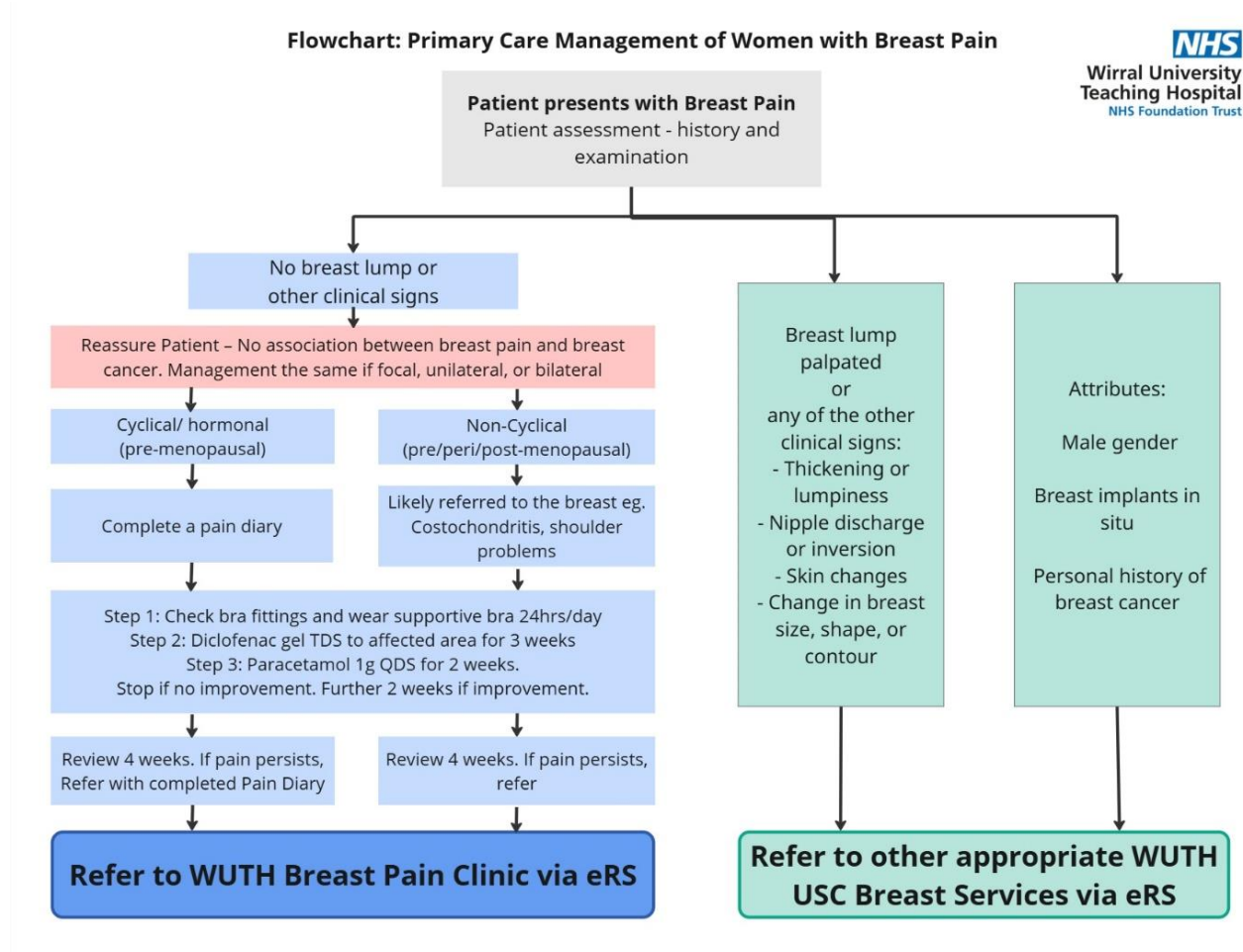


Breast Pain Management – Information for GPs

Flowchart for primary care management of women with breast pain



More detailed information for GPs

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 new 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. Unlike hormonal mastalgia (35-50yrs).

Careful clinical examination is essential to help determine the site/origin of the pain. 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 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 troublesome pain, providing that there are no contraindications, nonsteroidal 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.

Ask the patient about her bra and ensure that if she is wearing an underwire bra it is fitting comfortably and not pressing on lateral chest wall. Firm or total support non-wire bras may be more comfortable. Encourage a range of exercise that will gently stretch all muscle of chest wall and shoulder. Most gyms have exercise classes for different age groups and water based classes- aqua aerobics, aqua-jogging/running or aqua-Zumba will provide an excellent workout of all muscle groups without any impact on joints. For any land based exercise we would advise a sports bra (these are different from support bras). Sports bras are designed to hold the breasts firmly against the chest wall (squash) to decrease movement and they should not be worn for long periods. A good support bra will lift the breasts upwards and off the chest wall and are for all day, everyday use. A breast pain chart can be used to report pain levels and levels of activity and success.

True mastalgia (cyclical mastalgia/hormonal breast pain)

Pain arising in the breast tissue itself is often associated with cyclical swelling and nodularity. 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.

Treatments for true mastalgia

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. All treatment advice is the same for both types of pain but after 23 month diary and gentle but increasing activity we would consider endocrine blocking treatment. This would be quite rare now though compared to in the past and must be instigated by a breast consultant with a clear management plan for the GP. It is unusual for the breast unit to prescribe Tamoxifen or danazol (only danazol is currently licensed). Both have significant side effects and breast pain is not a disease but a symptom of cancer and it is important for the patient to make changes that will not only help the breast pain but improve health and quality of life.

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.

Possibly helpful

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.

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 micronised 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.

Previous treatment now thought to be incorrect

Caffeine:

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

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.

Within the breast unit we only very rarely give tamoxifen or danazol. We would wish all patients to complete an activity and pain diary. Both pains are likely to benefit from aerobic activity. The benefit of aerobic activity is the overall improvement in physical and mental health. If maintained, government guidelines recommends 150 mins per week of moderate aerobic activity (slightly short of breath-activity).