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Efficacy of a Combined Diloxanide Furoate–Metronidazole Preparation in the Treatment of Amoebiasis and Giardiasis

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A combined formulation of diloxanide furoate and metronidazole was used to treat amoebiasis and giardiasis (cysts and vegetative forms) in 54 patients. Of these, 34 patients had amoebiasis, 19 had giardiasis and one had mixed infection. Each patient took one tablet (containing 500 mg diloxanide furoate and 400 mg metronidazole), three times daily for 5 days, and the response to therapy was checked by clinical examination and by examination of fresh stools on days 3, 5 and 10. Abdominal pain was completely relieved in 91% and 84% of patients with amoebiasis and giardiasis, respectively, while parasitic clearance was 100% in both groups. Tolerance to the drug was adequate.

KEY WORDS: Diloxanide furoate; Metronidazole; Antiprotozoal drugs; Amoebiasis; Giardiasis

54 مریضوں میں امیبیاسِس (amoebiasis) اور جیارڈیاسِس (giardiasis) (سِسٹس یعنی جَوفی اور ویجیٹیٹو یعنی روئیدہ کیفیات) کے علاج کے لئے ڈائی لاکسانائڈ فیورو ایٹ (diloxanide furoate) اور میٹرو نیڈازول (metronidazole) کو ملا کر استعمال کیا گیا تھا۔ اِن میں سے 34 مریضوں کو امیبیاسِس کی، 19 کو جیارڈیاسِس کی اور ایک کو ملے جلے انفیکشن کی شکایت تھی۔ ہر مریض کو پانچ دنوں تک دن میں تین بار (500 ملی گرام ڈائی لاکسانائڈ فیرو ایٹ اور 400 ملی گرام میٹرو نیڈازول پر مشتمل) ایک ایک گولی دی گئی اور اثرات کا طبّی طور پر جائزہ لیا جاتا رہا اور تیسرے، پانچویں اور دسویں دن مریضوں کے تازہ پاخانے کا معائنہ کیا گیا۔ امیبیاسِس کے 91 فی صد مریضوں میں اور جیارڈیاسِس کے 84 فی صد مریضوں میں پیٹ کے درد کو

مکمل طور پر آرام آگیا جبکہ دونوں قسم کے مریضوں میں طفیلی جرثومے (parasitic) سے 100 فی صد نجات حاصل ہو گئی۔ مریضوں میں دوا کی برداشت مناسب رہی۔

INTRODUCTION

Amoebiasis and giardiasis have been a major cause of morbidity and mortality in humans for centuries. Global statistics show that amoebiasis ranks third amongst the most common causes of parasitic death, and that giardiasis is the most common cause of diarrhoea.[1] The discovery of metronidazole in 1959 was a major breakthrough in the treatment of protozoal diseases.[2] Subsequently, the problems associated with metronidazole – short duration of action, repeat dosage requirement and possible drug resistance – prompted scientists to look for a better drug.[3] As a result, drugs with a longer half-life and more convenient dosage regimen, and combinations with other active drugs were marketed to meet these demands.[3]

Entamizole®, a combination of diloxanide furoate and metronidazole, represents a new therapeutic approach for the treatment of amoebiasis and giardiasis. Diloxanide furoate is a luminal amoebicide, whereas metronidazole works both in the lumen and the tissues.[4]

The aim of the present study, was to assess the efficacy of this combined formulation of diloxanide furoate and metronidazole in the treatment of amoebiasis and giardiasis.

PATIENTS AND METHODS

PATIENTS

Fresh stool samples from all adult patients suffering from diarrhoea were examined at our laboratory. Slides made using 0.85% saline and iodine preparation of the stool samples were examined microscopically under low- and high-power objectives. Only those patients whose stool samples showed cysts or vegetative forms either of amoeba or giardia were included in the study. Patients already taking antiamoebics or antibiotics were excluded, as were patients with known sensitivity to metronidazole.

A total of 56 patients were enrolled in the study. Of these, two were lost to follow-up and were therefore excluded from the study. Of the 54 evaluable patients, 26 were male and 28 were female. Amoebiasis was seen in 34 patients (23 passed cysts, seven passed vegetative forms and four passed both cysts and vegetative forms), 19 had giardiasis (four passed cysts and 15 passed vegetative forms), and one had a mixed infection (amoeba cyst and giardia trophozoite).

In the amoebiasis group all of the patients had abdominal pain, 11 had diarrhoea, 11 had excessive passage of mucus in the stool, and 10 had tenesmus on presentation. None had bleeding *per rectum*. In the giardiasis group all of the patients had abdominal pain, 12 had diarrhoea, six had excessive passage of mucus in the stool, six had tenesmus, and two had bleeding *per rectum*, along with diarrhoea.

METHODS

After informed consent had been obtained from each patient, the combined diloxanide furoate–metronidazole preparation was administered. Each patient took one tablet containing 500 mg diloxanide furoate and 400

Entamizole® is the registered tradename of Knoll Pharmaceuticals, Karachi, Pakistan.

mg metronidazole orally, three times daily for 5 days. Clinical and parasitological responses, compliance and side-effects were checked on days 3, 5 and 10 by clinical examination and by examination of fresh stool samples, using the method described above.

RESULTS

Clinical examination revealed persistence of abdominal pain in three of 34 (9%) patients with amoebiasis and three of 19 (16%) patients with giardiasis at the end of the treatment period. All other symptoms such as diarrhoea, tenesmus, mucus and bleeding *per rectum* subsided by day 5 in all cases. Parasitological clearance was 100% in both groups. Clearance of both infections was also achieved by day 10 in the patient with mixed infection. None of the stool samples checked on days 3, 5 or 10 showed persistence or recurrence of infection in patients with either disease. With the exception of a metallic taste in the mouth reported by 7 patients and occasional nausea reported by 3 patients, the drug was well tolerated by all patients.

DISCUSSION

Pakistan is an over-populated, developing country with poor sanitary conditions, which therefore has a very high frequency of water-borne diseases.[5] High temperatures in the summer, floods and leaking water pipes further accentuate the situation.[6] Studies carried out in our department show that the frequencies of amoebiasis and giardiasis in the adult population are 36% and 44%, respectively.[7] Duodenal aspirates from adults undergoing upper gastrointestinal endoscopy for various reasons have shown a 9% prevalence of giardiasis among these patients.[8]

Metronidazole and its derivatives are still prescribed as the treatment of choice, and these drugs are also taken by patients as self-medication. Because of the massive use and abuse of these drugs, there is a general fear amongst prescribers and users that their efficacy may be reduced. Metronidazole alone may fail to eliminate intraluminal infection, especially at low doses, and therefore clinical relapse can occur.[9] In trials carried out primarily in asymptomatic individuals passing trophozoites or cysts, or in patients with non-dysenteric, symptomatic intestinal amoebiasis, treatment with diloxanide furoate resulted in a high percentage of cure.[10]

As cultures and sensitivity tests for amoeba and giardia are not available in Pakistan, simple drug trials are used to check the clinical responses to new drugs in this country.

The efficacy of a recently introduced combined formulation of diloxanide furoate and metronidazole was assessed in present study. A clinical response rate of 91% for amoebiasis and 84% for giardiasis was observed, while a 100% parasitological response was observed for both diseases. These results are very encouraging and are in line with the 90% and 100% responses reported by others.[4,11 – 13]

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