Revisión de tema

Mastodynia

Mastalgia

Oscar Alejandro Bonilla Sepulveda[1] CvLAC, Diana Carolina Giraldo Santa[2]

Fecha correspondencia:
Recibido: octubre 15 de 2018.
Revisado: abril 22 de 2019.
Aceptado: abril 30 de 2019.

Forma de citar:
Bonilla Sepulveda OA, Giraldo Santa DC. Mastodynia. Rev. CES Med. 2019 33(2): 111-118.

DOI: http://dx.doi.org/10.21615/cesmedicina.33.2.4
ISSN 0120-8705
e-ISSN 2215-9177

Sobre los autores:

1. Specialist in Gynecology and Mastology. Professor PostGraduate Gynecology and Obstetrics UniRemington, Medellín, Colombia.

2. Medical surgeon, specialist in Epidemiology, Universidad de Caldas.

Abstract

Introduction: Mastalgia is a frequent clinical symptom in general and gynecological medicine consultation. The objectives of this bibliographical review are: to define the diagnostic concept, classification and treatment of mastalgia. **Methods:** literature search in Pubmed, Scielo, Cochrane and Google Scholar, using the MeSH terms: mastodynia, mastalgia, breast pain, chest pain. The search limits were: full texts in English and Spanish, in humans and published during the last 10 years. **Results:** the physiopathology of the mastodynia is not caused by a single mechanism, but by different causes with independent pathways. The main mechanisms are hormonal, mammary density, neuropathic and extra-mammary. **Conclusion:** It is important to know the pathophysiology and classification of mastodynia, due to its therapeutic implications and possible association with breast cancer.

Keywords: Mastodynia, Mastalgia, Pain; Review.

Resumen

Introducción: la mastalgia es un síntoma clínico frecuente en la consulta medicina general y ginecológica. Los objetivos de esta revisión bibliográfica son: definir el concepto diagnóstico, clasificación y tratamiento de la mastalgia. **Métodos:** búsqueda bibliográfica en Pubmed, Scielo, Cochrane y Google Académico, utilizando los términos MeSH: *mastodynia, mastalgia, breast pain, chest pain*. Los límites de búsqueda fueron: textos completos en idioma inglés y español, en humanos y publicados durante los últimos 10 años. **Resultados:** la fisiopatología de la mastodinia no es causada por un solo mecanismo, sino por diferentes causas con vías independientes. Los mecanismos principales son de tipo hormonal, densidad mamaria, neuropático y extra-mamaria. **Conclusion:** es importante conocer la fisiopatología y clasificación de mastodinia, debido a sus implicaciones terapéuticas y posible asociación con cáncer de seno.

Palabras claves: Mastodinia, Mastalgia, Dolor; Revisión.

Introduction

Mastalgia is defined as the pain originated in the mammary gland, its study is difficult to quantify due to subjectivity, the most used method to objectify it is the visual analogue scale or pain graph, when the intensity of the mastalgia is moderate to severe, and lasts more than five days, is a major cause of discomfort and is considered pathological (1).

Methodology

A search plan was made by exploring the PubMed, Cochrane, Scielo and Google Academic databases where the MeSH terms *mastodynia, mastalgia, breast pain, chest pain,* were used. The search limits were reviews and human clinical trials published the last ten years with full texts in English and Spanish. The search results identified 59 documents that met the search criteria, of which 40 articles were selected due to their relevance, relevance and updating.

Overview

Mastodynia is the most common symptom with a prevalence of 70% in women under 55 years (2), 36% of women consult the doctor for this cause. Erroneously mastalgia is still considered a trivial complaint by many doctors, because it is often considered psychological despite the severity of the symptom, and medications are rarely prescribed.

Epidemiology

45% of women have mild symptoms and in 20% of cases, it is severe. But it is the latter that most affects quality of life: interferes in 48% of sexual activity, 36% in physical activity, 13% in social activity and 6% in work or study (3). No association with marital status, income, education, or race has been found.

Innervation

Mastodynia is the most common symptom with a prevalence of 70% in women under 55 years and 36% of women consult the doctor for this cause.

The innervation of the breast is given by the antero-lateral and antero-medial branches of the intercostal nerves from T3 to T5. The irritation of these nerves anywhere along their course can arise from the breast tissue or the chest wall. A branch of T4 innervates the nipple and the intercostobrachial nerve innervates the inner side of the arm (2).

Etiology

The cause is not clear, but there are several theories. Hormonal etiology of mastalgia is suggested by the onset at the age of menarche, its relationship with the menstrual cycle and its resolution with menopause (4). However, hormone levels are similar among women with and without mastalgia. Theories suggest progesterone deficiency, excess estrogen and alterations in the progestin-estrogen ratio, alterations in the secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH), low levels of androgens, and high levels of prolactin (PRL), but none of them has been proven. It is speculated if instead of an alteration of the hormonal level, it could be a greater sensitivity of the receptor (5).

Measurements of PRL are difficult due to the variation in hormonal levels depending on the time of day. However, measurements of serum prolactin levels 24 hours and their concentration in breast tissue have been made, and no differences have been demonstrated between women with and without mastalgía (6).

The mental and emotional state of women has shown association: those with symptoms of anxiety and adaptive disorders are more associated with severe mastalgia (6).

There is some evidence that suggests that women with mastalgia have increased levels of saturated fatty acids and reduced those of essential fatty acids, especially gamma-linoleic acid (GLA) (7); apparently, this makes the cell membranes more sensitive to nociceptive depolarization and allows the estrogen receptor to be more available.

Mastodynia has been attributed to water retention; however, a study measuring the total body water with radioactive water (D_2O) in patients with mastalgia and asymptomatic, showed that there were no significant differences in the increase in body water between days 5 and 25 of the menstrual cycle (8).

Classification

Mastalgia is generally classified as cyclic (MC), non-cyclic (MNC), and chest wall pain (PTD). This distinction is important because the presentation, spontaneous remission rates and the likelihood of response to treatment It differs for each of these.

MC represents 70% of the cases of mastalgia. It presents as a predictable pattern of pain with the menstrual cycle, often before menstruation, occurs 1 to 2 weeks before menstruation. Pain is usually diffuse and bilateral, located preferably in the upper external quadrants and lasting from 1 to 4 days. It has been called mild cyclic mastalgia (MCL) or physiological considered normal (9).

It can be more severe in one breast than in another and is relieved with the onset of menstruation. Patients are usually between 30 and 40 years. This kind of pain can have a spontaneous resolution in 22% of the women and persist in 65% even after treatment. Usually, improves with pregnancy or menopause and because of this, a possible hormonal cause is postulated. It is considered a chronic disorder that does not tend to improve without treatment (9).

Mastalgia is generally classified as cyclic (70% of cases), non-cyclic (25%) and chest wall pain.

Non-cyclic mastalgia is described as a constant or intermittent breast pain with irregular exacerbations and is not related to menstruation, usually unilateral and located in a specific quadrant. Patients are usually older: between 40 and 50 years old and are often perimenopausal. There are several possible causes including cysts, periductal mastitis, stretching of Cooper's ligaments, traumatic fat necrosis, Mondor's disease, diabetic mastopathy, and neoplasia. MNC represents 25% of the cases of mastalgia (10), its duration tends to be shorter, with spontaneous resolution in 50% of the patients.

The pain of the chest wall, its characteristics differentiate it from breast pain in that it is unilateral, caused by the activity, very lateral or medial to the breast, is triggered by pressure in a specific area of the chest wall (trigger point), of the underlying muscles and ribs.

Osteochondritis or Tietze syndrome represents 7% of consultation for mastalgia, this pain is usually chronic, tends to occur in medial quadrants, and is reproducible with pressure on the affected cartilages (10).

Associated factors

A study found a significant but small association, among some lifestyle factors, among these smoking (RR 1.52), stress (RR 1.88) and high caffeine intake (RR 1.53), (3). Ernster *et al*. reported that caffeine restriction produces an improvement in symptoms; however, subsequent randomized and controlled studies have not shown this benefit (11). On the other hand, nutrition and alcohol consumption are not related to mastalgia (3).

The association between mastalgia and premenstrual syndrome (PMS) is controversial; although cyclic mastalgia is a component of the syndrome, more than 80% of women do not meet criteria for PMS. This implies that treatments for the syndrome

may not be effective for cyclic mastalgia. Some studies have found that oral contraceptives can reduce moderate to severe pain of cyclic mastalgia (RR 0.45) and somatic symptoms of premenstrual syndrome (3). However, oral contraception did not show any advantage over placebo for any premenstrual mood symptom (3).

Association with cancer

The two most common concerns of patients with mastalgia are fear of breast cancer and the presence of severe pain that affects the quality of life. It is considered that the risk of breast cancer among patients who present mastalgia as the only symptom is approximately 0.8% to 2% (12). Here, it is important to note that mastalgia can be presented in breast cancer in advanced stages, when the tumor presents peri neural invasion and in the sensory structures. This pain is usually unilateral, persistent, localized and constant; however it can be diffuse, as in inflammatory carcinoma (12).

The most important thing in the doctor's responsibility is to rule out cancer; doing this most patients calm down and have pain improvement. Many can be managed with simple analgesics (9) and rarely need specialized treatment.

Treatment

First, it is recommended to classify the type of pain and focused according to its possible cause. Clinical examination is very useful in some cases with palpable mass, spider vein, trigger points in the chest wall, but most cases will have a normal mammary examination (2), which together with an imaging examination (such as ultrasound or normal mammography) the possibility of undetected breast malignancy is less than 5%. It can make many patients (85%) calm down and will not require treatment (5,10). This confirms the theory that many women are looking for tranquility in the face of fear of cancer. A subgroup of women which will have moderate to severe pain, for more than 5 days, in the last 6 months, or if the pain interferes with their daily activities (15%), will require treatment.

It is considered that the risk of breast cancer among patients who present mastalgia as the only symptom is approximately 0.8% to 2%.

In general, 92% of patients with cyclical mastalgia and 64% with non-cyclical mastalgia can obtain pain relief with conventional treatment. It is important to know that 20% of women with mastalgia respond to placebo and 20% of the mastalgias are resistant to any treatment (1).

It is recommended to start with general measures, such as improving the support of the brassiere, to be sports relieve pain by reducing excessive stretching of the Cooper's ligament, especially in women with large breasts. It is estimated that up to 70% of women wear incorrect bras (13).

In one study four weeks of relaxation therapy reported that it provided improvement of mastalgia in 60% of patients. It has been said that exercising can improve mastalgia through the release of endorphins (13).

Anxiety and other psychological disorders seem to be more frequent among women with mastalgia. Psychiatric evaluation and a therapeutic trial with antidepressants may be useful in patients who do not respond to standard interventions. A meta-analysis of 10 randomized double-blind controlled trials with selective serotonin reuptake inhibitors (SSRIs) used in women with premenstrual symptoms, showed to be effective for the relief of mastalgia (14).

Dietary recommendations such as reducing or avoiding methylxanthines (coffee beverages, tea, chocolate, soft drinks) have not been proven useful (15). There is no convincing evidence to support the use of vitamins in the treatment of mastalgia (16). However, vitamin A, B1, B6 and E are used by clinicians. These have no paper and should not be misused (20). On the contrary, a meta-analysis describes that long-term use of vitamin E may increase the risk of hemorrhagic stroke (RR = 1.22, 95% confidence interval 1-1.48) (17).

The intake of fats in the diet (<15% of the total calories for 6 months) has been associated with improvement of cyclic mastalgia; however this regimen is difficult to meet (18).

Evening primrose oil (EPO) is a polyunsaturated essential fatty acid from a flower, which contains gamma-linolenic acid (GLA), a precursor of prostaglandin E1. Its mechanism of action is not clear, women with cyclic mastalgia have low levels of GLA metabolites in plasma. A multicenter randomized study concluded that gamma-linolenic acid efficacy was similar to placebo, regardless of whether antioxidant vitamins were added or not (19). It was used in the treatment of mastalgia until October 2002, when it was withdrawn from the prescription by the Drug Control Agency of the United Kingdom.

In general, 92% of patients with cyclical mastalgia and 64% with non-cyclical mastalgia can obtain pain relief with conventional treatment. Non-steroidal anti-inflammatory drugs can be effective in up to 80% of women and their utility is often underestimated.

Phytoestrogens, such as genistein, isoflavones, and soy milk, which is rich in genistein, have been investigated as a treatment for mastalgia. Only soy milk has been subjected to a randomized double-blind controlled study, using cow's milk as a control. Symptoms improvement of 56% was observed against 10% in controls. Authors reported noncompliance for bad taste, and a possible placebo effect.

Simple anti-inflammatories: Non-steroidal anti-inflammatory drugs can be effective in up to 80% of women and their utility is often underestimated (20).

The application of diclofenac gel in the form of local massage in painful breast areas, has been found which is more effective than placebo gel and ibuprofen gel, without any secondary effect (20).

Endocrine therapy: Bromocriptine, danazol, and tamoxifen have been shown to be effective for cyclic mastalgia. The only drug approved by the US F.D.A. for this indication is Danazol, a synthetic derivative of testosterone, which mechanism of action is unknown (20). Its androgenic effects are very frequent, permanent and potentially serious. With a dose of 200 mg per day, improvement is reported from 60% to 80% (2, 21). Unfortunately, relapse rates after treatment termination are high (70%). Danazol is contraindicated in women with a history of thromboembolic disease. It is potentially teratogenic and may interfere with oral contraception (2). It is not recommended as a first-line drug.

Tamoxifen at a dose of 10 mg / day for <6 months, continuous or limited to the luteal phase of the menstrual cycle, has shown an improvement in cyclic mastalgia in 70 to 90% and no clyclic mastalgia in 56% of cases (22). Side effects at this low dose for 3 months are minimal and include irregular periods and hot flashes. About 53% of patients are pain-free until one year later, however the relapse rate after treatment interruption is around 30% (22).

Bromocriptine is an ergot alkaloid that acts as a dopaminergic agonist in the hypothalamic-pituitary axis. One result of this action is the suppression of prolactin secretion (23). It is administered at a dose of 2.5 mg twice a day and the response is approximately 50% to 65%. Its adverse effects nausea, vomiting and dizziness are frequent (50%), which causes suspension of treatment, and in 10% can be serious (23). Bromocriptine has lost approval by the US FDA for the prevention of physiological lactation, after several cases of seizures. It should not be used as a first-line treatment and may be recommended when danazol is contraindicated.

In a randomized placebo-controlled trial of 147 premenopausal women with Goserelin analogue at a dose of 3.6 mg subcutaneously monthly, showed a significant reduction, on the average of days with severe pain of 17.6 to 5, 9 days, that is, a reduction of 67% (24). But unfortunately, most patients report side effects in the short and long term. I is recommended in acute and severe cases of mastalgia.

Gestrinone, an androgenic derivative of 19-nortestosterone, antiestrogenic and antiprogestogenic, at a dose of 2.5 mg twice a week, has an improvement rate of 55%, can also be used as a contraceptive, but 41% of patients complains of adverse effects (25).

Topical, oral and parenteral progestogens have been studied, with variable results: medroxyprogesterone acetate of 20 mg / day oral, does not produce any benefit (26).

The response of oral contraceptives in mastalgia is variable in different individuals. Studies of low doses of oral contraceptives (20 mcg ethinylestradiol) have not found an increase in breast symptoms compared with placebo (27).

Hormone replacement therapy generally increases the risk of breast pain, and no studies have been done for the treatment of mastalgia due to the risk of side effects from chronic use.

In the case of non-breast chest pain, injection of 1% lidocaine (1 ml) and methyl prednisone (40 mg), or injection of 2% lidocaine (2 ml) plus long-acting steroid such as ethyl triamcinolone 1 ml, trigger point shows improvement in 50% to 90% of the pain, usually requires a second dose 2 to 3 months later (28).

Bilateral or unilateral mastectomy is not recommended, the response to surgery is unpredictable, must be used with extreme caution, warrants psychological assessment. Patients should be informed of the possible complications inherent in reconstructive surgery and warn that in 50% of cases their pain will not be improved (29).

Chronic pain after breast surgery may be present in up to 50%, possibly associated with neuropathic pain in the scar or intercostobrachial neuralgia, the use of medications such as pregabalin or amitriptyline is recommended (29).

Conclusion

The scientific evidence addresses different concepts of the physiopathology of mastalgia, it is necessary an adequate classification because it entails an etiological approach and therefore greater therapeutic effectiveness. Frequently associated with estrogen hormone influx, breast tissue density and pain not mammary, it is infrequently seen in cases of breast carcinoma in early stages, which are diagnosed adequately by breast imaging tests.

Bibliography

1. Davies EL, Gateley CA, Miers M, Mansel RE. The long-term course of mastalgia. J R Soc Med 1998; 91:462–464.

2. Dixon JM. Managing breast pain. Practitioner 1999; 243:484–486; 488–489; 491.

3. Ader DN, South-Paul J, Adera, Deuster PA. Cyclycal mastalgia: Prevalence and associated health and behavioral factors. J Psychosom Obstet Gynecol 2001; 22:71–76.

4. Gateley CA, Maddox PR, Pritchard GA, Sheridan W, Harrison BJ, Pye JK, et al. Plasma fatty acid profiles in benign breast disorders. Br J Surg 1992; 79:407–409.

5. Hughes LE, Mansel RE, Webster DJ, eds. Breast pain and nodularity. In: Benign disorders and diseases of the breast: concepts and clinical management. Philadelphia: Bailliere Tindall, 1989, pp 75–92.

6. Parlati E Travaglini A, Liberale I, menini E, Dell'Ácqua Al. Hormonal profile in benign breast disease: Endocrine status of cyclical mastalgia patients. J Endocrinol Invest 1988; 11:679–683.

7. Horrobin DF, Manku MS. Premenstrual syndrome and premenopausal breast pain (cyclical mastalgia): disorders of essential fatty acid (EFA) metabolism. Prostaglandins Leukot Essent Fatty Acids 1989; 37:255–261.

8. Preece PE, Richards AR, Owen GM. Mastalgia and total body water. Br Med J 1975; 4:498–500.

9. Kumar S, Rai R, Das V, Dwivedi V, Kumar S, GG A. Visual analogue scale for assessing breast nodularity in non discrete lumpy breasts: the Lucknow Cardiff breast nodularity scale. The Breast 2010; 19:238–242.

10. Wisbey JR, Kumar S, Mansel RE, Preece PE, Pye JK, Hughes LE. Natural history of breast pain. Lancet 1983;ii:672–674.

11. Ernster VL, Mason L, Goodson WH. Effects of caffeine free diet on benign breast disease: a randomized trial. Surgery 1982; 91:263– 267.

12. Klimberg SV. Etiology and management of breast pain. In: Bland KI, Copeland EM, eds. The Breast: Comprehensive Management of Benign and Malignant Diseases, 2nd Ed. Philadelphia: WB Saunders Co; 1998, pp 247–260.

13. Hadi MS. Sports brassiere: is it a solution for mastalgia? Breast J 2000; 6:407–409.

14. Fox H, Walker RG, Heys SD. Are patients with mastalgia anxious, and does relaxation therapy help? Breast 1997;6: 138–142.

15. Russell LC. Caffeine restriction as initial treatment of breast pain. Nurse Pract 1989; 14:36–37.

16. Ernster VL, Goodson WHD, Hunt TK, Petrakis NL, Sickles, Mike R. Vitamin E and benign breast disease: A double-blind, randomized clinical trial. Surgery 1985; 97:490–494.

17. Shurks M, Glynn RJ, Rist PM, Tzourio C, Kurth T. Effects of vitamin E on stroke subtypes: meta-analysis of randomized controlled trials. BMJ 2010;341:c5702–1315. doi: 10.1136/c5702

18. Sharma AK, Mishra SK, Salila M et al. Cyclical mastalgia: Is it a manifestation of aberration in lipid metabolism? Indian J Physiol Pharm 1994; 38:267–271.

19. Goyal A, Mansel RE. A randomized multicenter study of gamolenic acid (Efamast) with and without antioxidant vitamins and minerals in the management of mastalgia. Breast J 2005; 11:41–47.

20. Colak T, Ipek T, Kanik A Efficacy of topical nonsteroidal antiinflammatory drugs in mastalgia treatment. J Am Coll Surg 2003; 196:525–530.

21. Sutton GLC, O'Malley UP. Treatment of cyclical mastalgia with low-dose short-term danazol. Br J Clin Pract 1986; 40:68.

22. Fentiman IS, Powles TJ. Tamoxifen and benign breast problems. Lancet 1987; 26(8567):1070–1072.

23. Mansel RE, Dogliotti L. European Multicenter Trial of bromocriptine in cyclical mastalgia. Lancet 1990; 335:190–193.

24. Mansel RE, Goyal A, Preece P, Leinster S, Maddox PR (2004) European randomized multicenter study of goserelin (Zoladex) in the management of mastalgia. Am J Obstet Gynecol 2004; 191(6):1942–1949.

25. Peters F. Multicenter study of gestrinone in cyclical breast pain. Lancet 1991; 339:205.

26. Uzan S, Denis C, Pomi V, Varin C. Double-blind trial of promegestone (R 5020) and lynestrenol in the treatment of benign breast disease. Eur J Obstet Gynecol Reprod Biol 1992; 43:219–227.

27. Coney P, Washenik K, Langley RG, Harrison DD. Weight change and adverse event incidence with a low-dose oral contraceptive: two randomized, placebo-controlled trials. Contraception 2001; 63:297–302.

28. Steinbrunn BS, Zera RT, Rodriguez JL Mastalgia: tailoring treatment to type of breast pain. Postgrad Med 1997;102(5):183–184,187-9,193-4.

29. Maddox PR, Harrison BJ, Mansel RE et al. Non-cyclical mastalgia:An improved classification and treatment. Br J Surg 1989; 76:901–904.