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PRESCRIÇÃO E USO DE METRONIDAZOL PARA  
CONTROLE DO ODOR EM FERIDAS NEOPLÁSICAS

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## ORIGINAL ARTICLE

**PRESCRIPTION AND USE OF METRONIDAZOLE FOR THE CONTROL OF ODOR IN NEOPLASTIC WOUNDS**

Nauã Rodrigues de Souza<sup>1</sup>, Maria Theresa Camilo de Lima<sup>2</sup>, Rayanne Paulyne da Silva Batista<sup>3</sup>, Aline Milany da Silva Santos<sup>4</sup>, Magaly Bushatsky<sup>5</sup>, Isabel Cristina Ramos Vieira Santos<sup>6</sup>

**ABSTRACT**

**Objective:** To check aspects related to the prescription, preparation and administration of metronidazole for the control of odor in neoplastic wounds.

**Methodology:** Cross-sectional study with 80 health professionals from five reference hospitals in oncology in Recife-PE, between August and October 2017. The following variables were analyzed: professional characterization, criteria for prescription, presentation, dilution, application, frequency and care in the application. Mean and standard deviation were calculated for obtaining the discrete rational variables, and chi-square test with Yates correction was used for dichotomous categorical variables.

**Results:** The nurses had little professional experience (1-3 years), less specialization compared to physicians, but had greater expertise in palliative care. Regarding the prescription and use of the product, 14 (53.8%) professionals used alternative and empirical prescriptions, with maceration of tablets, and five (19.3%) used injectable solution.

**Conclusion:** According to the results obtained, there are few studies on the subject and protocols based on scientific evidence should be constructed.


**DESCRIPTORS:** Oncological nursing; Wounds and Injuries; Anti-Infective agents; Metronidazole; Odorants.


**HOW TO REFERENCE THIS ARTICLE:**


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## ARTIGO ORIGINAL / ARTÍCULO ORIGINAL

**PRESCRIÇÃO E USO DE METRONIDAZOL PARA CONTROLE DO ODOR EM FERIDAS NEOPLÁSICAS****RESUMO**

**Objetivo:** verificar os aspectos relacionados à prescrição, preparo e administração do metronidazol para controle do odor em feridas neoplásicas.

**Metodologia:** estudo transversal, com 80 profissionais de saúde de cinco hospitais referência em oncologia em Recife-PE, entre agosto e outubro de 2017. Foram analisadas as variáveis: caracterização profissional, critérios para prescrição, apresentação, diluição, aplicação, frequência e cuidados na aplicação. Calculou-se média e desvio padrão para as variáveis racionais discretas, e para categóricas dicotômicas, teste qui-quadrado com correção de Yates.

**Resultados:** os enfermeiros caracterizaram-se pelo pouco tempo de experiência (1-3 anos), menor frequência de especialização comparados aos médicos, porém maior frequência de atualização em cuidados paliativos. Quanto à prescrição e utilização do produto, observou-se prescrições alternativas e empíricas, com maceração de comprimidos 14 (53,8%) ou solução injetável em cinco (19,3%).

**Conclusão:** resultados evidenciam a escassa literatura sobre a temática e levantam a necessidade de construção de protocolos fundamentados em evidências científicas.

**DESCRIPTORIOS:** Enfermagem oncológica; Ferimentos e Lesões; Anti-Infecciosos; Metronidazol; Odorantes.

**ASPECTOS ASOCIADOS A LA PRESCRIPCIÓN Y USO DE METRONIDAZOL EN EL CONTROL DEL OLOR EN HERIDAS NEOPLÁSICAS****RESUMEN:**

**Objetivo:** verificar los aspectos asociados a la prescripción, preparación y administración del metronidazol para control del olor en heridas neoplásicas.

**Metodología:** estudio transversal, con 80 profesionales de salud de cinco hospitales referencia en oncología en Recife, PE, entre agosto y octubre de 2017. Se analizaron las variables: caracterización profesional, criterios para prescripción, presentación, dilución, aplicación, frecuencia y cuidados en la aplicación. Se calcularon el promedio y la desviación típica para las variables racionales discretas, y para categóricas dicotómicas, test chi cuadrado con corrección de Yates.

**Resultados:** los enfermeros se caracterizaron por el poco tiempo de experiencia (1-3 años), menor frecuencia de especialización en comparación con los médicos, pero con más frecuencia de actualización en cuidados paliativos. Acerca de la prescripción y uso del producto, se observaron prescripciones alternativas y empíricas, con maceración de pastillas 14 (53,8%) o solución inyectable en cinco (19,3%).

**Conclusión:** resultados evidencian la escasa literatura sobre la temática y apuntan a la necesidad de construcción de protocolos basados en evidencias científicas.

**DESCRIPTORIOS:** Enfermería oncológica; Heridas y lesiones; Anti-Infecciosos; Metronidazol; Odorantes.

## INTRODUCTION

Neoplastic wounds are defined as a tumor infiltration or skin metastasis that may involve blood and afferent lymphatic vessels and are more common in breast cancer patients, despite its also high incidence in patients with head and neck cancer<sup>(1,2)</sup>.

The prevalence of these wounds is unknown due to the lack of population-based studies. However, it is estimated that neoplastic wounds affect 5% of patients with cancer in advance stages and 10% of patients with metastasis, with an average life expectancy of 6 to 12 months<sup>(2,3)</sup>.

Neoplastic wounds produce various physical symptoms such as foul smell, pain, pruritus, exudate and bleeding. Among these, odor, often described by patients, family members and other caregivers including nurses, as similar to the foul odor of litterboxes, rotten meat and decomposing flesh, is attributed to the proliferation of aerobic and anaerobic bacteria. The latter thrive in necrotic, oxygen-free tissue found in the bed of these wounds<sup>(4)</sup> and contribute substantially to low self-esteem, social isolation and lower quality of life.

Interventions aimed at reducing suffering caused by the odor, among other physical and psychological symptoms, are part of palliative care and aim at ensuring the best possible quality of life, based on the best evidence, balancing care objectives with the available resources<sup>(4)</sup>.

Although odor is a symptom that greatly contributes to social isolation due to stigma, there is scarce evidence on the ideal topical therapy for its control. Several topical products have been used, such as metronidazole, an antimicrobial agent derived from imidazole that can interact with the DNA molecules of the microorganism, preventing the synthesis of enzymes essential for the survival of the pathogen and thus indirectly controlling the odor<sup>(5)</sup>.

In Brazil, the use of metronidazole 0.8% gel in neoplastic wounds has been recommended because of its excellent results in odor control, without the induction of the side effects of systemic therapy. In cases where metronidazole gel is not available, the proposed alternative has been the topical use of macerated tablets or the pure injectable solution<sup>(6)</sup>. Nonetheless, some review studies demonstrate the lack of robust evidence to recommend topical use, because of the small sample sizes and randomization methods used, generating uncertainties about the validity of the results<sup>(5-7)</sup>, as well as problems related to special prescription requirements that may influence its use<sup>(8)</sup>.

Moreover, there was no consensus on the recommended presentation of the drug or method of drug use based on the comparison of effectiveness in cost-effectiveness analyzes. Therefore, the institutions prepare different topical formulations of metronidazole for patients with neoplastic wounds<sup>(9)</sup>. More scientific evidence in Brazil is needed for the elaboration of protocols that systematize the care provided to patients with neoplastic wounds.

Since it is important to know how the healthcare institutions are using metronidazole to control the odor of neoplastic wounds, in order to add evidence and contribute to the standardization of clinical practices and the construction of care protocols, the present study aimed to verify aspects related to the prescription and use of metronidazole for odor control in neoplastic wounds.

## METHOD

Cross-sectional, descriptive study with a quantitative approach developed in five reference hospitals in oncology treatment located in the city of Recife. The population consisted of 80 participants, as follows: 51 nurses and 29 physicians.

The inclusion criteria were health professionals, physicians and nurses who performed their duties in clinical oncology units of the hospitals that participated in the study. The subjects who were on vacation or leave during the collection period, as well as those who worked in the night shift were excluded.

Data was collected in the August- October 2017 period, through the administration of two questionnaires elaborated by the researchers, specifically for each professional category, containing the variables of interest: professional characterization; knowledge about odor control; prescription criteria, form of presentation, form of application, frequency and care observed in the application.

Data were tabulated through SPSS version 21 and analyzed through descriptive statistics, with simple and absolute frequency distribution. Mean ( $\bar{x}$ ), median ( $\tilde{x}$ ) and standard deviation ( $\alpha$ ) were calculated for obtaining the discrete rational variables, while for dichotomous categorical variables the chi-square test ( $\chi^2$ ) with Yates continuity correction was used, and a level of significance of 5% ( $p < 0.05$ ).

This study complied with the ethical standards in the conduct of research, and the research was approved by the Research Ethics Committee of the Hospital Complex of Universidade de Pernambuco (HUOC/PROCAPE), under protocol no 2,332,974.

## RESULTS

Table 1 presents the characterization of the professionals who participated in the research. There was a higher percentage of nurses 23 (45.1%) aged between 31-40 years ( $\bar{x}$ : 34.5;  $\alpha$ : 6.9;  $\tilde{x}$ : 34.0). A higher percentage of physicians in the same age group: 18 (62.1%) ( $\bar{x}$ : 34.9;  $\alpha$ : 6.4;  $\tilde{x}$ : 34.0) was observed.

Table 1 – Sample characterization. Recife, PE, Brazil, 2017

Variable	Nurses (%)	Physicians (%)
Age range		
20-30 years	19 (37.3)	8 (27.6)
31-40 years	23 (45.1)	18 (62.1)
41 + years	9 (17.6)	3 (10.3)
Length of professional experience (in years)		
1-3 years	30 (58.8)	16 (55.2)
3-6 years	18 (35.3)	5 (17.2)
6 $\geq$ years	3 (5.9)	8 (27.6)
Specialization in Oncology		
Yes	22 (43.1)	23 (79.3)
No	29 (56.9)	6 (20.7)
Refresher courses on palliative care		
Yes	27 (52.9)	14 (48.3)
No	24 (47.1)	15 (51.7)
Odor control		
Yes	28 (54.9)	10 (34.5)
No	23 (45.1)	19 (65.5)

As for the length of professional experience in each profession, 30 nurses (58.8%) ( $\bar{x}$ : 3.3;  $\alpha$ : 2.3;  $\tilde{x}$ : 3.0) and 16 (55.2%) physicians ( $\bar{x}$ : 5.1;  $\alpha$ : 5.0;  $\tilde{x}$ : 2.0) had one to three years of experience, and most of the latter 23 (79.3%) had specialization in oncology, unlike the nurses, and this difference was statistically significant.

Asked whether the "Odor Control" theme was addressed during refresher courses, 28 (54.9%) nurses said yes.

Figure 1 shows the products for odor control of neoplastic lesions that nurses and physicians knew. Metronidazole was most frequently reported by both groups 41 (80.4%) and 24 (82.7%), respectively, followed by activated charcoal 21 (41.2%) and seven (24.1%); and silver sulfadiazine 18 (35.3%) and three (10.3%).

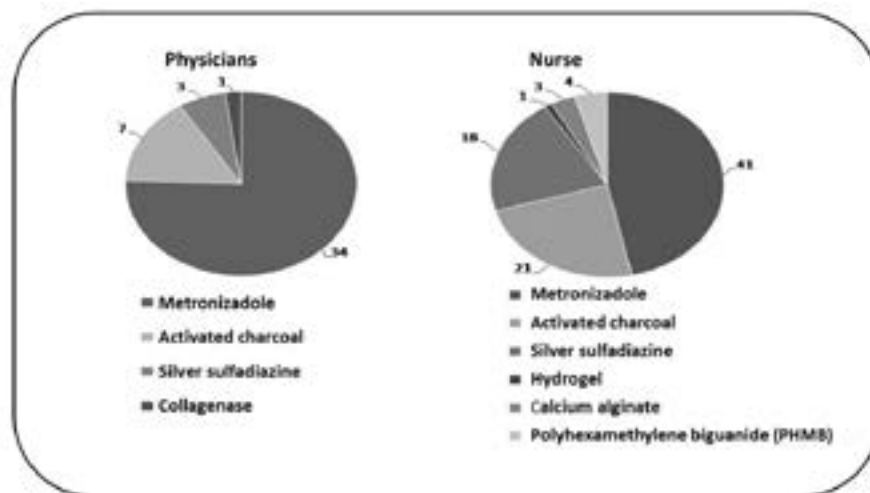


Figure 1 - Knowledge of odor control products by nurses and physicians. Recife, PE, Brazil, 2017

Table 2 shows the criteria for prescription of metronidazole and drug use. Most physicians: 12 (15%) prescribe the antimicrobial according to the availability of the product. The most prescribed form of presentation was macerated tablets: 14 (53.8%).

Table 2 - Criteria for prescription and use of metronidazole. Recife, PE, Brazil, 2017 (continues)

Variable	n (%)
Criteria for prescription	
Product availability	12 (15)
Clinical evaluation	11 (13.8)
Indication communicated by nurses	2 (2.5)
Form of presentation prescribed	
Macerated tablets	14 (53.8)
Gel	7 (26.9)
Injectable solution	5 (19.3)

Dilution of the injectable solution	
10mg/100ml	2 (40)
500mg/100ml	2 (40)
15mg/100ml	1 (20)

Table 3 shows the results obtained from the analysis of the use of metronidazole by nurses. It was found that the drug is directly applied to the wound bed, as referred by 20 (43.5%) nurses, while the same percentage of professionals applies the product with the aid of moist gauze. The frequency of use of the drug most commonly reported was 2 times a day by 21 (51.2%) nurses, while 19 (46.3%) of them reported application once a day, according to medical prescription. Regarding the care procedures performed during the administration of the drug, 17 (34.7%) performed wound cleaning with warm saline before the application of metronidazole.

Table 3 - Method of use of metronidazole by nurses. Recife, PE, Brazil, 2017

Variable	N (%)
Form of application	
Drug applied directly to the wound bed	20 (43.5)
In moist gauze	20(43.5)
Irrigation of wound	6 (13)
Frequency of applications	
1 time a day	19 (46.3)
2 times a day	21 (51.2)
Every 2 days	1 (2.4)
Care observed in the application	
Perform wound cleaning with warm saline before application of metronidazole	17 (34.7)
After application of metronidazole, occlude with dry gauze	12 (24.5)
Use metronidazole associated with other products/dressings	12 (24.5)
Perform escharotomy before application of the antimicrobial agent in the presence of hardened necrotic tissue in a wound	2 (4.1)

## DISCUSSION

Oncology is a complex area, and, thus, health professionals must have critical thinking skills and scientific basis to understand the circumstances and particularities of each patient and their clinical situation. The length of professional experience has a direct impact on knowledge and expertise. However, training and refresher courses about technological and scientific innovations are essential to assist these professionals in the decision-making process and the management of various situations, to improve the quality of care<sup>(10)</sup>.



Regarding the nurses, the length of professional experience was lower than the one found in a study on palliative care carried out in the Southeastern region of Brazil<sup>(11)</sup>. Although there is no consensus about the optimal amount of time needed to achieve nursing expertise, the number of years of professional experience are an important factor in the quality of care provided. However, it should be noted that although this is a necessary condition, it is not sufficient, since years of experience can provide fluidity and flexibility, but not the critical thinking required by expertise<sup>(12)</sup>.

Moreover, physicians had greater specialization in oncology than nurses, and this difference was statistically significant. However, the nurses had undergone refresher courses in palliative care in which the subject of odor control was more frequently addressed than physicians.

Knowledge of palliative care is essential for professionals dealing with patients who have neoplastic wounds, since cancer is difficult to cure. Thus, health care should be focused on the control of symptoms such as odor, comfort, prevention of injuries and disabilities, promotion of independence and autonomy, activation of emotional and social resources to cope with the process of illness and death, and support and guidance to family and caregivers<sup>(13)</sup>.

Some studies highlighted the limited knowledge in oncology in undergraduate courses and the existing gaps, which makes it difficult for the professionals to deliver care targeted to these patients<sup>(14,15)</sup>. On the other hand, the fact that most of the nurses who participated in this study had taken refresher courses in palliative care exemplifies the need perceived by them to be better qualified to meet the demands.

The expected increase in survival of cancer patients requires more attention to the training of nurses in oncology. Nursing knowledge will enable professionals to justify their actions or even avoid the use of unsafe practices. This implies the additional challenge of continuous professional development, since nursing knowledge is constantly evolving, and the expectation is to rely on the best evidence to provide the most appropriate care for each patient<sup>(16)</sup>.

Several authors focused on the need for scientific knowledge in the care of patients with wounds, to ensure the delivery of high quality care, since the rapid advances in the development of products and dressings used in health care practices in this area has considerably changed the practices of care of neoplastic wounds, and led to the establishment of new professional recommendations<sup>(11,17)</sup>.

According to the literature, the scientific knowledge of the principles of palliative care is essential for the process of caring for cancer patients with wounds. In fact, since the prospects of cure of these wounds is remote, palliative care focuses on two crucial aspects: physical and psychological. However, neoplastic wounds cause a wide variety of physical symptoms, much greater than other types of wounds. Therefore, care of physical symptoms is essential to improve the patients' self-esteem and restore their dignity<sup>(18)</sup>.

Several techniques and products have been developed to improve the treatment of neoplastic wounds. However, the specific topical therapy is still controversial. Metronidazole is one of the main products used in such treatment, as it is an antibiotic with anti-inflammatory properties and suppresses cells that mediate the immune system. The literature has demonstrated its odor-reducing effect from the first twenty-four hours of use of the product, which lasts for at least two weeks thereafter<sup>(19)</sup>. This may have justified the greater frequency of responses from doctors and nurses when asked about known odor control products.

Some studies recommend the application of metronidazole gel at 0.75 or 0.8% in the wound bed. However, since in Brazil there are no ready-to-use formulations of this topical 0.8% drug, its manipulation is necessary. This fact may have influenced the criteria adopted by prescribers, which in this study were based first on the availability of the product and then on clinical evaluation. It may also be related to the prescribed form, often macerated



tablets. This form of use meets the recommendations of the Brazilian Ministry of Health<sup>(5,8,9)</sup>.

Regarding the prescribed form of the injectable solution, the responses varied, ranging from dilutions of 10 mg/100 ml to 500 mg/100 ml of saline. This practice is consistent with clinical recommendations for the use of an injectable solution that should be administered pure, undiluted<sup>(6)</sup>.

Regarding the mode of use, most of the nurses who participated in the study reported applying metronidazole directly to the wound bed or through moist gauze, twice a day, after cleaning with a warm saline solution of 0.9%. According to a study on the current practice of wound odor management, with 1,444 professionals from 36 countries, there is not a standard protocol for the mode, dose and frequency of application of metronidazole. Thus, the institution prepare their topical formulations in different ways, making it impossible to determine the amount of the drug used in these practices. Commercial preparations range from 0.75% to 0.8%. However, from a clinical point of view, the amount of preparation that should be used in a wound to obtain the minimum concentration of the drug required to produce the desired therapeutic effect cannot be clearly determined<sup>(20)</sup>.

Despite the limitations related to the cross-sectional methodology used, the results of this study are important, in that they highlight issues that should be considered by hospital managers and training institutions, as well as by professionals concerned with improving care for the population affected by this pathology.

## CONCLUSION

The nursing professionals responsible for the prescription and application of metronidazole for odor control in neoplastic wounds had little experience and low qualification in the field of oncology, though they were more skilled in palliative care aspects.

Regarding the prescription and application of the product, the results demonstrated that it is primarily associated to the availability of the product and is prescribed alternately and empirically through tablet maceration or dilution of injectable solution.

The scarce literature on the subject suggests the need to build protocols based on scientific evidence, in order to assure that the application of drugs in patients with neoplastic wounds is safe and effective.

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Drafting the work or revising it critically for important intellectual content - MB

Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved - ICRVS

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