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Dr. S.A. Talari
Department of Parasitology,
Kashan University of Medical Sciences,
Kashan, Iran

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Comparison of Metronidazole and Furazolidone Against *Giardia lamblia* in Children

S.A. Talari, N. Momtazmanesh, A. Talebian, A. Khorshidi, A. Taghavi, E. Fakharian, M.R. Talari and Z. Mokhtari

This study was conducted on children infected by *Giardia lamblia* to evaluate the effectiveness and side effects of Metronidazole and Furazolidone drugs in Kashan. One hundred twenty two individuals infected with *Giardia lamblia* were assigned in 2 groups. They were 5-12 years old. Patients were surveyed four weeks following the therapy with Metronidazole and Furazolidone. Results were compared using chi-square method. Of 122 infected patients, 68.8% were urban residents, 43.4% were females and 56.6% were males. Abdominal pain was the most common clinical symptoms (84.2%). Four weeks after the therapy, the efficacy of metronidazole and furazolidone were 87 and 81.6%, respectively. Malaise (12.9%) and dark urine (25%) was the most frequents side effects of metronidazole and furazolidone, respectively. With respect to the efficacy of antiparasite drugs in the treatment of *giardiasis,* further studies in different parts of the country are highly recommended.

Key words: *Giardiasis*, treatment, drugs side effects

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Department of Parasitology, Kashan University of Medical Sciences, Kashan, Iran

INTRODUCTION

Giardia lamblia is a protozoan parasite of small intestine that cause extensive morbidity worldwide. It was first described in the late 17th century by the Dutch microscopist Antonine Van Leeuweenhoek (Dobell, 1920) and research into its epidemiology, pathogenesis and treatment his intensified since *G. lamblia* waterborne outbreaks were reported in Europe and the United States during the 1960 and 1970 (Craun, 1986; Farthing, 1992; Jephcott *et al*., 1986; Jokipii and Jokippii, 1974). WHO has reported 2-20% contamination's with *Giradia* throughout the world. The rate of contamination in developed countries is 1-6%, whereas in developing countries it is about 5 - 50% (Zeraatian, 1989; Sharifi and Elahi, 1995). The rate of contamination in Iran, is reported about 20% (Sharifi and Elahi, 1995).

Worldwide, the majority of patients infected with *G. lamblia* are asymptomatic However, typical clinical symptoms of giardiasis usually begin 1 to 3 weeks after ingestion of cysts and are marked by diarrhea, malaise, flatulence, greasy stools and abdominal cramps (Hill, 1993). Other symptoms commonly include bloating, weight loss and anorexia, vomiting and inadequate growth, the patients has to be diagnosed and treated immediately. The drug, which is used, must have the most effectiveness and least side effects. The different studies in recent years, have demonstrated that the effectiveness and side effects of metronidazole and furazolidone are (85-90% and 4.9-24%) and (77.2-80% and 5.2-19.8%), respectively (Zeraatian, 1989; Modarresi and Abdolmajid, 1994; Ghanaati, 1995; Sadjjadi *et al*., 2001; Wolf and Handler, 1998; Romero-Cabello *et al*., 1995).

Considering the difference in effectiveness and the side effects of these drugs, this study was conducted to compare the effectiveness and side effects of the Metronidazole and Furazolidone drugs in Kashan in 2003-2004.

MATERIALS AND METHODS

The clinical trial of this study was carried out on 122 patients with age range of 5 to 15 years old inflicted with *Giardia lamblia*. A parasitologist did confirm the diagnosis of giardiasis. Patients with other diseases or contaminated with other parasites and also the patients who were using drugs continuously deleted from the study.

After explaining the project for the selected patients and securing their agreement, a data form was provided for each of them in which their demographic features, such as age, sex, place of living, as well as the last medicine they were taking were recorded. Suspected patients, picked up by an pediatrician were referred to the Central Pathobiology Laboratory of Kashan University of Medical Sciences for stool examination. The samples from each person were collected in three consecutive days in a coded disposable plastic container and sent to the laboratory to be tested by a parasitologist by formalin-ether method (Ritchie, 1948).

Any children who had at least one positive test was considered a patient infected with *Giardia lamblia*. Families with three, three to five, or more than five members were considered respectively as under, average and over crowded. All data of the patients were kept confidentially and the patients with *Giardia lamblia* were visited and treated free of charge by pediatrician. The patients were requested to refrain from taking other drugs or changing their diet during the study.

The patients were randomly divided into two groups of 60-62 individuals matched for age and sex on the base of order of referral. Metronidzole was prescribed for the first group in doses of 15 mg kg^{-1} three time daily for 5 days and for the second group Furazolidone was administrated in doses of 6 mg kg^{-1} four time daily for 10 days.

The samples were collected according to demographic features, clinical symptoms and drug effectiveness. The data were analyzed by Chi-square method.

RESULTS

Out of 122 studied children, 53 cases (43.4%) were female and 69 cases (56.6%) were male and their age was from 5 to 12 years, 31.2% were living in cities and 68.8% in rural areas. The contamination of the samples on the base of genus and living site is shown in Table 1.

The most common clinical symptom in patients was abdominal pain (84.2%) and the least was belching (13.9%). Furthermore, the most prevalent symptom in male was abdominal pain whereas in females it was diarrhea; the least prevalent symptom between both sexes was belching. Other clinical symptoms according to the level of their prevalence were loss of weight (45%), anorexia (47.5%), nausea (69.7%) and vomiting (24.6%) (Table 2). There was differences in symptoms of *giardiasis* between males and females and the most prominent of these differences were in abdominal pain, loss of weight and anorexia. This was statistically significant at $p<0.05$.

One of our important findings was the effectiveness of the two above mentioned drugs on 95% of patients with giardiasis, after 4 weeks of treatment, documented by stool exam for patients. Stool examination was repeated

Table 1: Distribution of *giardiasis* in pediatric patients on the bases of genus and living place in Kashan, 2003-2004

Genus	Female		Male		Total	
Living site	No.	Percent	No.	Percent	No.	Percent
City	17	44.7	21	55.3	38	100
Rural	36	42.8	48	57.2	84	100
Total	53	56.6	69	43.4	122	100

Table 2: Distribution of symptoms in children patient with *giardiasis* on the base of sex, Kashan, 2003-2004

Genus symptom	Male 53 (100%)	Female 69 (100%)
Abdominal pain	44(83)	59(85.5)
Abdominal distension	24(45.3)	31(44.9)
Weight loss	42(79.3)	55(79.7)
Steatorrhea	30(56.6)	40(58)
Diarrhea	34(64.2)	46(66.7)
Abdominal cramps	38(71.7)	54(78.2)
Nausea	35(66)	50(72.5)
Anorexia	24(45.3)	34(49.3)
Malaise	19(35.8)	26(37.7)
Vomiting	13(24.5)	17(24.6)
Belching	7(13.2)	10(14.5)

Table 3: The comparison effectiveness of Metronidazole and Furazolidone on *giardiasis*

Genus Drug	Male	Female	Total
Metronidazole 62(100)	27(84/4)	27(90)	54(87)
Furazolidone 60(100%)	23(79/3)	26(83/8)	49(81.7)
Total 122(100%)	50(82)	53(86/9)	103(84.4)

after 4 weeks of treatment for all patients three times. Of 62 patients who received metronidazole, 8 (13%) did not respond to the drug and of 60 patients treated by furazolidone, 11 (18.3%) did not respond to the drug and their stool examination was positive.

We have considered persistence of contamination with *giardia* as negative response to drug after four weeks of treatment. Thus the effectiveness of treatment by metronidazole was 87% and furazolidone 81.7%. This difference was statistically significant at $p<0.05$ (Table 3). Then was no statistical difference between male or female.

The most common side effect of metronidazole was malaise in 8 patients (12.9%) and the least side effect was dizziness in four patients (6.4%). The most common side effect of furazolidone was the dark urine in 15 patients (25%) and the least side effect was dizziness in 5 patients (8.3%). In all of the above cases the side effects were tolerable and caused no obstacle for continuing the treatment. The patients were asked for the side effects up to two months and no long time side effects were reported.

DISCUSSION

This study showed that clinical symptoms caused by contamination with *Giardia lamblia* existed in 13.9-84.4% of children (Table 1). Worldwide, the majority of patients infected with *Giardia lamblia* are asymptomatic (Hill, 1993). However, clinical symptoms of *giardiasis* usually begin 1 to 3 weeks after ingestion of cysts and are marked by diarrhea, malaise, abdominal cramps, anorexia and vomiting. (Hill, 1993). With chronic illness, malabsorption of fat, lactose, vitamin A and vitamin B_{12} are reported and failure of children to thrive has been noted (Lengerich *et al*., 1994).

Some of the symptoms have no causal relationship with the disease and were only accidentally associated with it and continue after treatment (Gardner and Hill, 2001).

In this research the most common clinical symptom was abdominal pain (84.4%). Sharifi and Elahi in Kerman in 1994, showed a prevalence of 64% and in the study of Ghanaathi in Shiraz it was 85% (Ghanaati, 1995; Sharifi and Elahi, 1995).

In this study weight loss was the second most frequent symptom (79.5%). Since this study was done on children and it was different from other studies in quality and number of patients, this difference may be statistically significant.

Another finding of our study was the difference in effect of the drugs on patients with *giardiasis* so that 54 children (87%) were treated by metronidazole and 45 (81.7%) patients by furazolidone. These patients were not different in the severity of their illness. Our findings, like many others showed that the effect of metronidzole is more than the other drugs at $p<0.005$ (Modarresi and Abdolmajid, 1994; Ghanaati, 1995; Romero-cabello *et al*., 1995; Harris *et al*., 2001; Freeman *et al*., 1997; Wright *et al*., 2003). There is no definite explanation for this finding we recommend further clinical studies on this special subject.

The metronidazole and furazolidone used by clinicians as the mainstay of therapy of *giardiasis*. Metronidazole enters the trophozoite and once it is within the cell electron transport protein ferredoxins from the parasite donate electrons to the nitro group of the drug (Samuelson, 1999; Townson *et al*., 1994).

Metronidazole is quickly and completely absorbed after oral administration and penetrates body tissues and secretions such as saliva, breast milk, semen and vaginal secretion (Tracy and Webster, 1996). The drug is metabolized mainly in the liver and is excreted in the urine (Lau *et al*., 1992).

Furazolidone is approved for use in the United States and remains an important therapeutic agent worldwide.

Of the common Anti *Giardia lamblia drugs*, it is the only one available in a liquid suspension in the United States; therefore, its use is feasible in pediatric populations. (Lau *et al*., 1992).

When evaluating the clinical efficacy of agents used against *Giardia lamblia,* it is difficult to compare studies. They vary as to entry methodology, population studied outcome measure, different climate, nutrition, hygiene, socioeconomic conditions and so on (Romero-Cabello *et al*., 1995; Zeraatian, 1989; Ritchie, 1948).

The more findings of this study was the side effects of the administered drugs. The most common side effects of metronidazole treatment include headache, vertigo, nausea and a metallic taste in the mouth and of furazolidone was dark urine and headache, which was similar to findings of other researchers. (Modaarresi and Bdolmajid, 1994; Ghanaati, 1995; Sadjjadi *et al*., 2001). These were tolerable for the patients and produced no problem for completion of the treatment.

Considering the results of the study on the effects and side effects of the above drugs on the samples of the study, it seems that informing the patients at the time of prescribing the drug may have a significant role in curing them. Further researches for determining the effectiveness and the side effects of these drugs on children and adults with *giardiasis* in other parts of our country are recommended.

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