

DILEMMA OF MASTALGIA

M. NAJMUDDIN SHABBIR

Department of Surgery, Fatima Jinnah Dental College, Karachi

ABSTRACT:

Objective: To determine whether instances of mastalgia labelled as refractory were truly refractory to treatment or whether they were merely instances of inadequate treatment, by observing their response to non-pharmacological treatment.

Design & Duration: A prospective observational study carried out from 2003 to 2005.

Setting: The study was undertaken in an Out-patient Breast Clinic setting at Sarfaraz Rafiquee Shaheed Hospital and Tahir Medical Centre, Karachi.

Patients: Fifty-eight patients with "refractory mastalgia" were evaluated.

Methodology: The patients were treated by reassurance, low-fat, methyl xanthine restricted diet and dietary supplementation with 500 mg/day of evening primrose oil. The response was assessed at three and six months after beginning the treatment.

Results: There was a 94.3% overall response to non-pharmacological treatment, which indicated that they were all instances of inadequately treated mastalgia and not refractory mastalgia.

Conclusion: Cases of mastalgia labelled as refractory are usually due to inadequacy of treatment.

KEY WORDS: Mastalgia, Refractory, Non-Pharmacological Treatment

INTRODUCTION

Mastalgia is a commonly encountered condition, both in the primary care and the surgical outpatient settings in the subcontinent¹⁻³. The standard algorithms of management are not universally adhered to by the clinicians. This is not only true of Pakistan, but elsewhere in the world⁴ also. Inadequacy of treatment results in the instances of mastalgia being labelled as "refractory" to treatment with referral to breast clinics for specialized management. Delayed treatment results in unnecessary physical, emotional and financial strain on the patients. This is unacceptable in itself and particularly in the context of mastalgia which is a common benign breast disorder responding, in the majority of instances, to reassurance⁵.

PATIENTS & METHODS

A prospective observational study was undertaken in an outpatient breast clinic setting. Fifty-eight patients, referred for refractory mastalgia were enrolled to determine whether they were true instances of the refractory mastalgia or whether they were merely instances of inadequately treated mastalgia. This was done by observing their response to a protocol of the non-pharmacological management.

All patients were evaluated to determine the type of mastalgia, its duration, severity, past treatment and response. Further evaluation consisted of clinical breast examination, blood complete picture, thyroid, prolactin and lipid profile assessment. Investigations such as the mammogram, fine needle aspiration cytology (FNAC), etc. were undertaken only as and when required. All the patients were taught breast self-examination during the period of evaluation.

The treatment, initiated after assessment, comprised of reassurance, advice on a low-fat, methyl xanthine restricted diet and dietary supplementation with 500 mg/day of evening primrose oil capsules for the duration of the study i.e. six months. Literate patients or a family member in the case of sub-literate patients were taught to maintain a pain diary during the follow-up period.

Correspondence:

Dr. M. Najmuddin Shabbir, Associate Prof. & Head of the Department of General Surgery, Fatima Jinnah Dental College, Karachi.

Phones: 0300-8229833.

E-mail: drnajamshabbir461@hotmail.com

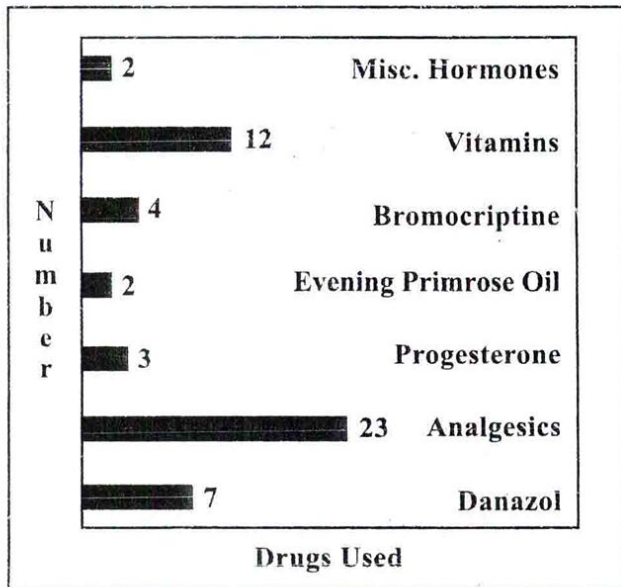


Fig. 1. Analysis of Past Drug Treatment for Mastalgia

The first review was undertaken three months later and the second, six months later. A simple visual analogue scale (using the individual patient as her own control) was used to quantify pain at initial assessment, and the response to treatment during the two reviews. The response was graded as Grade I (excellent), Grade II (substantial), Grade III (poor) and Grade IV (no response). During the review, compliance with breast self examination and evening primrose oil supplementation were noted specifically. Compliance of the advice regarding dietary fat changes and methyl xanthine restriction were not assessed objectively, but was merely reiterated as a health message.

RESULTS

Out of the 58 women enrolled into the study, five were lost to follow-up. Amongst the remaining, 30 (56.6%) patients had cyclical mastalgia, while 23 (43.4%) had

true non-cyclical mastalgia, of a severe degree. The median duration of cyclical mastalgia was three years (a mean of 3.93 years) and that of non-cyclical mastalgia one year (mean 2.35 years). The median age of cyclical mastalgia patients was 36.5 years (mean 36.63 years) and that of non-cyclical mastalgia patients was 39 years (mean 37.91 years).

Analysis of the past treatment revealed that none of these patients had been reassured about the nature of the pain and the absence of serious underlying breast pathology. Twenty-three (43.4%) patients had been prescribed analgesia (non-steroidal anti-inflammatory drugs) and 12 (22.6%) had been prescribed vitamins E. The rest (18 patients) had been treated with danazol, bromocriptine, progesterone, miscellaneous hormone combinations and evening primrose oil (Fig. 1). The dose and the duration of the treatment was not reliably discernable from the multiple prescriptions issued to most patients by multiple medical practitioners. No patient admitted to improvement with the past treatment.

Clinical breast examination revealed that 34 (64.2%) patients had nodularity in the breasts and 2 (3.8%) had a fibroadenoma (confirmed by FNAC), while 17 (32.1%) had normal breasts. Investigations in the form of blood complete picture, thyroid profile, prolactin and the lipid profile assessment revealed no statistically significant abnormalities.

Cyclical Mastalgia

At the 3-months review, the response to treatment was Grade I (excellent) in 13 (43.3%) cases, while 14 (46.7%) patients had Grade II (substantial) and three (10.0%) Grade III (poor) response. None had Grade IV response (Table I).

At the 6-months review, the response to treatment was Grade I (excellent) in 17 (56.6%) cases, while 11 (36.7%) patients had Grade II (substantial) and two (6.7%) had Grade III (poor) response. None had Grade IV response.

Table I. Treatment Response in Cyclical Mastalgia at 3 and 6 months

Grade	Response	Response at 3 months		Response at 6 months	
		No.	%	No.	%
Grade I	(Excellent)	13	43.3	17	56.6
Grade II	(Substantial)	14	46.7	11	36.7
Grade III	(Poor)	03	10.0	02	06.7
Grade IV	(None)	—	—	—	—

Grade	Response	Response at 3 months		Response at 6 months	
		No.	%	No.	%
Grade I	(Excellent)	11	47.8	14	60.9
Grade II	(Substantial)	10	43.5	08	34.8
Grade III	(Poor)	02	08.7	01	04.3
Grade IV	(None)	--	--	--	--

Table II. Treatment Response in Non-Cyclical Mastalgia at 3 and 6 months

Non-Cyclical Mastalgia

In the 3-months review 11 (47.8%) patients had Grade I (excellent) response, 10 (43.5%) had Grade II (substantial) response and two (8.7%) had Grade III (poor) response. None had Grade IV response (Table II).

In the 6-months review 14 (60.9%) patients had Grade I (excellent) response, eight (34.8%) had Grade II (substantial) response and one (4.3%) had Grade III (poor) response. None had Grade IV response (Table II).

Overall Response

At the end of the study an overall response of Grade I or II was seen in 50 (94.3%) patients (95% CI), while three (5.7%) patients had Grade III response (86.1% CI) as shown in Table III.

It was noted that 46 (86.8%) patients were adhering to monthly breast self-examination and all the 53 patients, complied with evening primrose oil supplementation.

DISCUSSION

More and more women are seeking treatment for mastalgia, because of the increasing awareness about breast cancer and the fear that breast pain may be indicative of it. However, most clinicians are ill-trained to handle mastalgia. As breast cancer seldom presents with pain^{6,7},

patients are often dismissed with no formal evaluation, no reassuring explanations and often with a prescription of drugs that has no established therapeutic value or those with irksome or even potentially dangerous side-effects. Such prescription patterns are not unique to our country Pakistan only.

The management of mastalgia has become increasingly refined and standardized in the hands of specialist surgeons. When confronted with a patient of mastalgia, the treatment protocol adopted takes into account the nature, the source and the duration of pain. In the majority of instances, where the pain is mild to moderate and the duration is short-lived (less than six months), after thorough evaluation, the patient is treated by reassurance only. This consist of an explanation that mastalgia is an aberration and not indicative of serious underlying disease. Because of the possibility of spontaneous remission⁸ (approximately 20% in cyclical mastalgia and 59% in non-cyclical mastalgia), pharmacological management is not indicated. This is effective in 80-85% of the patients⁹. In addition, advice is given on the use of supportive undergarments, adhering to a low-fat, methyl xanthine restricted diet and abstention from the drugs like oral contraceptive pill or hormone replacement therapy¹⁰.

In those instances, where the pain is severe or persistent,

Table III. Overall Response to the Treatment

Timing	Diagnosis	Response %			
		Grade I / II		Grade III	
Review at 3 months	Cyclical Mastalgia	90.0	(95% CI)	10.0	(71.5% CI)
	Non-Cyclical Mastalgia	91.3	(95% CI)	08.7	(79.8% CI)
Review at 6 months	Cyclical Mastalgia	93.4	(95% CI)	06.7	(84.6% CI)
	Non-Cyclical Mastalgia	95.7	(95% CI)	04.3	(87.4% CI)
Overall response	Cyclical + Non-Cyclical	94.3	(95% CI)	05.7	(86.1% CI)

in addition to the above steps, evening primrose oil capsules in a therapeutic dose of 3 g/day given orally was until recently the first line drug in the treatment of cyclical mastalgia and true non-cyclical mastalgia. In the UK clinical experience, the overall response rate to it was 44% in cyclical pain and 27% in non-cyclical pain¹¹. Danazol^{12,13} (overall response 70% in cyclical mastalgia and 31% in non-cyclical pain) and tamoxifen¹⁶ (overall response 75% differentiation) were reserved for treatment failure. However, the evening primrose oil does not possess the current standard of therapeutic efficacy (compared to danazol or tamoxifen) required for marketing authorisation as a drug for the treatment of mastalgia. Indeed it has never been listed in the USA, where danazol is the only drug approved by the FDA for the treatment of mastalgia¹⁷. With effect from October 2002, the UK Medicines Control Agency has withdrawn the marketing authorisation¹⁸ given earlier to evening primrose oil, and new drug protocols for the management of the mastalgia are now being drawn up. Evening primrose oil is, however, freely available as a food supplement around the world including Pakistan as there are no safety issues concerning its use.

In this study, analysis of past treatment revealed that none of the patients had been reassured about the nature of the pain and the absence of serious breast pathology. As reassurance is the cornerstone of the successful treatment of mastalgia, it is not surprising that these women continued to seek further treatment, for what they perceived as a serious problem. Forty (75.5%) patients had received analgesia¹⁹, vitamin-E²⁰, progesterone²¹ and miscellaneous hormone combinations²² which are considered non-standard drugs, as the literature supporting their use is conflicting and currently inconclusive. Only a minority of the patients have been treated with danazol, bromocriptine and evening primrose oil which are standard drugs used in the treatment of mastalgia. It is to be noted that use of both danazol and bromocriptine is fraught with side-effects (22% and 45% respectively)²³ and therefore usage needs to be carefully balanced against the severity of mastalgia. As some of these side-effects may be irreversible or even fatal, their use as first line management, particularly in the primary care set-up cannot be recommended.

In the present study patients were treated with a protocol of reassurance, advice on adhering to a low-fat, methyl xanthine restricted diet and dietary supplementation with 500 mg/day of evening primrose oil (not as a therapeutic drug, the dosage of which is 3 g/day). The importance of reassurance in the treatment of mastalgia dictates that it should be the first ingredient in the treatment protocol. The value of methyl xanthine restriction has not been proven²⁴. It has been suggested that low-fat

diets (15% of total calorie value for prolonged periods) may have a positive impact,²⁵ but the creation of randomized trials have proven difficult in practice owing to the lack of patient compliance to a drastic change in dietary habits. Despite lack of concrete evidence, mastalgia patients continue to be given advice on adhering to low-fat, methyl xanthine restricted diets in breast clinics around the world. In this study, while the patients were advised to adhere to such a restricted diet as a life style change, no rigid implementation with evening primrose oil is there as it remains to be established through randomized control trials.

CONCLUSION

The contribution of the individual components of the treatment (reassurance, dietary restriction and supplementation) is impossible to determine in an observational study of this nature. As 50 patients showed a Grade I-II and only three patients Grade III overall response at the end of six months, to non-pharmacological treatment, we may say that 50 out of the 53 (94.3%) patients were in fact instances of inadequately treated mastalgia and not refractory mastalgia, thus proving the aim of this study. The study also illustrates without doubt that there is a definite scope for improvement in mastalgia management.

REFERENCES

1. Shukla HS, Kumar S. Benign Breast Disorders in India (Part II). *World J Surg* 1989; 13:746-9.
2. Khanna AK, Tapodar J, Misra MK. Spectrum of Benign Breast Disorders in a University Hospital. *J Indian Med Assoc* 1997; 95: 5-8.
3. Krishnaswamy U. Profile of Benign Breast Disorders and Diseases in Urban India. *Indian J Surg* 2003; 65:178-81.
4. Pain JA, Cachill CJ. Management of Cyclical Mastalgia. *Br J Clin Pract* 1990; 44: 454-6.
5. Maddox PR, Mansel RE. Management of Breast Pain and Nodularity. *World J Surg* 1989; 13: 669-705.
6. Preece PE, Baum M, Mansel RE, Webster DJ, Fortt RW, Gravelle IH, et al. Importance of Mastalgia in operable Breast Cancer. *Br Med J Clin Res Edin* 1982; 284: 1299-300.
7. Hughes LE, Mansel RE, Webster DJ. Aberrations of normal development and involution (ANDI): a

- concept of benign breast disorders based on pathogenesis. In: *Benign Disorders and Diseases of the Breast: Concept and clinical management*. London: Bailliere Tindall; 1989. p.15-26.
8. Wisbe J, Mansel RE, Pye J. Natural history of the Breast Pain. *Lancet* 1983; 2: 672-4.
 9. Preece PE, Hughes LE, Mansel RE, Baum M, Bolton PM, Gravelle IH. Clinical syndromes of Mastalgia. *Lancet* 1976; 2: 670-3.
 10. Mansel RE, Fenn NJ, Davies EL. Benign Breast Disease and its management. In: *Recent Advances in Surgery* (21). Edinburgh: Churchill Livingstone; 1998. p.71-83.
 11. Pyc JK, Mansel RE, Hughes LE. Clinical experience of Drug treatments for Mastalgia. *Lancet* 1985; 2: 373-7.
 12. Gateley CA, Maddox PR, Mansel RE, Hughes LE. Mastalgia refractory to Drug treatment. *Br J Surg* 1990; 77: 110-2.
 13. Mansel RE, Wisbey JR, Hughes LE. Controlled trial of the antigonadotrophin danazol in Painful nodular Benign Breast Disease. *Lancet* 1982; 1: 928-930.
 14. Durning P, Sellwood RA. Bromocriptine in severe cyclical Breast Pain. *Br J Surg* 1982; 69: 248-9.
 15. Mansel RE, Dogliotti L. European multicentre trial of bromocriptine in cyclical mastalgia. *Lancet* 1990; 335: 190-3.
 16. Fentiman IS, Caleffi M, Hamed H, Chaudary MA. Dosage and duration of tamoxifen treatment in Mastalgia: a controlled trial. *Br J Surg* 1988; 75: 845-6.
 17. BeLieu RM. Mastodynia. *Obstet Gynecol Clin North Am* 1994; 21: 461-77.
 18. World Health Organization Consolidated List of Products whose Consumption and/or Sale have been Banned, Withdrawn, Severely Restricted or Not Approved by Governments. In: *Pharmaceuticals: 5/who-edm-qsm-2003-5.pdf*.
 19. Premenstrual syndrome in Cape Town. Part II. A double blind placebo-controlled study of the efficacy of mefenamic acid. *S Afr Med J* 1986; 70: 159-60.
 20. Emster VL, Goodson WH 3rd, Hunt TK, Petrakis NL, Sickless EA, Miike R. Vitamin E and Benign Breast Disease: a double-blind, randomized clinical trial. *Surgery* 1985; 97: 490-4.
 21. Maddox PR, Harrison BJ, Horobin JM, Walker K, Mansel RE, Preece PE, et al. A randomized controlled trial of medroxyprogesterone acetate in Mastalgia. *Ann R Coll Surg Engl* 1990; 72: 71.
 22. Colin C, Gaspard U, Lambotte R. Relationship of Mastodynia with its endocrine environment and treatment in a double blind trial with lyestrenol. *Arch Gynakol* 1978; 225: 7-13.
 23. Hinton CP, Bishop HM, Holiday HW, Doyle PJ, Blamey RW. A double-blind controlled trial of danazol and bromocriptine in the management of severe cyclical Breast Pain. *Br J Clin Pract* 1986; 40: 326-30.
 24. Ernster VL, Mason L, Goodson WH 3rd, Sickles EA, Sacks ST, Selvin S, et al. Effects of caffeine free diet on Benign Breast Disease: a randomized trial. *Surgery* 1982; 91: 263-7.
 25. Boyd NF, McGuire V, Shannon P, Cousins M, Kriukov L, et al. Effect of a low-fat, high carbohydrate diet on symptoms of cyclical Mastopathy. *Lancet* 1988; 2: 128-32.