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A PROSPECTIVE STUDY ON EFFECTIVENESS OF *AEGLE FOLIA* IN CASES OF IRRITABLE BOWEL SYNDROME - A SINGLE BLIND RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Background: Irritable bowel syndrome (IBS) is a gastrointestinal (GI) disorder characterized by altered bowel habits in association with abdominal discomfort or pain in the absence of detectable structural and biochemical abnormalities.[1] The vast population has suffered from IBS in some form or the other and due to ignorance by people, this disease has been suppressed or managed by taking inappropriate medication. So based on this fact purpose of the study is to give effective and long lasting relief in cases of IBS by Homoeopathic medicine. **Objectives:** To assess the effectiveness of *Aegle folia* in cases of irritable bowel syndrome by using Irritable Bowel Syndrome-Symptom Severity Scale (IBS-SSS) and to explore & identify other clinical symptom of *Aegle folia*. **Materials and Method:** A randomized single blind controlled trial was conducted at Dr. Madan Pratap Khunteta Homoeopathic Medical College, Hospital and Research Centre, Jaipur. 70 cases of IBS were enrolled in the study. Randomly selected 35 cases received *Aegle folia* (Group A), 35 cases received *Placebo* (Group B). Irritable Bowel Syndrome Symptom Severity Scale was used to assess the improvement in the study. **Result:** There was a significant role of *Aegle folia* in treating the cases of IBS as compared with placebo as determined by statistically significant differences between the means of both independent groups i.e. Group A- *Aegle folia* and Group B - *Placebo*. Levene's test indicated equal variance (F= .066, P= .798) so df= 68. There is significant ($p < 0.005$) improvement in IBS with *Aegle folia* (M=67.71, SD= 62.666) than *Placebo* (M= 160.29, SD= 63.373), t(68)=

6.145, p< 0 .005. **Conclusion:** This study showed that there was effectiveness in cases of IBS from *Aegle folia* and Placebo both, but the effect of *Aegle folia* was far better than Placebo. Cases of IBS if treated with *Aegle folia* (if the symptoms correspond can be improved to a great extent.

KEYWORDS: IBS, Homoeopathy, *Aegle folia*, Randomized, Irritable Bowel Syndrome, Symptom Severity Scale.

INTRODUCTION

Irritable bowel syndrome (IBS) is a functional bowel disorder characterized by abdominal pain or discomfort and altered bowel habits in the absence of detectable structural abnormalities.[2] No clear diagnostic markers exist for IBS, thus the diagnosis of the disorder is based on clinical presentation.[2] The Rome 3rd criteria is currently accepted in clinical practice.[3] Nevertheless, IBS is the most common cause of gastrointestinal referral and accounts for frequent absenteeism from work and impaired quality of life.[4] Young women are affected 2–3 times more often than men.[5]

Population- based studies estimate the prevalence of IBS at 10- 20% in western countries and incidence of IBS at 1-2% per year. Prevalence of IBS is 4.2-7.9% in India.[6]

IBS is a disorder that affects all ages, although most patients have their first symptoms before age 45years.Pain or abdominal discomfort is a key symptom for the diagnosis of IBS. These symptoms improve with defecation and/or have their onset associated with a change in frequency or form of stool. Supportive symptoms that are not part of the diagnostic criteria include defecation straining, urgency or a feeling of incomplete bowel movement, passing mucus, and bloating. The pathogenesis of IBS is poorly understood, although roles of abnormal gut motor and sensory activity, central neural dysfunction, psychological disturbances, mucosal inflammation, stress, and luminal factors have been proposed.[2]

IBS is a common health problem affecting a substantial proportion of the population. Many individual with symptoms of IBS do not seek medical attention or have stopped consulting because of disillusionment with current treatment options,[7,8] Modern therapies like Allopathy associated with poor efficacy & side effect in cases of IBS. So homoeopathy could become choice of treatment to give appropriate and lasting relief to the patients of IBS.

There are number of Indian drugs which were commonly used in Ayurvedic system of medicine since ancient time,[9] now being proved and showing significant role in Homoeopathy so lesser used Indian Homeopathic drug *Aegle folia* can also be beneficial for such conditions.

MATERIALS AND METHODOLOGY

❖ Study Setting

The study was undertaken at Dr M.P.K. Homoeopathic Medical College, Hospital & research centre, sindhi camp/saipura Jaipur. The cases were taken from the OPD /IPD. The study duration was for 1 year (June 2016-May2017) with minimum 6 follow- ups.

❖ Study Design

It was a prospective randomized placebo controlled study design.

Allocation- Patients fulfilling the eligibility criteria were enrolled and randomized systematically (computer generated randomization chart) to receive either homoeopathic interventions (*Aegle folia*) or *Placebo.* Group A (N= 35) medicine group and Group B (n=35) controlled group. Sample size was 70.[10]

The council's ethical committee approved the study protocol. Written informed consent was received from the patients.

❖ Inclusion Criteria

- ✓ Patient satisfying the Rome 3rd criteria,[11] of IBS.
- ✓ All patient were included in the study irrespective of their age, sex, caste, religion & duration of illness.
- ✓ Those who were willing to sign Informed Consent Form (ICF)**.**

❖ Exclusion Criteria

- ✓ Those who were taking regular medicine for GIT complaints other than IBS and systemic disease.
- ✓ Pregnant or breastfeeding females.
- ✓ According to investigator desertion.

❖ Withdrawal Cases

- ✓ Any condition requiring emergency treatment including IBS.
- ✓ Cases which discontinued treatment in between and cases without proper follow up.

✓ Patient withdraws consent.

❖ **Intervention**

Experimental group

Patients randomized to Group A received Homoeopathic medicine *Aegle folia* for six follow-ups customized to each patient, which started with 30C/TDS up to 1M potency according to patient's susceptibility and homoeopathic principles.

GMP certified medicine was used of globules no. 60 by oral route of administration by hospital dispensary from a certified pharmacist.

Controlled Group

Patients randomized to the Group B group received *Placebo*, which was similar in all the manners to that of Group A including the globules no, route of administration. However, it constituted un-medicated poppy size sugar globule impregnated with dispensing alcohol.

❖ **Data analysis & Statistical techniques**

- Subjects were assessed through the following indices i.e. on the basis of Rome 3rd criteria and outcome was measured according to symptom severity scale (IBS-SSS).[12]
- Statistical techniques - "Paired t-test" and "Independent t-test".

RESULTS AND DISCUSSION

For assessing the improvement of IBS cases Symptom Severity Scale was used. Scores before treatment and after treatment were compared in both groups. The analysis was conducted through the software SPSS (ver.16) applying Paired t- test & Independent t- test.

Table 1: Group A, Paired Samples Statistics.

		Mean	N	Std. Deviation	Std. Error Mean
Group A	ScoreA_before	218.71	35	45.703	7.725
	ScoreA_after	67.71	35	62.666	10.592

Table 2: Group A, Paired Samples Test

Group A	Paired difference					T	Df	Sig. (2- tailed)
	Mean	Std. Deviation	Std. Error Mean	95% confidence interval of the Difference				
				Lower	Upper			
Score A before Score A after	151.00	73.712	12.460	125.679	176.321	12.119	34	.000

A paired t-test was conducted to compare before and after score of Group A- *Aegle folia* in cases of IBS.

There was a significant difference in the scores for Group A- *Aegle folia.*
Before (M=218, SD=45.703) and after score (M=67.71, SD= 62.666) conditions; t (34) = 12.119, p = 0.000.

These results suggest that *Aegle folia* medicine had shown significant result in cases of IBS.

Table 3: Group B Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Group B	ScoreB_before	228.57	35	36.108	6.103
	ScoreB_after	160.29	35	63.373	10.712

Table 4: Group B Paired Samples Test

Group B	Paired difference					T	Df	Sig. (2- tailed)
	Mean	Std. Deviation	Std. Error Mean	95% confidence interval of the Difference				
				Lower	Upper			
Score B before Score B after	68.286	67.136	11.348	45.224	91.348	6.017	34	.000

A paired t-test was conducted to compare before and after score of Group B- Placebo in cases of IBS.

There was a significant difference in the scores for Group B- Placebo Before(M=228.57, SD=36.108) and after score(M=160.29, SD= 63.373) conditions; t(34)= 6.017, p = 0.000.

These results suggest that Placebo had shown significant result in cases of IBS.

Table 5: Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
Score_after	Exp.	35	67.71	62.666	10.592
	Control	35	160.29	63.373	10.712

Table 6: Independent Samples Test in IBS cases

		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
Score_after	Equal variances assumed	.066	.798	-6.145	68	.000	-92.571	15.065	-122.633	-62.510
	Equal variances not assumed			-6.145	67.991	.000	-92.571	15.065	-122.633	-62.510

Levene's test indicated equal variance (F= .066, P= .798) so df= 68. There is significant (P < 0.005) improvement in IBS with *Aegle folia* (M=67.71, SD= 62.666) than Placebo (M= 160.29, SD= 63.373), t(68)= 6.145, P< 0 .005, therefore rejecting null hypothesis(H_0) and accepting alternating Hypothesis (H_1) that *Aegle folia* has a significant role in treating the cases of IBS.

Taken together, these results suggests that intervention of *Aegle folia* appears to be significantly effective in treating cases of IBS as compared to *Placebo.*

A Discussion on various aspects observed in study has been given below.

Most of patients with IBS in India are of middle age group as in U.C. Ghoshal' study,[13] higher prevalence in mean age 39.4 yr. was recorded. Similar to previous studies, it has been observed that maximum incidence of IBS were observed in age group 20-30 yrs., i.e. in 24 cases (34%), followed by 30-40 yrs., i.e. in 22 cases (31%), 40-50 yrs. age group in 12 cases (17%) and the minimum patients were observed in age group of 60-70 yrs. i.e. in 1 case (1%) respectively.

IBS is more common in women then in men in most part of the world.[14,15,16] In India IBS is reported more often in male.[17] Interestingly, similar finding has been observed that maximum incidence of IBS were observed in males i.e. 55 cases (78.57%), whereas in females incidence was observed in 15 cases (21.43%). Similar to previous studies in India male dominance was recorded in Ghoshal's study.[13]

In this study, maximum incidence of IBS were observed in vegetarian patients i.e. 55 cases (79%), whereas in non-vegetarian incidence was 15 cases (21%) out of 70. No similar finding was found in previous studies.

There is increasing evidence regarding the role of immune activation in the etiology of IBS, which has mainly been shown in studies investigating mechanisms of Post Infectious IBS.[18] So similar to past studies this study had shown past history of Typhoid in 13 cases, Dengue in 9 cases, malaria history in 5 cases, chikungunya history in 2 cases.

Psychological stress is an important factor for the development of irritable bowel syndrome according to the research in the last decade.[19,20] Interestingly 11 cases had shown past history of acute stress disorder.

However, it remains unknown whether immune activation in IBS patients is largely dependent on infectious gastroenteritis and/or psychological stress. Additional studies are necessary to understand the precise mechanism of immune activation and its relationship to the development of IBS.[21]

In this study following modality were observed in patients

- 18 Cases had shown of aggravation of flatulence after eating.
- 24 Cases had shown amelioration after defecation in abdominal pain and discomfort.
- 30 Cases had shown aggravation in evening in upper abdominal pain, *Aegle folia* was given to 22 cases among which 18 showed improvement. Abdominal pain, aggravated from 4-5pm was given in CCRH clinical verification study.[22]
- 11 Cases had shown hard, knotty stool with mucous aggravated after eating.
- Dyspepsia aggravated after taking tea in 30 patients, *Aegle folia* was given to 14 cases among which 11 showed improvement.

- 25 Cases had shown constipation with incomplete evacuation and insufficient stool aggravated after stress, *Aegle folia* was given to 14cases among which 12 showed improvement.
- 8 Patient were with urticaria with itching aggravated in evening, out of which *Aegle folia* was given to 5cases among which 3 showed improvement.
- 10 Cases had shown loose, watery stool aggravated after stress.

Most studies report that around one third of patients have diarrhoea predominant IBS (IBS-D) and one third have constipation predominant IBS(IBS-C), the remainder having a mixed bowel pattern (IBS-M) with both loose and hard stool.[23,24,25] Previous Ghoshal's study,[13] showed that maximum patients were observed of M-TYPE (57%) then 39% of IBS-C and 4% of IBS-D.

In this study, maximum no. of IBS patients were observed of C-TYPE i.e. 42 cases (61%), as compared to M-type i.e. 15 cases (20%) & D- TYPE i.e. 13 cases (19%) out of 70.

In this study, 26 cases (37%) had shown Marked Improvement, out of which maximum cases were from Group A –*Aegle folia* i.e. 20 cases, 14cases (20%) had shown Moderate Improvement, out of which maximum cases were from both Group A- *Aegle folia* & Group B- *placebo* i.e. 7 cases each, 28cases (40%) has shown Mild Improvement, out of which maximum cases were from Group B- Placebo i.e. 20 cases and 2 cases (3%) become worse but as it was within the limits patho-physiologically, the subjects did not experienced any unfortunate incidence.

In this study it was observed that maximum no. of patients were observed with upper abdomen complaints i.e. 34 cases (48%), as compared to patients with whole abdomen complaints i.e. 20 cases (29%) & patients with lower abdominal complaints i.e. 16 cases (23%) out of 70 cases. Similar to previous studies,[26] in India upper abdominal complaints was recorded in this study.

Further Recommendations

- ❖ This study was conducted with small sample size. So, in future different population with large sample size is recommended for more reliable results.
- ❖ The study period was short. So, to confirm the conclusions long term studies are recommended.

CONCLUSION

This was a single blind randomized controlled trial with positive results. This study proved that intervention of *Aegle folia* can be significantly effective in treating cases of IBS as compared to placebo.

In this study, *Aegle folia* showed better result in the symptoms of Patients suffering from upper abdominal pain, which is aggravated in evening and constipation with incomplete evacuation and insufficient stool aggravated after stress and dyspepsia aggravated after taking tea.

This study showed that there was effectiveness in cases of IBS from Placebo and *Aegle folia* both, but the effect of *Aegle folia* was far better than Placebo. Placebo showed effect because of the life style management given to the patients. Cases of IBS if treated with *Aegle folia* (if the symptoms correspond) along with life style management, can be improved to a great extent.

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