed by the medical team for the case was oncologic surgery, with partial glossectomy performed in April 2018, plus association with exclusive radiotherapy. BMJ protocol consisted of 6MV nominal energy photons generated with MEVATRON linear particle accelerator. Tumor Dose/ Day: 200cGy and Total Tumor Dose: 7.000cGy, from 01/11/2018 to 28/12/2018. Before the beginning of radiotherapy, BMJ went to the dentistry service for oral adequacy.

The intraoral clinical examination showed bad oral hygiene, the presence of dental caries, and chronic periodontitis with marked mobility in all teeth present. Panoramic radiography of the jaws helped to complete the analysis, planning, and correct adequacy of the oral cavity. Multiple dental extractions were necessary to remove all compromised dental elements and root remnants, to minimize the side effects of radiotherapy.

It was instituted The Standard Oral Care Protocol (POP-Oral) for edentulous individuals, using a toothbrush with a small head and soft bristles, non-abrasive toothpaste, mouthwash with sodium bicarbonate solution (8/8h), mouthwash with oral nystatin solution (100,000 IU) four times a day and topical application of vitamin E (oily) 12/12h. Also, after signing the Consent and Authorization Form for the use of Copaiba Oral Hydrogel, it was used through mouthwash twice a week, once a day, throughout the radiotherapy treatment (Figure 2B).

At each consultation, the researchers applied the Numerical Pain Scale before topical application and mouthwash with the copaiba hydrogel. In the 18th session of radiotherapy, BMJ reported pain corresponding to grade 5 on the pain scale (Figure2A)and managed to reach the absence of pain symptoms, identified as grade 0, after the third session of topical application in the ulcer and mouthwash with the Copaiba-based hydrogel (Figure 2C).



Figure 2: *2A:* Clinical aspect of grade II OM presented at the 18th session of radiotherapy with pain complaint corresponding to grade 5, on the numerical pain scale. *2B:* Topical application of copaiba-based oral hydrogel for later mouthwash. *2C:* Clinical aspect of grade II OM in regression and control phase after the third session of topical application and mouth wash with Copaíba-based Hydrogel, with no pain symptoms, identified as grade 0, on numerical pain scale.

BMJ underwent weekly follow-up, and as can be seen in the last week of radiotherapy treatment, BMJ presented asymptomatic integral oral mucosa (Figure 3). BMJ is lucid, conscious, oriented, and very collaborative.

BMJ presented good tolerance to side effects of radiotherapy, developing throughout the treatment episodes of xerostomia and MO grade II (WHO scale) [6,14,15,16]. BMJ is currently undergoing an oral rehabilitation phase (removable total denture) and is being followed up by a multidisciplinary team.

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Figure 3 (A and B): Clinical aspect of the oral mucosa in the last week of radiotherapy treatment, showing recovered mucosa and absence of painful symptoms.

III. Discussion

Innovation in cancer treatment resulted in increased survival, as well as changes in the incidence, nature, and severity of oral complications, affecting the quality of life of these individuals. Thus, the need for dental follow-up of these patients has become increasingly recognized, in addition to establishing specific oral care for them, aiming to ensure their oral health and general well-being[17].

Since a lack of a balanced diet, poor oral hygiene, the presence of fractured teeth or defective restorations, root remnants, periodontal disease or poorly adjusted prostheses can all contribute to the development of local or systemic infections, it is consensus in the literature that dental treatment before the beginning of radiotherapy, as reported in this clinical case, optimizes antineoplastic protocol avoiding interruptions during its application and improving patients' quality of life[16,17,18].

Corroborating the clinical case described in this article, the study developed by Brennan [18], evaluated the level dental disease prior to radiotherapy. Based on dental examination, 163 (49.5%) of the participants had recommended dental treatment before radiotherapy, with dental cleaning in 137 (41.5%); recommended extractions in 116 (35.3%); a new dental restoration or replacement of a restoration in 82 (25%); pre-prosthetic surgery in 21 (6.4%); and endodontic therapy in 8 (2%).

Therefore, teeth with a poor prognosis, as in the case of advanced periodontal disease, high rate of dental caries, poor oral hygiene, need for endodontic treatment, or extensive restorations, have an indication of extraction, as described and performed in the clinical case of this article. The necessary extractions should be performed at least 14 to 21 days before the beginning of radiotherapy, in an atraumatic manner, eliminating bone spicules, with primary closure of the surgical wound and without soft tissue tension to promote rapid and complete healing[16].

Oral mucositis (MO) is an acutely painful inflammation that has age, oral hygiene, renal function, genetic factors, previous antineoplastic treatment, among others, as risk factors linked to the patient; whereas, the dose of chemotherapy and radiotherapy, the chemotherapy used, and the mode of application are factors related to therapy[5].

The routine eating behavior that was a habit in the life of these patients undergoes radical changes. Painful symptoms and difficulty in swallowing food cause extreme discomfort in patients with mucositis lesions, which makes eating difficult. Besides, the taste of food is altered as a result of head and neck radiotherapy and the use of chemotherapeutic agents and discourage eating. As the lesions evolve, they increase the sensation of pain and discomfort within the oral cavity and, as a result of these clinical manifestations, the patient opts to use pasty or liquid food. This complication may result in increased length of stay or hospitalization, as well as burdening treatment costs[6].

The severity of mucositis lesions interferes with the systemic treatment of the individual since the degree of morbidity is high and may lead to the suspension of antineoplastic therapy. In this context, mucositis classifications are of fundamental importance, as they are instruments for assessing the success or failure of a given therapy[11,19, 20].

The most commonly used scale to evaluate and measure oral mucositis is recommended by WHO, which classifies the OM in four degrees[6,14,15] as described in this article, in the methodology item. This case report demonstrates an OM grade II, which is characterized by the presence of ulcers, pain, but the patient still maintains oral feeding.

As demonstrated in the report of this clinical case, it is essential to establish before the cancer treatment a clinical and surgical dental treatment plan, when these needs are diagnosed in the initial dental evaluation, aiming to promote oral health as a

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fundamental role, enabling to minimize the risk of sequelae, as is the case with MO[9,16-18].

Also, for control of OM and other complications such as dehydration, cachexia, and infections[7,15], prophylactic approaches are indicated, as awareness for the improvement of oral hygiene, and adoption of POP-Oral as demonstrated in this case report [21]. With regular oral care, it is possible to reduce the influence of oral bacterial flora, pain symptoms, and bleeding related to anticancer therapy and prevent soft tissue infections, which may promote systemic sequelae. Also, maintaining oral hygiene reduces the risk of dental complications, including caries and gingivitis[7,9,16,17].

Still, the management of OM often recommends the use of chamomile, betamethasone, benzydamine, acetylsalicylic acid, lidocaine, polymyxin E, lozenges, tobramycin, LBP and cryotherapy, among others, as therapeutic resources[15].In this study, Copaiba-based Hydrogel developed and used as a preventive and therapeutic form for OM was able to reduce the severity of mucositis degree and also oral pain, providing rapid relief, inflammation control, maintenance of mucosal integrity, better tissue repair and greater patient comfort.

In other words, POP-Oral[21] associated with topical application and mouthwash with Copaíba-based Hydrogel showed a positive clinical and functional response, promoting excellent comfort and quality of life for patients under head and neck radiotherapy. Soon we will release data from the randomized controlled trial conducted.

Coupled with specific dental care, Copaiba Oral Hydrogel can represent a low cost and affordable possibility, and with anti-inflammatory and antimicrobial properties, corroborated in the literature, to be used as an alternative and effective method to control oral mucositis, considering the efficacy observed in this case report against radio-induced OM.

Acknowledgements

To patients and relatives, who agreed to use the copaiba hydrogel, allowing the development of this study. To CETENE for their support in the manufacture of the copaiba hydrogel for oral use. To the Secretariat of Health of the State of Pernambuco-SES/PE and Pernambuco State Science and Technology Support Foundation - BFT / FACEPE.

Financing

FINANCING Pernambuco State Health Secretariat - SES/PE (2016-2019).

Technician Fixing Grant of the Pernambuco State Science and Technology Support Foundation - BFT / FACEPE (Process number 0166-1.06/15).

Conflict of interest

The authors declare no conflicts of interests.

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* Previous Postdoctoral Research Note by Profa. Dr. Aurora Karla de Lacerda Vidal under the guidance of Prof. Dr. Teresinha Gonçalves da Silva (UFPE), Co-guidance of Profa. Dr. Ana Paula Pimentel Cassilhas (ICB/UPE) and collaboration of the others co- authors.

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