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Review article

Cyclic and non-cyclic breast-pain: A systematic review on pain reduction, side effects, and quality of life for various treatments



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ABSTRACT

Cyclic and non-cyclic breast-pain: A systematic review on pain reduction, side effects, and quality of life for various treatments.

Background: No clear systematic-review on all the various treatment regimen for (Non-) cyclical-breast-pain currently exists.

Objectives: The aim of this study was to assess the various forms of therapy for treatment of breast-pain and the evidence for their effectiveness.

Search strategy: Search-terms included 'mastalgia' and 'therapy' or 'hormones' or 'nsaid' or 'psychotherapy' or 'analgesia' or 'surgery', and synonyms.

Selection criteria: The review was conducted according to the Preferred Reporting Items for Systematic-reviews and Meta-Analysis guidelines. RCT's and pro-/retrospective studies reporting on treatment of breast-pain were considered eligible. Minimal follow-up and sample-size criteria were 6 months and 10 patients respectively.

Data collection and analysis: Data was extracted using standardized tables and encompassed number of subjects, type of breast-pain and treatment, efficacy of treatment and clinical complications/side-effects. No pooling of data could be achieved due to heterogeneity amongst studies.

Main results: Twenty-three studies were included, that reported on 2100 patients in total. Topical-Diclofenac was found to reduce pain by 58.7 and 63.3 on a Visual-Analogue-Scale (VAS) in cyclical and non-cyclical-breast-pain respectively. Persistent cyclical-breast-pain can be treated with short courses (2–6 months) of either Bromocryptine (VAS \downarrow = 25.4) or Danazol (VAS \downarrow = 33.6) as long as benefits outweigh the side-effects. Last-resort options for unresponsive and severe debilitating breast-pain include surgery in the form of bilateral mastectomy with reconstruction.

Conclusions: Pain reduction in patients with breast-pain can be achieved with analgesics, hormonal-regimen and possibly surgery as a last resort. Additional studies are needed with well-described patient-characteristics, robust study set-up, and longer follow-up times.

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Introduction

The term "breast-pain" is often used to describe pain in one or both breasts ranging from mild tension to agonizing pain [1–3], and dates from 1829 when first defined in this context by Cooper et al. [4] The definition has endured obscurity since then, because of a variety of different terms used to describe similar problems, such as mastalgia, mastodynia, fibrocystic-breast-disease or – syndrome. It can be categorized in three categories; cyclical, noncyclical and extra-mammary.

Cyclical-Breast-pain is associated with the menstrual-cycle, with an onset around the late-luteal phase and cessation or reduction around the menstrual phase and is caused by normal hormonal changes that stimulate the ductal elements (estrogen), stroma (progestin) or ductal secretion (prolactin). The pain is typically bilateral, localized in the upper lateral quadrant and can sometimes be associated with palpable lumps. However, a relation with fibrocystic-breast-disease or abnormalities in hormone levels could not be found [5]. Another biochemical abnormality thought to cause breast-pain is that of the lipo-acidic-profile with diets limiting fat intake possibly decreasing symptoms. However, no clear biochemical aberration in this lipo-acidic-profile has been found [6–8]. The onset is typically around the age of thirty to forty, with known cases of remissions during pregnancy, lactation or menopause [9].

Non-cyclical-breast-pain, mostly constant or intermittent in nature frequently involves post-menopausal women. It is typically manifested as a more diffuse unilateral pain and mostly involves one quadrant only. The onset is typically around the fourth and fifth decennia and causes – although found in only a small portion [9–11] – include; previous pregnancy, lactation, thrombophlebitis, cysts, benign tumors, duct-ectasia, side-effects, stretching of Cooper's ligaments, diet and lifestyle-factors, and hormone-replacement-therapy [2].

Extra-mammary-pain, which is most often referred-pain from sources outside the breast can be caused by musculoskeletal, cardiovascular, or biliary-pathologies and has also been attributed to neurological-pathologies (herpes zoster), or can be psychological in origin. The treatment of extra-mammary pain is beyond the scope of this review.

The most important first step is to screen for breast-cancer, not only to initiate therapy if breast-cancer is diagnosed, but also because *excluding* the possibility of cancer and reassuring the patient provides adequate relief in 78–85% of women [12,13]. In the remaining group breast-pain is described as moderate to severe and these women seek help because of significant interference with routine daily activities [14,15].

Treatments described for cyclical and non-cyclical-breast-pain partly overlap and include: symptomatic-relief (support-garments); psychological-counseling; non-hormonal-therapy; hormonal-therapy and surgery. Until now, of these treatments only reassurance and analgesics have been proven effective forms of therapy in small prospective studies and randomized controlled trials [16,17]. Furthermore, studies comparing different regimens of hormonal-therapy show great heterogeneity besides being partly effective and associated with significant side-effects. Three previously published (systematic)-reviews [18-20] provide good overviews of the current literature. Srivastava et al. [19] performed a meta-analysis of studies reporting on the most commonly used treatments (Bromocrpytine, Danazol, Tamoxifen and Evening-Primrose-oil) for breast-pain without specifying the type (cyclical vs non-cylcical). They included all follow-up periods and reported pain on various outcomes (i.e. pain-score, proportion of patients with pain-relief). Both Iddon et al., and Kataria et al. [18,20] while clearly describing the classification and etiology of breast-pain, give a compact description of the various treatment options, but do not provide comprehensive data on outcomes like pain-decrease, side-effects, drop-out and quality of life (QoL).

Objective

The objective of this study was to assess the various forms of therapy for treatment of breast-pain and the evidence for their effectiveness. We aim to give a comprehensive overview of the literature on the outcomes of various therapies for the different forms of benign breast-pain with regard to pain reduction, quality-of-life, side-effects and drop-out.

Methods

This is a systematic-review of literature reporting on breastpain of the female breast conducted according to the Preferred-

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