

An Open Comparative Randomized Clinical Study of Plant Based Drugs *Embelia Robusta Roxb* and *Mallotus Philippinensis Muell* on Intestinal Parasites

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Abstract

Background: Intestinal parasites are common cause of morbidity.**Aim:** To compare the efficacy and safety of two plant based drugs *Embelia robusta Roxb* and *Mallotus philippinensis Muell* on intestinal parasites.**Methods:** Forty Patients exhibiting symptoms of parasitic infection were diagnosed and confirmed by stool test. They were then randomized to either *Embelia* in a dose of 5 g or *Mallotus* in dose of 1 g with honey and jaggery as adjuvant respectively. Drugs were administered for a period of one week and follow-up was carried in 15 days and thereafter a month to observe symptomatic relief and presence or absence of ova/cyst in stool sample examination.**Results:** Symptomatic relief was found in *Mallotus* while some symptoms still persisted with *Embelia*. *Embelia robusta* had 40% cure rate while *Mallotus* had 70% cure rate, but both the drugs did not result in any adverse effects.**Conclusions:** It was observed that *Mallotus philippinensis* had better efficacy.**Keywords:** *Embelia robusta Roxb*; *Mallotus Philippinensis uell*; Intestinal parasites; Comparative study

Introduction

The prevalence of human diseases is increasing rapidly worldwide, as is the number of deaths from diseases [1]. Intestinal parasites are one of the most common infections in humans. It is estimated that 60% of the world's population is infected with gut parasites, which play role in morbidity [2,3]. 3.5 billion people are affected, 450 million are ill as a result of these infections, the majority being children. 44 million pregnant women have hookworm infections which cause chronic blood loss from the intestine and predisposes to the development of iron deficiency anaemia. 65,000 deaths are directly attributable to hookworm infections 60,000 to Ascaris [4]. These cause morbidity in human in different ways, by affecting nutritional equilibrium, including intestinal bleeding, inducing malabsorption of nutrients, competing for absorption of micronutrients, reducing growth, reducing food intake, causing surgical complications such as obstruction, rectal prolapse and abscess, affect cognitive development [5,6].

In spite of great measures in the control of parasites, it still continues to be a major health problem which has compelled to think over less toxic and more effective alternative source i.e. from plant source.

Embelia robusta burm. is one such plant claimed to be best in the treatment of pathogens as documented in Indian traditional system of Medicine [7] It is advocated to be used with honey as an adjuvant [8]. Also glands and hairs covering the fruit of *Mallotus philippinensis muell* have also been mentioned for the treatment of pathogens [9]. The adjuvant advised here is jaggery [10].

The study aims to compare the efficacy of these two drugs on selected parasites.

Methods

The study was open labeled, comparative, interventional randomized trial.

Preparation of the drug

Plant material: Market Samples of *Embelia robusta* and *Mallotus philippinensis Muell* were collected from different crude drug markets and subjected to High Performance liquid chromatography (HPLC), this being one of the widely used methods for separation and quantitative estimation of phenolic acid content present in them. The samples having highest cinnamic acid content was chosen for the study. Cinnamic acid is a phenolic acid with anthelmintic, anti-viral, antioxidant and antifungal property [11-14]. As per the references in the classics *Embelia robusta Roxb* was advised with honey [7] and *Mallotus philippinensis Muell* tablets was prepared by admixture of glands and hairs of *Mallotus* and jaggery in twice the proportion [10].

Administration of drug

Embelia robusta Roxb fruit powder in the dose of 5 g orally was advised to be taken with honey, glands and hairs of *Mallotus philippinensis Muell* was made into tablets and administered in the dose of 500 mg orally for children and 1g to the adults. This dose was arrived at after referring the Ayurvedic classics and Ayurvedic Pharmacopoea of India [15].

Methodology for clinical trial

Type of study- Interventional study

Study design - open randomized controlled clinical trial

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Patient selection- Allocation randomized open labelled clinical controlled trial.

End point classification- Clinical efficacy

Intervention model- Parallel assignment

Phase of trial- phase III trial

Locale of study

The study subjects were selected from the outpatient department, S.S. Hospital, Banaras Hindu University, Varanasi.

Screening and recruitment of the patients

Twenty patients of different age groups who exhibited symptoms of parasitic infection were selected for each test drug and their stools were examined microscopically in the Department of Microbiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi to confirm the presence of ova/cyst of helminthes. Before the commencement of the trial Institutional Ethics committee approval was obtained .Written informed consent and assent was obtained prior to enrollment of the patients. Also it was conducted in accordance to ICMR ethical guidelines for biomedical research on Human Participants, 2006.

Sample size

A total number of forty patients were enrolled in this trial.

Study Design

Grouping of the patients

Group A: Twenty patients presenting with symptoms and signs of infestation were treated with powder of *Embelia* with Honey.

Group B: Twenty patients exhibiting the signs and symptoms of infestation received *Mallotus* with jaggery.

Procedure Of clinical trial

Forty patients were selected from O.P.D. of S.S. Hospital, I.M.S; B.H.U. Twenty patients were treated with *Embelia* and twenty with *Mallotus*. Their age varied from 3-45 years. Patients of both sexes were selected. The diagnosis was based on their symptoms and signs and confirmed by examining their stools microscopically for the presence of ova/cyst. Follow-up of patient was done at the end of 7 days, 15 days and one-month duration of the treatment. Each week their stool was examined in the lab for the presence of ova/cyst and results were noted.

Diets and habits

The patients were advised to avoid sweet substances and to maintain personal hygiene particularly to wash hands before food and after defecation.

Diagnosis of the patients

Clinical diagnosis has been done on the basis of signs and symptoms exhibited by the patients.

Laboratory diagnosis - ova/cysts and parasite examination of the stool was done which included direct wet mount. A drop of saline was placed on left half of the slide and one drop of iodine on the right half. With a wooden stick, a small portion of stool was introduced into the drop of saline and iodine. A cover slip was placed on this and examined under the microscope in systemic manner. Low power examination (x100) of entire 22 by 22 mm cover slip preparation (both saline and

iodine); high dry power examination (x400) of at least one third of the cover slip area (both saline and iodine) was done. In low power, larvae, ova, segments, RBCs and WBCs can be seen while in high power trophozoites, cysts etc can be screened.

Parameters for efficacy assessment

The results were assessed on the basis of repeated negative stool report for three consecutive days and relief in symptoms and signs were classified as follows:

Cured - Those cases who had symptomatic relief with negative stool report after the treatment.

Improved - Cases showing symptomatic relief but positive stool reports for ova.

Unchanged - Cases whose stool reports were negative for ova and only partial or no symptomatic relief was noted.

Results

The results of the study are presented under the following headings:

Demographic profile

Clinical profile

Results of Study Drugs

Demographic profile presents distributions of patients suffering from infestation according to age, sex, domicile status, socio-economic status, religion, personal hygiene, occupation, dietary habit and residential sanitation.

Clinical profile comprises of incidence of general signs and symptoms, also characteristic symptoms.

Treatment and response include comparison of baseline characteristics, concomitant medication and follow up in different study groups.

Demographic profile

Most of the patients i.e. out of 40, 15 (37.5%) belonged to 11-20 years of age group followed by 1-10 yrs (35%), 21-30 yrs (15%) and 31-40 yrs (12.5%) (Table 1). Also 67.5 percent patients were male whereas female were 32.5percent (Table 2). The incidence of worm infestation is more in rural areas than in urban. A maximum of 30 patients constituting 75 percent of the study sample were rural people, whereas 25 percent belonged to urban area (Table 3). The incidence of worm infestation was seen highest in patients with poor hygiene (55%) (Table 4).

Distribution of patients (%) according to age (n = 40)		
Age Group (in years)	No. of patients	Percentage (%)
1 – 10	14	35.0
11 – 20	15	37.5
21 – 30	6	15.0
31 – 40	5	12.5
Total	40	100

Table 1: Incidence of Age.

Distribution of patients (%) according to sex (n = 40)		
Sex	No. of patients	Percentage (%)
Male	27	67.5
Female	13	32.5
Total	40	100

Table 2: Incidence of Sex.

It was been observed that this condition is more common in students (72.5%) followed by housewives (12.5%), farmer (7.5%), businessmen (5%) and 2.5% were from service class (Table 5). Vegetarian and non-vegetarian diet has nearly the same significance as worm infestation can be equally transmitted through improperly washed vegetables, improperly cooked vegetarian as well as non-vegetarian diet, as they carry ova/cyst forms (Table 6).

Clinical profile

Among forty patients examined for the presence of ova/cyst by stool examination, sixteen were positive for ova of *Ascaris*, followed by cyst of *Entamoeba histolytica* in seven patients, cyst of *Giardia lamblia* in 5 patients and ova of *Hymenolepis nana* in four patients. Mixed infestation was seen in four patents. *Ancylostoma* and *Taenia* was observed in only two patients (Table 7).

Results of study drugs

Table 8 shows comparison of demographic variables in different study groups. There is no statistically significant difference among both groups with respect to age, sex domicile status, socio-economic status, personal hygiene, occupation, diet and residential sanitation.

Total relief was seen in patients treated with *Embelia* in relation to Fatigue, Anal pruritis, and Anemia. Some symptoms i.e. Anorexia (25%), Loss of Appetite (23.07%), Dizziness (20%), Pain abdomen (20%) persisted. Patients treated with *Mallotus* had relief with Diarrhoea, Anorexia, Fatigue, Pruritis, Anemia, Loss of appetite, Hypopigmented skin patches with persisting symptoms with regards to Anal pruritis

Distribution of patients (%) on the basis of domicile status (n = 40)		
Domicile Status	No. of cases	Percentage (%)
Rural	30	75
Urban	10	25
Total	40	100

Table 3: Incidence according to Domicile Status.

Distribution of patients (%) according to personal hygiene (n = 40)		
Personal Hygiene	No. of cases	Percentage (%)
Poor	22	55
Moderate	18	45
Good	-	-
Total	40	100

Table 4: Incidence of Personal Hygiene.

Distribution of patients (%) according to occupation (n = 40)		
Occupation	No. of cases	Percentage (%)
Student	29	72.5
Housewife	5	12.5
Businessman	2	5.0
Serviceman	1	2.5
Farmer	3	7.5
Total	40	100

Table 5: Incidence of occupation.

Distribution of patients (%) according to dietary habits (n = 40)		
Dietary Habits	No. of cases	Percentage (%)
Vegetarian	21	52.5
Non-vegetarian	19	47.5
Total	40	100

Table 6: Incidence of dietary habits.

Number of patients in whose stool samples different ova/cysts were detected (n = 40)		
S.N.	Ova / Cyst	No of cases
1.	<i>Ascaris lumbricoides</i>	16
2.	<i>Hymenolepis nana</i>	4
3.	<i>Ancylostoma duodenale</i>	2
4.	<i>Entamoeba histolytica</i>	7
5.	<i>Giardia lamblia</i>	5
6.	<i>Taenia saginata</i>	2
7.	Mixed infestation <i>Ascaris + Giardia</i> <i>Ascaris + trichuris</i> <i>Cyclospora + Idamoeba</i> <i>Ascaris + Taenia + trichuris</i>	4

Table 7: Incidence of ova/cysts.

Variables	A N=20	B N=20	Total N=40	χ^2
Age Groups	1 – 10	4	10	7.38 p > 0.05 NS
	11 – 20	11	4	
	21 – 30	3	3	
	31 – 40	3	2	
Sex	Male	14	13	0.11 p > 0.05 NS
	Female	6	7	
Domicile status	Rural	14	16	0.53 p > 0.05 NS
	Urban	6	4	
Religion	Hindu	19	19	χ^2 not applicable as expected frequency < 5
	Muslim	1	1	
	Christian	-	-	
Personal hygiene	Poor	10	12	0.40 p > 0.05 NS
	Moderate	10	8	
	Good	-	-	
Occupation	Student	13	16	χ^2 not applicable as expected frequency < 5
	Housewife	2	3	
	Businessman	-	2	
	Serviceman	-	1	
Diet	Vegetarian	10	11	0.65 p > 0.05 NS
	Non-vegetarian	10	10	

Table 8: Comparison of demographic profile in different study groups.

(25%) and Dizziness (11.11%) (Table 9).

In patients treated with *Embelia* it was observed that there was persistence of ova/cyst in patients positive for *Giardia* and *Taenia*, 50% persistence with *Ancylostoma* and *Entamoeba*, and 37.5% persistence with *Ascaris* and 33.3% with *Hymenolepis nana*. While those with *Mallotus* there was persistence of ova of *Ascaris* in only 12.5% of the patients and *Entamoeba* in 25%. Rest showed negative report after treatment (Table 10).

The cure rate was 40% in *Embelia* treated group with improvement in 35% and no improvement in 25% of the cases. While 70% of the cases treated with *Mallotus* were cured with improvement in 15% of the cases and no improvement in other 15% of cases (Table 11).

Table 12 shows that the initial mean \pm SD for *Embelia* Group was 10.37 \pm 0.97 and after a month's drug therapy it increased to 11.55 \pm 0.81. The improvement of Hb gm% was statistically highly significant (p < 0.01) while in *Mallotus* Group initial mean \pm SD was 10.30 \pm 0.78

Specific symptoms	Group A				Group B			
	B.T.		A.T. (persisting)		B.T.		A.T. (Persisting)	
	No.	%	No.	%	No.	%	No.	%
Diarrhoea	19	(95%)	3	(15.78%)	10	(50%)	-	-
Anorexia	8	(40%)	2	(25%)	2	(10%)	-	-
Fatigue	2	(10%)	-	-	2	(10%)	-	-
Pruritis	7	(35%)	-	-	8	(40%)	2	(25%)
Anemia	2	(10%)	-	-	2	(10%)	-	-
Loss of appetite	13	(65%)	3	(23.07%)	13	(65%)	1	-
Dizziness	10	(50%)	2	(20%)	18	(90%)	2	(11.11%)
Pain abdomen	10	(50%)	2	(20%)	12	(60%)	-	-
Hypopigmented skin patches	-	-	-	-	2	(10%)	-	-

Table 9: Effect of trial drugs on Clinical Signs and symptoms of (%)Intestinal parasites (n = 20).

Ova/cysts	Group A			Group B		
	B.T.	A.T. (Persisting)		B.T.	A.T. (Persisting)	
	No.	No.	%	No.	No.	%
Ascaris lumbricoides	8	3	(37.5%)	8	1	(12.5%)
Hymenolepis nana	3	1	(33.31%)	3	0	-
Ancylostoma duodenale	2	1	(50%)	1	0	-
Entamoeba histolytica	2	1	(50%)	4	1	(25%)
Giardia lamblia	1	1	(100%)	1	0	-
Taenia saginata	2	2	(100%)	1	0	-
Trichuris trichuira	0	0	-	0	0	-
Mixed infestation	1	0				
α. Ascaris + Giardia	1	1			0	
β. Ascaris + trichuris				1	1	
γ. Cyclospora + Idamoeba						
δ. Ascaris + Taenia Trichuris	2	1	(50%)	2	1	(50%)

Table 10: Persistence of ova/cyst (%) after treatment with drug A and drug B (n = 20).

Response of the Drug	Embelia		Mallotus	
	No.	(%)	No.	(%)
Cured	8	40	14	70
Improved	7	35	3	15
Unchanged	5	25	3	15

Table 11: Overall response of Embelia and Mallotus (%) (n = 20).

Groups	BT	F ₁	F ₂	F ₃	F ₃ -BT	Paired 't' test	
Embelia (n = 20)	10.37 ± 0.97	11.23 ± 0.92	11.45 ± 0.81	11.55 ± 0.81	1.175 ± 0.92	t = 5.70 p<0.01	NS
Mallotus (n = 20)	10.30 ± 0.78	10.88 ± 0.72	11.00 ± 0.63	11.08 ± 0.59	0.775 ± 0.752	t = 4.61 p<0.01	NS

Intergroup Comparison

Group	't' value	'p' value
Embelia Vs Mallotus	1.51	p>0.05 NS

Table 12: Change in blood Hb g% before and after treatment in both groups (n = 20).

and after treatment it increased to 11.08 ± 0.63. The improvement of Hb g% was statistically significant (p<0.01). No significant difference was observed between both the groups, when intergroup statistical comparison was done.

The above data shows that the initial mean of eosinophil count is 8.35 ± 4.45, which decreased to 2.94 ± 0.90 in Group A. It was statistically significant. Group B also showed statistically significant result. Difference among the study groups was not statistically significant (Table 13).

Discussion

On the basis of the findings recorded in the clinical cases it is evident most of the patients belonged to age group between 11-20 years, majority of patients were males and belonged to rural area. The incidence of disease was more in patients with poor hygiene i.e. improper cleaning of hands after defaecation or before meals. Vegetarians and non-vegetarians were equally affected; this may be due to food borne infections commonly transmitted by the ingestion of ova and cysts attached on raw vegetables and improperly cooked meat and uncooked vegetarian meals.

Groups	BT	F ₁	F ₂	F ₃	BT Vs F ₃	Paired 't' test	
Embelia	8.35 ± 4.45	4.65 ± 2.06	3.53 ± 1.18	2.94 ± 0.90	6.00 ± 4.20	5.89 p < 0.001	HS
Mallotus'	7.40 ± 3.52	4.78 ± 2.29	4.00 ± 1.33	3.56 ± 1.29	4.39 ± 3.16	5.88 p < 0.001	HS

Intergroup Comparison

Group	't' value	'p' value
Embelia Vs Mallotus	1.29	p>0.05 NS

Table 13: Response of treatment on eosinophil count (%) in *Embelia* and *Mallotus* (n = 20).

Patients treated with *Embelia robusta* had a cure rate of 40%, improvement in 35% and no improvement in 25%. Patients who received *Mallotus* showed better response with cure rate of 70%, improvement in 15% and no improvement in 15%. There was statistically significant increase in Hbg% and decrease in eosinophil in both groups.

No adverse effects were observed with either of the drugs.

Hence, it can be concluded that comparatively *Mallotus* has a better clinical response over *Embelia robusta*. The accepted species is *Embelia ribes* Burm. While *Embelia robusta* is the substitute. Looking into the market dominance *Embelia robusta* was chosen for the study. A study comparing the actual species *Embelia ribes* is recommended as it is said to be the best for all infective pathogens. Also the study is to be performed on large number of patients.

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