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Evaluation of some agents for Controlling Mastalgia in Patients with Fibrocystic Diseases

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Abstract

Mastalgia, often known as breast discomfort (or mastodynia), is a common complaint experienced by women of reproductive age worldwide. The majority of mastalgia medications are pricy and come with unwanted effects. The aim of this study was to evaluate the effect of evening primrose oil, danazol, Cabergoline and tamoxifien for controlling mastalgia in patients with fibrocystic disease. This prospective random comparative study has been carried out in Derna university, Elwehda Hospital during the period between December 2021 to June 2022 on 136 patients enrolled with 3 months period of follow up. In the cabergoline group 17.6% of patients showed complete resolution and 38.2% showed partial improvement. In the Evening primerose oil group 32.4.% of patients showed complete resolution and 50% showed partial response. In Tamoxifen group 47.1% of patients showed complete resolution while 52.9% showed partial improvement. The danazol group received, 58.8% of patients showed complete resolution and 41.2% showed partial improvement. Evening prime rose oil is effective in reducing the severity of mastalgia with minor tolerable side effects. Danazol is the most effective agent, but its side effects make it less favorable agent. Tamoxifen is the second most effective agent among the other agents with reversible tolerable side effects. Cabergoline significantly decrease breast pain especially cyclic mastalgia.

Keywords: Mastalgia, Cyclical mastalgia, Fibrocystic disease

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1. Introduction

One of the most prevalent benign lesions that hurt women is fibrocystic breast alterations. The most typical sign of fibrocystic breast alterations is mastalgia, or cyclic breast discomfort. Mastalgia lowers quality of life and generates dread and anxiety about breast cancer [1]. Cyclic mastalgia is classically related to the menstrual cycle. It is bilateral, diffuse, poorly localized, and generally described as a heaviness or soreness that often radiates to the axillae and arms. It occurs most often during the luteal phase as a result of increased water content in breast stroma caused by increasing hormone levels. Cyclic breast pain occurs more often in younger women, mostly resolves spontaneously, and should be separated from premenstrual syndrome. Noncyclic pain is not related to the menstrual cycle, and may be unilateral. It is usually described as a sharp, burning pain that appears to be localized in the breast. Noncyclic mastalgia is most common in women of 40–50 years of age [2]. The aetiopathogenesis and treatment of mastalgia are highly debated topics. In non-medical therapy, comfort and a supportive sports bra with strong external breast support are key components. Many medications, including topical and oral non-steroidal anti-inflammatory medicines, centchroman, tamoxifen, evening primrose oil, and bromocriptine, have been attempted to treat mastalgia [3]. Gamma-linolenic acid (GLA) can be found in evening primrose oil (EPO) in amounts as high as 7% to 14%. GLA inhibits the production of prostaglandins, which may be the cause of breast pain [2]. Danazol is derived from ethisterone, a modified form of testosterone, a synthetic steroid. In the early 1970s, the U.S. Food and Drug Administration (FDA) approved it as the first medication intended particularly for the treatment of endometriosis. The FDA has approved it for the treatment of mastalgia and it reduces gonadotropin secretion, stops luteinizing hormone surge, and inhibits ovarian steroid synthesis [3]. Both cyclical and noncyclical mastalgia have been reported to be relieved by tamoxifen at a dose of 10 mg per day. Hot flashes and irregular periods are among the few side effects that occur at this low dose over the course of three months. For mastalgia, tamoxifen is the recommended medication in the majority of Western breast clinics. Informing the patient that tamoxifen is not being prescribed for cancer is necessary [4]. Although it hasn't been used for mastalgia, cabergoline has been used extensively for hyperprolactinemia for a number of years, and compared to bromocriptine, it appears to have less adverse effects. Thus, we postulated that cabergoline, with fewer side effects, would be just as useful as bromocriptine for treating the symptoms

of mastalgia [5]. It has been shown that cabergoline, another powerful, long-lasting dopamine, is just as effective as bromocriptine while having fewer adverse effects [6].

Aim of the study

The aim of this study was to evaluate the effect of evening primrose oil, danazol, Cabergoline and tamoxifien for controlling mastalgia in patients with fibrocystic disease.

2. Patients and Methods

This prospective random comparative study has been carried out in Derna university, Elwehda Hospital during the period December 2021 to June 2022 on 136 patients enrolled with 3 months period of follow up. Written informed consent was obtained from all participants' parents and the study was approved by the research ethical committee of Faculty of Medicine, Derna University. The work has been carried out in accordance with The Ethical Code of the World Medical Association (Declaration of Helsinki) for studies involving humans. Inclusion Criteria: Patients age of 18 years old and above complaining of mastalgia with fibrocystic disease

Exclusion Criteria: Pregnant or lactating patients. Patients who have history of breast cancer or family history of breast cancer. Patients who have dermatological or musculoskeletal disorder causing breast pain. Patients with any previous breast surgery.

All patients were subjected to:
Full history taking including: Demographic data; name, age, residence, occupation, marital status, special habits of medical importance, menstrual and obstetric history were recorded.

Medical history including: mastalgia onset, course and duration as well as co-morbidities and cyclic or noncyclic characters of the breast pain.

Clinical examination including: general and complete breast examinations(CBE) to assess breast size ,tenderness, nipple changes or discharge ,lumpiness or localized nodularity and any hotness redness and thorough examination to the axillary lymph node .

Ultrasound breast was done to all patients at first visit and three months post treatment to assess nodularity and the response to treatment regarding to nodularity and to discover any other breast mass which may not be seen by clinical examination. Patients in this study was divided into four equal groups using a computer-generated randomization list as follow:

First group: included 34 patients received evening primrose oil capsule 1000 mg once daily for period of three months.

Second group: included 34 patients received danazol tablet 200mg once daily for period of three months.

Third group: included 34 patients received Cabergoline tablet 0.5mg once weekly for period of three months.

Fourth group: included 34 patients received tamoxifien 10mg once daily for period of three months.

Follow up:

Patients are followed up as outpatients monthly for 3 months. Patients seen monthly and their pain assessed by careful history to the pain and its intensity measured by pain analogue scale in each visit, any side effect of the drug developed has been sought and recorded, Patients are also seen at the outpatient clinic instantly if they developed any new or concerning symptoms or side effects between their follow-up visits.

Parameters of evaluation:

Patient improvement and relief according to visual analogue scale ranging between 0 to 10 (0 experiencing no pain and 10 experiencing the worst unbearable pain) which shown to each patient as numerical scale and explained to each patient individually as the main goal of our study is to control mastalgia. Clinical improvement assessed by breast examination which requested at first visit then after three months to assess nodularity, although most of patients came to our clinic complain of mastalgia rather than nodularity or lumpiness which are not uncommon among patients with fibrocystic diseases. Reported drugs side effects which revised monthly till the end of period of trial, side effect of each drugs explained to each patient in simple language and reported in every monthly visits.

Statistical analysis:

SPSS version 20 was used for statistical analysis, a description was given of the demographic variables in the overall sample, with measures of central tendency (mean) and standard deviation for the quantitative variables, and percentages for the categorical variables. A search was subsequently made for differences in variable distribution between the two study groups. A Student's t test was used for the quantitative variables, and a Chi-square test was used for the categorical variables. Measurement of the incidence of the outcome variables was then continued, after which the relative risk of prediabetes as a function of the outcome variables and the corresponding confidence interval were estimated. Level of significance was considered for $P < 0.05$ and high significance $P < 0.001$.

3. Results and discussion

Table (1), showed that there is statistically significant difference between the studied groups regarding age. On Least Significant Difference (LSD) comparison, the difference is significant between Tamoxifen group and both Evening primrose oil and Cabergoline groups. Similarly, the difference is significant between danazol and evening primerose groups. patients received tamoxifen and danazol were the oldest. There is statistically non-significant difference between the studied groups regarding marital status. Table (2), showed that There was no statistical significant difference between the studied groups regarding baseline ultrasonographic findings. There was a statistical significant difference between the studied groups regarding ultrasonographic finding at 3 months with significant difference between Cabergoline group and both Tamoxifen

and Danazol groups. Table (3), showed that there was statistically significant difference between the studied groups regarding change in fibroadenois among the studied patients. The difference is significant between Cabergoline group and both danazol and tamoxifen groups. Table (4), showed that there was no statistical significant difference between the studied groups regarding baseline VAS score. There was statistically significant difference between the studied groups regarding VAS score in the second month (Cabergoline group had the most significant higher VAS score in comparison with each other group). Also, There is statistically significant difference between the studied groups regarding VAS score in the third month (Cabergoline group had the most significant higher VAS score in comparison with each other group). There is also significant difference between Danazol, Tamoxifen groups and both Cabergoline group and evening Primeroe group). Table (5), showed that there was a statistically significant difference between the studied groups regarding percent decrease in VAS score with Cabergoline group had the least value. Danazol showed the highest percent of pain improvement followed by tamoxifen then evening primrose oil. Table (6), showed that there was statistically significant difference between the studied groups regarding occurrence of adverse effects with significant difference between tamoxifen and both evening primrose oil and Danazol groups. Table (7), showed that 26 patients (76.5%) had no side effect, dizziness was noticed an associated side effects in 6 out of 34 patients (17.6%) and 2 (5.9) patient had headache. Table (8), showed that in studied patients received evening primerose oil, 32 patients (9431%) had no side effect, two patient (5.9%) of the side effect represented in minor tolerable GIT upset. Table (9), showed that studied patients received evening primerose oil, 18 patients (52.9%) had no side effect, while 10 patients (29.4%) had hot flashes and 6 (17.6%) patients had vaginal discharge. Table (10), showed that 21 patients (61.7%) had no side effect, while 4 patients (11.8%) had delayed menses and 3 patient (8.8%) had scanty menses and 3 patient (8.8%) had urticaria and 3 (8.8%) had vaginal discharge.

Discussion

Mastalgia is a medical term used for breast pain, one of the most common complaints among women of 15 to 40 years of age (child-bearing age). Approximately two-thirds of women during their reproductive lives suffer from this condition and seek medical help. It is a dull, aching pain while some women may describe it as heaviness, tightness, discomfort, or burning sensation in the breast tissue, which may be unilateral or bilateral. Most often, it is located in the upper outer quadrant of the breast and can sometimes radiate to an ipsilateral arm. It is most common in premenopausal and perimenopausal women, but postmenopausal women can also rarely develop such pain. The breast pain ranges from mild to severe, could be intermittent or constant throughout the day, and may interfere with the female's quality of life [7]. Fibrocystic breast change is a common and benign condition which are experienced by 13.5–42% of women usually of reproductive ages. The breast fibrocystic involves both nonproliferative and proliferative changes occurred concurrently or separately. The proliferative changes include breast nodularity (presence of macro and micro cysts) which could be localized or diffused. Furthermore, it could be adenosis which means an increase in the size or number of cysts, or apocrine metaplasia and fibrosis. Non-proliferative changes might be sclerosing adenosis and intraductal papillomatosis which both increase the risk of breast cancer. Cyclic mastalgia may occur with breast fibrocystic [8]. However, some women experience continuous pain. The breast pain is usually bilateral and lasts more than 5 days in a menstrual cycle. This pain is more severe before menstruation and ends up after menopause. Other symptoms such as nipple discharge and changes in the appearance of the nipple may also occur [9]. The prevalence of breast pain is different between societies, but approximately 41–69% of women suffer from cyclic mastalgia. In 25–30% of patients, the breast pain lasts more than 5 days in a cycle. Those women experiencing pain receive mammography 4–7 times more often than women without symptoms [8]. Mastalgia whether cyclic (associated with menstrual periods) or noncyclic may be severely incapacitating for the woman. Cyclical mastalgia is a common problem that can be sufficiently severe to interfere with usual activities and has been associated with elevated mammography usage in women. Many women with mastalgia worry more about the consequences of cancer than about the pain itself [10]. The exact reason for breast fibrocystic is unknown, however an imbalance in reproductive hormones may contribute to breast fibrocystic, such as an increase in the level of estrogen, progesterone deficiency, and hyperprolactinemia, thyroid hormones, stress, methylxanthines, and deficiency of unsaturated fatty acids [11]. The purpose of medical interventions is relieving mastalgia, cessation of its progression, and finally reversing the changes. The treatment options for breast fibrocystic changes are classified into nonpharmacological and pharmacological modalities. Nonpharmacological recommendations are the first-line which include education, relaxation training, and wearing a bra. Furthermore, lifestyle modifications may relieve symptoms, such as limiting fat intake, consuming more daily fiber and avoiding caffeinated beverages (methylxanthines). Pharmacological interventions involve hormonal (oral contraceptives, progestins, bromocriptine, danazol, and tamoxifen) and nonhormonal therapies (herbal supplements) [12]. Despite not having proven efficacy in previous studies, the use of evening primrose oil is warranted as supportive measures if pain persists despite treatment and advice. A 3 to 6 month period is the suggested timeframe to observe the desired effect. If breast pain is severe for more than six months and disrupts daily activities, other therapies such as tamoxifen, bromocriptine, or danazol can be options. Due to the recurrent nature and long duration of these symptoms, several months of treatment is necessary[13].

This prospective random comparative study has been carried out in Derna university, Elwehda Hospital during the period from October 2021 to March -2022 on 136 patients enrolled with 3 months period of follow up to evaluate the effect of evening primrose oil, danazol, Cabergoline and tamoxifien for controlling mastalgia in patients with fibrocystic disease.

The current study showed that age range between 20 - 48 years where the median age was 37 years which in agreement with the study conducted by Aydin et al [5],who found that the mean age of the patients in their study was 38years. There was statistically significant difference in the

mean age between the four different groups where danazol and tamoxifen group had the oldest patients. There was no statistically significant difference between the studied groups regarding the base line ulatrasonography findings at time of presentation. In accordance with the results reported Jain et al [14], study regarding baseline ultrasonography findings. However Regarding to the ultrasonography findings 3 months post treatment, we found that ,in the cabergoline group 6 patients (17.6%) achieved complete resolution, and 15 patients (44.2%) showed partial improvement in the degree of fibroadenosis compared to the base line ultrasound and 13 patients (38.2%) showed no changes which in agreement with the study of Memon et al [15], who found that 73% of cyclic nodularity reduced using cabergoline , but they used dose of 1.5mg over period of three months.

While the patients treated with evening primerose oil showed complete resolution in 11 patients (32.4%) of total group and 20 patients (58.8%) showed different degrees of response and 3 patient (8.8%) showed no change at all, these findings agreement with the study of Khadka et al [16], who stated a similar results in their study. Patients treated with tamoxifen showed complete resolution in 16 patients (47.1%) of total group and 18 patients (52.9%) respond by different degree of improvement in fibroadenosis changes and no recent study found regarding to the effect of tamoxifen on cyclic nodularity but the role of tamoxifen in reducing nodularity need to be evaluated, as most studies concentrate on its effect on pain control. Patients have been treated with danazol showed complete resolution in 20 patients (58.9%) and 14 patients (41.1%) have been improved radiologicaly comparing to the first ultrasound, which near match the result of Gayatri et al [17], who showed that 85% of resolution can be achieved in breast nodularity. All patient included in the four groups of our study had cyclic mastalgia with VAS more than 7 where the patient with non-cyclic breast pain has been excluded and this does not typically match the study conducted by Aydin et al [5], whose patients included in the study had cyclic mastalgia with visual analogue scale above 4 which considered moderate mastalgia. The four drugs' groups showed significant difference alleviating the pain of cyclic mastalgia, where patients in the danazol group had achieved most significant degree of decrease in the VAS of pain followed by tamoxifen, evening primerose oil and then cabergoline. The patients of cabergoline group at time of presentation had a cyclic mastalgia with VAS of (7-9) that decreased to (6-8) after 1 month of treatment and further decreased to (3-6) after 3 months post treatment.

While patients in evening primerose oil group had (7-9) VAS which decreased to (4-7) and down to (2-5) over period of three month of treatment. The VAS of patients in tamoxifen group at first visit was (8-9) and decreased with treatment to (4-7) in second month and (2-3) after 3 months of treatment. In danazol group all patients had VAS ranged between (8-9) which decreased to (4-7) in the second month of treatment and further decreased to (2-3) at the end of follow up period. The difference in VAS between firs visit and after first months of treatment was insignificant in all four groups, the baseline characteristics and initial pain score were similar in the four groups and no statically significant difference. The percentage of decrease of the VAS been significant after the completion of the third month where the percentage of decrease in VAS in cabergoline group was 45.76% who received 0.5 mg/week over three months and that different from the study conducted by Aydin et al [5], who achieved 66.2% with 70 patients enrolled in cabergoline group with the dose similar to what has been used in our current study. Evening prime rose oil group had 62 % decrease in VAS in the third month comparing to 50% which was achieved in study Conducted by Nigam et al .,2018 on 98 patients in which 62 patients had cyclic mastalgia treated by 1000 mg once daily dose ,another study carried out by Kumar et al [18], achieved 68% decrease in the VAS after 12 weeks which in concordance with our current study. Patients in tamoxifen group who have been on 10mg/day tablets over 3 month , showed 70.75% decrease in their VAS at the third months, in disagreement with prospective randomized control trial conducted by Gupta et al [10], where the response achieved in the tamoxifen group was 33.3% in study include 72 patients in which cyclic mastalgia constitute 66.67% of total number of patients complaining of mastalgia but in their study the dose was 20mg and the follow up period was 18 months. In another study conducted by Khadka et al [16], which include 106 patients received 10mg tamoxifen over 3 months period ,which resemble our parameters in our present study, the decrease in VAS was 60 % which near match our current study, while Jain et al[14], reported decrease in the cyclic pain around 71% of total group.

In the meanwhile patients in danazol group had achieved the most significant percentage of the decrease on cyclic pain according to the VAS which reached to 75% at the end of follow up period and that seem to be similar to results obtained by prospective randomized study conducted by Kumar and hasan [19], which included 64 patients and showed 71%. improvement in patients treated by danazol 200mg over 12 weeks with side effect reached 30%, in another study conducted by Gupta et al[10], in which the decrease in VAS achieved was 71% supported by another study conducted by cornell et al.,2016 reported 77% reduction of pain in VAS which all support the results of our current study. Regarding the cabergoline group, dizziness was noticed an associated side effects in 6 out of 34 patients (17.6%) And 2 (5.9) patient had headache and this in agreement of Aydin et al [5], who mentioned (16.4 %) occurrence of dizziness in study included 70 patients in cabergoline group. two patient (5.9%) in evening primerose oil group reported side effect represented in minor tolerable GIT upset and this correlate with data in study conducted by Nigam et al [20], which showed insiginicant side effect of the study included 45 patients and reported safe profile of this drug, Sarayloo et al [21], stated that no side effects of evening prime rose oil, where Kumar et al [18], reported 8% of side effects occurrence.

Table 1: Comparison between the studied groups regarding demographic data

Demographic data	Groups	Test

	Cabergoline group	Evening primerose oil group	Tamoxifen group	Danazol group	F/ χ^2	P
	N=34 (%)	N=34 (%)	N=34 (%)	N=34 (%)		
Age:						
Mean ± SD	35.12 ± 10.66	32.29 ± 6.62	40.35 ± 5.51	39.47 ± 4.8	4.608	0.006*
Range	24 – 54	20 – 40	34 - 48	34 – 48		
Marital status:						
Married	34 (100)	32 (94.1)	26 (76.5)	26 (76.5)	6.531	0.113
Single	0 (0)	2 (5.9)	8 (23.5)	8 (23.5)		

*p<0.05 is statistically significant

Table 2: Comparison between the studied groups regarding ultrasonographic findings at time of presentation and after the third month.

Ultrasonographic findings	Groups				Test	
	Cabergoline group	Evening primerose oil group	Tamoxifen group	Danazol group	χ^2	P
	N=34 (%)	N=34 (%)	N=34 (%)	N=34 (%)		
At time of presentation:						
Fibroadenosis	28 (82.4)	26 (76.5)	34 (100)	34 (100)		
Normal study	6 (17.6)	8 (23.5)	0 (0)	0 (0)	8.122	0.055
At third month:						
Fibroadenosis	15 (44.2)	6 (17.6)	0 (0)	0 (0)	16.455	0.010*
Partial resolution	13 (38.2)	17 (50)	18 (52.9)	14 (41.2)		
Complete resolution	6 (17.6)	11 (32.4)	16 (47.1)	20 (58.8)		

*p<0.05 is statistically significant

Table 3: Comparison between the studied groups regarding change in ultrasonographic findings

Change in ultrasonographic features in fibroadenosis	Groups				Test	
	Cabergoline group	Evening primerose oil group	Tamoxifen group	Danazol group	χ^2	P
	N=34 (%)	N=34 (%)	N=34 (%)	N=34 (%)		
Third month:						
No change	13 (38.2)	3 (8.8)	0 (0)	0 (0)	21.24	<0.001**
Partial resolution	15 (44.2)	20 (58.8)	18 (52.9)	14 (41.1)		
Complete resolution	6 (17.6)	11 (32.4)	16 (47.1)	20 (58.9)		

**p≤0.001 is statistically highly significant

Table 4: Comparison between the studied groups regarding VAS score at the first, second and third months

VAS	Groups	Test

	Cabergoline group	Evening primerose oil group	Tamoxifen group	Danazol group	F	P
	N=34 (%)	N=34 (%)	N=34 (%)	N=34 (%)		
1st month: Mean ± SD Range	8.059 ± 0.827 7 – 9	8.412 ± 0.795 7 – 9	8.471 ± 5.145 8 - 9	8.647±0.493 8 – 9	2.269	0.089
2nd month: Mean ± SD Range	6.941 ± 0.748 6 – 8	5.765 ± 1.091 4 – 7	5.471 ± 1.179 4 - 7	5.529±0.943 4 – 7	7.995	<0.001**
3rd month: Mean ± SD Range	4.353± 1.169 3 – 6	3.118 ± 1.111 2 – 5	2.471 ± 0.514 2 – 3	2.176±0.728 2 – 3	18.678	<0.001**

*p<0.05 is statistically significant

Table 5: Comparison between the studied groups regarding percent change in VAS score at the third months

% change in VAS	Groups				Test	
	Cabergoline group	Evening primerose oil group	Tamoxifen group	Danazol group	KW	P
	N=34 (%)	N=34 (%)	N=34 (%)	N=34 (%)		
Third month: Mean ± SD Range	45.76 ±14.19 25 – 66.7	62.00 ± 14.53 37.5 – 77.78	70.75 ± 6.36 62.5 – 77.78	75.00 ±8.55 62.5 – 88.89	28.719	<0.001**

Table 6: Comparison between the studied groups regarding occurrence of adverse effects

Adverse effects	Groups				Test	
	Cabergoline group	Evening primerose oil group	Tamoxifen group	Danazol group	χ^2	P
	N=34 (%)	N=34(%)	N=34 (%)	N=34 (%)		
No	26 (76.5)	32 (94.1)	18 (52.9)	22 (64.7)		
Yes	8 (23.5)	2 (5.9)	16 (47.5)	12 (35.3)	20.09	<0.001**

*p<0.05 is statistically significant

Table 7: Distribution of the studied groups regarding adverse effects of the studied drugs

Adverse effects	Cabergoline group
	N=34 (%)
No	26 (76.5)
Dizziness	6 (17.6)
headache	2 (5.9)

Table 8: Distribution of the adverse effects in the Evening primerose oil group

Adverse effects	Evening primerose oil group
	N=34 (%)
No	32 (94.1)
GIT upset	2 (5.9)

Table 9: Distribution of the adverse effects in the Tamoxifen group

Adverse effects	Tamoxifen group

	N=34 (%)
No	18 (52.9)
Hot flashes	10 (29.4)
Vaginal discharge	6 (17.6)

Table 10: Distribution of the adverse effects in the Danazol group

Adverse effects	Danazol group
	N=34 (%)
No	21 (61.7)
delayed menses	4 (11.9)
scanty menses	3 (8.8)
urticaria	3 (8.8)
vaginal discharge	3 (8.8)

In the tamoxifen group 18 patients (52.9%) had no side effect at all while 10 patients (29.4%) had hot flashes and 6 (17.6%) patients had vaginal discharge intermittently over three months that does not exactly correlate with the results obtained by Jawade & Bande [22], where they report 58.28% occurrence of reversible side effects mainly hot flash. In Danazol group 21 patients (61.7%) had no side effect, while 4 patients (11.8%) had delayed menses and 3 patient (8.8%) had scanty menses and 3 patient (8.8%) had urticaria and 3 (8.8%) had vaginal discharge, while Kumar et al [18], reported 32 % occurrence of side effects among patients in danazol group which near match our result. Again, the difference between the four drugs regarding to the occurrence of the side effect was significant with tamoxifen has higher incidence of side effect followed by danazol, cabergoline and lastly the evening primerose oil, which has the less incidence.

4. Conclusions

Evening prime rose oil is effective in reducing the severity of mastalgia with minor tolerable side effects. Danazol is the most effective agent, but its side effects make it less favorable agent. Tamoxifen is the second most effective agent among the other agents with reversible tolerable side effects. Cabergoline significantly decrease breast pain especially cyclic mastalgia.

Recommendations

Further studis with larger groups of patients with longer period follow up to confirm our results and to assess the recurrence of breast pain after 3 months.

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