

Mastalgia

This guideline has been reviewed by the Breast Disease Committee and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada. This guideline has also been developed in collaboration with the Breast Health Centre, Winnipeg Regional Health Authority.

PRINCIPAL AUTHORS

Vera Rosolowich, RN, SCM, IBCLC, Winnipeg MB

Elizabeth Saettler, MD, FRCSC, Winnipeg MB

Beth Szuck, BA, HEc, CACE, RD, Winnipeg MB

BREAST DISEASE COMMITTEE

Robert H. Lea, MD, FRCSC, Glen Haven NS

Pierre Levesque, MD, FRCSC, Rimouski QC

Fay Weisberg, MD, FRCSC, Toronto ON

James Graham, MD, FRCSC, Halifax NS

Lynne McLeod, MD, FRCSC, Halifax NS

Vera Rosolowich, RN, SCM, IBCLC, Winnipeg MB

Abstract

Objective: To review the current management of women with breast pain.

Options: The effect of various treatment modes and health practices, including medications, was considered for the management of both cyclical and noncyclical breast pain.

Outcomes: Effective and timely management of the woman with breast pain and improved quality of life.

Evidence: A literature search was performed to identify reports published in English between 1975 and July 2003 using MEDLINE and Cochrane Database of Systematic Reviews.

Values: Levels of evidence, as outlined, have been determined using the criteria outlined by the Canadian Task Force on the Periodic Health Examination. Participants were the principal authors: a clinical dietitian, a surgeon oncologist, and a nurse.

Benefits, Harms, and Costs: Utilizing the information will increase knowledge, enabling a consistent approach, which will reduce the number of ineffective interventions and ensure appropriate use of medications.

Validation: Comparison has been made with management protocols in the literature, but no clinical guidelines have been located. No formal clinical testing has taken place.

Key words: Mastalgia, breast pain, mastodynia

Sponsor: The Society of Obstetricians and Gynaecologists of Canada (SOGC). Work on these guidelines was initiated by team members to fill a need for practice guidelines at Winnipeg Regional Health Authority Breast Health Centre, Winnipeg, MB.

Recommendations

1. Education and reassurance is an integral part of the management of mastalgia and should be the first-line treatment. (II-1 A)
2. The use of a well-fitting bra that provides good support should be considered for the relief of cyclical and noncyclical mastalgia. (II-3 B)
3. A change in dose, formulation, or scheduling should be considered for women on HRT. HRT may be discontinued if appropriate. (III C)
4. Women with breast pain should not be advised to reduce caffeine intake. (1 E)
5. Vitamin E should not be considered for the treatment of mastalgia. (1 E)
6. There is presently insufficient evidence to recommend the use of evening primrose oil (EPO) in the treatment of breast pain. (II-2 C)
7. Flaxseed should be considered as a first-line treatment for cyclical mastalgia. (I A)
8. Topical non-steroidal anti-inflammatory gel, such as diclofenac 2% in pluronic lethicin organogel, should be considered for pain control for localized treatment of mastalgia. (I A)
9. Tamoxifen 10 mg daily or danazol 200 mg daily should be considered when first-line treatments are ineffective. (I A)
10. Mastectomy or partial mastectomy should not be considered an effective treatment for mastalgia. (III E)

J Obstet Gynaecol Can 2006;28(1):49-60

INTRODUCTION

This document addresses the need for a review of the current management and treatment of breast pain with recommendations based on the best available evidence. Treatments were reviewed, including dietary changes, non-prescription medications, prescription drugs, and other therapies. In evaluating the evidence, the importance of randomized, double-blind, placebo-controlled trials was emphasized. Mastalgia has a natural history of remission and relapse, and placebo response in most trials is significant, approaching 40%. Some interventions widely recommended in the past have not been found to have any

This guideline reflects emerging clinical and scientific advances as of the date issued and are subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed. Local institutions can dictate amendments to these opinions. They should be well documented if modified at the local level. None of these contents may be reproduced in any form without prior written permission of the SOGC.

Table 1. Criteria for quality of evidence assessment and classification of recommendations

Level of evidence*	Classification of recommendations†
I: Evidence obtained from at least one properly designed randomized controlled trial.	A. There is good evidence to support the recommendation that the condition be specifically considered in a periodic health examination.
II-1: Evidence from well-designed controlled trials without randomization.	B. There is fair evidence to support the recommendation that the condition be specifically considered in a periodic health examination
II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group.	C. There is poor evidence regarding the inclusion or exclusion of the condition in a periodic health examination.
II-3: Evidence from comparisons between times or places with or without the intervention. Dramatic results from uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category.	D. There is fair evidence to support the recommendation that the condition not be considered in a periodic health examination.
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.	E. There is good evidence to support the recommendation that the condition be excluded from consideration in a periodic health examination.

*The quality of evidence reported in these guidelines has been adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on the Periodic Health Exam.⁸⁵

†Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the Canadian Task Force on the Periodic Health Exam.⁸⁵

useful effect when tested in clinical trials with appropriate blinding and controls. In addition, interpretation of the literature is difficult because most of these studies were performed in an era when breast lumpiness was felt to represent a disease, variously described as fibrocystic disease, cystic mastopathy, or “dysplasia,” and studies focused on physician-assessed nodularity and tenderness, rather than patient-assessed pain.

INCIDENCE AND CLASSIFICATION

In Western societies mastalgia, or breast pain without underlying pathology, is a common complaint that may affect up to 70% of women in their lifetime.^{1,2} Interestingly, it is less common in Asian cultures, affecting as few as 5%.³ It is not unusual for women to have 2–3 days of mild breast pain premenstrually but 8–30% of women report moderate to severe breast pain with a duration of 5 or more days each month.^{2,4} It can be severe enough to interfere with quality of life rating,⁵ and when compared with other conditions the mean pain-index has been found to be similar to chronic cancer pain.⁶ Fifteen percent of women who present to a breast clinic will need drug treatment.⁷ Breast pain may be bilateral, may be in only one breast or part of one breast, and may radiate to the axilla and down the medial aspect of the upper arm. The affected breast is often extremely tender to touch and pain may be accompanied by swelling. Although breast nodularity is sometimes associated with breast pain, it is a separate entity^{3,8} and should be assessed independently.

A recent classification, first described by the Cardiff Mastalgia Clinic⁹ is useful in making clinical decisions and consists of 3 components: cyclical, noncyclical, and chest-wall pain. Cyclical pain is most prominent towards the end of the menstrual cycle.⁶ Cyclical mastalgia affects up to 40% of women before menopause, most often in their thirties.¹⁰ In approximately 8% of these women pain will be severe and interfere with their normal activities. A minority of women with the most severe pain will also experience it during menstruation.⁶ The pain can continue for many years but will usually disappear after menopause. In 20% of women it subsides without intervention. Cyclical mastalgia is not to be confused with premenstrual syndrome (PMS) which, by definition, is associated with the menstrual cycle but differs in presentation, effective treatment, and likely etiology.⁸

ETIOLOGY

The etiology of mastalgia is not well understood. Hormonal assays of estrogen, progesterone, and prolactin have shown no consistent abnormalities despite the relationship to the menstrual cycle. Even so, pregnancy, lactation, menopause, oral contraceptives, and hormone replacement therapy variously affect the course of breast pain.⁵ Some studies have shown hyperresponsiveness of prolactin to stimulation by thyrotropin-releasing hormone,¹¹⁻¹³ while others have suggested elevated levels or abnormalities of lipid metabolism.^{14,15} It has been proposed that breast pain during the luteal phase of the menstrual cycle may be due to higher serum estrogen-to-progesterone ratios. This may be related more to an insufficiency of progesterone rather than an

Table 2. Classification and description of mastalgia^{6, 9}

Cyclical	Pronounced pattern; pain experienced around luteal phase of menstrual cycle; associated with ovulatory cycles; more common in pre-menopausal women; often bilateral; often described as sharp, shooting, stabbing; heaviness, aching, deep tenderness, throbbing.
Noncyclical	No pattern; no association with menstrual events; pain tends to be well-localized; often sub-areolar or medial; may be bilateral; often described as heavy, aching, tender, fearful, burning, pulling, stabbing, pinching.
Chest wall pain	No pattern; any age; almost always unilateral; consider costochondritis (Tietze's syndrome), musculo-skeletal origin, surgical trauma, referred pain.

excess of estrogen. Preece et al. found no correlation between women with mastalgia and controls when determining total body water.¹⁶ Therefore, as fluid retention is not a factor, there is no rationale for the use of diuretics or sodium restriction. A recent study¹⁷ investigated morphological structures by ultrasound of 335 women in Germany, 212 of whom had breast pain. The intensity of pain showed a significant positive correlation with the width of the milk ducts, suggesting an association between duct ectasia and mastalgia. Moreover, the site of pain positively correlated with the site of duct dilatation in the noncyclical type.

MASTALGIA AND BREAST CANCER

Rarely is mastalgia the only symptom of breast cancer. In a retrospective study of 2332 new patients attending a breast clinic in South Wales, only one carcinoma presented with pain alone.¹⁸ However, breast pain has been reported as a presenting symptom of breast cancer in a range of 5–18% of breast cancers.^{19–22} Two studies^{23,24} have found an increase in relative risk for developing breast cancer in women who had a history of cyclical mastalgia. The first²³ is a case-control study of 420 premenopausal women matched with age and age at first full-term pregnancy. A history of cyclical mastalgia was associated with an increased risk of breast cancer. A second study²⁴ included 192 premenopausal women recently diagnosed with node-negative breast cancer, age-matched with 192 controls. Breast tenderness scores were significantly higher premenstrually. The investigators identified an association of cyclical breast tenderness with breast cancer risk in premenopausal women. A third,²⁵ later study examined the association between mastalgia and breast cancer by analysing data for 5463 women who presented at a Breast Care Centre. Of these, 1532 had initially reported breast pain and 861 were diagnosed with breast cancer. After adjusting for risk factors, the authors found that women who experienced pain were less likely to be diagnosed with breast cancer. They acknowledged that further investigation is warranted.

Although an association between mastalgia and the subsequent development of breast cancer may exist, the nature of

the relationship is not clear, based on current evidence. Clinical examination of the breasts and assessment of the patient's individual risk for breast cancer should be the main determinants of the need for imaging or other investigation.

Psychological Factors

Whether stress is a result of the pain or a contributing factor, psychological assessment and support is an integral part of the management of mastalgia. Two studies found elevated anxiety and depression among women with mastalgia. In a small study²⁶ consisting of 20 premenopausal women with severe cyclical breast pain and 12 women with no symptoms, it was found that the women with mastalgia had higher levels of anxiety and depression. The authors concluded that women who sought treatment for severe cyclical mastalgia were psychologically different from those in the control group. Another study,²⁷ which compared several groups of women, reported the high levels of mood disturbance in women with severe mastalgia were comparable to those of women with newly diagnosed breast cancer on the morning of their surgery. Levels of anxiety, depression, and social dysfunction were also shown to be significantly higher in women with severe mastalgia compared with those who had non-severe mastalgia. Some of the women who had improvement after drug treatment continued to experience some residual anxiety that suggests psychosocial factors may also contribute to the complaint of mastalgia. The authors suggested that women with severe breast pain be screened for psychological problems and be provided with support. Those who might benefit from a specific psychological intervention should be referred to a psychiatrist or a clinical psychologist.

Are explanations and reassurance enough? In a randomized controlled study (n = 121)²⁸ evaluating the intensity of the breast pain following a treatment based on explanations and reassurance, an overall success rate of 70% was verified. Reassurance was found to be 85.7% efficient in mild cases, 70.8% in moderate cases, and 52.3% in severe cases. It was also found to be more effective for those whose symptoms were more intense in the premenstrual period. Relaxation

therapy has been shown to have potential in the treatment of mastalgia. A 4-week randomized controlled study²⁹ involving 30 women evaluated the effects of keeping a pain diary and listening to a relaxation audio tape versus keeping a pain diary alone (control group). In 61% of the relaxation therapy patients versus 25% of the control patients, there was a complete or substantial response. In addition, there was an increase in the number of pain-free days in the treatment group. The data also suggested that this treatment might be more effective for cyclical rather than noncyclical mastalgia. Despite the smallness of the study and a dropout rate of 34%, relaxation therapy does show promise in the treatment of cyclical and noncyclical mastalgia.

Recommendation

1. Education and reassurance is an integral part of the management of mastalgia and should be the first-line treatment. (II-1 A)

Well-Fitting Support Bra

Although randomized controlled trials (RCTs) are lacking, there is evidence that a well-fitting bra may provide relief for mastalgia. In two prospective studies^{30,31} where women wore an individually fitted bra or a sports bra, a 75–85% improvement in mastalgia was reported.

Recommendation

2. The use of a well-fitting bra that provides good support should be considered for the relief of cyclical and noncyclical mastalgia. (II-3 B)

HORMONES

Hormone Replacement Therapy (HRT)

Mild and temporary to severe and persistent breast tenderness can result from taking estrogen replacement.³² Product monographs cite breast pain as an adverse effect of HRT. One small ($n = 44$) RCT³³ compared HRT with tibolone, a synthetic steroid prescribed in Europe, with no treatment. The objective was to evaluate the effect of hormone replacement therapy and tibolone on the breast. Breast pain was found to be significantly increased in women on HRT versus tibolone after one year. Two studies found that moderate to severe breast pain was significantly less frequent with intranasal 17β estradiol than with the patch³⁴ or oral administration.³⁵ No methodical studies on modifying or eliminating hormone replacement therapy with regard to mastalgia have been reported. Suggested management includes discontinuing HRT if appropriate or trying a low dose and increasing slowly.^{2,10,36}

Recommendation

3. A change in dose, formulation, or scheduling should be considered for women on HRT. HRT may be discontinued if appropriate. (III C)

Oral Contraceptives

When breast pain occurs in women taking oral contraceptives, it often resolves after a few cycles.^{13,37} In the case of severe pain that does not resolve, a lower dose or a different preparation could be tried. If this is not effective, consideration should be given to changing to alternative methods of birth control.¹⁰ In a RCT³⁷ of 1417 women comparing contraceptives, breast pain was cited by 18% of those using transdermal therapy versus 5.8% of those using oral therapy and was described by 85% as mild-moderate in severity. A multi-institutional cross-section prevalence study³⁸ found that women receiving long-acting parenteral progestones for contraception reported significantly less breast pain than the control group. It is unclear whether oral contraceptives relieve or cause cyclic mastalgia.

CAFFEINE

Interest in caffeine as a causative agent in fibrocystic breast disease arose from two observational studies by Minton^{39, 40} in which resolution of signs and symptoms occurred in 85% of subjects who abstained from methylxanthines for a period of 8 weeks or more.

Seven case-control studies have addressed the relationship between methylxanthines and fibrocystic breast disease, 4 negative⁴¹⁻⁴⁴ and 3 positive.⁴⁵⁻⁴⁷ These studies are of limited relevance to mastalgia because cases were identified by a clinical or biopsy diagnosis of benign breast disease, and not by the presence of breast pain.

Three RCTs have been done to determine the efficacy of methylxanthine avoidance in treating fibrocystic disease. The only positive trial¹ is significantly marred by its failure to blind the examiner to the patients' treatment status and by the absence of a placebo intervention. In addition, the observed effect, although statistically significant, was judged too small to be clinically important. The 2 negative trials,^{48,49} although smaller, are methodologically sound. In both, no benefit was observed after 6 months of a caffeine-free diet.

Recommendation

4. Women with breast pain should not be advised to reduce caffeine intake. (1 E)

VITAMINS

Vitamin E

Three RCTs have been done,⁵⁰⁻⁵² all showing vitamin E to be no better than placebo in the treatment of benign breast disease. In the first,⁵⁰ patients were asked whether their breast pain was better, worse, or unchanged after 2 to 3 months of therapy. In each group, 40% reported improvement. The second trial⁵¹ did not assess breast pain, but found no improvement in nodularity. The third⁵² found no improvement in nodularity or mammographic density, and although a larger proportion of women in the vitamin E group reported improvement in breast tenderness, this was not statistically significant.

Recommendation

5. Vitamin E should not be considered for the treatment of mastalgia. (1 E)

Vitamin B6

In uncontrolled studies^{53,54} vitamin B6 has been used to treat cyclical mastalgia with mixed results. A small (n = 42), double-blind, controlled study⁵⁵ found vitamin B6 did not significantly improve cyclical mastalgia at a dose of 200 mg daily as compared with a placebo.

FAT

Evening Primrose Oil

All RCT evidence in support of evening primrose oil (EPO) comes from 2 centres in Wales and Scotland. Two studies have been published,^{56,57} both with serious methodologic flaws, and neither of them in a peer-reviewed journal. Patients with at least a 6-month history of cyclic or noncyclic mastalgia were randomized to 3 months of EPO or placebo, followed by 3 more months of open-label EPO. Noncyclic mastalgia showed no response to EPO. Patients with cyclic mastalgia had significant improvement in pain after 3 months on EPO, but not on placebo. Pain levels returned to baseline by 6 months, despite continued therapy in the EPO group, and the placebo group showed no reduction in pain when they were treated at "crossover" with open-label EPO.

Three randomized, placebo-controlled, double-blind clinical trials⁵⁸⁻⁶⁰ have shown no efficacy for EPO in the treatment of cyclic mastalgia. One of these⁵⁸ used a non-standard dose of EPO (3 g daily given during the luteal phase only). A second study⁵⁹ randomized 27 women with premenstrual syndrome (PMS) in a double-blind, placebo-controlled crossover trial. Patient-assessed breast discomfort was the same in both arms of the trial, before and after crossover. The third study⁶⁰ also dealt with patients diagnosed with PMS. After an initial cycle with no

treatment, patients received 3 months of EPO or placebo and then crossed over. Thirty-eight women were entered and results analyzed. EPO had no effect on breast pain. The latter 2 studies are methodologically rigorous and used a standard dose and duration of EPO. However, they may not be generalizable to the mastalgia population because patients were selected from a premenopausal group deemed to suffer from PMS.

Recommendation

6. There is presently insufficient evidence to recommend the use of EPO in the treatment of breast pain. (II-2 C)

Dietary Fat

There is support for lipid metabolism playing a role in the pathophysiology of cyclical mastalgia.^{3,61} However, only one small randomized single-blinded controlled study (n = 21)⁶² assessed the effect of a low fat diet (15% energy from fat) on severe cyclical mastalgia. Reduced swelling, tenderness, and nodularity were reported in 6 out of 10 patients in the intervention group. More research is needed before any recommendation can be made.

PHYTOESTROGENS

Isoflavones

To date only one small double-blind RCT⁶³ has looked at the role of isoflavones in the treatment of cyclical breast pain. Eighteen women were randomized to receive a placebo or 40 mg isoflavones or 80 mg isoflavones. It demonstrated isoflavones reduced cyclical breast pain. More studies are required before any recommendation can be made about the use of isoflavones to treat cyclical mastalgia.

Flaxseed

A Canadian study⁶⁴ examined the effects of dietary flaxseed in women with severe cyclical mastalgia. One hundred sixteen women were enrolled in the double-blind placebo-controlled trial with the treatment group receiving 25 g of flaxseed daily, in a muffin, and followed for up to four menstrual cycles. However, there was no long-term follow-up. Breast pain was alleviated in both treatment groups but was reduced to a significantly greater degree in the flaxseed group. This one study shows promise and merits further research.

Recommendation

7. Flaxseed should be considered as a first-line treatment for cyclical mastalgia. (I A)

HERBS**Ginseng**

Ginseng has been cited by 2 references as contributing to mastalgia.^{65,66} No controlled studies were found.

Chasteberry

The effect of chasteberry on cyclical mastalgia has been researched. In a double-blind placebo-randomized controlled trial with 97 women, chasteberry (*vitex agnus castus*) was found to be useful and tolerable in the treatment of cyclical breast pain.⁶⁷ Another clinical trial⁶⁸ was published in German, and no English abstract is available (Tschudin et al. 1999).

MEDICATIONS**Progesterone Cream**

Topical progesterone locally applied to the breast has been used in France for many years, but in a small randomized controlled cross-over trial have not proved superior to a placebo.⁶⁹

However, a vaginal cream of micronized progesterone was found to be effective in reducing pain in 64.9% of cases compared with 22.2% of controls in a randomized double-blind placebo-controlled study in Italy.⁷⁰ A small randomized double-blind crossover study (n = 26) concluded that the therapeutic response of medroxyprogesterone acetate in cyclical mastalgia is no better than a placebo in the management of breast pain.⁷¹

Topical non-steroidal anti-inflammatory drugs

A small (n = 26) prospective pilot study⁷² demonstrated the potential for effective treatment of cyclical and noncyclical mastalgia using stronger types of topical NSAID — diclofenac and piroxicam. There is some indication that weaker types like ibuprofen gel are not effective in relieving breast pain.^{53,72} A larger prospective randomized blinded, placebo-controlled study (n = 108)⁷³ demonstrated significant improvement with diclofenac diethylammonium (Voltaren emulgel) in the treatment group for both cyclical and noncyclical mastalgia with minimal side effects. This is a reasonable alternative to a systemic analgesic for those who prefer topical therapy.

Recommendation

8. Topical, non-steroidal anti-inflammatory gel, such as diclofenac 2% in pluronic lethicin organogel (PLO), should be considered for pain control for localized treatment of mastalgia. (I A)

Tamoxifen

Two RCT's^{74,75} found tamoxifen superior to placebo in premenopausal women with cyclic or noncyclic mastalgia. Tamoxifen 20 mg daily alleviated pain (defined as 50% reduction in linear analogue score) in 71% of patients at 3 months, compared with 38% who received placebo.⁷⁴ Tamoxifen 10 mg daily eliminated symptoms in 89% of women at 6 months, compared with 38% who experienced “partial improvement” in the placebo group.⁷⁵ The 2 doses were then compared directly and found to have equivalent response rates (86% for the 20 mg dose, 90% for the 10 mg dose) in a further trial.⁷⁴ Side effects were significantly reduced at the lower dose. Response rates were superior in cyclic mastalgia: 94% versus 56% in the noncyclic group.

Side effects of tamoxifen commonly observed in short-term treatment for mastalgia include hot flashes (10%), menstrual irregularity/amenorrhea (10%), weight gain, nausea, vaginal dryness, and bloating (5% or less). Thromboembolic events, endometrial cancer, and cataracts are rare but serious side effects of tamoxifen; their incidence in short-term, low-dose treatment regimens for mastalgia is not known. Tamoxifen 10 mg daily is effective in the treatment of mastalgia. As it is significantly cheaper, it can be used as a first medication except in women with a history of thromboembolic disease.

Danazol

Two RCT's have compared danazol with placebo in premenopausal women with cyclic mastalgia^{76,77} and one 3-arm trial compared tamoxifen with danazol with placebo.⁷⁸ The first of these,⁷⁶ a double-blind crossover trial, compared danazol 200 mg/day with placebo in 28 women with cyclic mastalgia. Crossover occurred at 3 months. Mean pain scores showed significant response to danazol. The second trial⁷⁷ used danazol 200 mg/day in the luteal phase of the cycle only. One hundred women were randomized and followed for 3 menstrual cycles. Danazol was found to reduce breast discomfort without any increase in side effects in comparison with placebo. The third trial, comparing danazol with both tamoxifen and placebo,⁷⁸ randomized 93 patients with cyclic mastalgia to 6 months of danazol 100 mg bid, tamoxifen 10 mg od or placebo. Treatment success was defined as >50% reduction in mean pain score and was achieved in 65% of those on danazol, 72% of those on tamoxifen, and 38% of those on placebo. Statistically, tamoxifen and danazol were equivalent, and both were significantly better than placebo.

Side effects of danazol at the 200 mg daily dose included weight gain (30%), menstrual irregularity/amenorrhea or menorrhagia (50%), deepening of the voice (10%), and hot flashes (10%).⁷⁶ Danazol 200 mg daily is effective in the

Table 3 Selective treatment, side effects and relative cost

Drug	Usual dose	Side effects	Relative cost
Tamoxifen	10 mg od	Hot flashes, menstrual irregularity, (nausea, bloating, vaginal dryness, rarely DVT, pulmonary embolus)	+
Danazol	100 mg bid	Amenorrhea, menstrual irregularity. Weight gain, (hirsutism, deepening voice, hot flashes)	++++
Bromocriptine	2.5 mg bid after gradual increase	Nausea, dizziness, headache, postural hypotension, (rarely seizures, stroke or hypertension)	+++
Evening Primrose Oil	3000 mg od	Soft stool, headaches	++

DVT: Deep vein thrombosis.

Note: parentheses denote rare side effects.

treatment of breast pain. To minimize side effects, it can be given in the luteal phase only.

Recommendation

9. Tamoxifen 10 mg daily or danazol 200 mg daily should be considered when first-line treatments are ineffective. (I A)

Bromocriptine

Bromocriptine, 5 mg daily, has been found effective in the treatment of cyclic mastalgia in 2 randomized, placebo-controlled trials.^{79,80} The first,⁷⁹ carried out in Pakistan, found that bromocriptine reduced breast pain, tenderness, and nodularity after 3 months of treatment. There was an absolute reduction of 40% (relative reduction of 50%) in mean linear analogue scores for pain, and 65% of patients on bromocriptine were reported as experiencing complete relief of symptoms. Side effects were experienced by 40% of patients taking the drug, and included nausea, dizziness, postural hypotension, and headache. The second RCT, a multicentre European trial,⁸⁰ analyzed 187 premenopausal women with cyclic mastalgia. Both arms (bromocriptine and placebo) showed significant improvement in breast pain, but bromocriptine was more effective, with an absolute 45% reduction in mean linear analogue score for pain. Side effects of bromocriptine included nausea (32%), dizziness (12%), and vomiting (7%). Overall, 11% of patients in the bromocriptine group and 6% in the placebo group discontinued treatment because of side effects.

Surgical Intervention

The experience with surgery for relief of mastalgia is very limited. Only 4 patients in a British breast clinic had undergone mastectomy for mastalgia in 12 years¹⁰ and only 12 out of 1054 patients seen in the Cardiff Mastalgia Clinic over 25 years underwent surgery. A retrospective chart analysis⁵ of this latter group found that only those women who had

had a mastectomy for mastalgia were pain-free following surgery. Other forms of surgery did not bring relief.^{81,82}

It is necessary to differentiate true mastalgia from other causes such as muscular-skeletal and referred pain. Sutton et al. report 5 cases of breast pain relieved by surgical decompression of the thoracic outlet.⁸³ These patients all had arm pain together with breast pain. Davies et al.⁵ concluded that surgery for mastalgia should be considered only in a minority of women who are resistant to all other forms of treatment. Patients must be informed of possible complications and warned that in 50% of cases their pain will not be improved.

Recommendation

10. Mastectomy or partial mastectomy should not be considered an effective treatment for mastalgia. (III E)

Evaluation of Evidence

The quality of evidence and classification of recommendation reported in these guidelines has been described using the Evaluation of Evidence criteria outlines in the Report of the Canadian Task Force on the Periodic Health Exam.⁸⁴

REFERENCES

- Ernst VL, Mason L, Goodson WH III, Sickles EA, Sacks ST, et al. Effects of caffeine-free diet on benign breast disease: a randomized trial. *Surgery* 1982;91(3): 263-7.
- Ader DN, South-Paul J, Adera T, Deuster PA. Cyclical mastalgia: prevalence and associated health and behavioral factors. *J Psychosom Obstet Gynaecol* 2001;22:71-6.
- Goodwin PJ, Miller A, Del Giudice ME, Singer W, Connelly P, Knox Ritchie JW. Elevated high-density lipoprotein, cholesterol and dietary fat intake in women with cyclic mastalgia. *Am J Obstet Gynecol* 1998;179:430-7.
- Ader DN, Browne MW. Prevalence and impact of cyclic mastalgia in a United States clinic-based sample. *Am J Obstet Gynecol* 1997;177:126-32.
- Davies EL, Gateley CA, Miers M, Mansel RE. The long-term course of mastalgia. *JR Soc Med* 1998;91:462-4.
- Khan SA, Apkarian AV. The Characteristics of cyclical and non-cyclical mastalgia: a prospective study using a modified McGill Pain Questionnaire. *Breast Cancer Res Treat.* 2002;75:147-57.

7. Holland PA, Gateley CA. Drug therapy of mastalgia. What are the options? *Drugs* 1994;48(5):709–16.
8. Ader DN, Shriver CD, Browne MW. Cyclical mastalgia: premenstrual syndrome or recurrent pain disorder? *J Psychosom Obstet Gynaecol* 1999;20(4):198–202.
9. Preece PE, Mansel RE, Bolton PM, Hughes LE, Baum M, Gravelle IH. Clinical syndromes of mastalgia. *Lancet* 1976;02(7987):670–3.
10. Mansel RE, Hughes LE. Breast pain and nodularity. In: Hughes LE, Mansel RE, Webster DJT, eds. *Benign disorders and diseases of the breast. Concepts and clinical management*. 2nd ed. London: WB Saunders; 2000:95–121.
11. Rea N, Bove F, Gentile A, Parmeggiani U. Prolactin response to thyrotropin-releasing hormone as a guideline for cyclical mastalgia treatment. *Minerva Med* 1997; 88(11):479–87.
12. Kumar S, Mansel RE, Scanlon MF, Hughes LE, Edwards CA, Woodhead JS, et al. Altered responses of prolactin, luteinizing hormone and follicle stimulating hormone secretion to thyrotropin releasing hormone/gonadotrophin releasing hormone stimulation in cyclical mastalgia. *Br J Surg* 1984;71(11):870–3.
13. BeLieu RM. Mastodynia. *Obstet Gynecol Clin North Am* 1994;21(3):461–77.
14. 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;79:407–9.
15. Preece PE, Hanslip JI, Gilbert L, Walker D, Pashby, NL, Mansel RE, et al. Evening primrose oil (efamol) for mastalgia. In: Horrobin DF, ed. *Clinical uses of essential fatty acids*. Montreal: Eden Press;1982:147–54.
16. Preece PE, Richards AR, Owen GM, Hughes LE. Mastalgia and total body water. *BMJ* 1975;4:498–500.
17. Peter F, Diemer P, Mecks O, Behnken LJ. Severity of mastalgia in relation to milk duct dilatation. *Obstet Gynecol* 2003;101:54–60.
18. Cochrane RA, Singhal H, Monypenny IJ, Webster DJT, Lyons K, Mansel RE. Evaluation of general practitioner referrals to a specialist breast clinic according to the UK national guidelines. *Eur J Surg Oncol* 1997;23:198–201.
19. Preece PE, Baum M, Mansel RE, Webster JDT, Fortt RW, Gravelle IH, et al. Importance of mastalgia in operable breast cancer. *Br Med J* 1982;284:1299–300.
20. Haagensen CD. *Diseases of the breast*. 3rd ed. Philadelphia: WB Saunders;1986:502.
21. Smallwood JA, Kye DA, Taylor I. Mastalgia; is this commonly associated with operable breast cancer? *Ann R Coll Surg Engl* 1986;68:262–3.
22. The Yorkshire Breast Cancer Group. Symptoms and signs of operable breast cancer 1976–1981. *Br J Surg* 1983; 70:350–61.
23. Plu-Bureau G, Thalabard JC, Sitruck-Ware R, Asselain B, Mauvains-Jarvis P. Cyclical mastalgia as a marker of breast cancer susceptibility: results of a case-control study among French women. *Br J Cancer* 1992;65(6):945–9.
24. Goodwin PJ, DeBoer G, Clark RM, Catton P, Redwood S, Hood N, et al. Cyclical mastopathy and premenopausal breast cancer risk. *Breast Cancer Res Treat* 1994;33:63–73.
25. Khan SA, Apkarian AV. Mastalgia and breast cancer: a protective association? *Cancer Detect Prev* 2002;26:192–6.
26. Downey HM, Deadman JM, Davis C, Leinster SJ. Psychologic characteristics of women with cyclical mastalgia. *Breast Dis* 1993;6:99–105.
27. Ramirez AJ, Jarrett SR, Hamed H, Smith P, Fentiman IS. Psychosocial adjustment of women with mastalgia. *The Breast* 1995;4:48–51.
28. Barros AC, Mottola J, Ruiz CA, Borges MN, Pinotti JA. Reassurance in the treatment of mastalgia. *Breast J* 1999;5(3): 62–5.
29. Fox H, Walker LG, Heys SD, Ah-See AK, Eremin O. Are patients with mastalgia anxious, or does relaxation therapy help? *The Breast* 1997;6:138–42.
30. Wilson MC, Sellwood RA. Therapeutic value of a supporting brassiere in mastodynia. *Br Med J* 1976;2(6027):90.
31. Hadi MS. Sports brassiere: is it a solution for mastalgia? *Breast J* 2000;6(6):407–9.
32. Speroff L, Rowan J, Symons J, Genant H, Wilborn W. The comparative effect on bone density, endometrium and lipids of continuous hormones as replacement therapy (CHART study). *JAMA* 1996;276(17):1397–403.
33. Colacurci N, Mele D, De Franciscis P, Costa V, Fortunato N, De Seta L. Effects of tibolone on the breast. *Eur J Obstet Gynecol Reprod Biol* 1998;80:235–8.
34. Lopes P, Merkus H, Nauman J, Bruschi F, Foidart J, Calaf J. Randomized comparison of intranasal and transdermal estradiol. *Obstet Gynecol* 2000;96(6):906–12.
35. Mattsson, LA, Christiansen C, Colau J, Palacios S, Kenemans P, Bergeron C, et al. Clinical equivalence of intranasal and oral 17 β -estradiol for postmenopausal symptoms. *Am J Obstet Gynecol* 2000;182 (3):545–52.
36. Klimberg VS. Etiology and management of breast pain. In: Bland KI, Copeland EM III, eds. *The Breast. Comprehensive management of benign and malignant diseases*. 2nd ed. Philadelphia: WB Saunders;1998:255.
37. Audet M, Moreau M, Koltun WD, Waldbaum AS, Shangold, G, Fisher AC, et al. Evaluation of contraceptive efficacy and cycle control of a transdermal contraceptive patch vs an oral contraceptive. *JAMA* 2001;285(18):2347–54.
38. Euhus DM, Uyehara C. Influence of parental progesterones on the prevalence and severity of mastalgia in pre-menopausal women: a multi-institutional cross-sectional study. *J Am Coll Surg* 1997; 84:596–604.
39. Minton JP, Foecking MK, Webster DJ, Matthews RH. Caffeine, cyclic nucleotides, and breast disease. *Surgery* 1979;86:105–9.
40. Minton JP, Abou-Issa H, Reiches N, Roseman JM. Clinical and biochemical studies on methylxanthine-related fibrocystic breast disease. *Surgery* 1981;90(2):299–304.
41. Marshall J, Graham S, Swanson M. Caffeine consumption and benign breast disease: a case-control comparison. *Am J Public Health* 1982;72(6):610–2.
42. Schairer C, Brinton LA, Hoover RN. Methylxanthines and benign breast disease. *Am J Epidemiol* 1986;124:603–11.
43. Lubin F, Ron E, Wax Y, Black M, Funaro M, Shitrit A. A case-control study of caffeine and methylxanthines in benign breast disease. *JAMA* 1985;253(16):2388–92.
44. Lawson DH, Jick H, Rothman KJ. Coffee and tea consumption and breast disease. *Surgery* 1981;90(5):801–3.
45. Odenheimer DJ, Zunzunequi MV, King MC, Shipler CP, Friedman GD. Risk factors for benign breast disease: a case-control study of discordant twins. *Am J Epidemiol* 1984;120(4):565–71.
46. Boyle CA, Berkowitz GS, LiVolsi VA, Ort S, Merino MJ, White C, et al. Caffeine consumption and fibrocystic breast disease: a case-control epidemiologic study. *J Natl Cancer Inst* 1984;72(5):1015–9.
47. La Vecchia C, Franceschi S, Parazzini F, Regallo M, Decarli A, Gallus G, et al. Benign breast disease and consumption of beverages containing methylxanthines. *J Natl Cancer Inst* 1985;74(5):995–1000.
48. Allen SS, Froberg DG. The effect of decreased caffeine consumption on benign proliferative breast disease: a randomized clinical trial. *Surgery* 1987;101(6):720–30.
49. Parazzini F, La Vecchia C, Riundi R, Pampallona S, Regallo M, Scanni A. Methylxanthine, alcohol-free diet and fibrocystic breast disease: a factorial clinical trial. *Surgery* 1986; 99(5):576–81.
50. London RS, Sundaram GS, Murphy L, Manimekalai S, Reynolds M, Goldstein PJ. The effect of vitamin E on mammary dysplasia: a double-blind study. *Obstet Gynecol* 1985;65:104–6.

51. Ernster VL, Goodson WH, Hunt TK, Petrakis NL, Sickles EA, Miike R. Vitamin E and benign breast "disease": a double-blind, randomized clinical trial. *Surgery* 1985;97(4):490-4.
52. Meyer EC, Sommers DK, Reitz CJ, Mentis H. Vitamin E and benign breast disease. *Surgery* 1990;107(5):549-51.
53. McFayden IJ, Forrest AP, Chetty U, Raab G. Cyclical breast pain - some observations and the difficulties in treatment. *Br J Clin Pract* 1992;46(3):161-4.
54. Wetzig NR. Mastalgia: a 3 year Australian study. *Aust N Z J Surg* 1994;64:329-31.
55. Smallwood J, Ah-kye D, Taylor I. Vitamin B6 in the treatment of pre-menstrual mastalgia. *Br J Clin Pract* 1986;40(12):532-3.
56. Preece PE, Hanslip JI, Gilbert L, Walker D, Pashby NL, Mansel RE, et al. Evening primrose oil (efamol) for mastalgia. In: Horrobin DF, ed. *Clinical uses of essential fatty acids*. Montreal: Eden Press; 1982:147-54.
57. Mansel RE, Pye JK, Hughes LE. Effects of essential fatty acids on cyclical mastalgia and non-cyclical breast disorders. In: Horrobin DF, ed. *Omega-6 essential fatty acids: pathophysiology and roles in clinical medicine*. New York: Wiley-Liss; 1990:557-67.
58. Puolakka J, Makarainen L, Viinikka L, Ylikorkala O. Biochemical and clinical effects of treating the premenstrual syndrome with prostaglandin synthesis precursors. *J Reprod Med* 1985;30(3):149-53.
59. Collins A, Cerin A, Coleman G, Landgren B-M. Essential fatty acids in the treatment of premenstrual syndrome. *Obstet Gynecol* 1993;81:93-8.
60. Khoo SK, Munro C, Battistutta D. Evening primrose oil and treatment of premenstrual syndrome. *Med J Aust* 1990;153:189-92.
61. Sharma AK, Mishra SK, Salila M, Ramesh V, Bal S. Cyclical mastalgia-is it a manifestation of aberration in lipid metabolism? *Indian J Physiol Pharmacol* 1994;38(4):267-71.
62. Boyd NF, Shannon P, Kriukov V, Fish E, Lockwood G, McGuire V, et al. Effect of a low-fat high-carbohydrate diet on symptoms of cyclical mastopathy. *Lancet* 1988;2:128-32.
63. Ingram DM, Hickling C, West L, Mahe LJ, Dunbar PM. A double-blind randomized controlled trial of isoflavones in the treatment of cyclical mastalgia. *The Breast* 2002;11:170-4.
64. Goss PE, Li T, Theriault M, Pinto S, Thompson L. Effects of dietary flaxseed in women with cyclical mastalgia. *Breast Cancer Res Treat* 2000;64:49.
65. Staba EJ, Staba JE. Ginseng (Panex species). In: Chandler F, ed. *Herbs: everyday reference for health professionals*. Ottawa: Canadian Pharmacist Association and the Canadian Medical Association. 2000:130-5.
66. Natural Medicines Comprehensive Database. Ginseng-American, Siberian, panex. Available at: www.naturaldatabase.com. Accessed December 21, 2005.
67. Halaska M, Raus K, Beles P, Martan A, Paithner KG. Treatment of cyclical mastodynia using an extract of Vitex agnus castus: results of a double-blind comparison with a placebo. *Ceska Gynecol* 1998;63(5):388-92.
68. Tschudin S, Huber R. Treatment of cyclical mastalgia with a solution containing a Vitex agnus castus extract: results of a placebo-controlled double-blind study [article in German]. *Breast* 1999;8:175-81.
69. McFadyen IJ, Raab GM, MacIntyre CC, Forrest AP. Progesterone cream for cyclic breast pain. *Br Med J* 1989;298:931.
70. Nappi, C, Affinito P, DiCarlo C, Esposito G, Montemagno U. Double-blind controlled trial of progesterone vaginal cream treatment for cyclical mastodynia in women with benign breast disease. *J Endocrinol Invest* 1992;15:801-6.
71. Maddox PR, Harrison BJ, Horobin JM, Walker K, Mansel RE, Preece PE, et al. *Ann R Coll Surg Engl* 1990;72(2):71-6.
72. Irving AD, Morrison SL. Effectiveness of topical non-steroidal anti-inflammatory drugs in the management of breast pain. *J R Coll Surg Edinb* 1998;43:158-9.
73. Colak T, Ipek T, Kanik A, Ogetman Z, Aydin S. Efficacy of topical nonsteroidal drugs in mastalgia treatment. *J Am Coll Surg* 2003;196:525-30.
74. Fentiman IS, Caleffi M, Hamed H, Chaudary MA. Dosage and duration of tamoxifen treatment for mastalgia: a controlled trial. *Br J Surg* 1988;75(9):845-6.
75. Messinis IE, Lolis D. Treatment of premenstrual mastalgia with tamoxifen. *Acta Obstet Gynecol Scand* 1988;67(4):307-9.
76. Mansel RE, Wisbey JR, Hughes LE. Controlled trial of the antigonadotropin danazol in painful nodular breast disease. *Lancet* 1982;1(8278):928-30.
77. O'Brien PMS, Abukhalil IEH. Randomized controlled trial of the management of premenstrual syndrome and premenstrual mastalgia using luteal phase-only danazol. *Am J Obstet Gynecol* 1999;180:18-23.
78. Kontostolis E, Stefanidis K, Navrozoglou I, Lolis D. Comparison of tamoxifen with danazol for treatment of cyclical mastalgia. *Gynecol Endocrinol* 1997;11(6):393-7.
79. Nazli K, Syed S, Mahmood MR, Ansari F. Controlled trial of the prolactin inhibitor bromocriptine (Parlodel) in the treatment of severe cyclical mastalgia. *Br J Clin Pract* 1989;43(9):322-7.
80. Mansel RE, Dogliotti L. European multicentre trial of bromocriptine in cyclical mastalgia. *Lancet* 1990;335(8683):190-3.
81. Davies EL, Cochrane RA, Stansfield K, Sweetland HM, Mansel RE. Is there a role for surgery in the treatment of mastalgia? *The Breast* 1999;8:285-8.
82. Gately CA, Maddox PR, Mansel RE, Hughes LE. Mastalgia refractory to drug treatment. *Br J Surg* 1990;77:1110-2.
83. Sutton GCJ, Palmer JD, Royce GT. Breast pain and the thoracic outlet compression syndrome. *The Breast* 1993;2:250-2.
84. Woolf SH, Battista RN, Angerson GM, Logan AG, Eel W. Canadian Task Force on the Periodic Health Exam. Ottawa: Canada Communication Group; 1994. p. xxxvii.