

Efficacy of albendazole in giardiasis

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نجاعة الألبندازول في معالجة داء الجيارديات

رخشند بقائي، سروار زبيري، هما قريشي، وقار الدين أحمد وسليم حافظ

الخلاصة: عُقدت مقارنة بين مفعول الألبندازول ومفعول المترونيدازول في 68 شخصاً كان تشخيصهم إيجابياً لداء الجيارديات عن طريق إعطاء جرعة واحدة من الألبندازول مقدارها 1200 ميلي غرام لأربعة وعشرين من المرضى، وجرعتين يومياً من الألبندازول مقدار كل منهما 400 ميلي غرام، مدة ثلاثة أيام لثلاثة وعشرين آخرين، وجرعة من المترونيدازول مقدارها 400 ميلي غرام ثلاث مرات يومياً مدة خمسة أيام للمرضى الواحد والعشرين الباقين. وتم رصد الاستجابة للمعالجة بالفحص السريري وتحليل عينات من البراز الطازج قبل بدء المعالجة، وفي اليوم الثالث وفي اليوم السابع وفي اليوم العاشر. وبلغت نسبة الاستجابة للجرعة الوحيدة من الألبندازول 55%، ونسبة الاستجابة للجرعة المجرّاة منه 70% ونسبة الاستجابة للمترونيدازول 84%. ويتضح من النتائج أن الألبندازول الذي يُوصى به أصلاً لعلاج العدوى بالديدان، يمكن أيضاً أن يُستخدم لعلاج المرضى المصابين بعدوى مختلطة بالأوالي، أو لعلاج العدوى المقاومة للمترونيدازول.

ABSTRACT Albendazole and metronidazole were compared in 68 patients diagnosed positive for giardiasis. Albendazole 1200 mg. one dose was given to 24 patients, albendazole 400 mg twice a day for 3 days was given to 23 patients, and metronidazole 400 mg 3 times a day for 5 days to 21 patients. Response to therapy was monitored by clinical examination and analysis of fresh faecal samples on days 0, 3, 7 and 10. Response to the single dose of albendazole was 55%, to the divided dose of albendazole 70%, and to metronidazole 84%. The results show that albendazole, originally recommended for helminthic infection, can also be used in patients with mixed protozoal infection or for infections resistant to metronidazole.

Efficacité de l'albendazole dans la giardiase

RESUME L'albendazole et le métronidazole ont été comparés chez 68 patients ayant un diagnostic positif de giardiase. On a administré 1200 mg d'albendazole en une dose à 24 patients, 400 mg d'albendazole deux fois par jour pendant 3 jours à 23 patients, et 400 mg de metronidazole 3 fois par jour pendant cinq jours à 21 patients. La réponse au traitement a été suivie par examen clinique et par analyse d'échantillons de selles fraîches les jours 0, 3, 7 et 10. La réponse à la dose unique d'albendazole était de 55 %, elle était de 70 % pour la dose divisée d'albendazole, et de 84 % pour le métronidazole. Les résultats montrent que l'albendazole, recommandée à l'origine pour l'helminthiase, peut être également utilisée chez les patients ayant une protozoose mixte ou pour les infections résistantes au métronidazole.

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Received: 16/10/00; accepted: 23/01/01

Introduction

Giardiasis is a common cause of diarrhoeal disease in Pakistan [1-3] and other countries [4-6]. Various drugs have been used in its treatment. Albendazole is widely used for the treatment of helminthic infection, hydatid disease [7] and microsporidial infection [8]. As its efficacy in giardiasis has not been established, this study aimed to determine the response of patients to this drug.

Methods

Sixty-eight (68) patients presenting with abdominal pain and diarrhoea at our gastroenterology clinic were clinically examined and their medical history recorded. Faecal samples were screened by direct microscopy, *Giardia lamblia* trophozoites or cysts were detected by the concentration method and *G. lamblia* antigen by immunofluorescence. Patients taking antibiotics or antiprotozoal therapy were excluded from the study.

For direct microscopy slides were made by saline and iodine preparation and examined under low- and high-power objectives. The faecal parasite concentration method (FPC, Evergreen Scientific, California, United States of America) was also used. Some faecal samples that were negative by direct microscopy were positive by this method.

The *Giardia-Col* IF test (Cellabs Pty Limited New South Wales, Australia) was used. A drop of faecal sample prepared in phosphate buffered saline (PBS) was placed on a clean slide. The spot was air dried and fixed in acetone for 1 minute. Then 25 µL (microlitres) of fluorescent-labelled monoclonal antibody was applied to both the faecal specimens and the positive control, and incubated for 30 minutes at

room temperature in a humidified chamber. The slides were washed gently with water, drained, and mounting fluid applied. Cover slips were placed on the slides, which were then scanned by fluorescent microscopy at $\times 400$ magnification.

Patients diagnosed positive for *G. lamblia* were selected for study. After giving their informed consent the patients were divided into three groups and were given the drug as follows:

- albendazole 1200 mg as a single dose (24 patients);
- albendazole 400 mg twice daily (total 800 mg) for 3 days (23 patients);
- metronidazole 400 mg three times daily (total 1200 mg) for 5 days (21 patients).

Clinical and parasitological response, patient compliance and any adverse events were noted on days 0, 3, 10 and 17 using the following criteria:

- Responders: patient with no clinical symptoms and with negative stools from day 3 to day 17.
- Non-responders: patients in whom symptoms or presence of parasite persisted during the course of treatment, or in whom the parasite reappeared.
- Defaulters: patients who did not complete the follow-up.

Results

A total of 68 patients (38 males and 30 females), with ages ranging from 16 to 68 years, were included in the study. The main presenting symptoms were abdominal pain and persistent diarrhoea. Some patients had nausea, vomiting, flatulence, anorexia and weight loss.

In the first group, albendazole 1200 mg was given as a single dose to 24 patients. Of these, 4 defaulted, while 11 of the re-

maintaining 20 (55%) responded to the drug and were considered cured. In 2 patients the parasite cleared on day 10 and 17 respectively. Two patients were non-responders as the parasite had reappeared, one on day 10 and the other on day 17.

In the second group of 23 patients, albendazole 400 mg was given twice a day for 3 days. Of these patients, 6 did not complete the treatment. Of the 17 evaluated cases, 12 (70%) responded. Two patients responded on day 10 and one on day 17. In 2 patients the parasite reappeared on day 10 but had cleared on day 17. Two patients were classed as non-responders as the parasite reappeared on day 10 in one case and on day 17 in the other.

In the third group, metronidazole 400 mg was given to 21 patients for 5 days, 2 of whom defaulted. Of the 19 evaluated cases, 16 (84%) responded to the drug. In 2 patients, the parasite cleared on day 17, while 2 patients were non-responders as the parasite reappeared on day 10 and on day 17 respectively.

There was no statistically significant difference between the cure rates of the three groups ($\chi^2 = 3.94$, $P = 0.139$).

Discussion

The efficacy of albendazole at different dose regimes was compared with metronidazole in this clinical study. Metronidazole has been a popular drug for the treatment of giardiasis, but its side-effects, prolonged duration of treatment and frequent dosing regime have prompted a search for new

drugs with fewer side-effects that can be taken once daily. Single-dose therapy is recommended to improve compliance and response and reduce side-effects [9]. Secnidazole, a nitroimidazole with a prolonged duration of action, has been used as a single dose in 22 patients suffering from giardiasis and a cure rate of 77% was observed [9].

Variation in drug response *in vitro* suggests that treatment with two drugs of different classes would be more effective for chemotherapy of *G. lamblia* infection than a single drug [10]. Patients treated with a combination of diloxanide furoate and metronidazole had a clinical response rate of 84% for giardiasis [11].

Clinical resistance to metronidazole in patients suffering from giardiasis has been reported [12,13]. Lactum-substituted nitroimidazole has been found to be most effective against metronidazole-resistant *Giardia* species [14]. As drug resistance and toxicity has restricted the use of metronidazole, the benzimidazole albendazole is regarded as a promising alternative. Efficacy of albendazole has been reported against *G. lamblia in vitro* at a concentration 30 times lower than metronidazole [15]. Albendazole has high efficacy against *Giardia* species with a wide margin of safety, although there has been one report of severe bone marrow suppression in animals treated with albendazole [16]. Use of albendazole is therefore recommended when metronidazole resistance develops or there is a mixed protozoal and helminthic infection.

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