Efficacy of Metronidazole & Diloxanide Furoate in Amoebiasis and Giardiasis

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This study was done to evaluate the efficacy of metronidazole & diloxanide combination in amoebic/giardiasis. It was an open prospective study on cases of diarrhea / dysentery. The children included were between the ages of 2 and 10 years. This cohort included 300 cases presenting with diarrhea / dysentery. The infected cases wer selected on the basis of positive stool examination.There were 30 cases of amoebiasis, 14 of giardiasis and 6 of mixed infection. The presenting features of the cases of amoebiasis included dysentary (87%), diarrhoea (13%), abdominal pain (97%), vomiting (40%) and fever (30%) whereas those of giardiasis included diarrhoea (79%), abdominal pain (93%), and fever (7%). These children were prescribed a combination of metronidazole and diloxanide in therapeutic doses for five days. 92% parasitological cure of giardiasis and 98% of amoebiasis was observed after five days of treatment. Clinical cure rate in both cases was 98%. This combination is well tolerated and is logical, for cure of amoebiasis and giardiasis.

Key words : Metronidazole, Diloxanide, Amoebiais, Giardisis.

Amebiasis and giardiasis are parasitic diseases which have world-wide distribution. Their prevalence is more in the tropical areas of under developed countries like Pakistan. 500 million people carry Entamoeba histolytic (the causative organism of amoebiasis) in the world[1,2]. And 50 million develop invasive amoebiasis[2]. Similarly giardiasis is also one the commonest pathogenic intestinal protozoal infection world-wide[3]. E histolytica was first discovered by Lamble in 1859[4] where as Giardia lamblia (the causative organism of giardiasis was originally identified by Leuwenhoek in 1600s but was also first recognized by Lamble as the etiological agent of dysentry[5].

Various drugs have been used for the treatment of these parasitic diseases. Metronidazole which was discovered in 1959 was a major breakthrough in the treatment of protozoal diseases[6]. After its use problems were associated with use of metronidazole that included short duration of action, repeated dosage requirement and possible drug resistance, which prompted scientists to look for other drugs[7]. As a result diloxanide furoate was discovered. A combination of diloxanide furoate and metronidazole was subsequently used for treatment of amebiasis and giardiasis[8]. Metronidazole works both in the lumen and the tissues where as diloxanide furoate is a luminal drug[9].

Aims and objectives

The aims of this study were to determine the frequency of amebiasis and giardiasis in children presenting with acute diarrhea/dysenteric and to evaluate the efficacy of combination of metronidazole and diloxonide furoate.

Patients and methods

This will be an open prospective study to be conducted in the Department of Pediatrics, King Edward Medical College & Mayo Hospital, Lahore over a period of 6 months from June to November 2002. A total of 300 children from age 2 to 10 years of either sex presenting with diarrhea and dysentery associated with constitutional symptoms will be enrolled. Fresh samples of stool treated with 0.85% saline/iodine will be taken on day 0. These samples will be examined under low and high power objectives. Only those children *(50 out of 300)* found to be positive for E histolytica and/or G lamblia (cyst/vegetative) will be included in the study for further follow-up and analysis. Cases will be excluded from the study even if stool positive but there was history of anti amoebic/giardia drug intake recent past or thosehaving severe/advanced systemic diseases like meningitis and sepsis etc. or if there is history of hypersensitivity to any drugs being used in the study. The children in the study group would be treated with combination of metronidazole of (30 mg/kg) and diloxanide furoate for a period of 5 days. Follow up will be done on day 3, 5 and 10, clinical examination and stool test to be repeated on each occasion. Outcome variables will be parasitological and clinical cure on days 3, 5 and 10.

Results

A total of 300 patients were enrolled for the study out of which 50 cases were selected on the basis of positive stool examination. These children were between ages of 2 and 10 year with the peak age of 4 year. Out of these 50 cases , 30 were positive for E histolytica, 14 had giardiasis and

the rest 6 had mixed infection (Fig. 1). In amebiasis group prominent features were abdominal pain (97%), dysentery (87%), vomiting (40%), fever (30%) and watery diarrhea (13%). In Giardiaisis cases abdominal pain (93%), diarrhoea (79%) and fever (7%). In the mixed group the presenting features were dysenteric stools with recurrent abdominal pain. The male to female ratio showed almost equal distribution (26:24) (Fig. 2)

Figure 1:Sex distribution

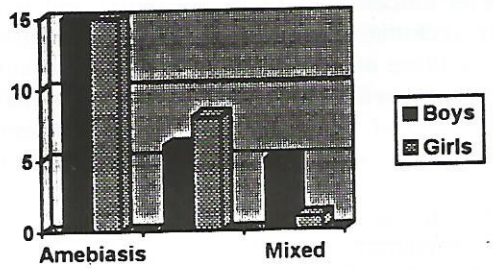


Figure 2:Distribution of E histolytic and G lamblia.

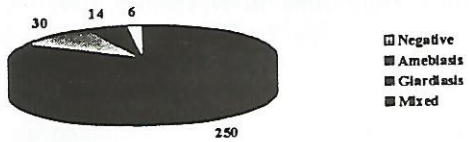
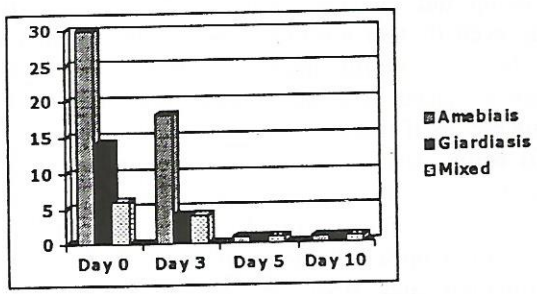


Figure 3: Parasitological cure



The patients were treated with recommended doses of metronisazole/dilaoxanide and followed up as mentioned above. Clinical evaluation on day 5 and day 10 showed that all patients were symptom free except one patient with mixed infection group who was still passing blood on day 5. However he was also symptom-free at the end of the study. A total of 92% parasitological cure of giardiasis and 98% of amoebiasis was observed after five days of treatment. Clinical cure rate in both cases was over 98%. In this study no side effects were observed and the tolerability of the drug was excellent in all patients.

Table 1: Clinical cure rate

Symptoms	Day 3	Day 5	Day 10
Dysentery	96%	98%	100%
Diarrhea	38%	100%	100%
Tenesmus	75%	100%	100%
Pain abdomen	90%	100%	100%
Nausea	95%	100%	100%
Vomiting	96%	100%	100%

Table 2: Parasitological clearance.

	Day 0	Day 3	Day 5	Day 10
Amebiasis	30	18	01	01
Giardiasis	14	4	01	01
Mixed	6	4	01	01

Discussion

Both amebiasis and giardiasis are common childhood parasitic infections. These diseases are prevalent in countries like Pakistan where hygienic conditions are unsatisfactory[10]. We observed that 17% of children who presented with diarrhea or dysentery had amebiasis or giardiasis or both. Other studies have shown that the frequency of amebiasis is as high a 36% and giardiasis 44% in the general population in Karachi[11]. World-wide prevalence rates of giardiasis vary from 4 – 42%[12].

In the present study statistical analysis of results show that metronidazole/diloxanide furoate combination is effective treatment for both amebiasis and giardiasis. This is supported by parasitological and clinical cure rates of 92 – 98% and 98% respectively. Qureshi et al[8] in a similar study from Pakistan have demonstrated a clinical response rate of 91% for amebiasis, 84% of giardiasis and 100% parasitological response for both diseases. Clinical response rate in our study and the study conducted by Qureshi et al is better than the rates of 90% reported by many researchers form India[9, 13, 14, 15] where socioeconomic conditions are similar to those in Pakistan.

The regimen with metronidazole/diloxanide furoate was very well tolerated by children and no side effects were observed. In the present study we conclude that every 5th child with diarhoea or dysenteric symptoms in the age group of 2 – 12 years had parasitic infection. Metronidazole and diloxonide combination provided more than 98% parasitic and 100% clinical cure in 5 days treatment. Five days treatment is adequate for treatment of amebiasis and giardiasis.

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