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ROLE OF MAINTAINING CAUSE AS IGE MEDIATED ANTIBODIES IN THE MANAGEMENT OF EOSINOPHILIC ESOPHAGITIS PRESENTING GERD - A SINGLEBLIND RANDOMIZED PLACEBO CONTROL TRIAL

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ABSTRACT

Objectives: To compare the pre and post treatment between two groups of eosinophilic esophagitis using GERD-Q questionnaire. To assess predominant miasm in cases of eosinophilic esophagitis with the aid of Hahnemann's chronic disease. **Study Design:** Single blind, randomised, placebo control trial. **Materials and Methodology:** A total of 100 cases of Eosinophilic esophagitis were randomly allocated to the two treatment groups, *Individualized Homeopathic Medicine* group- Group A (n=50) and *Placebo* group- Group B (n=50). Potency selection, dosage and repetition of medicine of Group A were done according to patient's susceptibility and homoeopathic principles. The outcome measures werelowering of GERD score in both groups after three months of treatment with removal of maintaining cause. **Results:** Observations and result show that among 100 cases of Eosinophilic esophagitis enrolled in the study: Patients treated with Individualized Homeopathic medicine selected on the basis of totality have significant improvement as compared to Placebo with removal of maintaining cause. The most frequently prescribed homoeopathic medicines in Group A were *China* (n=6), *Arsenic*

(n=5), *Nux Vom.* (n=5), *Phosphorus* (n=4), *Pulsatilla* (n=4) and *Lycopodium* (n=4). Symptoms of heartburn, regurgitation, nausea, vomiting and sleep disturbances were highly improved. Among the 50 cases of Eosinophilic Esophagitis enrolled in Group A in which Individualized Homoeopathic Medicine was given with removal of maintaining cause showed marked improvement in 22 (44%) cases. Whereas among 50 cases of Eosinophilic esophagitis enrolled in Group B belonging to Placebo with removal of maintaining cause showed mild improvement in 28 (56%) cases by lowering the GERD Q score. The predominant miasm found in this study was mainly psora. **Conclusion:** From the study "Role Of Maintaining Cause As IgE Mediated Antibodies in The Management of Eosinophilic Esophagitis Presenting GERD - A Single Blind Randomized Placebo Control Trial" it is evident that removing of maintaining cause along with Individualized Homoeopathic medicine is a useful approach in cases of Eosinophilic Esophagitis presenting GERD as compared to only removal of maintaining cause. There were significant changes in GERD Q in Medicinal group. The most commonly indicated medicine are China, Nux vom., Arsenic, Phosphorus, Pulsatilla, Lycopodium. From this study it can be concluded that Psora is the predominant miasm lying in the background of the patients suffering from Eosinophilic esophagitis.

KEYWORDS - Eosinophilic esophagitis, Individualised Homoeopathic Medicine, Placebo, GERD, SPT.

INTRODUCTION

Eosinophilic esophagitis (EoE) is a chronic immune/antigen-mediated esophageal disease characterized clinically by symptoms associated with esophageal dysfunction and histologically by eosinophil-predominant inflammation.[1]

Eosinophilic esophagitis is a common diagnosis in patients with refractory Gastroesophageal Reflux Disease (GERD). Patients with eosinophilic esophagitis are usually young men, present with a history of intermittent solid food dysphagia, and often have a history of food impaction.[2,3]

The current prevalence in developed countries is between 45 and 55 cases per 100,000 population. In Egypt, The prevalence of EoE is about 3.3% in adult patients presenting with upper gastrointestinal symptoms.[4]

Previous study, included 354 patients with various upper gastro-intestinal symptoms, 10.2% of them had EoE. A prospective study in India included 185 patients with reflux symptoms, 3.2% of them had EoE. When patients with both GERD and EoE were compared to patients with GERD only, the former group had higher percent of allergic history 16.6% versus 0.11% in the latter group, in addition to non-response to PPI. These two factors were considered predictors of EoE among GERD patients.[5,6]

Skin prick testing (SPT) could be a reliable method to diagnose IgE-mediated allergic disease in patients with rhinoconjunctivitis, asthma, urticaria, anapylaxis, atopic dermatitis and suspected food and drug allergy.[7]

The removal of all food antigens from the adult diet is also effective in resolving EoE, with improvements in endoscopic and histologic features in 72% of subjects after 4 weeks of treatment.[8,9]

Maintaining cause is the avoidable harmful influence responsible for the maintenance of the chronic disease process or development of pseudo-chronic disease. Without the removal of causa occasionalis (maintaining cause), permanent cure of the chronic disease is not possible.[10]

MATERIALS AND METHODS

Study setting

The subject for this study were collected from OPD/IPD of Mangilal Nirban Homoeopathic Medical College & Research Institute, Bikaner, Rajasthan.

Study duration

The study was undertaken for a period of 12 months out of which cases were registered in first nine months so that minimum 3 months of observations could be obtained from the last case. Each case was followed for a period of 3 months and called at every 7th day for regular follow up.

Selection of sample

Sample size: To see the effect of Individualised Homoeopathic Medicine and Placebo in Group A and in Group B. Mean difference in effect of Group A and Group B was seen. By taking standard effect size= 0.6 at 80% power, size of sample in each group is 45. Assuming the drop out is 10%, the effective sample size for each group is 50 and total sample to be taken is 100

cases.[11]

Group A- 50 casesGroup B- 50 cases.

Inclusion criteria

- Age group 25-45 years were included in the study irrespective of gender, race,religion andsocio-economic status.
- Patient with symptoms of heartburn, regurgitation, nausea and sleep disturbance occuringmore than 3-4 days as per GERD-Q questionairre.
- Endoscopy and SPT of patients were done to determine other systemic disease and Foodallergy.

Exclusion criteria

Patient with esophagitis with other systemic disease like scleroderma and other collagen diseases, Crohn's disease, oesophageal carcinoma, fungal and oesopheal infections, erosive GERD were excluded.

- Pregnant and lactating women with eosinophilic esophagitis were excluded.

Drop outs

- Cases who discontinue treatment in between and cases without 6 follow up were excluded from the study.
- Cases requiring emergency treatment.

Intervention

Double group assignment, random allocation.

Group- A- Individualised homoeopathic medicine and removing maintaining cause.

- Potency- Selection of potencies was done according to patient susceptibility and homoeopathic principles.
- Manufacturer- Medicine was obtained from a GMP certified company.
- Form- Globules no.30
- Route of administration- Oral
- Dispensing- This was done by the college dispensary from a certified pharmacist.Group-B- Placebo and removing maintaining cause.
- Manufacturer- Medicine was obtained from a GMP certified company.
- Form- Globules no.30

- Route of administration- Oral
- Dispensing- This was done by the college dispensary from a certified pharmacist.

Outcome assessment

GERD-Q –changes in mean scores of GERD-Q.[12]

Following parameters were used fixed according to the type of response obtained after the treatment -

Improvement criteria

Baseline score- after score/ Baseline score X 100100% -75% - Marked improvement.

74% - 50% - Moderate improvement.

49% - 25% - Mild improvement.

< 25% - Non significant.0% - Status Quo.

Data Analysis & Statistical technique

The data will be summarized in the form of master chart in MS Excel. The statistical test was used for the analysis of data using statistical softwareIBM SPSS 20.0 version.

- Independent t-test was used to compare two treatment groups.
- Paired t-test was used to assess the before and after scores in each patient.

Ethical clearance

Ethical clearance was obtained from the institutional ethics committee.

OBSERVATIONS AND RESULTS

Table 1: Baseline characteristics of patients studied under modified intention-to-treat.

	Groupa (Individualized Homoeopathic medicines) No. Of cases (n = 50)	**Group b (*Placebo*) No. Of cases (n = 50)**
Age (%)		
20-25	3(6%)	1(2%)
26-30	5(10%)	5(10%)
31-35	14(28%)	17(34%)
36-40	11(22%)	13(26%)
41-45	11(22%)	8(16%)
46-50	6(12%)	6(12%)
Gender (%)		
Male	27(54%)	21(62%)
Female	23 (46%)	19(38%)
Socioeconomic status (%)		
Lower	16(32%)	16(32%)
Middle	22(44%)	15(30%)

Upper	20(40%)	27(54%)
Occupation (%)		
Business	9(18%)	3(6%)
Clerk	5(10%)	3(6%)
Housemaker	7(14%)	4(8%)
Shopkeeper	8(16%)	22(44%)
Student	14(28%)	12(24%)
Teacher	7(14%)	6(12%)
Allergen (%)		
Cheese	6(12%)	6(12%)
Egg	4(8%)	5(10%)
Fish	3(6%)	10(20%)
Milk	12(24%)	7(14%)
Paneer	4(8%)	0(0%)
Peanuts	3(6%)	5(10%)
Soyabean	5(10%)	8(16%)
Tomato	3(6%)	0(0%)
Wheat	10(20%)	9(18%)
Addiction (%)		
No addiction	35(70%)	35(70%)
Smoking	13(26%)	12(24%)
Smoking+tobacco	1(2%)	1(2%)
Tobacco	1(2%)	1(2%)
Smoking+alcohol	0(0%)	1(2%)
Diet (%)		
Vegetarian	16(32%)	19(38%)
Non- Vegetarian	34(68%)	31(62%)
Predominant miasm (%)		
Psora	32 (64%)	32 (64%)
Psora syphilis	10(20%)	9(18%)
Psora sycosis	8(16%)	9(18%)
Area of residence (%)		
Rural	10(20%)	20(40%)
Urban	40(80%)	30(60%)

Table 2: Patient Distribution in Group A According to GERD Q Cut Points Before and After Treatment.

Cut pointsof GERD Q	GERD Q in GroupA before treatment n=50	GERD Q in GroupA after treatment n=50	%
0-2	0	8	8
3-7	0	30	30
8-10	1	11	12
>11	49	1	50
TOTAL	50	50	100

GERD Q cut points indicate the intensity of symptoms of eosinophilic esophagitis as heartburn, nausea, regurgitation, sleep disturbance. Increased score show increase in severity of symptoms, so this table indicate that after taking medicine and removing maintaining cause the score of GERD Q reduces in Group A.

Table 3: Patient Distribution in Group B According to GERD Q Cut Points Before and After Treatment.

Cut pointsof GERD Q	GERD Q in GroupA before treatment n=50	GERD Q in GroupA after treatment n=50	%
0-2	0	1	1
3-7	0	17	17
8-10	2	25	27
>11	48	7	55
TOTAL	50	50	100

GERD Q cut points indicate the intensity of symptoms of eosinophilic esophagitis as heartburn, nausea, regurgitation, sleep disturbance. Increased score show increase in severity of symptoms, so this table indicate that there is not much improvement in symptoms of eosinophilic esophagitis in Group B (placebo group) as only maintaining cause was removed and no medicine was taken.

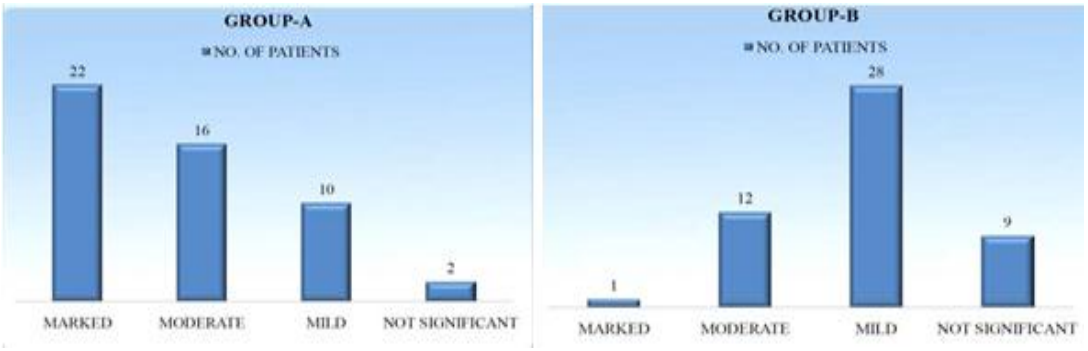

Fig. 1: Distribution of cases of Eosinophilic Esophagitis according to result obtained in both groups.

Table 4: Distribution of Cases of EoE According to "Indicated Medicine & Result Obtained" in Group A.

Sr. No	Medicine	No. of Patients	Marked improvement	Moderate improvement	Mild improvement	Non – significant	Status Quo
1.	*China officinalis*	6	2	1	3		
2.	*Nux Vomica*	5	3		2		
3.	*Arsenicum*	5	4		1		

	Album						
4.	*Lycopodium clavatum*	4	2	1	1		
5.	*Phosphorus*	4	1	3			
6.	*Pulsatilla nigricans*	4	1	2		1	
7.	*Argenticum nitricum*	3	2		1		
8.	*Natrum muriaticum*	3	1	1	1		
9.	*Carbo vegetabilis*	3	1	2			
10.	*Sulphur*	3	2	1			
11.	*Acidum sulphuricum*	2		1	2		
12.	*Sepia officinalis*	2	1	1			
13.	*Natrum phosphoricum*	2	1	1			
14.	*Bryonia alba*	1				1	
15.	*Antimonium crudum*	1	1				
16.	*Thuja occidentalis*	1		1			
17.	*Medorrhinum*	1	1				

Table 3: Independent t-test result.

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	T	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
VAR00009	Equal variances assumed	1.251	.266	-7.554	98	.000	-3.58000	.47395	-4.52054	-2.63946
	Equal variances not assumed			-7.554	96.161	.000	-3.58000	.47395	-4.52076	-2.63924

Levene's Test indicated equal variances (F = 1.25, p = .26) so df = 98. There is significant difference between lowering of GERD-Q scale by eliminating maintaining cause in cases of Eosinophilic Esophagitis along with Individualised Homoeopathic Medicines (M= 4.66, SD= 2.52) as compared to Placebo(M= 8.24, SD= 2.19), with the mean difference between the groups being M= -3.58, SE= .47.

Therefore rejecting Null hypothesis removing maintaining cause in cases of Eosinophilic Esophagitis along with Individualised Homoeopathic Medicines is more effective as compared

to only removing of maintaining cause with placebo, with difference of mean= -3.58.

DISCUSSION

The study entitled **"Role of Maintaining Cause As IgE Mediated Antibodies in The Management of Eosinophilic Esophagitis Presenting GERD - A Single Blind Randomized Placebo Control Trial"** was undertaken at OPD /IPD of M. N. Homoeopathic Medical College & R.I. Bikaner, Rajasthan.

In this study 100 cases of Eosinophilic Esophagitis were taken by Random Allocation Sampling Method. These cases were randomly allocated into 2 treatment groups- Group A - Individualized Homoeopathic Medicine Group B – Placebo. A discussion on the interpretation derived from the study has been given below:- Among 100 cases of eosinophilic esophagitis 54 (54%) cases were found to be male while 46 (46%) cases were female similar results were seen in a retrospective, multicenter, cross-sectional analysis where predominantly male patients (72%) were found affected with EoE.[13]

Previous studies showed similar results regarding habitat of patients as seen in our study, i.e. maximum incidence of eosinophilic esophagitis seen in urban area with 70 (70%) cases and 30 (30%) cases of rural area. On the contrary study done by Jensen showed increased incidence of EoE in rural areas.[14]

Among 100 cases of eosinophilic esophagitis 14 (14%) cases belong to age group of 20-30 years showing minimum incidence, 55 (55%) cases belong to age group 31-40 years showing maximum incidence and lastly 31 (31%) cases belong to age group 41-50 years, similar results were seen in the study done by Potter in 2004, where in adults, eosinophilic esophagitis presented in the third or fourth decades of life.[2]

Increased incidence of eosinophilic esophagitis among upper class people in 47 (47%) cases, followed by middle class people 37 (37%) cases and least seen in lower class i.e. in 16 (16%) cases similar results were found in previous studies done in the Asian region have shown that high socioeconomic status people are at risk EoE presenting GERD.[15]

Among 100 cases of eosinophilic esophagitis it was seen that 70 (70%) cases had no addictions while 25 (25%) cases were addicted to smoking, with similar results in previous studies where smoking, alcohol use, and hiatus hernia were found to be risk factors for EoE presenting GERD.[15]

Previous studies showed that non-vegetarian people have higher incidence of eosinophilic esophagitis similar results were seen, in our study where non-vegetarian cases were 65 (65%) and 35 (35%) cases were vegetarian.[16]

Predominance of eosinophilic esophagitis as occupation wise among 100 cases was seen in shopkeeper 30 (30%) cases and students 26 (26%) cases, followed by teachers in 13 (13%) cases, 12 (12%) cases of business men, housemakers were 11 (11%) cases and lastly clerk were found to be in 8 (8%) cases.

As mentioned in table (4) indicated medicines for eosinophilic esophagitis were found to be *Cinchona officinalis=6, Arsenic=5, Lycopodium, Phosphorus, Pulsatilla=4, Carbo veg., Sulphur, Natrum mur., Argentum nit.=3, Sepia, Acid sulph., Natrum phos.=2, Antim crud., Medorrhinum, Bryonia, Thuja=1*. These figures relate to previous studies done by Mittal et al where *Lycopodium clavatum, Nux vomica,* and *Pulsatilla nigricans* were the commonly indicated medicines.[81]

Predominant miasm among 100 cases of esinophilic esophagitis was found to be psora in 64 (64%) cases, psora-syphilis in 19 (19%) cases and psora-sycosis in 17 (17%) cases.

Among 50 cases of eosinophilic esophagitis, in Group-A, marked improvement was seen in in 22 (44%) cases, while moderate improvement was seen in 16 (32%) cases, 10 (20%) cases showed mild improvement and non-significant result was obtained in 2 (4%) cases and as shown in fig. (29) in Group-B among 50 cases, 1 (2%) cases showed marked improvement, 12 (24%) cases showed moderate improvement, 28 (56%) cases showed mild improvement while in 9 (18%) cases non-significant result was found.

CONCLUSION

From the study **"Role Of Maintaining Cause As IgE Mediated Antibodies in The Management of Eosinophilic Esophagitis Presenting GERD - A Single Blind Randomized Placebo Control Trial"** it is evident that removing of maintaining cause along with Individualized Homoeopathic medicine is a useful approach in cases of Eosinophilic Esophagitis presenting GERD as compared to only removal of maintaining cause. There was significant changes in GERD Q in Medicinal group.

- Severity and Intensity of symptoms of Eosinophilic esophagitis like heartburn, regurgitation,nausea, vomiting and sleep disturbance also reduces as compared to placebo

group.

- From this study it can be concluded that Psora is the predominant miasm lying in thebackground of the patients suffering from Eosinophilic esophagitis.
- The most commonly indicated medicine are *China, Nux vom., Arsenic, Phosphorus, Pulsatilla, Lycopodium.*

Limitations

- There are also some limitations of this study. Since, the sample size was also small in this study, so generalizing the result and conclusions of this study need to be done very cautiously.
- Globally, there was no specific scale found for the assessment of the treatment outcome in case of Eosinophilic esophagitis infection. So, the results of this study cannot be generalised to any population. The findings of this study need to be further evaluated using better study designs with large sample size and enhanced methodological rigor. Hence, further more extensive studies will be required with better statistical tools to establish the outcome results of this study.

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