Research Article

Advances in Hematology and Oncology Research

Evaluation of the use of Orasol Plus®, A Mouthwash Based on Plant Extracts, in Mucositis in Patients with Breast Cancer Receiving Chemotherapy

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Submitted: 28 Mar 2020; **Accepted:** 04 Apr 2020; **Published:** 02 May 2020

Abstract

Breast cancer is the first and most common cancer in women and represents the leading cause of female cancer death. To treat cancer, the treatment that is giving more results is the conventional poly-chemotherapy with numerous other substances that have specific action, called target therapy. During the treatment of breast cancer, chemotherapy drugs lead to the frequent detection of side effects, first of all, the Oral Mucositis. Oral mucositis (OM) is a common in cancer therapy, found in a percentage of 15-40%, and cause severe sequelae and strong impact on a patient's quality of life (QoL), health care costs, and ultimately outcome by influencing the treatment dose. There are some and limited therapeutic options to help reduce the severity of OM. Our study evaluated the action of a mix of natural supplements (swallowable solution, Orasol plus®, for reduction of mucositis during chemotherapy, with Lapacho (Tabebuia Avellanedae Lorentz ex Griseb.), Camellia Sinensis L. Kuntze, Calendula Officinalis L, Malva Sylvestris L, Sisymbrium Officinale (L) Scop, Plantago Major L e Propoli) in 15 breast cancer patients under treatment with chemotherapy and target therapy. No patients had stopped the treatment because of mucositis. From 11 patients that have mucositis during treatment, 5 had complete remission at the and of the first cycle in the 4 patients who took Orasol Plus®, as a preventive measure, none developed mucositis during antiblastic treatments. The data of our study depose for the effectiveness of Orasol Plus® in the treatment of oral mucositis, in patients undergoing chemotherapy for breast cancer. They need a larger study to insert Orasol Plus® in a standardized pathway in the treatment of oral mucositis during chemotherapy.

Keywords: Oral Mucositis, Breast Cancer, Chemotherapy, Natural Supplements

Introduction

Breast cancer is the first and most common cancer in women and represents the leading cause of female cancer death. Oral mucositis (OM) is a common and often dose-limiting adverse event (AE) of cancer therapy with the potential to cause severe sequelae and have a strong impact on a patient's quality of life (QoL), health care costs, and ultimately outcome by influencing the treatment dose [1]. During the treatment of breast cancer, chemotherapy drugs lead to the frequent detection of side effects, first of all the Oral Mucositis [2]. OM can be observed in patients with breast cancer treated with conventional chemotherapeutic drugs as well as in patients receiving targeted therapies such as the tyrosine kinase inhibitor (TKI) lapatinib and the mammalian target of rapamycin (mTOR) inhibitor everolimus [3]. Mucositis of the oro-pharyngeal cavity is found in a percentage of 15-40% of patients treated for cancer with conventional chemotherapy [4]. In principle, OM is initiated by an inflammatory process affecting the mucosa of the oral cavity or other areas of the gastrointestinal tract. The lesions can sometimes be large in size and are often associated with intense pain which can compromise nutrition and oral hygiene [5]. In addition, there is an increased risk for local and systemic infections due to treatment-induced compromised immunity and damaged oral mucosa [6]. The establishment of mucositis can therefore represent a serious impairment of the prognosis, worsening the prospects of life to the extent of doubting the effectiveness of the therapy itself. Impairment of the integrity of the oral mucosa leads to burning and pain that can make proper nutrition, hydration and patient relationship difficult until impossible. The consequence of the interruption of the treatments and their restart in a discontinuous way prolongs the disease, increases the days of hospitalization and undermines the patient's trust seriously compromising the emotional state in an anxious-depressive sense. The severity and incidence of OM in patients with breast cancer depend on a number of specific factors such as the underlying systemic disease, type of treatment, dosage and frequency of chemotherapeutic agents, and patient-related risk factors [7]. Several standard chemotherapeutic agents such as 5-fluorouracil (5-FU), anthracyclines and taxanes are known to be associated with high rates of OM (Fig. 1) [8]. A systematic comparative study from 2015, published in the International Journal of Hemathology-Oncology and Stem Cell Research, reports that the use of the taxane, alone or in combination, for the treatment of breast CA, involves the establishment of a picture of oral mucositis in 89.3% of cases (P = 0.009) [2].

Regimen	Grade ¾ risk, %
All breast	4,08
A-T-C: doxorubicin, taxane*, and cyclophosphamide (administered sequentially)	2,29
AT-C: doxorubicin, cyclophosphamide, and taxane* (administered sequentially)	2,8
A-CT: doxorubicin, cyclophosphamide, and taxane* (administered sequentially)	5,26
A-T: doxorubicin and taxane* (administered sequentially)	4,17
AT- doxorubicin and taxane*	8,33
FAC (weekly): 5 FU, doxorubicin and cyclophosphamide	3,33
AC (weekly): doxorubicin and cyclophosphamide	13,64
Paclitaxel (weekly)	2,87
TAC	4,92
* Paclitaxel or Docetaxel	
5 FU= 5- Fluorouracil	

Figure 1: Risk of NCI-CTC Oral Mucositis with frequently used chemiotherapeutic regimens (Keefe, 2007)

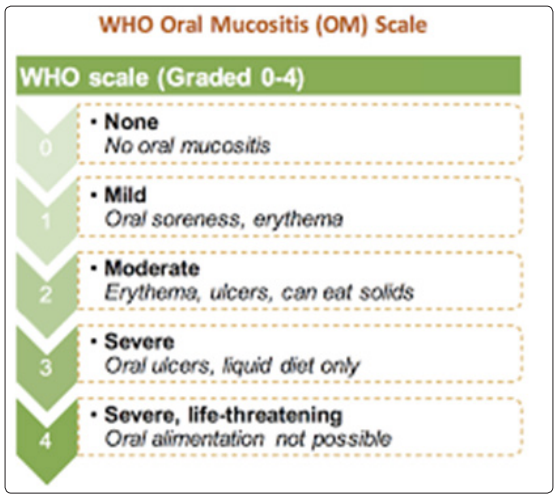

Figure 2: WHO,Handbook for reporting results of cancer treatment; Geneva 1979

In this context, the adoption of a therapy useful to prevent, limit and treat oral mucositis is of central importance. Although a great number of therapeutic options have been developed and evaluated in recent years, research remains scanty and thus proven preventative and treatment approaches to help reduce the severity of OM are still limited [9]. In our study we have considered Orasol plus®: is a nutritional supplement, swallowable solution, with Lapacho (Tabebuia Avellanedae Lorentz ex Griseb.) and other herbal ingredients (Camellia Sinensis L Kuntze, Calendula Officinalis L, Malva Sylvestris L, Sisymbrium Officinale (L) Scop, Plantago Major L e Propoli) (Tab. 1) useful to support the defenses of the oropharyngeal mucosa. Lapacho promote the functionality defenses with anti-infiammatory, analgesic and antimicrobic action. Hyaluronic Acid prevents tissue damage caused by pharmacological stress and promote healing of the lesions in case of mucositis. Green Tea has antioxidant and antimicrobial activity. Calendula has antioxidant activity useful in case of lesions of the mucous of mouth and pharynx. Erisimo has emollient activity useful against disorders of the throat. Propolis has antibacterial proprieties. Marigold, mauve and plantain have emollient action and soothing effect on the oropharyngeal mucosa and tone of voice. Previous studies had shown the efficacy of this product in the prophylaxis of mucositis:

1) In a study conducted at the European Cancer Institute of Milan Orasol plus® has proven effective in preventing mucositis in hematological patients undergoing autologous transplantation [12].

2) In a phase II study conducted at the University of Florence Orasol plus® has proven effective in reducing the incidence and severity of mucositis in patients undergoing radiation therapy [13].

This supplement seemed particularly interesting to us as the substances contained in it have characteristics particularly indicated in the repair and protection of tissues: ability to spread a protective mucilaginous veil on the mucosa, soothing, anti-inflammatory, analgesic, antimicrobial and antifungal properties. In addition, this supplement can be swallowed with an extension of the protective activity also on the esophageal mucosa which, like the oral one, can present mucosal pictures. As it is not alcoholic, this supplement can be used safely even in children.

Table 1: Orasol Plus® nutritional supplement formulation

Average contents	Per 30 ml
E. F. Lapacho, Tabebuia Avellanedae Lorentz ex Griseb- bark	3 gr
E. D. Calendula officinalis L. capolini	0,3 gr
E. D. Gree Tea leaves Camellia Sinensis L. Kuntze	0,3 gr
E. D. Erisimo Sysimbrium Officinale (L.) Scop. top of the flowers	0,2 gr
E. D. Malva Malva Sylvestris L. , leaves	180 mg
E. D. Piantaggine Plantago Mayor L. herb and flowers	40 mg
Sodio Ialuronato	20 mg
E. D. Propoli	100 mg

Materials And Methods

We carried out a study to evaluate the progress of oral mucositis in a group of 15 breast cancer patients undergoing treatment with chemotherapy and/or target therapy. A group of patients between the ages of 38 and 65 receiving chemotherapy for breast cancer has been observed. 3 of 15 patients showed metastatic lesions at the beginning of treatment and 2 patients was in second line of chemotherapy. The PS was 80-90. All the chemotherapy drugs used in standard dosage (mg/m^2), even in their various associations, had a strong correlation for the onset of oral mucositis.

Chemotherapy treatments:

3 patients: Epirubicin + Cyclophosphamide (4 cycles: 1 cycle every 21 days) + Paclitaxel (4 cycles: 1 cycle every 21 days).
2 patients: Docetaxel or Paclitaxel (6 cycles: 1 cycle every 21 days)

+ Pertuzumab and Trastuzumab (6 cycles: 1 cycles every 15 days).
2 patients: Epirubicin + Cyclophosphamide (4 cycles: 1 cycle every 21 days) + 12 Paclitaxel (12 cycles: 1 cycle every week).
1 patient: 4 cycles (1 cycle every 21 days) of Epirubicin + Cyclophosphamide
1 patient: 4 cycles (1 cycle every 21 days) of Taxol + Cyclophosphamide
1 patient: Enantone (every 28 days) + Everolimus (per os, every day) + Exemestane (per os, every day)
1 patient: Adriamicyn + Cyclophosphamide (4 cycles: 1 cycle every 21 days) + paclitaxel (12 cycles: 1 cycle every week) + Herceptin (every 15 days for 1 year)
1 patient: 4 cycles (1 cycle every 21 day) of Nab-paclitaxel.
1 patient: Cisplatin (4 cycles: 1 cycle every 21 days) + Capecitabine **(4 cycles:** 1 cycle per os, every day for 14 days) + Vinorelbine (4 **cycles:** 1 cycle every 21 days)
1 patient: 12 cycles (1 cycle every 15 days) of Trastuzumab.
1 patient: 12 cycles (1 cycle every 15 days) of Palbociclib + Letrozole (per os every day) + Enantone (every 28 days).

At baseline (T0) (Tab.2) 11 of the patients (73.3% of the sample) included in the study had grade 2 oral mucositis on the WHO scale and 4 (26, 7 %) had no mucositis but Orasol Plus® was administered with the start of chemotherapy for preventive purposes.

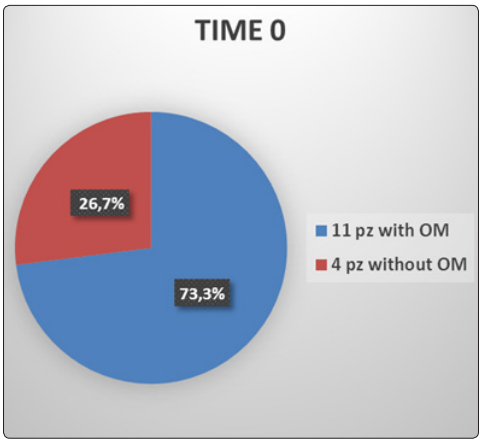

Table 2: Time 0 -Start treatment of chemotherapy and administration Orasol Plus® (OM: oral mucositis)

Results

None of the patients had to stop chemotherapy because of oral mucositis.
In the 11 patients who presented with mucositis at the beginning of the observation, the administration of Orasol Plus® resulted in complete remission of mucositis during the first cycle of chemotherapy in 5 patients (33%), remission that remained so until the end of the chemotherapy itself. In 3 patients (20%) there was a great improvement in symptoms until a disappearance of the mucosal picture at the end of chemotherapy. In 3 patients (20%) Orasol Plus® was used only as needed end for short time because the mucositis passed quickly.

In the 4 patients in whom the administration of Orasol Plus® was given prophylactically with the start of chemotherapy, there were no manifestations of oral mucositis during the entire duration of the chemotherapy itself. (Tab.3)

None of the patients resorted to antalgic drugs, for the control of mucosal pain, during chemotherapy.

In no case did side effects occur due to taking Orasol Plus®.

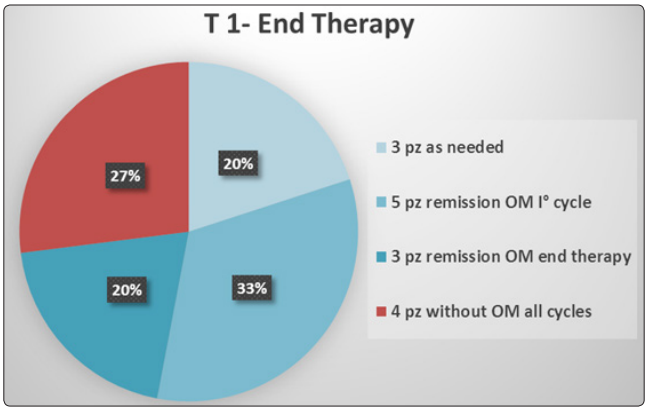

Table 3: T1 End of chemotherapy and/or target therapy treatment (OM: oral mucositis)

Discussion

Oral mucositis, in patients with breast cancer, is the most common complication of chemotherapy and is perhaps among the most disabling aspects of the toxicity of the chemotherapy drugs themselves.

The establishment of a picture of oral mucositis strongly influences the patient's quality of life for pain, for the inability to eat and for the psychological-relational effect.

The oral mucositis treatment protocols are not standardized and are often entrusted to personal, and therefore always different, experiences of each oncology department with encouraging but difficult direct correlation results.

The results obtained in our study with the administration of Orasol Plus® are encouraging, both from the point of view of the remission of the pictures of oral mucositis, and from the point of view of prevention. In fact, Orasol Plus® has proved to be an effective and manageable product for treatment and prevention of OM during chemotherapy.

To the characteristics of the individual components are added those of extreme handling of the product which can be swallowed without fear of significant side effects. The swallowing of the product, in addition to presenting the benefits of an extension of the surface of contact with the protection, therefore, also of the esophageal mucosa, also poses favorably for a possible enhancement of the effects given by the general absorption, at the gastrointestinal level, of the components. Furthermore, being a non-alcoholic mouthwash, Orasol Plus® can be used safely throughout the period of chemotherapy treatment as opposed to alcoholic mouthwashes that can only be used in the preventive phase of oral mucositis Regarding efficacy, in 33% of patients who had mucositis at the start of treatment there was complete remission of mucositis already in the first cycle of chemotherapy, remission that remained so until the end of the chemotherapy itself.

In 20% of patients the OM was severely attenuated during chemotherapy and completely ceased at the end of the chemotherapy treatment itself which, however, never had to be stopped. In another 20% of cases, patients with oral mucositis saw the symptoms of mucositis disappear concurrently with the administration of Orasol Plus®, so they arbitrarily decided to use it as needed.

Conclusions

The data of our study depose for the effectiveness of Orasol plus® in treatment of oral mucositis, in patients undergoing chemotherapy for breast cancer.

In particular, the sample that stopped autonomously the continuous administration of the mouthwash and used it as needed, showed a direct correlation between the administration of Orasol Plus® and the remission of oral mucositis.Orasol Plus® is an easy, safe and effective approach t for the treatment and prevention of OM during chemotherapy. Data from our study are encouraging and they need to be confirmed by larger study in order to insert Orasol Plus® in a standardized pathway in the treatment of oral mucositis during chemotherapy.

Acknowledgement

A special thanks to Roberto Galante and Fabrizio Mira of GamFarma for the help given to us.

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