

Full Length Research Paper

## Comparison of allopathic and herbal medicine for the treatment of *Entamoeba histolytica*: A double blind clinical trial

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This parallel, randomized, double blind clinical trial was designed to compare allopathic drugs [a combination of metronidazole + diloxanide furoate (MDF)] with Endemali (herbal product) for therapeutic cure rate and side effects in order to find out the most suitable drug for this killer disease. This double blind randomized clinical trial was conducted in two areas of Karachi, Pakistan after approval from ethical committee of Hamdard University. All those confirmed for *Entamoeba histolytica* were included in the study. One hundred and seventy one patients selected for the study were randomly allocated to two arms of 86 and 85 for allopathic and herbal treatment, respectively. However 78 in allopathic and 75 in herbal group completed the study. Main outcome variable was treatment success or failure. Secondary outcome measures included side effects and association with age and sex. No significant difference was observed in the socio economic and demographic variables at the baseline. No significant difference was found between the cure rate of MDF and Endemali; hence both drugs were equally effective in treating amoebiasis. Significant differences were reported for the side effects observed among the two groups and the price. The failure rate for the two drugs was 28.7%. It is concluded that both Endemali and MDF are equally effective in treating amoebiasis. However, Endemali has fewer side effects than MDF. New drugs need to be researched for the treatment of *E. histolytica* because of high failure rate of the two drugs against this killer organism.

**Key words:** Comparison, *Entamoeba histolytica*, amoebiasis, herbal, Endemali, metronidazole, diloxanide furoate, clinical trial, double blind, parallel.

### INTRODUCTION

Human intestinal pathogenic parasites (HIPP), especially *Entamoeba histolytica* have significant effect on the health

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of the community (Mondal, 2006; Herbinger, 2011; Siddiqui, 2002). In highly uneducated societies, like Pakistan, where literacy rate is 34% and only 20% population has access to safe water supply and sanitation and even lesser in the rural area, the prevalence of parasitic infection is a common problem (Iliyas, 2006) which requires effective treatment. Many options exist for the treatment of parasitic infection including herbal medicine, which are said to be more cost effective with less side effects (Dans, 2007; Shahab-ud-din, 2006; Al-Habbal, 1984; Calzada, 2005). Some work has been done regarding the prevalence of HIPP in Pakistan but there were few studies conducted to compare allopathic and herbal modalities for the treatment of amoebiasis (Khan, 2008; Ranque, 2004). Various options are available for the treatment of amoebiasis with a variable degree of failure rate (Dans, 2007) and include metronidazole, secnidazole, etc.

Huston (2003) conducted a randomized double blind study and found that natural herbal medicine showed significantly better result than placebo with a p-value < 0.04. One of the laboratories in Pakistan has also developed certain herbal medicine under the Unani pharmacopeia including Endemali to treat amoebiasis which has been tested for years for its efficacy and safety (Shahab-ud-din, 2006; Ozcan, 2004).

This double blind clinical trial was designed to compare allopathic drug metronidazole + diloxanide furoate (MDF) with the herbal medicine, Endemali to evaluate therapeutic cure rate and side effects in order to find out the most suitable drug for this killer disease.

### Objectives of the study

1. To find out the cure rate of MDF and Endemali.
2. To record the side effects reported by the two drugs.
3. To compare two drugs for efficacy and side effects.

### Null hypothesis

There is no difference in the efficacy and side effects of allopathic choice of MDF (metronidazole + diloxanide furoate) and herbal product Endemali for the treatment of *E. histolytica*.

### Alternate hypothesis

There is some difference in the efficacy and side effects of allopathic choice of metronidazole + diloxanide furoate (MDF) and herbal product Endemali for the treatment of *E. histolytica* (two tail hypotheses).

## MATERIALS AND METHODS

### Study design

It was a parallel randomized double blind clinical trial to evaluate these drug's effect by statistical analysis. Both physicians and patients were blinded about the type of treatment. Consolidated standards of reporting trials (CONSORT) flow chart and check list were used to write the methodology.

### Sample population

Two areas, one in Shifa-UI-Maluk Hospital, situated in the rural setting of Ali Goth, Gadap, Karachi and the other in Zahida Medical Centre, Sector 5-C, North Karachi were selected to randomly allocate the patients in two groups that is, allopathic group and herbal group.

### Sample size

To determine the sample size, we used  $\alpha < 0.05$  and power of study as 90%. The effect size considered to be clinically significant was a 0.15 difference between two groups based on a pilot study. "Hypothesis test for two population proportion with two sided test" was calculated with the help of World Health Organization (WHO) Manual (Lwanga, 1991). The sample size as calculated by sample size calculator was 152 that is, 76 in each group for the validation of result and statistical assessment to be true. Refusal to give consent and dropouts are inherent part of any given clinical trial and in developing world this factor is even more prevalent, so 50 more subjects were added in the calculated sample size to make it 202 (101 in each group).

### Sampling procedure

The selected patients were randomized by adopting blocking technique. This technique is used in clinical trial, to ensure that both treatment groups are similar in size (Crawford, 2009). The patients were divided into groups of 10. Marked papers were prepared by a person who was not part of research team. Half (five) of each block of 10 were marked "Treatment Group 1" (TR1) and the rest marked as "Treatment Group 2" (TR2). Each eligible participant was invited to pick blindly, one sheet out of 10 available for example, in one draw, first patient picked TR1, second also picked TR1, third picked TR2, fourth picked TR1, fifth picked TR2, sixth picked TR2, seventh picked TR2, eighth picked TR1, ninth picked TR1 and tenth was automatically allocated to TR2.

Once a sheet was picked up, after noting the treatment group allocation, it was put back in the drawer to make it 10 again so that every patient has an equal chance of being allocated in any of the treatment group. The procedure was repeated for second block of 10 and so on until all patients meeting inclusion/exclusion criteria were registered. These sheets were pulled out by the patient from a drawer at the time of informed consent, so allocation was concealed. Moreover physician and laboratory person were also blinded for the type of treatment. All patients were instructed to return back after following full course of treatment. However they were advised to report back immediately in case there is any side effect or any complication.

### Variables studied

Age, sex, education were main demographic variables. Stool was examined to confirm the diagnosis. Other variables included history of chronic disease, presenting complaints, general examination, investigations, treatment option, outcome such as success and failure, side effects etc.

### Treatment group 1

This is a combination of metronidazole + diloxanide furoate available in Pakistan with brand name "Entamizole DS". This tablet contains metronidazole 400 mg + diloxanide furoate 500 mg. Entamizole DS was given 3 times a day for 5 days.

### Treatment group 2

This involved the use of Endemali®, a herbal product, available in 4 g sachet, containing *Boswellia glabra* 270.9 mg, *Kaolinum ponderosum* 255 mg, *Ocimum pilosum* 580 mg, *Pistacia terbinthus* 116.1 mg, *Plantago ispagula* 812.7 mg, *Vateria indica* 232.2 mg sweetening agent q.s. Endemali® was given 4 times a day for 10 days.

### Criteria for assessment of therapeutic evaluation

#### Success

Success had two components: Parasitological cure and clinical cure. (1) Parasitological cure: No cyst found in the stool five days after stopping treatment. (2) Clinical cure: Absence (partial or complete) of symptoms after stopping the treatment. Treatment success in our case was defined as:

- A. Normalization of abdominal and systemic signs or at least improvement in the symptoms.
- B. No trophozoites or cyst in stool.

#### Failure

Treatment was considered failure if there was cyst found in the repeated sample and/or there was no improvement of the symptoms within two weeks.

#### Inclusion criteria

All the patients reporting to out patient department (OPD) of the two centers between the ages 5 to 60 years, who were proven cases of amoebiasis, were included in the study.

#### Exclusion criteria

All patients having congenital malformation or any other infection (as found through lab investigation) were excluded from the study. At the beginning of study it was planned that while taking the history and before registration of patient, at the base line, chronic diseases like tuberculosis etc. and co morbid condition like hypertension and diabetes will be excluded and even infection and co morbid

condition revealed later on by laboratory investigation will also be excluded to assess the naive cases only. Those having known hypersensitivity to the drugs were also excluded.

### Ethical consideration

The protocol was reviewed and approved by ethical committee of Hamdard College of Medicine and Dentistry (Reference No was CMHCMD/001/2007 dated 16th January 2007) and finally permission was granted by Board of Advanced Studies (BASR), Hamdard University in its 25th meeting held on 19th July, 2007. A voluntary fully informed consent was obtained at the time of enrolment of patient. Later on trial was registered at <http://www.controlled-trials.com> and the registration number allocated was ISRCTN10942146 (Siddiqui, 2012).

### Constraints and compromises

It took a long time (From October, 2008 to December, 2009) for the survey to be completed because it was very difficult to find out the patients who fulfilled the inclusion/exclusion criteria. Some of the patients did not give consent. They were treated with routine procedure but their results were not included in the study. The standard test to differentiate between *E. histolytica* and *E. dispar* are enzyme linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR) and recommended for the diagnosis of amoebiasis to capture antigen. Due to insufficient funds, the routine microscopic procedure which is being used as basis for the choice of treatment in most part of the developing world was utilized, and as most of the prescriptions are based on stool microscopy, we used the same for general application. Moreover the focus of study was a comparison of two choices of treatment in the available set of facilities; any kind of bias would have affected both groups equally and not affected the primary objective of study as the allocation of the subject was random. However, a study to compare the two drugs based on the diagnosis of amoebiasis through either ELISA or PCR is necessary.

### Data collection procedure

The study was executed in three phases, which are as follows:

#### Phase I

Patients coming for the OPD treatment in two centers, Shifa-UI-Maluk Hospital, Gadap and Zahida Medical Centre, North Karachi, with the complaint of pain in abdomen, blood in stool or diarrhea were selected to find out the study subjects.

Training of the research team: The physicians and laboratory persons were explained to about the purpose and method of study. Principal investigator himself explained each and every variable in the performa and about the importance and method of consent.

**Pre-testing:** Pre-testing was carried out two weeks before the actual data collection to find out any ambiguity in the performa in another center, located in North Karachi. All the steps needed for the conduction of the study properly were carried out here also. This gave a chance of, not only a thorough evaluation of the performa, but also its ability to assess the patient's condition.

Physicians examining the patients were supervised individually and any weakness was noted for later rectification. The data was entered in the computer through statistical package for social sciences (SPSS) software version 20 and analyzed to find out any difficulty during entry and analysis of actual result. The result of the pre-testing was more than satisfactory and did not emanate any significant change in the strategy of the study.

**The research instrument:** The variables described earlier were transformed into performa. Both close type and open type questions were used for variables in the performa depending upon the type of variable.

### Phase II

The actual implementation of clinical trial took place in this phase of the study. All patients reporting to OPD of the two centers between 9.00 am and 1.00 pm, who fulfilled the inclusion/exclusion criteria, were included in the study. Any patient reported to the respective health centers for symptoms of amoebiasis was thoroughly investigated for the presence of cyst or vegetative form of *E. histolytica*. All the proven cases were asked for their consent to be included in the studies after signing informed consent.

### Phase III

This phase was devoted to data analysis and report writing. SPSS ver. 20 was used for the purpose of data entry. Level of confidence was set at 95% and the level of significance was set at 5%.

**Collection of stool samples:** Each person with symptoms of amoebiasis was briefed about the appropriate method of collecting stool. They were given a wide, clean container having tight lid, which allowed ready access and visualization of the stool specimen. The specimens were adequately identified by the labels indicating code no., age, sex, etc. The containers were given to the patient the same day; they reported to OPD and were explained to defecate in the container next morning and not to mix with urine or water. It was made sure that the stools were normally passed and no purgatives were used. It was also made certain that the study subjects were not on any therapy for example, antibiotic, anthelmintic, antidiarrheal agent, antacid and hypertonic salts. The specimens were collected by the principal investigator and his team and transferred as soon as possible to the laboratory to avoid loss of trophozoites. The specimens were examined immediately in the laboratory by well-trained, qualified technicians. "Macroscopically stool samples were examined for color, consistency, reaction, presence of mucus, presence of blood, presence of abnormal matter, presence of undigested food and presence of parasites. Microscopically, each specimen was examined as under: (1) One fresh normal saline preparation, (2) One fresh Lugol's iodine preparation, (3) Zinc sulfate floatation preparation. Formalin in ether sedimentation method was used for examinations of stools containing fatty substances that interfere with zinc sulfate centrifugal floatation method.

**Procedure for stool examination:** A small quantity of the selected fresh material was placed on a warm slide with a toothpick applicator or platinum wire, thoroughly emulsified in one or two drops of warm physiologic sodium chloride solution and mounted with a cover glass. In fluid and semi fluid stools, the bloody mucous or tiny specks of tissue were selected and in formed feces the

material was scraped from surface in several parts of fecal mass. The preparation was made such that it was slightly opaque but thin enough to allow newspaper print to be legible through it. The specimens were examined first by the low power 16 mm objective and then suspicious objects or selected fields were studied with the high power 40 mm objective. Trophozoites and cysts of protozoa and helminthic eggs and larvae appeared in their natural shapes and colors.

**Iodine and supravital staining:** The treatment of fresh glass mounts with iodine or supravital staining aids in the differentiation of protozoa. The iodine mount which was made on the same slide as the plain mount was used for the identification of eggs and cysts.

**Concentration methods for protozoan cysts and helminthic eggs and larvae:** Concentration methods fall into two main classes: sedimentation and flotation each with a number of techniques. Sedimentation is less effective than flotation technique. Hence we used flotation technique. This technique is based on the difference of specific gravity of certain chemical solutions. Sugar, sodium chloride or zinc sulphate were employed chiefly. The eggs and cysts float to the surface in the heavier solutions while fecal matter sinks to the bottom gradually. Zinc sulphate is a preferable solution so we used the same. The optimal timings were 5 to 20 min, since the cysts tend to disintegrate after 30 min.

**Zinc sulfate centrifugal flotation technique:** This valuable method of concentrating cysts and eggs employs a zinc sulphate solution of S.G. 1.180, which was made by dissolving 331 g of granular zinc sulphate technical grade in 1000 ml of water and adjusting to exact S.G. using a hydrometer; filtered through glass wool. For formalized feces a solution of higher S.G. 1.200 was used. It is considered to detect about 80% of eggs and cyst in light infections. It destroys trophozoites but does not impair the morphology of cyst for about an hour.

**Procedure:** A fine suspension was made by comminuting one gram of freshly passed feces in about 10 ml of luke warm tap water. In order to remove the coarse particles, the suspension was strained through one layer of wet cheese cloth in a funnel into a small test tube, 100 by 13 mm. The suspension was centrifuged for 1 min at 2300. The supernatant fluid was poured off, about 2 ml of water was added, the sediment was broken up by shaking or tapping and additional water was added to fill the tube. The washing and centrifuging was repeated until the supernatant was fairly clear. Usually it was necessary to do it three times. The last supernatant fluid was poured off, about 2 ml of zinc sulfate of specific gravity 1.180 was added, the sediment was broken up and sufficient additional zinc sulfate to fill the tube to the rim was added. A cover glass was placed over the top of the tube, which was centrifuged again for one minute at 2300 cycles/minute. The cover glass was removed and mounted on a clean slide in a drop of Lugol's iodine solution for microscopic examination" (Siddiqui, 2002).

### Drugs used in this study

Entamizole DS contains two drugs Metronidazole and Diloxanide furoate in a strength of 400 mg and 500 mg, respectively.

### Metronidazole

Mode of action: It is used to destroy amoebae that have invaded

tissue. It kills trophozoites of *Entamoeba histolytica* in intestine and tissue but does not eradicate cysts from intestines.

#### **Diloxanide furoate**

Mode of action: It is a luminal amebicide and acts primarily in bowel lumen because it is poorly absorbed. It is used to eradicate cysts of *E. histolytica* after treatment of invasive disease.

#### **Endemali**

Each strip contains the following herbs;

(a) *Boswellia glabra* (270.924 mg). Mode of action: It was found to improve blood supply to the joints and restore integrity of vessels weakened by spasm.

(b) *Kaolinum ponderosum* (255.443 mg). Mode of action: Harmonization of motility and secretion in digestive disorders of the gastrointestinal tract, for example, digestive weakness.

(c) *Ocimum pilosum* (580.552 mg). Mode of action: Antibacterial, antifungal, anti-inflammatory, antipyretics, hepatoprotective, anti-infective

(d) *Pistacia terbinthus* (116.110 mg). Mode of action: Antitussive, nutritive, diuretic, anti-inflammatory, antirheumatic, appetizer, antiulcerative, hepatoprotective.

(e) *Plantago ispagula* (Husk) (812.727 mg). Mode of action: laxative, antiacidic, anti diuretic, demulcent, antidiarrheal, antihyperlipidemic.

(f) *Vateria indica* (232.221 mg). Mode of action: Antitumor, anti-oxidant, antidiarrheal, astringent, antibacterial, anti-inflammatory, sweetening agents and excipients q.s.

## **RESULTS**

This randomized, double blind clinical trial was conducted to compare herbal medicine Endemali and a combination of allopathic preparation, metronidazole and diloxanide furoate (MDF) in order to evaluate the effectiveness of these medicinal preparation for the treatment of amoebiasis. A total of 202 patients fulfilled the inclusion/exclusion criteria. However a total of 78 in allopathic and 75 in herbal group completed their study (Figure 1). Both groups were compared for the basic characteristics and there was no significant difference between the two with respect to age, weight, height, sex, marital status, body mass index (BMI), race, occupation etc. at alpha level 5%,  $P < 0.05$ . Mean and standard deviation of the ages for Treatment group 1 and Treatment group 2 were  $28 \pm 9.3$  and  $29.24 \pm 13.9$ , respectively. The skewness and kurtosis of the data were 0.79 and 0.15, respectively. The standard error of mean was 0.95 and the variable age was normally distributed. Mean height of the population of interest was 152.3 cm with a standard deviation value of 29.0, while mean height for group one and group two was  $156 \pm 21$  and  $149 \pm 35$ , respectively. Mean weight of the population of interest was 59.4 kg with a standard deviation value of  $\pm$

13.14 while the mean weights for group one and group two were  $58 \pm 10$  and  $60 \pm 15.1$ , respectively (Table 1).

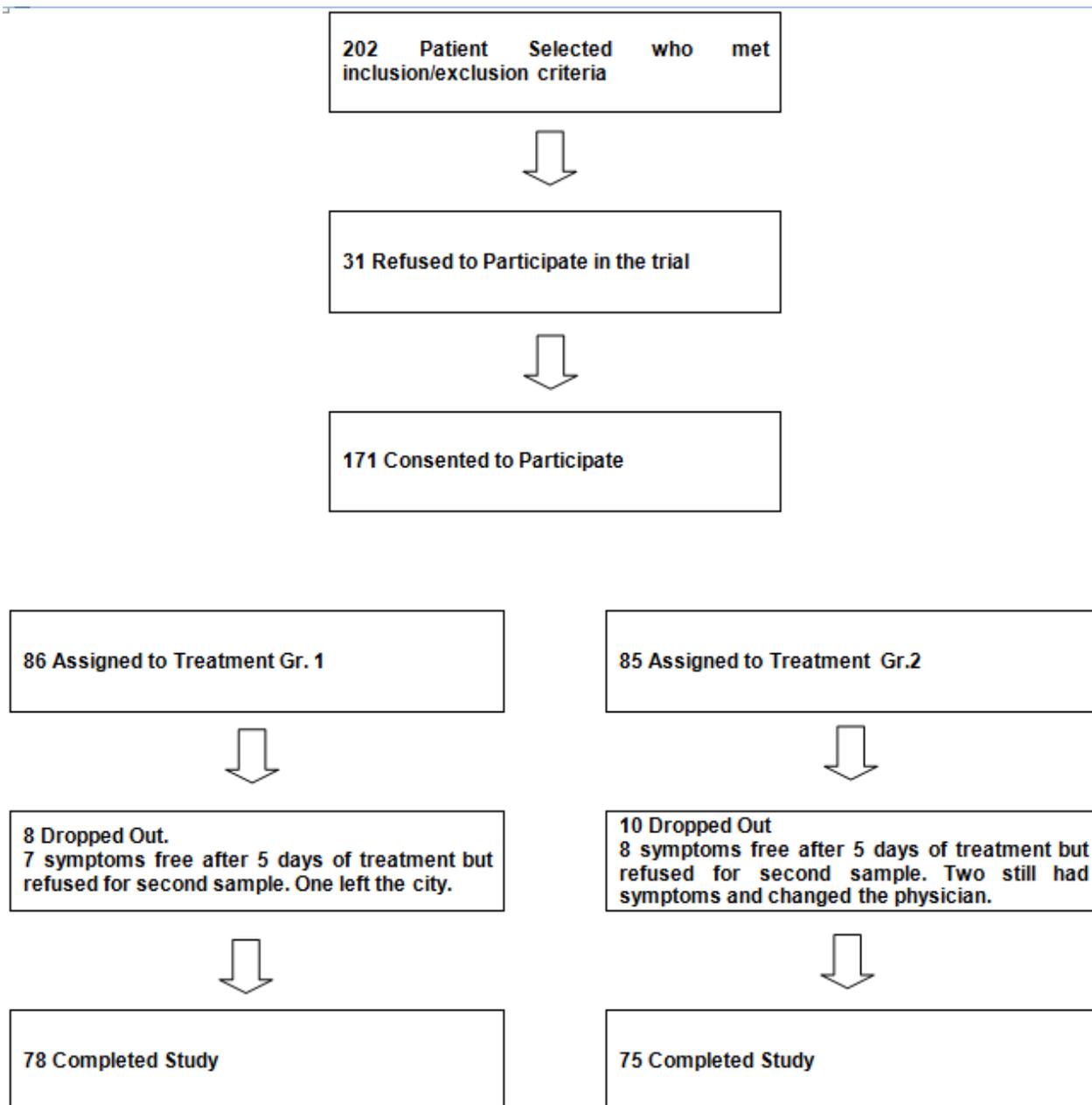
With respect to absence of cyst and trophozoites, 60 out of 78, on allopathic medicines, had no cyst after full course of treatment while 55 out of 75 on herbal medicines had no cyst after the full course of treatment. There was no significant difference between the two groups with respect to cure rate (Table 2). Regarding improvement of symptoms, 21 in allopathic group and 23 in herbal group did not show any improvement but there was no significant difference between the two groups (Table 3). However there was a significant difference regarding side effects reported between two options that is, allopathic and herbal with a chi square value of 27.09 and  $p$  value = 0.000 (Table 4).

Forty four (28.8%) patients reported side effects of drugs. Sixteen (10.5%) reported anorexia after medication, 9 (5.9%) metallic taste and 6 (3.9%) headache after medication. Patients receiving allopathic form of treatment reported more side effects than herbal (Table 5).

## **DISCUSSION**

Amoebiasis is one of the commonest problems especially in the developing countries (WHO, 1969). The prevalence rate varies from country to country with as low as 0.2% in endemic areas of developed countries to as high as 40% in developing countries (Haque, 2006; WHO, 1981). It is estimated that 80% of the world population utilize plant as their main source of medicinal agent. Moreover traditional medicine is still the only health source available to most of the world population. The importance of herbal medicine can be realized by the fact that South Africa flora consists of 30,000 species of higher plants and nearly 10% (3000) of these are used in medicine (Taylor, 2001). It is claimed that herbal formulas produce high cure rates with few or no side effects because of the more close formulation to human interior milieu. Moreover it improves the general well-being of the patient and has better compliance (Shahab-ud-din, 2006). Bland (1986) reported that the herbal medicine, though lack defined doses, but have advantage of lesser side effects. However contrary to the claim, as in preceding lines, Ernst (1998) described that herbal products can lead to hypersensitivity reactions ranging from transient dermatitis to anaphylactic shock (Ernst, 1998).

Traditionally, metronidazole is prescribed for the treatment of amoebiasis and taken as drug of choice (Tasanor, 2007; Gupta, 2004; Khairnar, 2007) but studies have shown that it is not effective against the cyst, as it is rapidly absorbed from the lumen (Powell, 1969). The present recommendations are to combine this drug with some luminal amoebicidal like paromycin or diloxanide



**Figure 1.** Flow chart demonstrating random allocation of the subjects to two arms of allopathic and herbal treatment.

furoate. Though metronidazole is effective in treating the amoebiasis but it resulted in failure due to development of resistance by *E. histolytica* against it (Orozco, 2002; Gonzales, 2009).

This study used combination of metronidazole and diloxanide furoate (MDF) as the drug of choice from allopathic form of treatment and Endemali, a herbal product, to compare the cure rate and side effects of the

two products.

In the present study, we enrolled 202 patient confirmed for the diagnosis of amoebiasis but only 153 completed their study which included 78 on allopathic and 75 on herbal therapy. As the drop out was considered as potential factor in the design phase an extra sample of 50 patients proved sufficient to meet the required number for the application of test of statistical significance. Both

**Table 1.** Distribution of base line Characteristics of the two treatment groups.

Characteristics	Treatment	Treatment	Test of significance	P value
	Group 1	Group 2		
	Allopathic (n=78)	Herbal (n=75)		
Age	28±9.3	29.24±13.9	0.357 Student t test	0.759
Weight	58±10.	60±15.1	1.041 Student t test	0.300
Height	156±21	149±35	0.361 Student t test	0.719
<b>Race</b>				
Sindhi	15	12	7.3 (Fischer Exact)	0.126
Punjabi	15	15		
Urdu	27	33		
Pashto	9	3		
Balochi	9	12		
Any other	3	0		
<b>Sex</b>				
Male	42	48	1.632 (Chi Square)	0.201
Female	36	27		
Body Mass index (kg/m <sup>2</sup> )	23.07+3.29	23.84+3.09	2.245 (ANOVA)F	0.136
<b>Marital status</b>				
Married	27	36	2.8 (Chi Square)	0.10
Unmarried	51	39		
<b>Occupation</b>				
Student	21	30	5.62 (Chi Square)	0.22
House wife	15	9		
Sales man	9	9		
Gardner	3	6		
Any other	30	21		
<b>History of Move</b>				
Yes	15	9	1.51 (Chi Square)	0.219
No	63	66		

groups were compared for the homogeneity by applying test of significance, at baseline and no significant difference was found between the two groups of treatment with respect to confounding variables, like, socio-economic and demographic variables. We used mean, standard deviation, Student t-test, Chi square test, Mann-Whitney U test, Kendall tau-b and analysis of variance (ANOVA) for comparison of data, depending upon the nature of grouping variables.

Our result for mean age of the population of interest, 28.94, are less than Mohiuddin (2007) (33 years) and in agreement with Shahab (2006) (28 years). It was

probably due to the reason that we included patients from age 5 to 60 years while Mohiuddin (2007) included from a minimum of 15 to 68 years. However all three studies result demonstrates that disease affects young and productive age group in the population, resulting in economic losses. Regarding the cure rate we found no significant difference between MDF and Endemali while Shahab (2006) reported a significantly better result with MDF as compare to Endemali. About 25% patients were passing cyst even after completing the full course of therapy in both the groups with no significant difference between the two treatment groups.

**Table 2.** Treatment option by presence of cyst after treatment.

Characteristics	Category	Cyst present	Cyst absent	Chi square value	P value
Treatment option	Allopathic	18	60	0.26	0.6
	Herbal	20	55		

**Table 3.** Treatment option by type of improvement.

Characteristics	Category	Allopathic	Herbal	Kendall's tau-b	P value
Slight improvement	Slight improvement	14	6	0.004	0.959
	Moderate improvement	19	22		
	Completely recovered	24	24		
	No improvement	21	23		

**Table 4.** Distribution of side effects by treatment options.

Side effects reported	Treatment option		Total
	Allopathic	Herbal	
Yes	37	7	44
No	41	68	109
Total	78	75	153

Pearson Chi-Square Value = 27.094 p value < 0.000.

**Table 5.** Distribution of types of side effects by treatment option.

Types of side effects	Treatment option		Total
	Allopathic	Herbal	
Anorexia	14	2	16
Metallic taste	7	2	9
Headache	5	1	6
Flatulence	5	0	5
Pain in abdomen	4	1	5
Any other	2	1	3
Total	37	7	44

Tasanor (2007) tested *in vitro* three of the allopathic drugs as control (Metronidazole, Dehydroemetine and Dihydroartemisinin) and seven herbs (leaves, root and stem bark of *Agalia eleagnoidae* (Ae), leaves from *Stemona tuberosa* (St), stem bark and leaves of *Agalia odutis* (Ao), and leaves of *Agalia odorata* (Aod). Stem bark extract of Ae demonstrated the highest activity with the lowest IC99 (495.5 ng/ml) and the steepest slope 1.1325 (Tasanor, 2007). The study showed a better response of all herbal medicines as compared to

Metronidazole, tested against *E. histolytica*.

There was a highly significant difference between the side effects reported by allopathic form of treatment than its herbal counterpart in the current study. However the symptoms in no case were serious enough to drop out of the study. The most common side effect reported was anorexia (n = 14) followed by metallic taste (n = 7) in the allopathic group while herbal medicine presented with the same side effects that is, anorexia (n = 2) and metallic taste (n = 2).

The result of the study depicts that null hypothesis for the effectiveness of two drugs, cannot be rejected. However the null hypothesis for the side effects of the two drugs was rejected with a highly significant difference and Endemali had significantly less side effects as compared to MDF.

## Conclusion

Based on this study, it is concluded that, there is no significance difference between the cure rate of MDF and Endemali. So both drugs are equally effective in treating amoebiasis. Endemali is a better tolerated drug and friendlier to internal environment of human body as there were significantly more side effects reported due to MDF as compared to Endemali. Both the drugs had high failure rate, hence there is a need to search for new salts for this killer disease. This study may be taken as a platform for the development of new therapeutics as we have used gold standard for the clinical trial protocol that is, double blind clinical trial.

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## Conflict of interest

Authors declare that there are no conflicts of interest.

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