Evaluation of Correlation Between Azathioprine and Methotrexate With Response to Treatment in Patients With Idiopathic Granulomatous Mastitis.

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Aim & Methods

AIM: Idiopathic granulomatous mastitis, also called lobular idiopathic granulomatous mastitis, is a benign inflammatory disease of the breast with unknown etiology. The disease most often occurs in young women of childbearing age, although it has been seen in nulli-parous people and even in men. The age of onset of IGM varies from 11 to 83 years, but the most common age is in the 3rd and 4th decades in women. It is mostly found in the Mediterranean region and in developing Asian countries. In recent years prevalence of idiopathic granulomatous mastitis (IGM) in women of child-bearing age is increasing. The main problem is long course of disease and need medical and surgery treatment. In many cases treatment with glucocorticoids alone is ineffective and necessary to immunosuppressive. Some studies have showed corticosteroid therapy as successful and In patients who do not respond well to corticosteroids, immunosuppressive drugs such as methotrexate and azathioprine have been used in combination with corticosteroids. This study aimed to investigate azathioprine and methotrexate response in patients with IGM.

Methods: In this study, which is designed as a historical cohort, All patients referred to the clinic of Shahid Beheshti Hospital in Kashan with pain, mass and tenderness in the breast that underwent open biopsy or core biopsy and in the pathology of breast tissue, findings in favor of non-caseating granulomatous mastitis were identified. In the initial studies, bacterial and fungal cultures were negative and in the pathology found, no malignancy was mentioned. After obtaining informed consent from all patients, they entered the study. This study was performed on 52 patients with IGM that did not respond to prednisolone (20 - 30 mg per day for 2 month). Finally 25 in methotrexate and 27 in azathioprine group were entered. Treatments included azathioprine at a dose of 50 in first and then increased to 100 mg per day and methotrexate at a dose of 10 to 15 mg per week. Then demographic and clinical characteristics, ultrasound and pathology findings of all patients were recorded. Response to treatment was evaluated by repeated examination and clinical judgment by single rheumatologist and ultrasound was done every 3 to 6 follow-ups. No response was considered if the clinical and Para clinical symptoms improved by less than 25% and In case of improvement 25 to 75% the was considered relative response and in case of improvement above 75% the response was considered complete. Then the information was entered into the software and statistically analyzed.

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Results

In this study, 53 patients with granulomatous mastitis were studied, all of whom were female, and in all patients the diagnosis was based on pathology indicating granulomatous. Based on the findings of Table 1, there is no significant difference between the two groups in terms of age, involved breasts and unilateral or bilateral breast involvement, clinical findings and physical examination, sonographic findings and pathology findings (p <0.05). According to the findings of this study there isn't significant difference in type of biopsy, number of surgical and abscess discharges, and the duration of treatment (p <0.05) between two group of patients with IGM.

Table1: Distribution of variables according to clinical & physical findings in Prednisolone + MTX and Pre+ AZA groups.

Results

The results showed that patients with IGM in two groups did not have significant difference of response to treatment in third, sixth and eighteenth months (p <0.05) .while response to treatment showed a significant difference in twelfth month (p <0.05). The results also showed that duration of treatment in patients with IGM in two groups receiving azathioprine and methotrexate did not show a significant difference in terms of age and number of lesions (p <0.05). The two groups of patients did not show a significant difference in terms of the number of surgical cases (p = 0.84), the number of abscess discharges (p = 0.75), and the number of lesions. Also, there is no significant difference in the pathology of the lesion and infiltrated cells in the two groups (p <0.05).

Table2: Outcomes of treatment in Pred + MTX and Pre+ AZA groups.

Variables		Prednisolone+ MTX N=26	Prednisolone + AZA N=27	Total N=53	P-Value
Age Meant SD		32.65 ± 6.462	35.67 ± 7.791	34.19 ± 7.262	0.199
Right Breast		13 (50.0)	11 (40.7)	24 (45.3)	0.5
Left Breast		13 (50.0)	16 (59.3)	29 (54.7)	
Unilateral involve		25 (96.2)	25 (96.2)	50 (94.3)	1.0
Bilateral involve		1 (3.8)	2 (7.4%)	3 (5.7)	
Pain		24 (92.3)	27 (100)	51 (96.2)	0.24
Mass in Breast		23 (88.5)	26 (96.3)	49 (92.5)	0.35
Discharge		6 (23.1)	9 (33.3)	15 (28.3)	0.41
Erythema		17 (65.4)	16 (59.3)	33 (62.3)	0.65
Fever		4 (15.4)	3 (11.1)	7 (13.2)	0.7
Chills		3 (11.5)	0 (.0)	3 (11.5)	0.11
Tenderness		16 (61.5)	15 (55.6)	31 (58.5)	0.66
Abscess formation		6 (23.1)	4 (14.8)	10 (18.9)	0.44
Fistula		13 (50.0)	11 (40.7)	24 (45.3)	0.5
Location of Breast	Upper, Internal	10 (38.5)	8 (29.6)	18 (34.0)	0.56
	Upper, External	12 (46.2)	10 (37.0)	22 (41.5)	
	Lower, External	1 (3.8)	4 (14.8)	5 (9.4)	
	Lower, Internal	1 (3.8)	3 (11.1)	4 (7.5)	
	Nipple	2 (7.7)	2 (7.4)	4 (7.5)	
Antibiotic usage		15 (57.7)	9 (33.3)	24 (45.3)	0.08
Arthritis			3(11.1)	3(11.5)	
OCP usage		8(30.4)	8(29.6)	16(30.2)	
Erythema Nodosum		1 (3.8)	2 (7.4)	3(11.5)	
ESR elevation		3 (11.5)	10 (37.0)	13 (24.7)	
CRP elevation		7(26.9)	9 (33.3)	10 (37.0)	
ANA positive		1 (3.8)	3 (11.1)	4 (7.5)	
History of Mastitis		10 (38.5)	8 (29.6)	18 (34.0)	
Relapse of Mastitis		1 (3.8)	2 (7.4)	3(11.5)	

Variables		Pred + MTX	Pred+ AZA	Total	P-Value
Length of treatment (in month) Mean ± sd		8.7±5.83	7.8±4.42	8.2±5.05	0.81
Response to treatment in 1 month N (%)	Complete	0	0 (.0)		0.24
	Relative	5 (19.2)	9 (33.3)	14 (26.4)	
	No	21 (80.8)	18 (66.7)	39 (73.6)	
Response to treatment in 3 month N (%)	Complete	4 (15.4)	5 (18.5)	9 (17.0)	0.77
	Relative	17 (65.4)	19 (70.4)	36 (67.9)	
	No	5 (19.2)	3 (11.1)	8 (15.1)	
Response to treatment in 6 month N (%)	Complete	10 (45.5)	12 (54.5)	22 (50.0)	0.33
	Relative	9 (40.9)	10 (45.5)	19 (43.2)	
	No	3 (13.6)	0 (.0)	3 (6.8)	
Response to treatment in 12 month N (%)	Complete	1 (8.3)	6 (60.0)	7 (31.8)	0.02
	Relative	10 (83.3)	4 (40.0)	14 (63.6)	
	No	1 (8.3)	0 (.0)	1 (4.5)	
Response to treatment in 18 month N (%)	Complete	5 (45.5)	2 (50.0)	7 (46.7)	1.0
	Relative	5 (45.5)	2 (50.0)	7 (46.7)	
	No	1 (9.1)	0 (.0)	1 (6.7)	

Conclusion

According to the results of this study, treatment with prednisolone plus methotrexate or azathioprine are both effective in the treatment of IGM. But response to prednisolone with azathioprine is higher than methotrexate especially in 12 month. Therefore we can used Azathioprine in equal of methotrexate in treatment of IGM.

Key Word: Azathioprine, Methotrexate, Response to treatment, Idiopathic granulomatous mastitis.