NITAZOXANIDE COMPARED WITH QUINFA MIDE AND MEBENDAZOLE
IN THE TREATMENT OF HELMINTHIC INFECTIONS AND INTESTINAL PROTOZOA IN CHILDREN

CESAR E. DAVILA-GUTIERREZ, CLEMENTE VASQUEZ, BENJAMIN TRUJILLO-HERNANDEZ, AND MIGUEL HUERTA

Abstract. The present study was carried out to evaluate the effectiveness of nitazoxanide compared with that of quinfamide, mebendazole, or both in the treatment of intestinal protozoa and helminthic infections. A total of 677 stool specimens from children aged 2–12 years living in 3 communities of Colima, México, were analyzed in order to detect the presence of cysts, trophozoites, eggs, or larvae of intestinal protozoa or helminths. A total of 275 infected children were enlisted in a double-blind controlled study and randomly assigned to one of 2 treatment groups: Group A, nitazoxanide (200 mg for 3 days) and Group B, quinfamide (100 mg for 1 day), mebendazole (200 mg for 3 days), or both. A posttreatment fecal examination was conducted on Day 14 from treatment initiation. In Group A (n = 143), the parasitosis eradication rate was superior to that of Group B (n = 132). However, there was no significant difference between the 2 groups (P > 0.05).

INTRODUCTION

The variety of intestinal parasites is amazing. Many of them are conspicuous for their high frequency and morbidity rates and the important social cost these imply. In México and other Latin American countries, the 3 most frequent parasitoses are amebiasis (24–30.6%), ascariasis (1.4–11.2%), and giardiasis (3.7–22.3%). Among all treatments, quinfamide and mebendazole have had effective and safe results. As more becomes known about parasite metabolism, new broad-spectrum antiparasitic drugs are being produced. One such drug, nitazoxanide, was first synthesized by Rossignol and Cavier in 1976 and was used as an antiparasitic on the basis of its structural similarity to nitrobenzamide. Since then, several reports have been published describing the action of nitazoxanide on different intestinal parasitoses. Nitazoxanide is effective in the treatment of the following parasites: Hymenolepis nana, Cisticercus pisiforme, Uncinaria stenocephala, Trichuris trichiura, Entamoeba histolytica, Toxocara canis, Giardia lamblia, Ascaris lumbricoides, Enterobius vermicularis, Taenia saginata, Cryptosporidium parvum, Helicobacter pylori, and Fasciola hepatica. It has been seen to have even antibacterial effects.

MATERIALS AND METHODS

The study was carried out in the Mexican Institute Social Security Hospital with children from 3 different communities in Colima, México. According to Mexican Health Authority reports, Colima is a state that has one of the highest rates of intestinal parasitoses, primarily in children. The present study was approved by the ethical committee of the health center. An informed-consent form was signed before the study by the children’s parents.

The work team obtained 677 stool specimens from children aged 2–12 years. The specimens were subjected to direct examination by means of a coproparasitoscopic test and Kato-Katz technique. Parasite identification was exclusively morphological, so pathologic and nonpathologic species differentiation was not possible. For this reason, when amebic cysts were encountered, they were reported as Entamoeba histolytica/Entamoeba dispar or simply as amebiasis.

A total of 275 patients were included in the study, all with intestinal parasitoses detected by the aforementioned tests. Each patient underwent a complete physical examination. After this, the children were randomly assigned to one of the 2 treatment groups in a double-blind design. Group A patients received nitazoxanide 200 mg administered in a 10-mL suspension (100 mg/5 mL twice daily for 3 days), regardless of which parasite or parasites they presented, and Group B patients received quinfamide 100 mg administered in a 5-mL suspension (single dose) only if E. histolytica/E. dispar was observed, and they received mebendazole 200 mg administered in a 10-mL suspension (100 mg/5 mL twice daily for 3 days) when a single parasite other than E. histolytica/E. dispar was observed. They received quinfamide and mebendazole together when any mixed parasitosis was detected.

To compare the effectiveness of the treatments, each parasitosis was classified as single parasitosis or nonassociation with other parasites when only one parasite was detected in the fecal sample; and as mixed parasitosis or association with other parasites when 2 or more parasites were detected. A feces control study was performed 14 days after treatments.
Children that did not complete the treatment or did not provide the posttreatment fecal sample were not included in the final analysis of the study.

Treatment effectiveness was estimated in proportion to the patients with negative parasitological examinations after treatments. Parasitosis was determined as present or absent and measured proportionately. Comparisons between treatment groups were made with the chi-square test, Yates correction, and McNemar test (95% confidence interval). The differences were considered significant at $P < 0.05$.

**RESULTS**

From 275 children infected with parasites, 143 (52%) were assigned to Group A and 132 (48%) to Group B. The mean age ($\pm$ standard deviation) was 7.6 $\pm$ 2.2 years for Group A and 7.4 $\pm$ 2.7 years for Group B. There were 126 girls (70 in Group A and 56 in Group B) and 149 boys (73 in Group A and 76 in Group B).

Table 1 shows treatment distribution by age in children with parasites. The parasites found most frequently in the fecal examinations were as follows: Entamoeba histolytica/Entamoeba dispar, 38.1% ($n = 105$, 25 single and 80 associated parasitoses), Giardia lambia, 37.0% ($n = 102$, 51 single and 51 associated parasitoses), Ascaris lumbricoides, 30.4% ($n = 84$, 35 single and 49 associated parasitoses), Endolimax nana, 25.8% ($n = 71$, 20 single and 51 associated parasitoses), Trichuris trichiura, 13.4% ($n = 37$, 1 single and 36 associated parasitoses), and Hymenolepis nana, 13.0% ($n = 36$, 17 single and 19 associated parasitoses). Treatment effectiveness for single parasitoses is presented in Table 2. There was no statistically significant difference between groups (Group A, 70.8%; Group B, 68%, chi-square $= 0.17$, degree of freedom $[df] = 1$, $P = 0.7$). A comparison of associated parasitoses treatments was made (Table 3). Many samples had more than only one parasite; some had up to 6, thus accounting for the varying number of patients per group.

There was no statistically significant difference between either group (Group A, 79.2%; Group B, 73.6%, chi-square $= 1.2$, $df = 1$, $P = 0.2$). Finally, the effectiveness of both treatments was compared with the global frequency of parasites. The results of this analysis is shown in Table 4. There was no statistically significant difference (Group A, 76.3%; Group B, 69.0%, chi-square $= 0.9$, $df = 1$, $P = 0.1$). Interestingly, in this case, a significant difference in the amebiasis treatment ($P < 0.02$) with nitazoxanide was observed. It is important to mention that nitazoxanide had the best eradication rate in the treatment of Hymenolepis nana (90–100%) and the worst in the treatment of G. lambia (56.2–75.9%). Similar results were obtained with quinamide and mebendazole. In this group, a 100% eradication of Hymenolepis nana and a 57.1–64.1% eradication of G. lambia were obtained. Both treatments were well tolerated by the patients.

**DISCUSSION**

Intestinal parasites in the child population is still a public health problem in México. It is related to child morbidity and mortality because of its frequent association with malnutrition, anemia, and growth and development alterations. Thus, it is important to take corrective measures to decrease its prevalence. Poverty and poor education are key factors in the existence of this condition. Prevention campaigns have had little success, and so for several years, in an effort to reduce the incidence of parasitoses, public health institutions have engaged in massive therapeutic programs against the most common and frequently found parasites.

Quinamidine and mebendazole are very effective drugs in the eradication of amebiasis, giardiasis, and ascariasis.\(^8\)–\(^11\) Similarly, nitazoxanide has demonstrated its effectiveness as a broad-spectrum antiparasitic drug in different open-level and in vitro studies.\(^16\)–\(^36\) None of the reports compared nitazoxanide’s broad-spectrum antiparasitic action with that of other treatments. The relevance of the present report is that it was a double-blind, controlled, and randomized study comparing the effect of nitazoxanide with that of quinamide, mebendazole, or both in a sample of children aged 2–12 years.

In order to include the different types of parasitic associations observed in children, several kinds of statistical analyses...
against nitazoxanide was said to have had an effectiveness of 78.0% slightly lower than those reported in previous studies, where 57.4% for Groups A and B, respectively. These rates are in infections, the eradication rates for single parasitosis and as-

with mebendazole and quinfamide together. In with nitazoxanide versus 69% with mebendazole and 66.6% for single and associated parasitoses were 62.5 and 73.6% possible drug synergism.

cation rate interval for a given parasite and also indicated associated with other parasites allowed us to have an eradica-
tion rate. Classifying the parasitoses as single or as associated parasitoses, which differed slightly from previous reports –

100%.20 This difference is probably because people of different age groups were analyzed. In our study, the 6 most prevalent parasites found in the parasitological tests were E. histolytica/E. dispar, G. lamblia, A. lumbricoides, Hymenolepis nana, T. trichiuria, and E. nana. The double-blind, randomized comparison of the treatments by parasite type are conducive to better determining the true eradication rate. Classifying the parasitoses as single or as associated with other parasites allowed us to have an eradication rate interval for a given parasite and also indicated possible drug synergism.

In A. lumbricoides infection, the eradication percentages for single and associated parasitoses were 62.5% and 73.6% with nitazoxanide versus 69% with mebendazole and 66.6% with mebendazole and quinfamide together. In G. lamblia infections, the eradication rates for single parasitosis and associated parasitosis were 56.2% and 63.6% versus 61.0 and 57.4% for Groups A and B, respectively. These rates are slightly lower than those reported in previous studies, where nitazoxanide was said to have had an effectiveness of 78.0% against G. lamblia.21 Nitazoxanide had a higher eradication rate in amebiasis treatment: 85.1% and 93.3% for single and associated parasitoses, respectively, which was significant when compared with treatment with quinfamide, mebendazole, or both. Although there were no statistically significant differences in the remaining comparisons, nitazoxanide had a higher eradication rate than did the combined treatment (quinamide, mebendazole, or both).

In conclusion, nitazoxanide had a single parasitoses eradication rate of 70.8% and an associated parasitoses eradication rate of 79.2%. There was no statistically significant difference in the rates when compared with treatment with quinfamide, mebendazole, or both. However, nitazoxanide could be a safe alternative treatment in associated parasitoses and intestinal amebiasis, and treatment of the latter would be shorter than others, which lasted at least 7 days.

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Reprint requests: Benjamín Trujillo-Hernández, MD, PhD, Calle Colibrí # 65, Colonia Colinas de Santa Bárbara, Colima, Colima México, CP 28020, Telephone: +52 (312) 31-31649, Fax: +52 (312) 31-31013, E-mail: trujillobenjamin@hotmail.com.

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