




THERAPEUTIC MANAGEMENT OF NON-PUERPERAL MASTITIS

MANEJO TERAPÊUTICO DA MASTITE NÃO PUERPERAL

MANEJO TERAPÉUTICO DE LA MASTITIS NO PUERPERAL

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ABSTRACT

Non-puerperal mastitis (NPM) is a benign, heterogeneous, and uncommon inflammatory breast condition, characterized by its occurrence outside the gestational-puerperal cycle, chronic course, and high recurrence rate, significantly impacting quality of life. The most prevalent clinical forms are Periductal Mastitis (PMD), strongly associated with smoking and nipple inversion, and Granulomatous Lobular Mastitis (GLM), linked to autoimmune disorders and hyperprolactinemia. Due to its similarity to breast carcinoma on imaging, histopathological biopsy is considered the gold standard for differential diagnosis and exclusion of malignancy. Therapeutic management, given the absence of a universal protocol, should be multimodal and individualized. Strategies range from conservative treatment (corticosteroids for GLM and antibiotics for PMD) to surgical interventions, indicated in cases of persistent abscesses and recurrence, always aiming to reduce the high recurrence rates. Systemic risk factors (such as diabetes and hypertension), as well as immunometabolic indicators (e.g., elevated fibrinogen and reduced HDL-C), also influence prognosis and recurrence. Thus, the present study aimed to analyze recent scientific evidence on NPM management strategies, highlighting the need for a multidisciplinary approach and strict control of risk factors to ensure favorable outcomes and preservation of breast health.

Keywords: Non-puerperal Mastitis. Granulomatous Mastitis. Therapeutics. Recurrence.

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RESUMO

A Mastite Não Puerperal (MNP) é uma afecção inflamatória benigna da mama, heterogênea e incomum, caracterizada por sua ocorrência fora do ciclo gravídico-puerperal, evolução crônica e alta frequência de recorrência, impactando significativamente a qualidade de vida. As formas clínicas mais prevalentes são a Mastite Periductal (MPD), fortemente associada ao tabagismo e inversão mamilar, e a Mastite Lobular Granulomatosa (MLG), correlacionada com distúrbios autoimunes e hiperprolactinemia. Devido à semelhança com o carcinoma mamário em exames de imagem, a biópsia histopatológica consolida-se como o padrão-ouro para o diagnóstico diferencial e exclusão de malignidade. O manejo terapêutico, dada a ausência de um protocolo universal, deve ser multimodal e individualizado. As estratégias variam entre o tratamento conservador (corticosteroides para MLG e antibioticoterapia para MPD) e intervenções cirúrgicas, indicadas em casos de abscessos persistentes e recidiva, buscando sempre a redução das elevadas taxas de recorrência. Fatores de risco sistêmicos (como diabetes e hipertensão), além de indicadores imunometabólicos (ex: fibrinogênio elevado e redução de HDL-C), também influenciam o prognóstico e a recidiva. Dessa forma, o presente estudo objetivou analisar as evidências científicas recentes sobre as estratégias de manejo da MNP, reforçando a necessidade de uma abordagem multidisciplinar e do controle rigoroso dos fatores de risco para garantir desfechos favoráveis e a preservação da saúde mamária.

Palavras-chave: Mastite Não Puerperal. Mastite Granulomatosa. Terapêutica. Recorrência.

RESUMEN

La mastitis no puerperal (MNP) es una afección inflamatoria benigna de la mama, heterogénea y poco común, caracterizada por su aparición fuera del ciclo gestacional-puerperal, evolución crónica y alta frecuencia de recurrencia, impactando significativamente la calidad de vida. Las formas clínicas más prevalentes son la Mastitis Periductal (MPD), fuertemente asociada al tabaquismo y la inversión del pezón, y la Mastitis Lobular Granulomatosa (MLG), relacionada con trastornos autoinmunes e hiperprolactinemia. Debido a la similitud con el carcinoma mamario en estudios de imagen, la biopsia histopatológica se consolida como el estándar de oro para el diagnóstico diferencial y la exclusión de malignidad. El manejo terapéutico, dada la ausencia de un protocolo universal, debe ser multimodal e individualizado. Las estrategias varían entre el tratamiento conservador (corticosteroides para MLG y antibioticoterapia para MPD) y las intervenciones quirúrgicas, indicadas en casos de abscesos persistentes y recurrencia, buscando siempre reducir las elevadas tasas de recurrencia. Factores de riesgo sistémicos (como diabetes e hipertensión), además de indicadores inmunometabólicos (p. ej., fibrinógeno elevado y reducción de HDL-C), también influyen en el pronóstico y la recurrencia. De este modo, el presente estudio tuvo como objetivo analizar la evidencia científica reciente sobre las estrategias de manejo de la MNP, reforzando la necesidad de un enfoque multidisciplinario y del control riguroso de los factores de riesgo para garantizar resultados favorables y la preservación de la salud mamaria.

Palabras clave: Mastitis No Puerperal. Mastitis Granulomatosa. Terapêutica. Recurrencia.



1 INTRODUCTION

NPM non-puerperal mastitis is a benign inflammatory condition of the breast that manifests outside the gestational and lactation periods, and is considered an uncommon condition among breast diseases. Despite its non-malignant nature, it is a pathology of clinical relevance due to its often prolonged evolution, recurrent character, and significant impact on the quality of life of patients (Li et al., 2024; Tang et al., 2024). NPM is estimated to account for a small portion of benign breast diseases, affecting mainly young and middle-aged women, with a higher incidence between the third and fourth decades of life (Tang et al., 2024).

NPM encompasses different forms of breast inflammation, including periductal mastitis and granulomatous lobular mastitis, which are considered the most frequently reported subtypes in the literature. These conditions have similar clinical manifestations, including breast pain, erythema, edema, and the presence of palpable nodules, which can progress to abscesses, ulcerations, or fistula formation in more advanced stages of the disease (Shi et al., 2022; Li et al., 2024). Due to these characteristics, the clinical course of NPM is usually prolonged and, in many cases, marked by episodes of recurrence.

Although several studies have investigated the mechanisms involved in its occurrence, the etiology of non-puerperal mastitis has not yet been completely established. Evidence suggests that multiple factors may be associated with the development of the disease, including hormonal changes, immune factors, smoking, metabolic disorders, and possible infectious agents (Shi et al., 2022). In addition, some subtypes have specific risk factors, reinforcing the hypothesis that NPM has a multifactorial nature and distinct pathophysiological mechanisms among its different clinical forms.

Another aspect that makes this condition particularly challenging is the similarity of its clinical and radiological manifestations with those observed in breast cancer. Inflammatory nodules, skin changes, and nipple retraction may give rise to suspicion of malignancy, which often requires further investigation to confirm the diagnosis. In this context, imaging methods such as ultrasound, mammography, and magnetic resonance imaging can aid in the initial evaluation, but histopathological examination remains the most reliable method to establish the definitive diagnosis (Li et al., 2024; Tang et al., 2024).



Prevention of non-puerperal mastitis involves controlling for modifiable risk factors. Smoking cessation, appropriate management of hormonal disorders, and follow-up of patients with hyperprolactinemia are important measures to reduce the risk of developing and recurrence of the disease. Health education plays a fundamental role in this context, allowing patients to recognize early signs and symptoms suggestive of breast inflammation and seek medical assistance in a timely manner (LIU et al., 2025; JIAO et al., 2023).

Considering the diagnostic and therapeutic complexity of non-puerperal mastitis and the absence of universally established therapeutic protocols, the present study aims to analyze recent scientific evidence on therapeutic management strategies for non-puerperal mastitis, highlighting its main etiological factors, diagnostic methods, and therapeutic approaches.

In view of this scenario, it is essential to broaden the understanding of the clinical characteristics, associated factors, and possible mechanisms involved in non-puerperal mastitis. The advancement of research in this area can contribute to the improvement of diagnostic and therapeutic strategies, favoring more effective management and reducing the impact of the disease on the physical and psychological health of patients.

2 METHODOLOGY

The present investigation is characterized as a narrative literature review, developed with the objective of synthesizing and analyzing the most recent scientific evidence related to the Therapeutic Management of Non-Puerperal Mastitis. The search was carried out in the PubMed database, using the descriptors "Non-Puerperal Mastitis" and "Treatment", combined using the Boolean operators AND and OR, according to the terminology of Medical Subject Headings (MeSH). Articles published in the last five years, available in full and written in Portuguese or English, that directly addressed the topic, were included. Studies that did not have a direct relationship with the central theme, duplicate publications, narrative reviews with low methodological rigor, and articles not indexed in the database used were excluded. The selection of studies was conducted in two stages: screening of titles and abstracts, followed by the evaluation of full texts to confirm relevance. The information extracted was organized in a descriptive way.



3 RESULTS AND DISCUSSION

3.1 ETIOPATHOGENESIS AND CLINICAL DIFFERENTIATION

NPM presents distinct profiles according to its pathological classification. Periductal mastitis (PDM) occurs predominantly in young women, affecting the subareolar ducts, and smoking is the main risk factor, possibly due to the direct damage caused by toxins to the mammary ducts (Jiao et al., 2023; Liu et al., 2025). In contrast, granulomatous lobular mastitis (FFM) affects the terminal lobules and is associated with factors such as hyperprolactinemia, use of psychotropic medications, and obesity (Liu et al., 2025; Jiao et al., 2023). In adolescents, NPM is often associated with congenital nipple retraction and trauma, presenting a clinical course that requires cautious surgical intervention to preserve breast development (Tang et al., 2024).

3.2 SYSTEMIC, IMMUNOMETABOLIC AND PARTICULAR RISK FACTORS IN ADOLESCENTS

In addition to local clinical and morphological aspects, recent evidence highlights that NPM is deeply associated with systemic, metabolic, and mental health factors. An extensive meta-analysis identified that underlying comorbidities, such as diabetes, hypertension, and heart disease, substantially increase the risk of developing the pathology (LIU et al., 2025). In addition, mental health status also exerts a strong influence, with emotional problems and the use of psychotropic medications — which often induce hyperprolactinemia — and risk factors independent and significant (LIU et al., 2025). From a biochemical point of view, patients with NPM have an altered profile characterized by a reduction in high-density cholesterol (HDL-C) and an increase in lipoprotein(a) and serum glucose when compared to patients with benign breast masses, which suggests an intrinsic link between lipid metabolism and the chronic inflammatory pathogenesis of the disease (SHI et al., 2022).

On the other hand, the immunological and coagulation microenvironment is also decisive for the prognosis of the disease. Advanced predictive models based on machine learning have revealed that the combination of elevated fibrinogen (FIB) levels, the presence of bacterial infection, and the reduction in CD4+ T cell count are the most robust indicators for predicting MNP relapse (LI et al., 2025). Finally, the etiological particularities of the disease extend to specific demographic groups, such as adolescents, in whom recent breast trauma and congenital nipple retraction (inverted nipple), often added to



high prolactin levels, act as independent primary triggers for the manifestation of the disease (TANG et al., 2024). In this age group, NPM presents rapid abscess formation (TANG et al., 2024), but responds quite favorably to surgical intervention, presenting rapid recovery, good aesthetic results, and absence of recurrence in short-term follow-up (TANG et al., 2024).

3.3 DIAGNOSTIC IMAGING APPROACHES AND BIOMARKERS

Ultrasound and magnetic resonance imaging (MRI) are fundamental tools, although the differentiation between MPD and MLG can be subtle. In MPD, ductal ectasia and subareolar abscesses are often observed, whereas in FFM, MRI reveals non-mass-forming lesions with heterogeneous enhancement patterns (Jiao et al., 2023; Tang et al., 2024). Laboratory lab, FFM has higher levels of inflammatory markers, such as C-Reactive Protein (CRP) and neutrophil count, compared to MPD (Shi et al., 2022). Additionally, activation of the IL-6/JAK2/STAT3 signaling pathway has been implicated in the pathogenesis of MLG, suggesting a more robust cytokine-mediated inflammatory component (Shi et al., 2022).

3.4 DIFFERENTIAL DIAGNOSIS

The differential diagnosis of non-puerperal mastitis includes several inflammatory and neoplastic breast conditions. Among the main diagnostic hypotheses are inflammatory carcinoma of the breast, bacterial abscesses, mammary tuberculosis, and other granulomatous mastitis secondary to systemic diseases. The clinical similarity between these conditions, characterized by the presence of erythema, edema, nodules, and skin changes, may make it difficult to distinguish the diagnosis solely on the basis of clinical and imaging findings. Thus, histopathological analysis remains essential for diagnostic confirmation and exclusion of malignancy (JIAO et al., 2023; TANG et al., 2024).

3.5 THERAPEUTIC STRATEGIES: CONSERVATIVE VERSUS SURGICAL

The management of NPM requires a specific approach, considering the complexity of the disease and its different clinical and etiological presentations. In the case of LGM, conservative treatment often involves the use of corticosteroids, such as prednisone or methylprednisolone. These drugs have an important anti-inflammatory and



immunosuppressive effect, inhibiting the production of inflammatory cells and the formation of granulomas in the breast tissue, which contributes to the regression of the inflammatory process. (Zhou et al., 2021). Initial use for approximately two weeks is generally recommended, with gradual reduction of the dose after clinical improvement and disappearance of symptoms.

The period required for a complete response can vary considerably, between 1.5 and 20 months. Studies indicate that oral corticosteroids have efficacy rates greater than 70% of occurrences. However, the prolonged use of these drugs by the oral route may be associated with the development of systemic adverse effects resulting from metabolic action. Among the main effects reported are glucose intolerance, centripetal obesity and ulcerations of the gastrointestinal tract. (Zhou et al., 2021; Jiao et al., 2023). In the case of periductal mastitis (PDM), conservative treatment is mainly based on broad-spectrum antibiotic therapy, especially directed against anaerobic microorganisms associated with acute episodes of the disease.

This approach aims to control the infectious process and reduce the local inflammatory response. Despite contributing to the initial control of the disease, antibiotic therapy alone is not always sufficient for the definitive resolution of the condition, especially when abscesses or fistula formation persist. In these situations, procedures such as aspiration or drainage of the abscess can be performed in association with clinical treatment, aiming at better control of the infection and prevention of recurrences (Zhou et al., 2021; Jiao et al., 2023). In view of the limitations of conservative treatment, the surgical approach is a relevant therapeutic alternative, since it allows the removal of the affected tissue and the resolution of the pathological process. In general, surgery is indicated in situations such as persistent abscesses, fistula formation, disease recurrence, or failure of clinical treatment. However, it is recommended that the procedure be performed preferably outside the acute phase of the inflammatory process, because during this period tissue edema and intense inflammatory reaction can hinder the adequate delimitation of the lesion, increasing the risk of intraoperative and postoperative complications. (Jiao et al., 2023). In the management of breast abscesses, drainage is one of the main therapeutic approaches.

For small abscesses, ultrasound-guided needle aspiration can be performed, a minimally invasive technique that allows the removal of purulent content with less damage to the glandular tissue and better aesthetic results. In contrast, larger abscesses require



incision and surgical drainage. This intervention consists of opening the absceded cavity to evacuate the pus and clean the infected tissue, contributing to the improvement of the inflammatory condition and relief of symptoms. In more complex cases, especially when there is fistula formation or persistence of inflamed areas, it may be necessary to perform surgical excision, a procedure known as fistulectomy. This technique involves removing the fistulous tract and compromised mammary ducts, with the goal of completely eliminating diseased tissue and reducing the risk of recurrence. (Zhou et al., 2021; Tang et al., 2024). In general, surgical treatment has success rates greater than 80% of cases. However, like any invasive procedure, it may be associated with some complications, including delayed incision healing, aesthetic deformities of the breast, formation of residual fistulas, hematomas, persistent infection, and postoperative pain. In addition, structural changes in the subareolar region can result in nipple retraction, a condition that can contribute to stasis of secretions in the breast ducts and favor the recurrence of the disease. (Zhou et al., 2021). Therefore, the therapeutic strategy of NPM requires careful evaluation of the clinical presentation and response to available therapies. The continuous advancement of research in this area can contribute to the development of more effective diagnostic and therapeutic approaches. (Jiao et al., 2023).

4 THERAPEUTIC DECISION-MAKING AND MULTIPROFESSIONAL INTEGRATION

In view of the therapeutic options available for non-puerperal mastitis, the definition of the most appropriate approach for each case requires an approach adjusted to the patient's needs, based on the evaluation of the clinical picture, the evolution of the inflammatory process and the patient's response to initial interventions. Unlike mastitis associated with lactation, this condition often has a prolonged course and greater variability of clinical manifestations, characterized by recurrent episodes that require careful analysis to define the most appropriate strategies (LIU et al., 2025; ZHOU et al., 2021). In this context, therapeutic decision-making involves consideration of multiple clinical factors, including the presence of an active infectious process, abscess formation, extent of breast tissue involvement, and possible association with chronic inflammatory conditions. The integrated evaluation of these elements allows the establishment of progressive approaches, which can range from pharmacological treatment to surgical interventions in specific situations (ZHOU et al., 2021). In cases associated with suspected bacterial infection, antibiotic therapy may be indicated as an initial approach,



particularly when there are evident inflammatory signs or evidence of infectious involvement. Microbiological studies have identified an association between *Corynebacterium kroppenstedtii* infection and lobular granulomatous mastitis, suggesting that early identification of the pathogen and the use of specific antibiotics, preferably lipophilic ones such as doxycycline and clarithromycin, may improve cure rates (JIAO et al., 2023). For cases refractory to corticosteroids, methotrexate emerges as an immunomodulatory alternative, expanding therapeutic possibilities beyond hormone therapy (JIAO et al., 2023). In addition to the choice of drug or interventional therapy, systematic clinical follow-up is an essential component of the management of NPM. Continuous monitoring of the response to treatment makes it possible to assess the regression of the inflammatory process, identify early signs of recurrence, and make therapeutic adjustments when necessary.

This follow-up becomes particularly relevant in view of the possibility of prolonged evolution of the disease and the occurrence of recurrent episodes documented in the literature (TANG et al., 2024). In this scenario, the integrated performance of different health professionals plays a fundamental role in the conduct of care. Collaboration between specialists in mastology, radiology, pathology, surgery, and other areas contributes to a more comprehensive clinical evaluation and the definition of more precise therapeutic strategies. In addition to medical practice, nursing plays a fundamental role in the management of NPM, especially in the care of surgical wounds and fistulas, in guidance for infection prevention, in emotional support in the face of changes in body image, and in health education about modifiable risk factors.

The nurse also acts in the articulation of care, ensuring the continuity of follow-up and therapeutic adherence. The histopathological diagnosis, considered the gold standard for excluding neoplasms and differentiating between MPD and FFM, exemplifies the need for this integration, since the subtypes have distinct etiologies — smoking and ductal alterations in MPD, while FFM involves autoimmune components and hyperprolactinemia — and, consequently, require specific therapeutic approaches (JIAO et al., 2023). This collaborative approach favors not only the proper management of treatment, but also the continuous monitoring of the clinical evolution of patients.

Thus, the effective management of non-puerperal mastitis depends on the combination of careful clinical evaluation, therapeutic decision-making based on scientific evidence, and structured multidisciplinary follow-up. The integration of these elements



allows optimizing treatment results, reducing complications, and improving the prognosis of patients affected by this complex inflammatory breast condition.

4.1 FUTURE THERAPEUTIC PERSPECTIVES

Recent advances in research on non-puerperal mastitis have explored new therapeutic approaches aimed at controlling the inflammatory and immune response associated with the disease. Studies point to the possible use of immunomodulatory therapies and strategies based on the identification of inflammatory biomarkers, capable of predicting the recurrence of the disease and guiding more individualized therapeutic approaches. The incorporation of predictive models based on machine learning also emerges as a promising tool for risk stratification and optimization of the clinical follow-up of these patients (LI et al., 2025; SHI et al., 2022).

4.2 PROGNOSIS AND RECURRENCE MODELS

Recurrence is the biggest obstacle in the treatment of NPM, with rates that can vary considerably. Factors such as age, periareolar location of the lesion, and the duration of the disease are significant predictors of recurrence (Li et al., 2025). Machine learning models suggest that the surgical approach may offer a lower recurrence rate compared to conservative treatment alone in certain subgroups of patients, although surgical trauma may also act as an inflammatory trigger (Li et al., 2025; Zhou et al., 2021). Multimodal management, combining steroids and salvage surgery, appears to be the most effective strategy for recalcitrant cases (Zhou et al., 2021).

4.3 PSYCHOSOCIAL IMPACT OF NON-PUERPERAL MASTITIS

In addition to the clinical repercussions, non-puerperal mastitis can have a significant impact on the quality of life of patients. The presence of chronic pain, breast deformities resulting from abscesses or surgical interventions, and frequent recurrence of the disease can generate psychological distress, anxiety, and changes in body self-image. Recent studies indicate that the prolonged nature of the disease and the need for multiple therapeutic interventions contribute to increased emotional stress and reduced quality of life, reinforcing the importance of multidisciplinary follow-up and psychosocial support during treatment (LIU et al., 2025; TANG et al., 2024).



5 CONCLUSION

Non-puerperal mastitis (NPM) remains a significant clinical challenge, characterized by a chronic course and high propensity for recurrences that negatively impact patients' quality of life. The analysis of the current evidence demonstrates that the success of therapeutic management resides, fundamentally, in the precise distinction between the pathological subtypes, periductal mastitis (PDM) and granulomatous lobular mastitis (FFM), and in the rigorous exclusion of malignancies through histopathological examination.

Treatment strategies should evolve from purely empirical approaches to multimodal and individualized protocols. While FFM responds favorably to corticosteroid use, MPD requires control of modifiable risk factors, such as smoking, and surgical correction of ductal anomalies. In addition, the integration of new biomarkers, such as fibrinogen and lipid profiles, associated with prediction models based on machine learning, emerges as a promising tool to identify patients at higher risk of recurrence and adjust the intensity of clinical follow-up. In summary, the transition to multidisciplinary management, which combines optimized pharmacological therapy and precise surgical interventions, is essential to reduce treatment failure rates and ensure a favorable long-term prognosis.

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