Clinical Evaluation of Mastalgia

Houman Tavaf-Motamen, MD; Deborah N. Ader, PhD; Matrice W. Browne, MD; Craig D. Shriver, MD

Objective: To describe an accurate and reproducible method to quantify a patient’s subjective experience of breast pain.

Design: Prospective diary study.

Setting: Military tertiary care hospital.

Patients: Thirty female military health care beneficiaries from the Walter Reed Army Medical Center, Washington, DC, gynecology and general surgery clinics.

Main Outcome Measures: Daily mastalgia was recorded using a visual analog scale and menstrual symptoms were measured using a daily questionnaire. These measures were correlated with results of a screening questionnaire completed prior to study entry.

Results: Patients identified as having cyclical mastalgia based on the screening questionnaire (n=15) were found to have higher peak perimenstrual mastalgia according to their daily diaries than patients who did not meet diagnostic criteria (n=15) (5.3±0.7 vs 3.5±0.5, P<.001). Applying the same criteria used in the screening questionnaire to the diary data, 17 of 30 patients met diagnostic criteria for cyclical mastalgia. The ability of the screening questionnaire to predict the results of the prospective diary data was calculated, and positive and negative predictive values were 73% and 60%, respectively. Most patients with cyclical mastalgia also have other perimenstrual psychological and somatic complaints, although a subset of patients has high levels of mastalgia with minimal associated symptoms.

Conclusions: Accurate assessment of mastalgia cannot be done with a retrospective questionnaire and requires prospective diary evaluation, owing to the variable and subjective nature of symptoms and recall bias. A daily visual analog scale provides reproducible results and is easy for patients to use.

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Mastalgia is the most common breast-related complaint of patients seeking care at both primary care clinics and breast referral centers. Two thirds of screened patients in most series complain of breast pain, of which more than 50% is cyclical in nature.1-3 While most patients only require reassurance of the benign nature of their complaint, up to 15% will require further therapy.2 Despite the pervasive nature of this condition, it has received little attention clinically or in the US medical literature, with the majority of references originating in Great Britain and western Europe. This relative inattention may be due to the misconception that breast pain is a normal part of the perimenstrual symptom complex and that there is no acceptable treatment available. To study and treat mastalgia effectively, an accurate and reproducible method to record a patient’s subjective experience of breast pain is needed.

Patients identified as having cyclical mastalgia based on the screening questionnaire were found to have higher peak perimenstrual breast pain noted in their daily mastalgia diaries than those who did not meet screening questionnaire diagnostic criteria (5.3±0.7 vs 3.5±0.5, P<.001). Applying the same criteria used to make a diagnosis of cyclical mastalgia on the screening questionnaire (ie, duration ≥5 days and peak intensity >4), 17 of 30 patients met diagnostic criteria for cyclical mastalgia using the diary data. The positive predictive value, negative predictive value, sensitivity, and specificity of the screening questionnaire were calculated using the prospective

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SUBJECTS AND METHODS

All human studies were performed in accordance with the protocol approved by an institutional review board and informed consent was obtained from all subjects prior to study enrollment. Patients seeking care at the Walter Reed Army Hospital, Washington, DC, gynecology and general surgery breast clinics were asked to complete a screening questionnaire regarding the intensity and duration of their perimenstrual breast pain. Intensity of mastalgia was measured with a visual analog scale. Responses were quantified by measuring the distance marked in centimeters, from 0 (no breast pain) to 10 (extreme breast pain). A diagnosis of cyclical mastalgia, using a modification of the criteria proposed by the mastalgia clinic at Cardiff, Wales, was made if a patient claimed perimenstrual breast pain for 5 days or more per cycle with a symptom severity score greater than 4 cm on the visual analog scale.

Thirty patients were given diaries in which symptoms of mastalgia were recorded daily an average of 141 days, using the same visual analog scale. Half of these 30 patients met the screening questionnaire diagnostic criteria for cyclical mastalgia, while the remaining 15 had lesser and nondiagnostic breast pain. Duration of mastalgia and peak mastalgia was determined for each menstrual cycle and averaged for each patient.

The same diagnostic criteria used in the screening questionnaire, namely, mean duration of at least 5 days per cycle and mean peak perimenstrual mastalgia greater than 4 cm on the visual analog scale, were applied to the prospectively gathered diary data. The positive predictive value, negative predictive value, sensitivity, and specificity of the screening questionnaire were calculated using the prospective diary data as the diagnostic criterion standard.

Patients completing the mastalgia diary were also evaluated regarding 33 other psychological and somatic complaints (Table 1) using a standard Menstrual Symptom Severity List. Each symptom was scored from 0 (absent) to 4 (extreme) daily. The scores for each symptom were summed for a cumulative daily symptom score. Peak perimenstrual symptom score was determined for each menstrual cycle and averaged for each patient.

Results are reported as mean±SEM. Pearson correlations were computed and comparisons between groups were made with the Student t test. The α limit was set at P<.05, 2 tailed, for all tests.

diary data as the diagnostic criterion standard, and were 73%, 60%, 65%, and 69%, respectively.

Overall, prospectively measured breast pain was significantly correlated with other menstrual complaints with a correlation coefficient of 0.54 (P<.001). Most patients experience mastalgia in association with high levels of other menstrual complaints, although a subset of patients (12% of patients with cyclical mastalgia) has high levels of mastalgia but relatively minimal associated symptoms. Figure 1 demonstrates the experience of a patient in whom catamenial symptoms mirror mastalgia time course. In contrast, Figure 2 represents a patient who has significant cyclical breast pain but minimal associated symptoms.

Cyclical mastalgia is an under-recognized and poorly understood disorder that is common among patients in the primary care setting and those referred for surgical consultation. Studies have shown that in a standard breast clinic or general surgery practice setting, 15% of premenopausal women will have clinically significant cyclical mastalgia. However, this disorder will not be appropriately diagnosed unless patients are properly evaluated for it. Our own data at the Walter Reed breast clinic demonstrates that, of those women diagnosed with cyclical mastalgia, the disorder significantly interferes with social, physical, and sexual activities in 13%, 35%, and 45% of patients, respectively. Moreover, we have shown that there is a significant increased utilization of health care resources, specifically mammography, in women younger than 35 years who reported a history of cyclical mastalgia.

See Invited Commentary at end of article

Study of cyclical mastalgia is confounded by the variable and subjective nature of symptoms as well as recall bias, prompting some authors to mandate the use of prospective studies in the evaluation of mastalgia. Our results corroborate this sentiment. When patients were assigned to a diagnostic group based on their answers to a mastalgia screening questionnaire, the agreement with the prospectively gathered diary data was only moderate, with a positive and negative predictive value of 73% and 60%, respectively. These figures will vary with the prevalence of mastalgia in the study population and with

Table 1. Menstrual Symptom Severity List

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Severity</th>
</tr>
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<tbody>
<tr>
<td>Abdominal bulging</td>
<td>Hot flash/sweating</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>Hand/feet swelling</td>
</tr>
<tr>
<td>Anger</td>
<td>Increased sleepiness</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Inertia</td>
</tr>
<tr>
<td>Backache</td>
<td>Irritable</td>
</tr>
<tr>
<td>Breast pain*</td>
<td>Irritable</td>
</tr>
<tr>
<td>Can’t get to sleep</td>
<td>Lonely</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>Mood swings</td>
</tr>
<tr>
<td>Decreased concentration</td>
<td>Night awakening</td>
</tr>
<tr>
<td>Decreased decisiveness</td>
<td>Out of control</td>
</tr>
<tr>
<td>Decreased sexual desire</td>
<td>Rash</td>
</tr>
<tr>
<td>Desire to be alone</td>
<td>Sad</td>
</tr>
<tr>
<td>Early awakening</td>
<td>Sensitivity to cold</td>
</tr>
<tr>
<td>Food craving</td>
<td>Tearful</td>
</tr>
<tr>
<td>Guilt</td>
<td>Tension</td>
</tr>
<tr>
<td>Headache</td>
<td>Weight gain</td>
</tr>
<tr>
<td>Hostility</td>
<td></td>
</tr>
</tbody>
</table>

*Breast pain was omitted when calculating the perimenstrual symptom score and when calculating correlation to visual analog scale mastalgia levels.

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the threshold at which the diagnosis of mastalgia is arrived. We believe that the standard of care for the study, diagnosis, and treatment of cyclical mastalgia is to perform a diary study for a minimum of 2 cycles before and after an intervention. We have found a daily mastalgia visual analog scale to provide reproducible results and to be intuitive and easy for patients to use. In our experience, a questionnaire relying on patient recall is useful for screening, but is not adequately sensitive or specific to determine who is an appropriate candidate for treatment.

As more research is completed on this topic, common clinical practices are being called into question and new treatments for cyclical mastalgia are gaining acceptance. Despite multiple studies showing no advantage to treatments including diuretic use, abstinence from methylyxanthines (such as coffee, chocolate, and other derivatives), or vitamin supplementation, these modalities are still being advocated in the United States.8-10 Research has shown that for most patients, reassurance that mastalgia is not associated with a malignant neoplasm is all that is required.1,4 For patients with refractory symptoms, multiple hormonal agents such as gestrinone,11 danazol,12 bromocriptine,13 and tamoxifen14 have been shown to be efficacious when compared with placebo. Unfortunately, these medications are associated with high degrees of adverse reactions, including hirsutism, hot flashes, and dysfunctional uterine bleeding, among many others. γ-Linolenic acid (GLA), found in evening primrose oil, is an over-the-counter nonhormonal agent with minimal adverse effects that has proven efficacy in European placebo-controlled trials,15 but is not approved by the US Food and Drug Administration for treatment of mastalgia. It is thought that GLA works by increasing the ratio of essential unsaturated fatty acids to saturated fatty acids in the body. Our center is embarking on a prospective, double-blind, placebo-controlled trial of GLA for the treatment of cyclical mastalgia.

Diary data show a correlation between mastalgia and other cyclical somatic and psychological complaints; however, there seems to be a subset of patients (12% with cyclical mastalgia in our study population) with significant mastalgia but minimal associated symptoms. This divergence of symptom complexes suggests that, at least for some patients, mastalgia is distinct from other menstrual complaints. It will be interesting to note whether this subset of patients differs in response to mastalgia-specific treatments such as GLA.

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The opinions or assertions herein are those of the authors and do not necessarily represent the views of the US Army or the US Department of Defense.

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REFERENCES

In this issue of the ARCHIVES, Tavaf-Motamen and associates give a wake-up call to physicians who study or treat mastodynia. They compared the recall questionnaires of 30 women with breast pain with each patient’s daily visual analog scale for breast pain and found poor agreement. Only 73% of those identified as having cyclic mastalgia based on the questionnaire met the same criteria based on their daily diaries. Furthermore, the intensity of other somatic menstrual complaints was not always in accord with the severity of breast pain on the analog scales. Their data emphasize the complexity of this problem and the necessity for objective means of evaluating its course and treatment. In the United States, breast pain is almost the norm. In my surgical practice, only 2.5% of patients referred for breast-related problems are seen primarily for breast pain, but on questioning, the majority report some degree of mastodynia. Only when the pain is severe or debilitating does it become the focus of attention. In postmenopausal women, the problem is often related to hormone replacement therapy. If the cause is not obvious, the tendency is to recommend relatively harmless remedies and reserve danocrine for resistant cases. The former include caffeine and tyramine restriction, vitamin E, and evening primrose oil, each with a tenuous rationale. The subjectivity and variable course of symptoms often preclude an accurate assessment of results. The authors provide few clues about their enrollment questionnaire, and the periods evaluated with the questionnaire and the daily diary were not coincident, surely a problem when the course of a clinical problem is uneven. While it comes as no surprise that patients’ histories are not always accurate, the message is clear that understanding mastodynia and its treatment requires more than hearsay.

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A Comparison of Estrogen Replacement, Pravastatin, and Combined Treatment for the Management of Hypercholesterolemia in Postmenopausal Women
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Objectives: To evaluate and compare the lipid-altering effects of conjugated estrogens and pravastatin, alone and in combination, in postmenopausal women with hypercholesterolemia.

Methods: This was a double-blind, randomized, placebo-controlled clinical trial with 4 parallel groups. Participants (N=76) were randomly assigned to receive conjugated estrogens, 0.625 mg/d; pravastatin sodium, 20 mg/d; conjugated estrogens plus pravastatin; or a placebo for 16 weeks.

Results: Primary end points were changes in serum lipid parameters. Among participants treated with conjugated estrogens, levels of non–high density lipoprotein cholesterol (non–HDL-C) (13.0%) and calculated low density lipoprotein cholesterol (LDL-C) (13.5%) decreased, while levels of HDL-C (22.5%) and triglycerides (4.2%) increased. Participants in the pravastatin group achieved reductions of 23.7% and 25.4% in non–HDL-C and calculated LDL-C levels, respectively. Levels of HDL-C increased slightly (3.7%) and triglycerides decreased by 12.1%. Among participants treated with a combination of conjugated estrogens plus pravastatin, the non–HDL-C (−25.2%) and calculated LDL-C (−28.7%) responses were similar to those of the pravastatin group, and the HDL-C response (21.2%) was similar to that observed in the conjugated estrogens group. Triglyceride levels remained similar to baseline (−0.9%) in the combined treatment group.

Conclusions: Administration of conjugated estrogens resulted in potentially antiatherogenic changes in levels of non–HDL-C, HDL-C, and calculated LDL-C. The HDL-C response to combined treatment was similar to that observed in women taking conjugated estrogens alone, while the non–HDL-C and LDL-C responses to combined treatment were similar to those produced by pravastatin therapy alone. These findings support the position of the National Cholesterol Education Program that estrogen replacement, with a progestin where indicated, should be given consideration as a therapeutic option for the management of hypercholesterolemia in postmenopausal women. Arch Intern Med. 1997;157:1186-1192

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