

CHAPTER 3

Mastalgia

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OVERVIEW

- Breast pain alone or painful lumpiness is common and accounts for approximately 50% of all referrals of new patients to clinics
- Breast pain is a rare symptom of breast cancer
- Pain in the breast can arise from the breast or from the underlying chest wall
- Careful examination can differentiate chest wall pain from true breast pain
- Few patients with breast pain need treatment with drugs

Mastalgia is pain in the breast. Up to 70% of women will experience this at some time during their life. The pain women describe as breast pain can arise either in the breast tissue itself or it can be referred pain, which is felt in the breast. The nerve supply to the breast is from the anterolateral and anteromedial branches of the intercostal nerves from T3 to T5 and irritation of these nerves anywhere along their course can lead to pain that is felt in the breast or nipple. A branch of T4 penetrates the deep surface of the breast and runs up to the nipple. Irritation of this nerve can result in the shooting pain up to the nipple that many women describe. Pain can also be referred from the breast or chest wall through the intercostobrachial nerve to the inner aspect of the arm.

Breast pain is a rare symptom of breast cancer. In a 10-year survey in Edinburgh of 8504 patients presenting with breast pain as their major symptom, 220 (2.7%) were subsequently diagnosed with breast cancer. During this period 4740 patients had breast cancer, which means that 4.6% of women with breast cancer had pain as an important presenting symptom.

It is important to differentiate between pain referred to the breast from the chest wall and true breast pain, because management of these two conditions is different. It is less important to differentiate cyclical mastalgia – pain that occurs only in the premenstrual part of the menstrual cycle – from non-cyclical mastalgia, as management of these conditions is similar. Pain may last throughout the cycle or bear no relation to the menstrual cycle.

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Table 3.1 Classification of non-cyclical mastalgia.

Chest wall causes	Non-breast causes
Such as tender costochondral junctions (Tietze's syndrome)	Cervical and thoracic spondylosis Lung disease Gall stones
True breast pain	Exogenous oestrogens, such as hormone replacement therapy
Diffuse breast pain Trigger spots in breast	Thoracic outlet syndrome

Primary care studies indicate that the most common type of mastalgia is pain referred from the chest wall. In breast clinics chest wall pain is now also more common than true breast pain. Clinical examination reveals that even in women with a classic history of cyclical breast pain, the chest wall is most often the site of origin of the pain (Table 3.1).

Chest wall pain

Features suggesting that breast pain is referred rather than originating in the breast include pain that

- is unilateral, and brought on by activity;
- is very lateral or medial in the breast; and
- can be reproduced by pressure on a specific area of the chest wall.

Women who are postmenopausal and not taking hormonal supplements or who are known to have spondylosis or osteoarthritis are much more likely to have musculoskeletal pain rather than true breast pain.

Careful clinical examination is essential to help determine the site of origin of the pain (Table 3.2; Figures 3.1–3.3). Any patient complaining of breast pain should have a complete breast examination including palpation with the woman lying on each side, allowing the breast to fall away from the chest wall, and palpation

Table 3.2 Principles of mastalgia treatment.

Exclude cancer	Assess site of pain
<ul style="list-style-type: none">• Clinical examination• Mammography in women aged >40• Ultrasonography if localised area of pain	<ul style="list-style-type: none">• True breast pain• Chest wall pain
Provide reassurance and information	



Figure 3.1 How to examine for lateral chest wall tenderness. The patient is rolled on her side with the breast falling away from the site of the pain laterally. The underlying chest wall is then palpated to identify any area of localised tenderness.



Figure 3.2 How to examine for medial chest wall tenderness over the costochondral junctions. The patient is rolled on her side with the breast falling away from the site of the pain medially. The underlying chest wall is then palpated to identify any area of localised tenderness.

of the underlying muscles and ribs. The patient should be asked to indicate whether there is any localised tenderness on palpation of the chest wall and whether any discomfort evident during examination is similar to the pain they normally experience. If the patient has pain in the lower part of the breast the underlying chest wall is examined by lifting the breast with one hand while palpating the underlying chest wall with the other hand. Allowing the woman herself to confirm that the site of maximal tenderness is in the underlying chest wall rather than the breast is an effective method of reassuring patients of the site of the pain.

Treatment of chest wall pain

The mainstay of treating chest wall pain is reassurance that there is no serious underlying cause for the pain. In women with



Figure 3.3 How to examine for chest wall tenderness under the lower part of the breast. The breast is lifted upwards by one hand while the other hand presses gently on the underlying chest wall to identify any area of localised tenderness.

troublesome pain, providing that there are no contraindications, non-steroidal anti-inflammatory drugs (NSAIDs) are usually effective. Although there is no evidence to suggest that topical NSAIDs have any benefit over oral preparations, there is some evidence that topical agents cause fewer gastrointestinal problems. Women often report a recent increase in activities, such as gardening, decorating, lifting or increased visits to the gym, after which they become aware of pain. Lifestyle is important in relation to breast pain. It is more common in women who spend many hours sitting at a desk in front of a computer. Identifying any underlying behaviour and modifying lifestyle accordingly form the cornerstone of treatment.

If the pain is very localised to one specific spot, then infiltrating the affected chest wall with prednisolone 40 mg in depot form combined with long-acting local anaesthetic can produce long-lasting pain relief (Table 3.3). If the correct area has been targeted, the pain should disappear quickly. About half of women with a localised tender spot get enduring benefit from a single injection. Repeating the injection after 4–6 weeks increases both the number of women getting benefit and provides long-lasting pain control for two-thirds of women with very localised troublesome pain that ‘interferes’ with regular daily activities.

Table 3.3 Outcome of women with chest wall pain treated by local infiltration of bupivacaine (Marcain) plus depot steroid (injected group) or observation alone (comparative group).

	Injected group	Comparative group
No of women	104	34
No who attended follow up	100	29
No (%) with complete resolution of pain*	61* (61)	5 (17)
No (%) with partial resolution of pain	22 (22)	8 (22.5)
No (%) with successful outcome*	83* (83)	13 (44.8)

*Differences significant at $p < 0.0001$.

Chronic pain following breast surgery

Similar symptoms of chest wall pain are commonly reported after breast surgery, affecting up to 50% of women in some surveys. It is important to rule out underlying causes such as local recurrence or a prior underlying cause of chronic pain. Typically the introduction of gabapentin, pregabalin or amitriptyline is recommended in all forms of neuropathic pain such as scar pain or intercostobrachial neuralgia. The authors have used external neuromodulation for postoperative neuropathic pain with promising results. External neuromodulation consists of the application of electrical current through an external probe over the painful area, trigger zone or affected nerve. The pain reduction can be immediate and quality of life can be dramatically improved following regular applications. Further studies are required to establish the role of this treatment in chronic breast pain.

True mastalgia

Pain arising in the breast tissue itself is often associated with cyclical swelling and nodularity (Figure 3.4). Hormonal changes are thought to be responsible for these changes in the breast, as they are most commonly seen in the week before menstruation and are relieved by its onset. In addition, the pain can be brought on by hormonal manipulation such as oestrogen containing hormone replacement therapy. It is much less of a problem in women taking tibolone. There are several theories regarding the pathophysiology of mastalgia.

Too much oestrogen

Measurements of serum oestrogen concentrations have not shown any differences between women with pain and normal controls.

Not enough progesterone

A single study has shown reduced serum progesterone concentration in the luteal phase in women with mastalgia when compared with controls.

Too much prolactin

Measuring prolactin is complicated because of diurnal variation in hormone levels. Measurement of 24-hour serum prolactin profiles and of tissue concentrations of prolactin in breast biopsy samples taken either during the day or the night have not shown any differences between women with and without mastalgia. The prolactin response after stimulation has been studied, and women with mastalgia produced more prolactin for longer, suggesting that there may be a problem in the prolactin pathway at the level of the hypothalamus.

Increased receptor sensitivity in breast tissue/abnormal fatty acids

Women with mastalgia may have different fatty acid profiles to women without pain, in that they have an increased ratio of saturated fatty acids to essential fatty acids. Cell membranes that have a high proportion of saturated fats become rigid and membrane receptors are easier for ligands to bind to. If cell membranes are composed of unsaturated fats, they are more fluid and receptors can be enveloped in folds of the membrane, making it harder for ligands to access and stimulate the receptor. Because women with mastalgia have more saturated fatty acids, the theory is that oestrogen receptor is more available, making the cells in the breast more sensitive to the effects of oestrogen.

In reality there is no unifying hypothesis that explains why women get cyclical mastalgia.

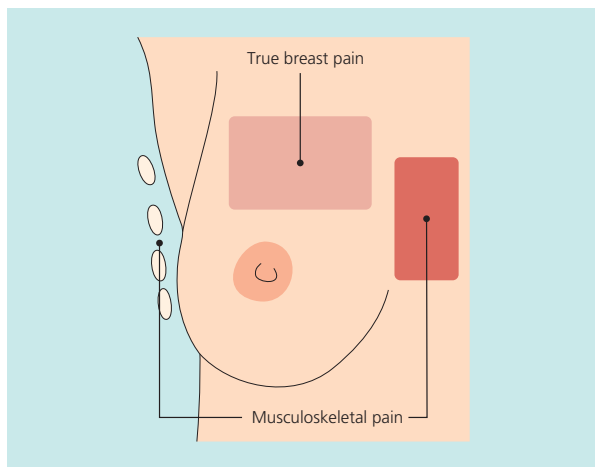


Figure 3.4 Classification of non-cyclical breast pain. Non-cyclical pain can be divided into true breast pain arising from the breast tissue or musculoskeletal pain arising from the ribs or chest wall. Musculoskeletal pain is commonly medially (Tietze's syndrome) or laterally at the edge of the breast.

Treatments for true mastalgia (Figure 3.5)

Reassurance

Breast pain often causes women to seek medical attention because they are afraid that it signifies serious pathology in the breast. Non-randomised studies have shown that reassurance is effective management in 70% of women (Figure 3.6).

Non-specific measures

Pain in bed at night is a problem for many women with both chest wall pain and true mastalgia. Wearing a soft, supportive bra at night stops the breast pulling down on the chest wall, supports tender breast tissue and helps many women to sleep. For chest wall pain, gentle exercise and stretching of the muscles, such as provided by swimming, seem sensible and are often advised, but this has not been studied. Lifestyle changes such as limiting the length of time spent sitting at a computer by taking regular breaks would also be sensible.

Researchers have suggested that some women get breast pain because of overstimulation of breast cells by methylxanthines as

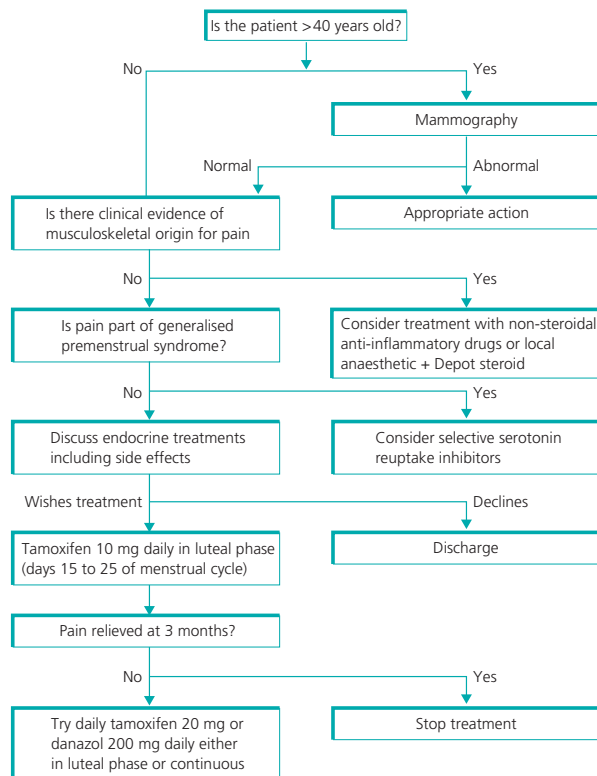


Figure 3.5 Management of breast pain in breast clinic.

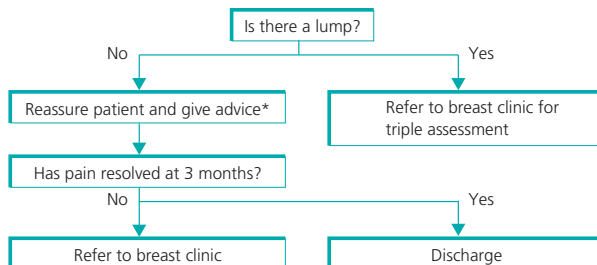


Figure 3.6 Patient presents to GP with breast pain (wear supportive, well-fitting bra, take simple analgesics for pain, regular gentle exercise).

a result of high caffeine intake from tea, coffee and soft drinks. However, one study found identical serum caffeine concentrations in women with and without mastalgia, and randomised trials have failed to demonstrate a benefit for caffeine restriction. Any association between mastalgia and caffeine intake thus remains unproved.

Evening primrose oil (EPO), gammalinoleic acid (GLA) and efamast

Preparations containing GLA were used in the treatment of mastalgia until October 2002, when they were withdrawn from prescription by the UK Medicines Control Agency, as it considered that

there was no good evidence to support their use. Two double-blind randomised controlled trials of EPO compared with placebo have been conducted and published. Neither study showed any difference in outcome between treatment and control groups. There was a reported improvement in symptoms during the first three months of treatment with a worsening of symptoms after crossover, regardless of whether patients received treatment or placebo first. A further study showed improvement in pain scores in the treated group for both cyclical and non-cyclical pain, but this study did not report results after crossover and there was a high drop-out rate in the placebo arm. While other studies have been published, these were not randomised or blinded.

Low-fat diet

Two randomised controlled studies have shown that a low-fat diet is effective in improving cyclical mastalgia. Both studies limited the dietary fat intake to less than 15% of calories, and patients who responded showed changes in their serum lipid profiles. These studies were not blinded, so a placebo effect cannot be excluded. Such low-fat diets are difficult to maintain for longer than a few weeks.

Danazol

One double-blind randomised controlled trial of danazol 200 mg/day compared with placebo showed a significant improvement in breast pain. A second, larger double-blind randomised controlled trial compared danazol 200 mg/day with tamoxifen 10 mg/day or placebo. Both danazol and tamoxifen were effective in treating breast pain compared with placebo, but women taking tamoxifen reported fewer side effects. Restricting the use of danazol to the luteal phase of the menstrual cycle reduces side effects. In a double-blind randomised controlled trial of danazol taken only during the luteal phase compared with placebo, mastalgia was improved by danazol without an excess of adverse events compared with the placebo.

Tamoxifen

Tamoxifen 20 mg/day has been shown to be superior to placebo in one double-blind randomised controlled trial, and pain relief was maintained in 72% one year after use. When tamoxifen 10 mg/day was compared with danazol 200 mg/day, tamoxifen was superior to danazol. Women reported fewer adverse events with tamoxifen and more tamoxifen patients (53%) were pain free at one year than in the danazol group (37%). Giving tamoxifen only in the luteal phase of the menstrual cycle abolished pain in 85% of women in one study, regardless of whether they took 10 mg/day or 20 mg/day. A quarter of the women in the 10 mg group had pain at one year compared with 30% in the 20 mg group; adverse events were reported in 21% and 35% respectively, and included hot flushes and vaginal discharge. A meta-analysis of treatments for mastalgia restricted to tamoxifen, bromocriptine, danazol, evening primrose oil and placebo showed that tamoxifen was the most effective treatment with the least side effects.

Studies with tamoxifen gel applied to the breast indicate that this is an effective treatment, but it is not in common use and not widely available.

Other hormone-based treatments

Progestogens and progesterone have been used orally, topically (applied to the skin of the breast) and vaginally. Compared with placebo, oral medroxyprogesterone acetate did not produce any benefit in a dose of 20 mg/day given during the luteal phase. Topical progesterone produced no benefit in two randomised controlled trials, but in a double-blind randomised controlled trial of microionised progesterone administered in the luteal phase, 65% of treated women and 22% of patients receiving placebo had a 50% reduction in pain. Gestrinone, a synthetic steroid similar to danazol, has the advantage that the woman does not require additional contraception. Compared with placebo, gestrinone 2.5 mg twice a week produced a greater reduction in pain, but 41% of the women complained of adverse events. Dopamine agonists, such as bromocriptine and lisuride maleate, which inhibit prolactin release, seem effective in reducing breast pain. Although bromocriptine is effective at relieving pain compared with placebo, it is less effective than danazol and up to 80% of women develop side effects including headaches and dizziness. It is thus no longer used to treat breast pain. A placebo controlled trial has shown that lisuride is effective in reducing breast pain.

Non-hormonal treatments

Individual phyto-oestrogens, such as genistein and isoflavins, and soya milk, which is rich in genistein, have been investigated as treatments for breast pain. Only soya milk has been subjected to a double-blind randomised controlled study, with cows' milk being used as a control. An improvement in symptoms was noted in 56% of test patients and 10% of controls, but the authors reported that non-compliance was a problem. Serum levels of phyto-oestrogens were not raised in some patients who reported a response to treatment, suggesting that they were not actually taking the soya. The major reason for non-compliance was that the soya drink was considered unpalatable.

Agnus castus, a fruit extract, has been subjected to a double-blind randomised controlled trial for the treatment of both premenstrual syndrome and mastalgia. Treatment with agnus castus showed a significant improvement in visual analogue pain scores and treatment was well tolerated. Meta-analysis of 10 double-blind randomised controlled trials of selective serotonin reuptake inhibitors (SSRIs) used in women with premenstrual symptoms, including four studies that specifically included physical symptoms, showed SSRIs to be more effective than placebo at relieving breast pain. Interestingly, SSRIs did have an effect on fatty acid profiles.

Conclusion

Several treatments are available to treat true mastalgia. There is no single ideal therapy. Reassurance is the mainstay of treatment and is effective. Tamoxifen 10 mg limited to the luteal phase of the menstrual cycle produces the highest rates of pain control with few short-term adverse events and the lowest recurrence rates of pain at one year, but it is not licensed for the treatment of mastalgia. Danazol given in the luteal phase is also effective and causes fewer adverse events compared to continuous treatment. For women

who have mastalgia as part of premenstrual syndrome, agnus castus and an SSRI are options. Further studies of more tolerable dietary manipulations are needed. Research evaluating more palatable soya supplements may be worthwhile. EPO has not been shown to be an effective agent. It is important to remember that the majority of sufferers have chest wall pain and these agents offer little if any benefit for such pain.

Tamoxifen is not currently licensed for breast pain. Concerns that long-term use in healthy women is associated with an increased risk of deep vein thrombosis and endometrial cancer are not an issue in premenopausal women, as studies have shown no significant increase in these conditions in women having regular menstrual cycles. Studies with tamoxifen gel applied topically to the breast suggest that this may be as effective as oral treatment without the side effects.

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