Print ISSN: 2321-6379
Online ISSN: 2395-1893
DOI: 10.17354/SUR/2017/93

Original Article

Role of Centchroman in Mastalgia: An Experience in a Tertiary Care Hospital of Vindhya Region

Varsha Shukla[1], Vishnu Patel[2], Rachna Gupta[3], Survind Kumar[1], A P S Gaharwar[4]

[1]Junior Resident, Department of Surgery, Shyam Shah Medical College, Rewa, Madhya Pradesh, India, [2]Assistant Professor, Department of Surgery, Shyam Shah Medical College, Rewa, Madhya Pradesh, India, [3]Associate Professor, Department of Surgery, Shyam Shah Medical College, Rewa, Madhya Pradesh, India, [4]Head, Department of Surgery, Shyam Shah Medical College, Rewa, Madhya Pradesh, India

Abstract

Introduction: Mastalgia or breast pain is the common benign aberration in the breast. It may or may not be associated with nodularity. Centchroman, also known as ormeloxifene ($C_{30}H_{35}NO_3$), is weak estrogen receptor (ER) agonist, strong ER antagonist and therefore a selective ER modulator.

Materials and Methods: A prospective observational study was conducted in patients of mastalgia attending Surgery Outpatient Department of Sanjay Gandhi Memorial Hospital Associated with Shyam Shah Medical College, Rewa, Madhya Pradesh, from August 2015 to July 2016.

Results: Out of 70 patients in our study 30 patients (42.85%) presented with mastalgia alone and 40 patients (57.14%) presented with mastalgia along with nodularity. Mastalgia with or without nodularity was found to be common in the age group of 31-40 years, and the common pattern of presentation was of cyclical mastalgia. At the 12 weeks, 63 patients (90% of patients) of mastalgia showed significant response and had visual analog scale score ≤3. At the end of 12 weeks, 67.5% of patients were free of nodularity and had Lucknow Cardiff scale (LCS) grade 0. Moreover, 87.5% of patients had LCS grade ≤1.

Conclusion: The aim of the study was to observe the efficacy of the drug, centchroman, which can be used as a boon for the patients of exclusively benign but troublesome disorders of the normal development of the breast and in our study it is found effective and safe for mastalgia and nodularity.

Keywords: Mastalgia, Nodularity, VAS, LCS

INTRODUCTION

Diseases of the breast are known from eternity and their mention is found in manuscript of Hippocrates and Sushrut, "father of Indian surgery."

The first illustration regarding breast diseases was written by Sir Astley Copper. In his monograph "illustrations of diseases of breast,"[1] published in 1829. He described many benign breast disorders such as breast pain, nodularity, cystic change, and fibroadenoma.

Access this article online

www.surgeryijss.com

Month of Submission : 02-2017
Month of Peer Review: 03-2017
Month of Acceptance : 04-2017
Month of Publishing : 05-2017

Mastalgia or breast pain is the common benign aberration in the breast. It may or may not be associated with nodularity. Mastalgia may be cyclical or non-cyclical, intermittent or constant, localized or diffuse. Pronounced mastalgia may become a significant problem if the pain and tenderness interfere with woman's life, disturb her sleep and impair sexual activity. Breast tissue is a dynamic structure which undergoes cyclical changes of development and degeneration of lobular tissue with every menstrual cycle superimposed with pregnancy and lactation. Cyclical changes in the breast are mediated by a neuroendocrine response by endocrine and paracrine affect of estrogen, progesterone and prolactin directly, and other factors like methylxanthine which act indirectly. The imbalance between these factors leads to mastalgia and nodularity.[2]

With the social, economical and educational information, increasing number of women solicit medical opinion

Corresponding Author: Dr. Varsha Shukla, 14/140, Arun Nagar, Samiti Colony, Rewa - 486 005, Madhya Pradesh, India. Phone: +91-9425362881. E-mail: varshashukla77@yahoo.com

for breast pain and nodularity. The prime most fear is of malignancy, for which patients should be reassured and convinced about the benign nature of disease. Many pharmacological and non-pharmacological methods have been tried for mastalgia. The drugs used lead to hormonal manipulations such as danazol,[3] bromocriptine,[4] tamoxifene,[5] LHRH[6] analog such as goserelin, evening primrose oil and vitamin E. The non-pharmacological agents who have shown their efficacy are lifestyle modifications, reassurance,[7] breast support garments,[8] and non-steroidal anti-inflammatory gels[9] centchroman, also known as ormeloxifene ($C_{30}H_{35}NO_3$) is weak estrogen receptor (ER) agonist, strong ER antagonist and therefore a selective ER modulator. It is used as a non-steroidal, anti-estrogenic oral contraceptive pill and was developed by the Central Drug and Research Institute Lucknow, Uttar Pradesh, India in 1980's. It was introduced in July 1991 and was marketed in India in 1992 as Saheli, Choice-7 (Hindustan Latex Limited) and Centron (Torrent Pharmaceuticals India Limited). It is free from androgenic and steroidal side effects such as nausea, vomiting, weight gain, acne, and dizziness and it does not delay in fertility.[10] It is very little secreted in milk so no deleterious effect on breastfeeders. Babies born following user failure showed no congenital malformation or any development delay.[11]

MATERIALS AND METHODS

A prospective observational study was conducted in patients of mastalgia attending Surgery Outpatient Department of Sanjay Gandhi Memorial Hospital associated with Shyam Shah Medical College, Rewa, Madhya Pradesh from August 2015 to July 2016.

Women in the age group 20-50 years with mastalgia with or without modularity were included in the study with a sample size of 70. Women with past or family history of breast carcinoma, with discrete breast lump, with polycystic ovarian disease, uterine cervical hyperplasia, pregnant women, women during 6 months of lactation, and all male patients were excluded from the study.

A written and informed consent was taken, and the study was conducted. The patients were provided with the detail printed information in English or Hindi (language the patient understood easily), to explain about the benign nature of the disease, currently available therapies in the institutions with their side effects, the potential benefits of centchroman and its approval by the government of India as a contraceptive pill. For the purpose of the study, the proper clinical assessment was done. Ultrasound breast was done to rule out discrete lump, pelvis and gynecological valuation was done to exclude the patients of polycystic ovarian disease and cervical hyperplasia.

In patients of mastalgia assessment of pain was done using visual analog scale (VAS) which is a psychometric analysis with a line of length 100 mm (10 cm) with 10 points, with 10 lines 1 cm or 10 mm apart. The two end points mark the best imaginable and worst imaginable pain state. Patients were asked to mark their pain on the VAS. Patients were asked to keep record of their pain in breast diary. Breast pain chart in the diary was filled by the patient according to the amount of pain she experienced every day. Patients were asked to shade the blocks according to the severity of the pain. The chart was marked at the date of commencement of menses and at the bottom of the chart any side effects experienced were asked to mention.

In patient presenting with nodularity, Lucknow Cardiff scale (LCS) was used. This scale is a 5 point ordinal scale depicting increasing order of nodularity shown schematically in the upper outer quadrants of a paired breast. Grade 0 indicated a smooth textured breast with extreme extent of normalcy and grade 4 the maximum nodularity. There were five figures that provided a clue to chart nodularity in index breast. Patients were given tablet centchroman 30 mg on biweekly basis for 12 weeks. The serial assessment of the patients was done as per VAS, LCS, and clinical assessment. The patients were evaluated at the 1st week to assess about the side effects of the drug they experienced during the treatment. Further, follow ups were done at 2, 4, 8, 12 and 16 weeks. Self-reporting was taken as compliance. The reduction in VAS ≤3 on treatment was considered to be the efficacy of the drug.

OBSERVATIONS AND RESULTS

Out of 70 patients in our study, 30 patients (42.85%) presented with mastalgia alone and 40 patients (57.14%) presented with mastalgia along with nodularity. Mastalgia with or without nodularity was found to be common in the age group of 31-40 years, and the common pattern of presentation was of cyclical mastalgia.

Most of the patients (62.85%) presented with severe pain on VAS with VAS 10. The reduction in VAS to ≤3 on treatment was considered to be the efficacy of the drug. After administration of centchroman 30 mg on biweekly basis, there was a significant reduction in mastalgia.

In the follow-up at 2 weeks, 49 patients (70% of patients) were having VAS score ≤3. At 4 weeks, 56 patients had VAS score ≤3 (80%). At 8 weeks, 60 patients had VAS score ≤3. (85.7%). At the 12 weeks, 63 patients (90% of patients) of mastalgia showed significant response and had VAS score ≤3. At the 16 weeks (1 month after discontinuation of drug), 85.7% of patients had VAS

score ≤3. Three patients (4.28%) patient had relapse of pain after the discontinuation of the drug (Table 1).

At the start of the study, all the 70 patients had mastalgia on VAS ≤6. After the 2 weeks of treatment 49 patients which accounted for 70% had VAS score ≤3. Moreover, only 21 patients were left with VAS score of 6 or more than 6. At the end of 4 weeks, 56 patients had VAS score ≤3, accounting to be 80% and only 14 patients had VAS score6 or more than 6. At the end of 8 weeks, 60 patients (85.7%) had VAS score ≤3 and only 10 patients were left with VAS score 6 or more than 6. At the end of 12 weeks, 63 (90%) patients had VAS score ≤3. Moreover, only 7 patients were left with VAS score 6 or more than 6. At the end of 16 weeks, 60 patients (85.71%) had VAS score ≤3. The effect of the drug was still persistent insignificant amount of patients even after its discontinuation (Table 2).

Mastalgia with nodularity was present in 40 patients. At the presentation and at the end of 1st week, 30% of patients (12 patients) had LCS grade ≤1 (Graph 1). At the 2nd week, 37.5% of the patients (15 patients) had LCS grade ≤1 (Graph 2). At the end of 4 weeks, 50% of patients (20 patients) had LCS grade ≤1 and 35% were free of nodularity (Graph 3). At the end of 8 weeks, 50% of patients (20 patients) were free of nodularity and had LCS grade 0 and 67.5% of patients (27 patients) had LCS grade ≤1 (Graph 4). At the end of 12 weeks, 67.5% of patients were free of nodularity and had LCS grade 0. Moreover, 87.5% of patients had LCS grade ≤1 (Graph 5). This decrease is LCS grade was maintained even after discontinuation of treatment at 16 weeks (Table 3) (Graph 6, Graph 7).

Table 1: Decrease in VAS score (≤3) in follow-ups in patients of mastalgia (*n*=70)

Duration (weeks)	*n* (%)
2	49 (70)
4	56 (80)
8	60 (85.7)
12	63 (90)
16	60 (85.7)

VAS: Visual analogue scale

Table 2: Patients as per reduction in intensity of mastalgia on VAS score (*n*=70)

Visits in weeks	VAS score										
	0	1	2	3	4	5	6	7	8	9	10
0	-	-	-	-	-	-	7	3	12	4	44
1	-	-	-	-	-	-	7	3	12	4	44
2	2	-	41	6	-	-	11	3	6	1	-
4	13	-	34	9	-	-	8	1	5	-	-
8	25	-	30	5	-	-	6	-	4	-	-
12	31	-	29	3	-	-	4	-	3	-	-
16	31	-	24	5	-	-	7	-	3	-	-

VAS: Visual analogue scale

Table 3: Distribution of patients as per benign breast nodularity grade (LCS)

Visits in weeks	LCS grades				
	0	1	2	3	4
0	4 (10)	8 (20)	16 (40)	8 (20)	4 (10)
1	4 (10)	8 (20)	16 (40)	8 (20)	4 (10)
2	8 (20)	7 (17.5)	15 (37.5)	7 (17.5)	3 (7.5)
4	14 (35)	6 (15)	15 (37.5)	3 (7.5)	2 (5)
8	20 (50)	7 (17.5)	10 (25)	2 (5)	1 (2.5)
12	27 (67.5)	8 (20)	4 (10)	1 (2.5)	0 (0
16	27 (67.5)	8 (20)	4 (10)	1 (2.5)	0 (0)

Grades of LCS=0, 1, 2, 3, 4. LCS: Lucknow Cardiff scale

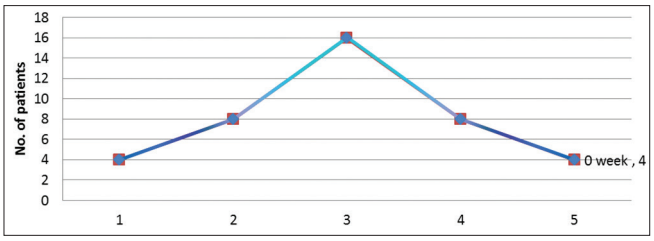
DISCUSSION

Mastalgia is a common complaint of patients presenting in surgical outpatient department. The main reason of women suffering from mastalgia coming for consultation is fear of malignancy or their daily life is affected due to severe mastalgia. There has always been a quest to find a beneficial drug with minimum side effects.

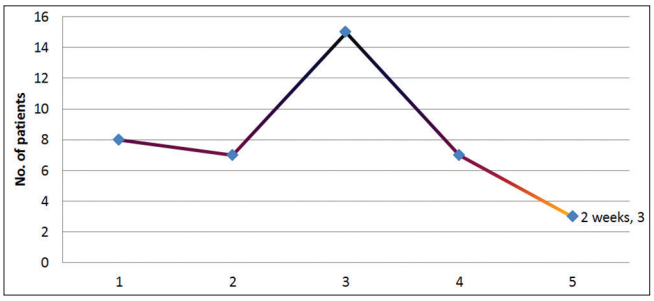
A pilot study was conducted at All India Institute of Medical Sciences, New Delhi, by Dhar and Shrivastava from August 2003 to September 2004. 60 patients were included in the study out of which 42 (70%) patients were of mastalgia and nodularity.[12] They were started of centchroman 30 mg on alternate day for the period of 3 months and were followed up for 6 months. In mastalgia group, VAS score 10 was recorded in 80% of the patients and remaining 20% had VAS score 7-10. There was good response in mastalgia group with decrease in VAS score from 10 to 3 in 90% of the patients in 1st week. Almost all the patients were painless at the end of the month with complete disappearance of the nodularity.

Centchroman regresses mastalgia: A randomized comparison with danazol: By done at All India Institute of Medical Sciences, New Delhi.[13] The study was done in 81 patients and 39 patients were analyzed for effect of centchroman. Centchroman was found to have response rate of 89.7% (reduction of pain to ≤3 on VAS score) at the end of 12 weeks. All the patients were relieved of nodularity at the end of 12 weeks.

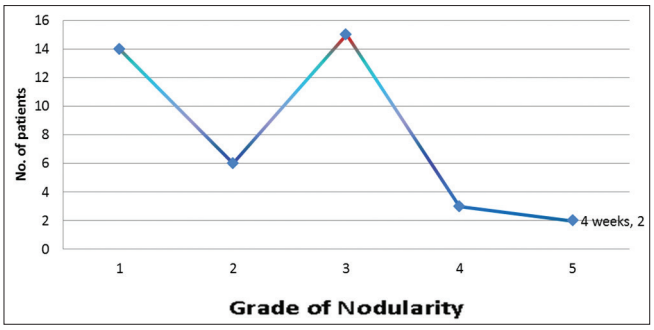
In a randomized double-blind placebo clinical trial done in 2008-2010 at the Department of Surgery, King George's (Chhatrapati Shahuji Maharaj) Medical University, Lucknow, Uttar Pradesh, India, by Kumar *et al*.[13] there was significant reduction in mean pain score from 5.71 at the start of the study to 1.3905 at the end of 3 months.



Graph 1: Distribution of patients as per benign breast nodularity grade (Lucknow Cardiff scale) - at the beginning



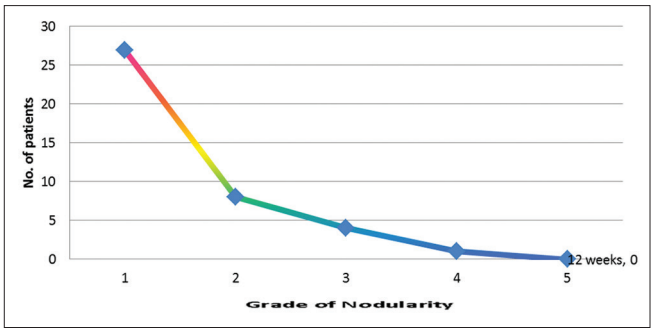
Graph 2: Distribution of patients as per benign breast nodularity grade (Lucknow Cardiff scale) - at 2 weeks



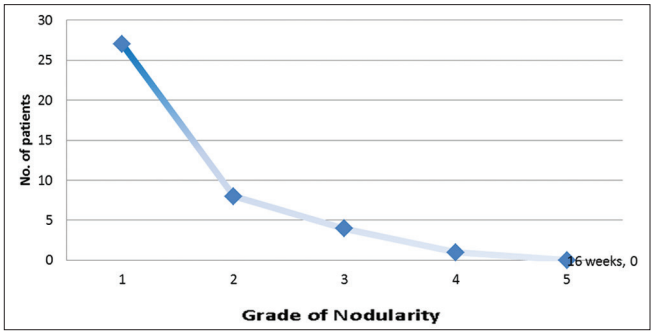
Graph 3: Distribution of patients as per benign breast nodularity grade (Lucknow Cardiff scale) - at 4 weeks

Graph 4: Distribution of patients as per benign breast nodularity grade (Lucknow Cardiff scale) - at 8 weeks

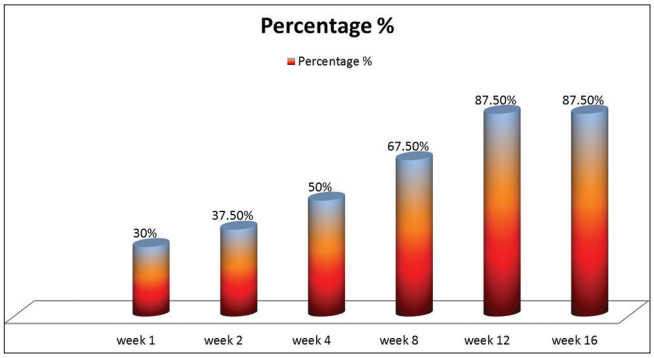
Bansal *et al*. in a study done at Jeevan Jyoti Hospital, Allahabad, reported the continuous decrease in mean pain level over five visits from 5.8 to 0.86 (2012-2015).[14]



Graph 5: Distribution of patients as per benign breast nodularity grade (Lucknow Cardiff scale) - at 12 weeks



Graph 6: Distribution of patients as per benign breast nodularity grade (Lucknow Cardiff scale) - at 16 weeks



Graph 7: Decrease in grade Lucknow Cardiff scale ≤1 in follow-ups in patients of mastalgia and nodularity

In our study, we had seen that out of 70 patients in our study 30 patients (42.85%) presented with mastalgia alone and 40 patients (57.14%) presented with mastalgia along with nodularity. VAS score 10 was seen in 44 patients (62.85%). All the patients had VAS equal to or more than 6.

At the end of 2nd week 49 patients had VAS score ≤3 (70%) and at the end of 12 weeks, 36 patients (90%) were relieved of their symptoms.

At the end of 2nd week 27 patients had VAS score ≤3 (67.5%) and at the end of 12 weeks, 63 patients (90%) were

relieved of their symptoms. A pilot study was conducted at All India Institute of Medical Sciences, New Delhi, by Dhar and Shrivastava from August 2003 to September 2004. They reported complete regression of nodularity at the end of 12 weeks.[12]

In the 1st clinical trial, randomized double-blind, placebo-controlled trial of ormeloxifene in breast pain and nodularity by Kumar *et al*. (2008-2010), at King George's Medical College, Lucknow, 151 patients were included in the study, out of which 75 were randomized to ormeloxifene. In this group, grade 1 and 2 nodularity were seen in 25 patients (33.3%), whereas grade 3, 4 and 5 were seen in 50 patients (66.7%). At the end of the 3 months of treatment 65 (86.7%) patients had grade 1 and 2 nodularity, 13.3% with grade 3, 4 and 5 nodularity[13] (for the purpose of data analysis the grade of breast nodularity were renumbered as 1-5 and labeled as normal, mild, moderate, severe and very severe, respectively, instead of ordinal scale of 0-4).

Bansal *et al*.[14] in study of 203 patients, at Jeevan Jyoti Hospital, Allahabad, Uttar Pradesh from 2012 to 2015 reported that in the beginning of the treatment, grade 1 or 2 nodularity were in 62 (30.5%) patients whereas grade 3, 4, 5 was seen in 141 (69.5%) patients. At the end of 3 months of the treatment, 134 patients (66.6%) were of grade 1 nodularity and 36 patients were of grade 2 nodularity (for statistical analysis the grades were renumbered 1-5, instead of ordinal scale of 0-4).

Khann *et al*. in study at Banaras Hindu University (September 2011-May 2013) reported that after 3 months of the treatment, 81.9% of patients had shown regression of nodularity.[15]

In our study, in the beginning grade 0 and grade 1 nodularity was seen in 12 patients (30%) and grade 2, 3, 4 was seen in 18 patients (70%). At the end of the 12 weeks, grade 0 nodularity was present in 67.5% of patients and grade 1 in 20% patients accounting for 87.5% of patients in total with grade 0 and 1 nodularity. Our study was consistent with the previous studies done.

In our study, oligomenorrhea was the major side effect and was reported in 27.32% patients. Amenorrhea was reported by 4.65% of patients. One patient presented with polymenorrhea (0.58%) and nipple discharge was reported by 2 patients (1.16).

CONCLUSIONS

The aim of the study was to observe the efficacy of the drug, centchroman, which can be used as a boon for the patients of exclusively benign but troublesome disorders of normal development of the breast; in our study, it is found effective and safe for mastalgia and nodularity.

REFERENCES

1. Cooper A. Illustrations of Diseases of the Breast. London: Longmans; 1829.
2. Hughes LE, Mansel RE, Webster DJ. Aberrations of normal development and involution (ANDI): A new perspective on pathogenesis and nomenclature of benign breast disorders. Lancet 1987;2:1316-9.
3. Asch RH, Greenblatt RB. The use of an impeded androgen – Danazol – In the management of benign breast disorders. Am J Obstet Gynecol 1977;127:130-4.
4. Mansel RE, Preece PE, Hughes LE. A double blind trial of the prolactin inhibitor bromocriptine in painful benign breast disease. Br J Surg 1978;65:724-7.
5. Fentiman IS, Caleffi M, Hamed H, Chaudary MA. Dosage and duration of tamoxifen treatment for mastalgia: A controlled trial. Br J Surg 1988;75:845-6.
6. Mansel RE, Goyal A, Preece P, Leinster S, Maddox PR, Gateley C, *et al*. European randomized, multicenter study of goserelin (Zoladex) in the management of mastalgia. Am J Obstet Gynecol 2004;191:1942-9.
7. Barros AC, Mottola J, Ruiz CA, Borges MN, Pinotti JA. Reassurance in the Treatment of Mastalgia. Breast J 1999;5:162-165.
8. Hadi MS. Sports Brassiere: Is It a Solution for Mastalgia? Breast J 2000;6:407-409.
9. Colak T, Ipek T, Kanik A, Ogetman Z, Aydin S. Efficacy of topical nonsteroidal antiinflammatory drugs in mastalgia treatment. J Am Coll Surg 2003;196:525-30.
10. Kamboj VP, Setty BS, Chandra H, Roy SK, Kar AB. Biological profile of Centchroman – A new post-coital contraceptive. Indian J Exp Biol 1977;15:1144-50.
11. Singh MM. Centchroman, a selective estrogen receptor modulator, as a contraceptive and for the management of hormone-related clinical disorder. Med Res Rev 2001;21:302-47.
12. Dhar A, Srivastava A. Role of centchroman in regression of mastalgia and fibroadenoma. World J Surg 2007;31:1178-84.
13. Kumar S, Rai R, Agarwal GG, Dwivedi V, Kumar S, DAS V. A randomized, double-blind, placebo-controlled trial of ormeloxifene in breast pain and nodularity. Natl Med J India 2013;26:69-74.
14. Bansal V, Bansal A, Bansal AK. Efficacy of SEVISTA (Ormiloxifene) in treatment of mastalgia and fibrocystic breast diseases. Int J Reprod Contracept Obstet Gynecol 2015;4:1057-60.
15. Khanna S, Gupta D, Shukla RC, Khanna AK, Khanna R. Comparative evaluation of the role of centchroman in benign breast diseases. Int J Biol Med Res 2016;7(2):5563-8.

How to cite this article: Shukla V, Patel V, Gupta R, Kumar S, Gaharwar APS. Role of Centchroman in Mastalgia: An Experience in a Tertiary Care Hospital of Vindhya Region. IJSS Journal of Surgery 2017;3(3):22-26.

Source of Support: Nil, **Conflict of Interest:** None declared.