

Comparison of the effect of surgical and medical therapy for the treatment of idiopathic granulomatous mastitis

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Background: Idiopathic granulomatous mastitis (IGM) is defined as a rare, inflammatory, chronic and benign disease mimicking malignant hyperplasia of mammary glands. There is no definitive therapeutic strategy for IGM; nevertheless, some approaches can be exploited as beneficial strategies. In this study, the surgery strategy was compared with coincident treatment with azithromycin and corticosteroid in IGM patients. **Materials and Methods:** This study was implemented as clinical trial during 2011-2013 in Isfahan, Iran. The target population comprised women whose IGM was substantiated. The medical group consisted of 20 patients, which were compared with a historical control group treated through surgical approach. Surgical group comprised 39 patients. Partial mastectomy was implemented in the surgical group whereas treatment protocol comprising azithromycin and prednisolone administered in medical group. Recurrence of mass was followed for 12 months. Fischer exact test, Chi-square test, Mann-Whitney and regression tests were applied for statistical analysis. This study was registered in Iranian Registry of clinical trial (IRCT number: IRCT 2013123015999N1). **Results:** No significant differences were recognized in side of lesions, lymphadenopathy, fever and pain; however, number of abscesses, number of lesions and size of lesions were significantly higher in the surgical group ($P < 0.0001$). Furthermore, probability of relapse correlated with the number of lesions, (odds ratio = 24.67 confidence interval [CI] = 2.2-269.3), whereas methods of IGM treatment did not contribute to the likelihood of relapse (odds ratio = 12.5 CI = 0.52-299). **Conclusion:** This clinical trial demonstrated that pharmaceutical treatment has appropriate efficacy, in treatment and prevention of IGM relapse. Moreover, this study presented hazf gardad number of the lesions as the most appropriate criteria for IGM prognosis, thus the probability of relapse decreases whether earlier IGM recognizing could be implemented.

Key words: Azithromycin, breast disease, idiopathic granulomatous mastitis, mastectomy, steroids

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INTRODUCTION

Idiopathic granulomatous mastitis (IGM) is defined as a rare, inflammatory, chronic and benign disease mimicking malignant hyperplasia of mammary glands.^[1-5] Risk factors contributing to IGM incidence are not precisely clarified; however, autoimmune and infectious diseases (such as *Corynebacterium* specious), contraceptive pills, hyperprolactinoma, trauma and alpha one antitrypsin deficiency are oriented as some critical risk factors contributing IGM cases in the society.^[1,3-7]

IGM is usually appeared as a unilateral, distinct and painful mass. Nonetheless, it is likely to appear as cutaneous lesion, nipple retraction, sinus formation, fistula, abscess and lymphadenopathy.^[1,8] Sonography findings comprise hypo echoic lobulated mass

associated with either tubular or oval structure. IGM in mammography is appeared as neither distinct nor symmetrical densities; however, it could be associated with not only micro calcification and speculate form calcification, but also lymphadenopathy. Pathological finding approach is exploited as the gold standard for IGM diagnosis; though pathology analyzing is strictly recommended for exclusion of malignancy likelihood.^[1,3]

There is no definitive therapeutic strategy for IGM; nevertheless, some approaches such as close and precise following up, surgery, antibiotic therapy, corticosteroid treatment can be exploited as beneficial strategies. Limited surgery strategy is associated with relapse risk whilst negative margin surgery affects patients with indispensable side-effects such as cosmetic aspects. Moreover, exertion is recommended when the

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differential diagnosis of IGM and malignancy is ambiguous.^[9] To demonstrate mastectomy is a high risk approach while tumor malignancy is not approved.^[3] Scientific findings show augmented relapses of IGM, whereas implementation of numerous surgeries is associated with augmented probability of wound infection, sinus formation and other cosmetic issue.^[4,9] In addition, scientists suggest application of immunosuppressive components such as corticosteroids due to implication of autoimmune disorders as a causative factor of IGM.^[5,7] Antibiotic therapy is not widely analyzed in IGM as well as other chemotherapy approaches; nonetheless, Antibiotics are widely used in IGM cases, due to high probability of *Corynebacterium* infections.^[8]

In this study, the surgery strategy was compared with concurrent azithromycin and corticosteroid treatment in IGM patients.

MATERIALS AND METHODS

This study was implemented as Clinical trial in Alzahra hospital located in Isfahan, Iran in 2011-2013. The target population comprised women whose IGM was substantiated via core biopsy method. Inclusion criteria involved women with mastitis disease showing neither staphylococcus nor TB infections as microbial agents of mastitis, nor treated via any interventional method. Informed consent was acquired from patients included in this intervention. The design of the study was approved by the Ethics committee of Isfahan University of Medical Sciences (project No. 291163). This study was registered in Iranian Registry of clinical trial (IRCT number: IRCT 2013123015999N1).

The medical group consisted of 20 consecutive patients, which was compared with a historical control treated through surgical approach. Surgical group comprised 39 patients who had operation of IGM (in their medical history) providing their treatment had been implemented more than 1 year (since the commencement of the research). IGM was confirmed through histopathological and bacteriological methods.

In the medical group, questionnaires included demographic information like age, marital status, number of children, situation of lactation and also, baseline clinical data such as lymphadenopathy, pain, abscess, fever and number, side and size of lesions. Some data such as lymphadenopathy, abscess, fever (temperature >37.2°C), number, and side of lesions were collected by physical examinations, whereas the size of lesions was measured through sonography and the other information such as the pain was collected through interview. Treatment protocol consisted of concurrent administration of azithromycin (250 mg twice daily) and prednisolone (60 mg daily) for 2 weeks.

Afterwards, prednisolone treatment was continued for 8 weeks (40 mg/day), then, it was tapered for 6 months. Patients were followed for recurrence of masses through physical examination for 12 months since initiation of treatment.

The surgical group consisted of patients who underwent partial mastectomy, as a conventional method, about more than a year before the study. We used medical documents of patients in order to gather information about age, marital status, number of children, situation of lactation, lymphadenopathy, pain, abscess, fever, number, side and size of lesions, and recurrence of mass. Indeed, relapse was evaluated for 12 months after the surgery.

The data were analyzed by SPSS for Windows version 20 (SPSS Inc., Chicago, IL, USA). Fisher exact test, Mann-Whitney U-test, and Chi-square test were used to analyze data whenever appropriate. To compare the recurrence rate after 12 months of the initiation of treatment in the two groups we used Chi-square test by jaye ghesmate neveshte shode ebarate zir neveshte gardad. In order to study the association of type of the treatment to the recurrence rate we used regression method to control factors contributing to relapse such as lacrimation, abscess, number of children, size and number of lesions.

RESULTS

A total of 59 women documented for IGM through biopsy technique were included in this study. 20 patients were treated through medical approaches in a clinical trial, whilst the efficacy of surgical treatment was analyzed in 39 cases of IGMs. One patient treated through medical approach was excluded due to pregnancy situation and one individual in the respective medical trial was transferred to surgical one due to failure of treatment.

Mean of ages of people included in medical approach and surgical approach were 30.3 (standard deviation [SD]=6.38) and 36.74 (SD = 13.51), respectively without significant statistical difference ($P=0.154$). Most of the women were of reproductive age (77.9%), though, there was no significant difference in above mentioned groups for marital status ($P=0.108$). Median of child numbers was two and three in medical and surgical groups respectively ($P=0.001$). Moreover, 80% in medical group and 97% in the surgical group had a history of lactation ($P=0.041$).

Information elaborating numbers, side and size of the lesions are presented in Table 1. No significant differences were recognized in baseline variables showing lymphadenopathy, fever and pain, however, number of the abscess was significantly higher in the surgical group [Table 1].

The rate of relapse in pharmaceutical treatment and surgical treatment was 6.2% and 82% respectively ($P < 0.001$). We used regression test due to the difference of factors contributing to relapse of the disease [Table 2].

Table 2 shows the number of lesions can prognoses the probability of the relapse, (odds ratio = 24.67 confidence interval [CI] = 2.2-269.3), whereas the methods of treatment did not contribute to its likelihood (odds ratio = 12.5 CI = 0.52-299).

DISCUSSION

This article makes a comparison between two different therapeutic methods comprising surgical approach, and special pharmaceutical regimen, which include corticosteroid and azithromycin without surgical approach.

This study demonstrates that there is no significant difference in recurrence of the IGM between surgical and pharmaceutical approaches, whereas the latter treatment shows less side effects (such as wound infection, abscess formation, and other cosmetic problems) furthermore, the last proceeded option could illustrate enough efficacy.

Table 1: Baseline characteristics in patients with idiopathic granulomatous mastitis

Lesion characteristics	Medical group	Surgical group	P value
Number of lesions (median)	1	2	<0.0001
R	9	17	0.999
Side of lesion L: (Number of patients)	10	19	
R and L	1	2	
Size of lesion (cm) (mean)	3.0955	4.0872	<0.0001
Fever (number of patients) (%)	2 (10)	6 (15)	0.567
Lymphadenopathy (number of patients) (%)	1 (5)	2 (15)	1.000
Abscess (number of patients) (%)	12 (60)	37 (94)	0.001

Table 2: Logistic regression of possible factors contributing in recurrence in the 1st year of treatment (surgical or medical) in patient with idiopathic granulomatous mastitis

Patients' characteristics	P value	Odds ratio (95% CI)
Treatment		
Surgical	0.169	Reference
Medical		0.11 (0.01-2.58)
Lacrimation		
Yes	0.999	Reference
No		0.000 (0-0)
Abscess		
Yes	0.525	3.02 (0.10-91.15)
No		Reference
Number of children	0.581	0.77 (0.30-1.94)
Number of lesion	0.008	24.96 (2.28-273.08)
Size of lesion	0.666	0.77 (0.24-2.46)

CI = Confidence interval

Hence, the pharmaceutical approach (without surgery) is strongly recommended; nonetheless, surgery could be suggested in the case of recurrent patients or lack of pharmaceutical efficacy.

However, there is no definite treatment in the case of IGM, whilst variety of methods has been testified in different studies. For example, DeHertogh *et al.* in 1980 were the first who investigated the efficacy of different treatments and they concluded that corticosteroid is an appropriate option for the treatment of the disease.^[10] Furthermore, Sakurai *et al.* sought this pharmaceutical approach and they authenticated that corticosteroid could be efficient in 87% of patients without any relapse.^[11] The proceeded results were validated by Hisuing *et al.* while their research implied that low doses of corticosteroids were efficient; though, more investigations in this field were recommended by them.^[12] Moreover, in 2010, it was authenticated that corticosteroids provide appropriate treatment, whereas first option should be allocated to surgery in the case of relapse, fistula, and abscess.^[13] Nonetheless, there are some investigations providing different results. For example, Boufettal *et al.* testified different approaches, which include tumorectomy plus antibiotic therapy with or without non-steroidal anti-inflammatory drugs in 16 patients, tumorectomy plus antibiotic therapy and corticosteroid in one individual, and finally corticosteroid plus antibiotic therapy in three individual. This research showed that combination of surgery and corticosteroid application were the most appropriate approach since corticosteroids could be recommended in order to avoid relapse of the disease. It is suggested that the diverse result of the latter study might be justified by the difference of the samples in comparison with the present study.^[14]

IGM, most of the times, occurs unilaterally and its clinical manifestations are defined as fever, lymphadenopathy, breast mass ranging from 0.5 to 15 cm.^[14,15] All of the patients in our study had breast masses and most of them were occurred unilateral in left breast. However, three patients had bilateral breast masses with proceeded clinical signs.

This study demonstrated that the number of breast masses was the only factor, which was significantly related to IGM relapse: The probability of IGM relapse increased 24 times per one increase in the mass numbers.

The limitation of our study was smallness of sample size due to the rare incidence of the disease.

CONCLUSION

This clinical trial demonstrated that pharmaceutical treatment has appropriate efficacy in IGM treatment relapse

as well as surgical treatment. Moreover, this study presented number of the lesions as the most appropriate criteria for IGM prognosis and relapse.

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AUTHORS' CONTRIBUTION

All authors have contributed in designing and conducting the study. MS, MM, SAT, MS, and MMS collected the data and HS and RT did the analysis. All authors have assisted in preparation of the first draft of the manuscript or revising it critically for important intellectual content. All authors have read and approved the content of the manuscript and are accountable for all aspects of the work.

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