Eficacia y tolerabilidad de Nitazoxanida para parasitismo intestinal en escolares atendidos en el Centro de Salud de la Universidad del Quindío

Efficacy and tolerability of Nitazoxanide for intestinal parasitism in students treated at the Health Center of the University of Quindío

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Abstract

Objective: To describe the effectiveness of the intestinal antiparasitic treatment provided to children from 4 to 9 years old that were attended at the Health Center of the University of Quindío between July 2017 and March 2018.

Materials and methods: Prospective observational study. Data were extracted from medical records of patients between 4 to 9 years old, who consulted at the Health Center of the University of Quindío and were diagnosed through coprological tests with Blastocystis or Giardiasis. The clinical records whose treatment was done with Nitazoxanide or Albendazole with coprological results of post-treatment check-up were selected. Descriptive statistics are presented along with percentage of efficacy and tolerability.

Results: From 15 children treated with Nitazoxanide, 10 responded to the treatment and no parasites in the coprological check-up were found. The remaining population presented some type of parasitic infection (n = 5). With an efficiency of 83,3% (IC95% 60 - 100) in blastocystis, and 57,1% (IC95% 32 – 82%) in giardiasis.

Conclusion: Percentage results were similar to those reported in the literature, being more effective in blastocystis than in giardiasis.

Key words: Nitazoxanide, Giardiasis, Blastocystis, efficacy, tolerability.

Resumen

Objetivo: Describir la efectividad del tratamiento antiparasitario intestinal brindado a niños de cuatro a nueve años atendidos en el centro de Salud de la Universidad del Quindío entre Julio de 2017 a marzo de 2018.

Materiales y métodos: Estudio observacional prospectivo. Se extrajeron datos de historias clínicas de pacientes con rango de edad de 4 a 9 años, quienes consultaron en el Centro de Salud de la Universidad del Quindío y se diagnosticaron mediante coprológico con blastocistosis o giardiasis. Se seleccionaron las historias cuyo tratamiento fuese Nitazoxanida y tuviesen un coprológico control postratamiento. Se presentan estadísticas descriptivas; porcentaje de eficacia y tolerabilidad.

Resultados: De 15 niños tratados con Nitazoxanida, respondieron al tratamiento 10, en quienes no se hallaron parásitos en el coprológico control. Con una eficacia del 83,3% (IC95% 60 – 100) en blastocistosis, 57,1% (IC95% 32 – 82%) en giardiasis.

Conclusión: Se evidenciaron resultados porcentuales similares a los reportados en la literatura, siendo más eficaz en blastocisotisis que en giardiasis.

Palabras clave: (DeCS) Nitazoxanida, Giardiasis, Blastocystis, eficacia, tolerabilidad.

Introduction

Intestinal parasitosis represent an important burden of morbidity (1), as well as a public health problem in developing countries (2). Given that children have the greatest impact (3), the study and control of intestinal parasitosis is a priority in Latin America and the Caribbean.

Gastrointestinal infection by protozoa such as Giardia lamblia, Isospora belli, Blastocystis hominis, Entamoeba coli and E. histolytica, is very common in the world, presenting asymptomatically or with mild symptomatology, although on some occasions it can compromise the health of the patient

«Giardia duodenalis also known as Giardia intestinalis is a protozoan parasite found mainly in warm and humid climates around the world.»

(4). Infections by intestinal parasites are treatable, preventable and are closely related to poor hygiene conditions (5).

In developing countries, parasitosis mainly affects children. According to WHO, it was estimated that 500 million children are infected with Entamoeba histolytica and 200 million with Giardia lamblia (2). The most common intestinal parasitosis are produced by protozoa such as Giardia, Cryptosporidium and Entamoeba histolytica among others (6). Within these parasites, infection by Blastocystis hominis has been reported as the most frequent in many sites (7). This parasite causes a great variety of symptoms such as abdominal pain, diarrhea, vomiting, anorexia, and general discomfort (8), besides, it presents a wide world distribution, with high prevalence reported in Brazil (40%), Argentina (27.7%), Cuba (38.5%), Indonesia (60%) and Egypt (33%) (9). In Colombia, prevalence is estimated between 22 and 38% (10), but studies on the treatment of Blastocystis are limited, specifically regarding treatment with Nitazoxanide (10).

Giardia duodenalis also known as Giardia intestinalis is a protozoan parasite found mainly in warm and humid climates around the world (11). The prevalence of G. duodenalis is between 2 and 7% in developed countries and between 20 and 60% in developing countries (12). Infections by this parasite are generally asymptomatic but may be associated with symptoms such as diarrhea and malabsorption syndromes (13). It is transmitted orally from person to person and is mainly associated with consumption of contaminated water (14). The places where it is most frequently found are schools, educational centers, nursing homes and day care centers (15). There is a great variety of drugs for its treatment, among which are Nitazoxanide and its derivatives Nitroimidazole, Metronidazole, Tinidazole or Secnidazole (2). It is of vital importance to know the effectiveness of these therapeutic options against several parasites, such as Blastocystis hominis and Giardia lamblia.

Currently there are few studies that have been conducted around the world, specifically against Blastocystis, and none of them have been conducted in South America. While when reviewing the studies related to Giardia Lamblia, only one was found to have been carried out in South America by Ortiz J. J. et al (18).

Nitazoxanide was discovered in 1976 by Jean Francois Rossignol, it is a drug derived from Nitrothiazole and is used in children and adults to treat diarrhea caused by a great variety of protozoa such as Giardia (16). Nita-

zoxanide is one of the drugs called antiprotozoal agents (17). Generally, it is administered orally with meals for 3 days in the treatment of diarrhea. It is important to clarify that it should be considered when prescribing in patients with renal insufficiency, diabetes, or hepatic dysfunction (17).

Materials and methods

Type of study: Observational-prospective study

Population: The children described in this study were selected based on a study in which the prevalence of parasites in students in Armenia (Quindío, Colombia) was identified by analyzing the presence of DNA (18). Subsequently, those children with the presence of parasites in the coprological examination were given follow-up appointments at the Health Center of the University of Quindío, a reference center for parasitology and tropical diseases in the Department of Quindío. The children consulted during the period from December 2017 to December 2018 and were assessed by the parasitologist of the institution who diagnosed, treated, and gave follow-up.

Inclusion and exclusion criteria: The medical records were reviewed and the records that met the selection criteria, were included for analysis, which were:

1. Pediatric patients with an age range of 4 to 9 years
2. Discharge diagnosis of parasitic infection by Giardia lamblia (ICD Code 10 A07.1) or Blastocystis hominis (ICD Code 10 A07. 9 Intestinal disease due to protozoa, unspecified) confirmed by coprological (fresh examination with saline and lugol) bearing in mind the criterion of the first one as the presence of Giardia duodenalis with one cross or more and the second one as the presence of Blastocystis hominis with two crosses or more and also those who reported the presence of cysts
3. Treatment with Nitazoxanide at a dose of 5 cc every 12 hours for 3 days
4. Coprological control report 7 days after the end of the treatment.

The following were excluded from the research:

1. Medical records reporting treatment with another medication
2. Non-adherence to treatment
3. Drug dosage different from that of inclusion.

Finally, sociodemographic data and adverse effects during treatment were extracted from the medical records. The information was tabulated in Microsoft Excel and the patient characteristics were analyzed. Proportions were used to describe the level of efficacy, determined as the absence of

cysts or parasites in the post-treatment coprological and tolerability of Nitazoxanide therapy and the adverse effects recorded in the clinical histories.

Results

After applying the inclusion and exclusion criteria, a total of 15 patients were selected, with a mean age of 5.5 years. 40% (n = 6) presented infection by Blastocystis spp, 46.6% (n = 7) infection by Giardia spp and 13.3% (n = 2) presented mixed infection. The results of the present study are shown in Table 1.

Table 1. Results of treatment with Nitazoxanide for Blastocystosis or Intestinal Giardiasis

Patient	Age	Infection		Follow-up result	
		Giardia spp	Blastocystis spp	Giardia spp	Blastocystis spp
1	7		+++		NPO
2	7		+++		NPO
3	7	+++		++	+++
4	9	+++		NPO	
5	6		+++		NPO
6	5	+		++	++
7	5	+		NPO	
8	7	+			+
9	4		+		+
10	5	+	+		++
11	8	++	+	NPO	NPO
12	4		+++		NPO
13	4	+++		NPO	
14	3	++		NPO	
15	2		++		NPO

+ = 10 cysts per field 10X; ++ = 10 - 20 cysts per field 10X; ++ > 20 cysts per field 10X. NPO: no parasites observed.

Of the 6 patients with Blastocystis spp infection who received Nitazoxanide, 5 had a negative post-control result, for an efficacy of 83.3% (95%CI 60 - 100). Of the 7 patients with Giardia spp infection who received Nitazoxanide, 4 had a negative post-control result, for an efficacy of 57.1% (95%CI 32 - 82%).

Of the two patients who received Nitazoxanide for the treatment of mixed infection, one had a negative post-control result and the other had Blastocystis spp. infection. The remaining 33.3% (n = 5) patients had some type of parasitic infection at post-control (95% CI 9 - 56%). The adverse effects reported by the patients during Nitazoxanide management are summarized in Table 2.

Table 2. Adverse effects presented during treatment with Nitazoxanide for Blastocystosis and intestinal Giardiasis

None	7 (46,6%)
Colored urine	4 (26,6%)
Abdominal pain	4 (26,6%)

Considering the above data, adverse effects occurred during treatment in 53.3% (n = 8) of the cases, which were colored urine and abdominal pain, both in equal proportion. This reflects a tolerability to treatment with Nitazoxanide for the management of blastocystosis and intestinal giardiasis of 46.6% (n = 7).

Discussion

Intestinal parasitosis generate an important health burden, being considered a public health problem, especially in Latin American countries (1,2). Currently, there are few studies around the world focused on the treatment of the parasites Blastocystis hominis or Giardia lambia, of which only one study was conducted in South America by Ortiz. J. J. in Peru where Nitazoxanide was compared with placebo as antiparasitic treatment, which showed that 85.4% of 55 patients with Giardia lambia responded to therapy with Nitazoxanide, compared with 80% of 55 patients in the placebo group (19).

In the present study, the efficacy of Nitazoxanide against the parasite Giardia lambia was 57.1% in 7 patients. It should be noted that the main limitation of the study was the small number of clinical histories collected. However, if the efficacy of Nitazoxanide is compared with a previous study, where it was 71.2% in 87 patients who responded to the therapy, although the sample size is significantly larger, the treatment efficacy does not exceed 80% (13).

Additionally, in another study where Nitazoxanide was compared with placebo, it was significantly superior to Nitazoxanide treatment (OR: 0.38), 78.3% of 74 patients responded to Nitazoxanide therapy, while 90.4% of 63 patients responded to placebo (7). Therefore, according to this study, Nitazoxanide as a treatment for giardiasis is not considered an alternative treatment.

This is not different when evaluating the efficacy of therapy against Blastocystis hominis. In the current study, the efficacy found for Nitazoxanide was 83.3% of 6 patients with blastocystosis, when compared to the study performed by Diaz with a comparable sample, it is observed that only 66.6%

of 9 patients responded to treatment (14). However, the sample sizes of both studies are unrepresentative. A study compared to placebo by Speich found that 56.7% of 37 patients in the Nitazoxanide-treated group responded to management, while 67.3% of 49 patients responded to the placebo intervention, concluding in their study that there is no significant difference in the use of Nitazoxanide compared to placebo for parasite elimination (15). Similarly, in the study conducted by Rossignol, where 85.7% of 42 patients responded to the intervention with Nitazoxanide, and 88.0% of 42 patients to placebo (16), it was found that the intervention with placebo was superior to management with Nitazoxanide.

The present study sought to evaluate the efficacy of Nitazoxanide as an antiparasitic treatment in pediatric population, according to the results and its relationship with the literature, we can conclude that Nitazoxanide did not provide enough statistically significant evidence to indicate that it is an alternative antiparasitic treatment against Blastocystosis and Giardiasis, so it is recommended to conduct more studies to demonstrate its efficacy.

Ethical aspects:

The protocol was presented and approved by the research bioethics committee of the Universidad del Quindío, under ACTA 08 RESEARCH BIOETHICS COMMITTEE, December 13, 2017.

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Conflicts of interest:

The authors declare that they have no conflicts of interest.

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References

1. Ramana K V. Intestinal parasitic infections: An overview. Ann Trop Med Public Health. 2012 ;5:279-81.
2. Werner A B. Infecciones por parásitos más frecuentes y su manejo. Rev Med Clin Condes. 2014; 25(3):485-528.
3. Ministerio de Salud y Protección Social, Universidad de Antioquia. Encuesta nacional de parasitismo intestinal en población escolar 2012 – 2014. [Internet] 2015[Consultado 05 Feb 2021]. Disponible en: https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/VS/PP/ET/encuesta-nacional-de-parasitismo-2012-2014.pdf
4. Fillot M, Guzman J, Cantillo L, Gómez L, Sánchez-Majana L, Marie-Acosta B, Sarmiento-Rubiano L. Prevalencia de parásitos intestinales en niños del Área Metropolitana de Barranquilla, Colombia. Revista Cubana de Medicina Tropical [Internet] 2015 [citado 20 Nov 2021]; 67 (3) Disponible en: http://www.revmedtropical.sld.cu/index.php/medtropical/article/view/93
5. Anderson VR, Curran MP. Nitazoxanide: a review of its use in the treatment of gastrointestinal infections. Drugs. 2007; 67:1947-1967.
6. Escobedo AA, Almirall P, Alfonso M, Cimerman S, Rey S, Terry SL. Treatment of intestinal protozoan infections in children. Arch Dis Child. 2009 ;94(6):478-82.
7. Devera Rodolfo, Finali Adriana, Casares José, Risco Mayra, Farias Ana, Ortega Luisa et al . Uso de la nitazoxanida en el tratamiento de niños infectados con Giardia Lamblia. Gen [Internet] 2015 Ene [citado 2021 Nov 21] ; 69(1): 7-12. Disponible en: http://ve.scielo.org/scielo.php?script=sci_arttext&pid=S0016-35032015000100003&lng=es.
8. Bances García Fary Betsy, Rodríguez Díaz David Rene, Albuquerque Fernández Pablo, Paz Marchena Aldo. Eficacia y seguridad de Nitazoxanida comparada con Albendazol en el tratamiento de Giardiasis sintomática en niños de Trujillo, Perú 2008 - 2009. Rev Cient Cienc Méd [Internet]. 2013 [citado 2021 Ago 15] ; 16(1): 6-11. Disponible en: http://www.scielo.org.bo/scielo.php?script=sci_arttext&pid=S1817-74332013000100003&lng=es.
9. Tan KS. New insights on classification, identification, and clinical relevance of Blastocystis spp. Clin Microbiol Rev. 2008;21(4):639-665. doi:10.1128/CMR.00022-08
10. Moreno-Brea M. R.. Tolerabilidad de Aspirina. Rev. Soc. Esp. Dolor [Internet]. 2005 Sep [citado 2021 Nov 21] ; 12(6): 357-372. Disponible en: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S1134-80462005000600006&lng=es.
11. Taylor-Orozco Viviana, López-Fajardo Alison, Muñoz-Marroquín Ineselena, Hurtado-Benítez Mario, Ríos-Ramírez Karina. Blastocystis sp: EVIDENCIAS DE SU ROL PATÓGENO. Biosalud [Internet] 2016 Dec [cited 2021 Aug 25]; 15(2): 69-86. Available from: http://www.scielo.org.co/scielo.php?script=sci_arttext&pid=S1657-95502016000200007&lng=en. https://doi.org/10.17151/biosa.2016.15.2.8.
12. Romero Cabello R, Guerrero LR, Muñóz García MR, Geyne Cruz A. Nitazoxanide for the treatment of intestinal protozoan and helminthic infections in Mexico. Trans R Soc Trop Med Hyg. 1997;91(6):701-703. doi:10.1016/s0035-9203(97)90531-9
13. Diaz E, Mondragon J, Ramirez E, Bernal R. Epidemiology and control of intestinal parasites with nitazoxanide in children in Mexico. Am J Trop Med Hyg. 2003;68(4):384–5.
14. Speich, B., Marti, H., Ame, S.M. et al. Prevalence of intestinal protozoa infection among school-aged children on Pemba Island, Tanzania, and effect of single-dose albendazole, nitazoxanide and albendazole-nitazoxanide. Parasites Vectors. 2013; 6 (3). doi. org/10.1186/1756-3305-6-3

15. Rossignol JF, Kabil SM, Said M, Samir H, Younis AM. Effect of nitazoxanide in persistent diarrhea and enteritis associated with Blastocystis hominis. Clin Gastroenterol Hepatol. 2005;3(10):987-991. doi:10.1016/s1542-3565(05)00427-1

16. Rossignol JF, Cavier R. New derivative of 2-benzamido-5- nitrothiazoles. Chem Abstr. [Internet] 1976 [Consultado Nov 20 2021]. Disponible en: patentimages.storage.googleapis.com/2e/00/47/e6a712386327e7/US3950351.pdf

17. Asociación Española de Pediatría [Internet]. Nitazoxanida: AEP; 2015 [Citado Nov 20 2021]. Disponible en: https://www.aeped.es/comite-medicamentos/pediamecum/nitazoxanida

18. Muñoz-Sánchez, GD, Hernández-Arango, N, Buitrago-Lopez, E, et al. Food protozoa safety assessment and risk in school restaurants in Armenia, Colombia. J Food Saf. 2019; 39:e12714. doi.org/10.1111/jfs.12714

19. Ortiz JJ, Ayoub A, Gargala G, Chegne NL, Favennec L. Randomized clinical study of nitazoxanide compared to metronidazole in the treatment of symptomatic giardiasis in children from Northern Peru. Aliment Pharmacol Ther. 2001;15(9):1409-1415. doi:10.1046/j.1365-2036.2001.01066.x