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Original Research Article

The Effectiveness of Oral Nitazoxanide Versus Oral Metronidazole in Pediatric Giardia lamblia-Induced Diarrhea

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Abstract: *Giardia lamblia is a common cause of diarrheal illness in children and contributes substantially to morbidity in low- and middle-income countries. Effective, well-tolerated, and short-course treatment options are important for improving clinical outcomes in pediatric patients.* ***Objective:*** *To compare the effectiveness of nitazoxanide versus oral metronidazole in pediatric Giardia lamblia-induced diarrhea at Khyber Teaching Hospital, Peshawar.* ***Methods:*** *This study was conducted on 340 children aged 1 to 15 years presenting with Giardia lamblia-induced diarrhea at the Department of Pediatrics, Khyber Teaching Hospital, Peshawar, from 14-August-2024 to 14-February-2025. Patients were allocated into two equal. Group A received oral nitazoxanide twice daily for three days. Group B received oral metronidazole twice daily for three days. Effectiveness was defined as resolution of diarrhea, with no abdominal cramps, bloating, or flatulence, and no unformed stools, three days after completing treatment. Data were analyzed using SPSS 23. The chi-square test was used to compare effectiveness between groups, with a p-value ≤ 0.05 considered statistically significant.* ***Results:*** *The study enrolled 340 children, 170 patients in group A (nitazoxanide) and group B (metronidazole). The mean age was 7.76±3.74 years in the nitazoxanide group and 8.68±4.18 years in the metronidazole group. Effectiveness was achieved in 145 (85.3%) patients receiving nitazoxanide compared to 123 (72.4%) patients receiving metronidazole. The difference was statistically significant (p = 0.003).* ***Conclusion:*** *Oral nitazoxanide was significantly more effective in pediatric giardia lamblia-induced diarrhea than oral metronidazole (85.3% versus 72.4%).*

Keywords: Giardia lamblia, diarrhea, pediatrics, nitazoxanide, metronidazole, effectiveness

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Introduction

Giardia lamblia is the predominant protozoan that infects the small intestine of humans. It is an important contributor to enteric infections globally among the youngsters (1). There have been reports of seven distinct genotypes/assemblages (A to G) of Giardia lamblia that display host specificity. Assemblages A and B have been recognized in humans, cattle and numerous other mammalian species (3). Common symptoms of giardiasis include diarrhea, oily feces, stomach pain, and weight loss. Reduced levels of intestinal enzymes and disaccharides are detected, as are impaired absorption of fat, vitamin A, and vitamin B12 (4, 5).

Giardia lamblia-induced diarrhea occurred in areas with few resources and among children, which is a prevalent intestinal ailment that affects millions of people worldwide (6). The parasite's ability to persist across diverse environmental conditions and its transmission via the fecal-oral route contribute to its resilience and widespread distribution as a pathogen (7). The clinical presentation of giardiasis spans a broad spectrum, from asymptomatic carriage to acute or chronic diarrhea, stomach pain, bloating, and malabsorption syndromes. These manifestations have a noteworthy influence on both the physical well-being and overall quality of life of affected individuals (7). A study compared the effectiveness of oral nitazoxanide (87%) versus oral metronidazole (75%) in pediatric Giardia lamblia-induced diarrhea (8). The initial diagnosis relies on the clinical manifestations observed in children. It is verified by identifying cysts and trophozoites in fecal samples via direct microscopic examination, which is widely regarded as the most reliable method for diagnosing Giardia. The enzyme-linked immunosorbent assay is the prevailing and highly sensitive method for detecting antigens in stool samples (9).

Due to the paucity of local literature on this subject, the goal of this study is to compare the effectiveness of oral nitazoxanide versus oral metronidazole in pediatric Giardia lamblia-induced diarrhea. By conducting a comparative study, we aim to clarify the relative effectiveness of nitazoxanide and metronidazole in pediatric patients, thereby informing clinical practice and guiding treatment decisions for this common and often debilitating condition.

Methodology

This Comparative Prospective Cohort study was conducted in the Department of Pediatrics, Khyber Teaching Hospital, Peshawar, from 14-August-2024 to 14-February-2025. Ethical approval (Ref # 563/DME/KMC) was obtained prior to commencing the study. Three hundred forty patients were selected for this study. The sample size was calculated using the OpenEPI web-based calculator, assuming an effectiveness of 87% for oral nitazoxanide versus 75% for oral metronidazole in pediatric Giardia lamblia-induced diarrhea. (8) Keeping Power 80%, and Confidence level 95%. Consecutive non-probability sampling was used.

Patients aged 1 to 15 years, of both genders, presenting with Giardia lamblia-induced diarrhea were enrolled in this study. Giardia lamblia-induced diarrhea was defined as children presenting with all of the following features: loose or watery stools (>three per day for more than 3 weeks), abdominal cramps, bloating, and flatulence. Diagnosis was made based on laboratory tests showing trophozoites in the stool sample and the presence of Giardia lamblia cysts on antigen testing. Children with allergy or intolerance to medications, celiac disease and inflammatory bowel disease were excluded.

The goal and benefits of this study were shared with the parents of all enrolled patients, and they were assured that participation posed no risk. Demographic data, including age, gender, weight, socioeconomic status, and residential area, were recorded. Patients were allocated to two groups in equal numbers (Group A and Group B). Patients in group A were treated with oral nitazoxanide 5 mL (ages 2-3 years) or 10 mL (ages 4-15

years), containing 100 mg of nitazoxanide per 5 mL, twice daily for 3 days. Patients in Group B were treated with oral metronidazole 5 mL of 125 mg per 5 mL (ages 2-5 years) or 250 mg per 5 mL (ages 6-15 years) twice daily for 3 days. Effectiveness was defined as resolution of diarrhea, i.e., no symptoms (abdominal cramps, bloating, and flatulence) and no unformed stools, after 3 days of treatment in both groups. The entire assessment was conducted under the guidance of a consultant with at least 5 years of post-fellowship experience.

For data analysis, SPSS 23 was used. Mean ± SD were determined for numerical variables such as age, weight, and duration of diarrhoea. Frequencies and percentages were used for categorical variables such as gender, effectiveness, socioeconomic status, and residence area. Effectiveness was compared between the two treatment groups using the chi-square test, with p-values <0.05 considered statistically significant. Effect modifiers such as age, weight, duration of diarrhoea, socio-economic status, and residence area were addressed through stratification. A post-stratification chi-square test was performed, with p-values < 0.05 considered statistically significant.

Results

The present study was conducted with 340 children, divided into two equal groups. The mean age of children receiving oral nitazoxanide was 7.76 ± 3.74 years. Those receiving oral metronidazole had a mean age of 8.68 ± 4.18 years. The average duration of diarrhea before treatment was 6.55±1.75 weeks in the nitazoxanide group and 6.30±1.73 weeks in the metronidazole group. The mean body weight was 25.11±8.69 kg in the nitazoxanide group and 27.49±10.14 kg in the metronidazole group.

In the nitazoxanide group 111 (65.3%) children were male, and 59 (34.7%) were female. In the metronidazole group, 95 (55.9%) were male, and 75 (44.1%) were female. Residence and socioeconomic distribution between the two groups are shown in Table 1.

In the nitazoxanide group, treatment was effective in 145 (85.3%) children. At the same time, only 123 (72.4%) children in the metronidazole group showed a favorable response. The difference between the two groups was statistically significant (p = 0.003).

Stratification of effectiveness by demographics in both groups is shown in Table 3.

Table 1: Demographic distribution of the patients

		Group			
		Group A (Oral Nitazoxanide)		Group B (Oral Metronidazole)	
		n	%	n	%
Gender	Male	111	65.3%	95	55.9%
	Female	59	34.7%	75	44.1%
Residence	Urban	75	44.1%	81	47.6%
	Rural	95	55.9%	89	52.4%
Socioeconomic status	Lower class	61	35.9%	56	32.9%
	Middle class	68	40.0%	79	46.5%
	Upper class	41	24.1%	35	20.6%

Table 2: Comparison of effectiveness between the two groups

		Group				P value
		Group A (Oral Nitazoxanide)		Group B (Oral Metronidazole)		
		n	%	n	%	
Effectiveness	Yes	145	85.3%	123	72.4%	0.003
	No	25	14.7%	47	27.6%	

Table 3: Stratification of effectiveness between both groups with respect to demographics

				Group				P value
				Group A (Oral Nitazoxanide)		Group B (Oral Metronidazole)		
				n	%	n	%	
Gender	Male	Effectiveness	Yes	99	89.2%	69	72.6%	0.002
			No	12	10.8%	26	27.4%	
	Female	Effectiveness	Yes	46	78.0%	54	72.0%	0.431
			No	13	22.0%	21	28.0%	
Residence	Urban	Effectiveness	Yes	62	82.7%	58	71.6%	0.101
			No	13	17.3%	23	28.4%	
	Rural	Effectiveness	Yes	83	87.4%	65	73.0%	0.014
			No	12	12.6%	24	27.0%	
Socioeconomic status	Lower class	Effectiveness	Yes	54	88.5%	40	71.4%	0.020
			No	7	11.5%	16	28.6%	
	Middle class	Effectiveness	Yes	55	80.9%	58	73.4%	0.28
			No	13	19.1%	21	26.6%	
	Upper class	Effectiveness	Yes	36	87.8%	25	71.4%	0.074
			No	5	12.2%	10	28.6%	
Age distribution (Years)	1 to 7	Effectiveness	Yes	71	83.5%	48	72.7%	0.107
			No	14	16.5%	18	27.3%	
	8 to 15	Effectiveness	Yes	74	87.1%	75	72.1%	0.012
			No	11	12.9%	29	27.9%	
Weight distribution	10 to 20	Effectiveness	Yes	46	82.1%	36	72.0%	0.213
			No	10	17.9%	14	28.0%	

	21 to 30	Effectiveness	Yes	48	85.7%	28	68.3%	0.040
			No	8	14.3%	13	31.7%	
	> 30	Effectiveness	Yes	51	87.9%	59	74.7%	0.054
			No	7	12.1%	20	25.3%	
Duration of diarrhea (Weeks)	4 to 6	Effectiveness	Yes	64	83.1%	67	71.3%	0.069
			No	13	16.9%	27	28.7%	
	> 6	Effectiveness	Yes	81	87.1%	56	73.7%	0.027
			No	12	12.9%	20	26.3%	

Discussion

The management of giardiasis in pediatric populations has remained a therapeutic challenge despite the availability of multiple antiprotozoal agents. Previous studies have consistently demonstrated that nitroimidazole compounds serve as the cornerstone of treatment for this intestinal infection. The study conducted by Ali et al. provided early evidence that a three-day course of nitazoxanide could achieve comparable, if not superior, outcomes to the standard seven-day metronidazole regimen in children with protozoal diarrhea. Their work reported a resolution of diarrhea in 82.3% of cases of giardiasis treated with nitazoxanide, compared with 76.47% with metronidazole. (10) The authors further noted that the shorter treatment duration with nitazoxanide offered meaningful advantages in terms of patient compliance and convenience, particularly given the frequent side effects associated with prolonged metronidazole use, including metallic taste, nausea and abdominal discomfort.

The work by Sami ul Haq and collaborators enrolled 230 children and found that nitazoxanide administered for 3 days produced a clinical response in 90% of cases, while metronidazole given for 5 days was effective in 93% of cases. Although the difference was not statistically significant, the study underscored that a shortened nitazoxanide regimen could be considered non-inferior to the longer metronidazole course. (11) Another study from Pakistan by Irfan et al. similarly demonstrated resolution of diarrhea in 90% of the nitazoxanide group compared with 85% for the metronidazole group, with a notable advantage in parasite clearance favoring nitazoxanide. (12)

Nitazoxanide interferes with the pyruvate ferredoxin oxidoreductase enzyme, which is essential for anaerobic energy metabolism in Giardia lamblia. This action leads to trophozoite swelling, membrane disruption and eventual parasite death. Metronidazole, a member of the 5-nitroimidazole (5-NI) family, by contrast, requires intracellular activation via reduction to toxic free-radical intermediates, which then bind to parasitic DNA and cause strand breakage. However, resistance to 5-nitroimidazoles has been increasingly reported, often related to reduced expression of pyruvate ferredoxin oxidoreductase or altered nitroreductase activity. (13)

Lopez Velez et al. reported patients with refractory giardiasis who were successfully treated with short-course combinations, such as metronidazole plus paromomycin plus albendazole, or tinidazole plus quinacrine. All combinations were administered for seven to ten days and were well tolerated. The authors also emphasized the importance of ruling out immunoglobulin A deficiency and co-infections before attributing treatment failure to true drug resistance. (14) In a separate trial, Vakkilainen et al. explored the use of rectal metronidazole as an alternative route for children who could not tolerate oral medications, demonstrating clinical cure in all symptomatic patients and acceptable caregiver acceptance. (15) Although that study was terminated early due to slow enrollment, it provided proof of principle that non-oral formulations may have a role in selected pediatric cases.

The present study contributes additional evidence by directly comparing oral nitazoxanide with oral metronidazole in a large cohort of 340 children with confirmed Giardia lamblia-induced diarrhea. The primary outcome of treatment effectiveness was defined as resolution of diarrhea, along with disappearance of abdominal cramps, bloating, and flatulence within 3 days of completing therapy. Effectiveness was achieved in 145 (85.3%) children receiving nitazoxanide, while only 123 (72.4%) children in the metronidazole group experienced similar clinical improvement. This difference was statistically significant (p =0.003). These findings are consistent with those of Ali et al., who reported a modest but statistically significant advantage of nitazoxanide over metronidazole in cases of giardiasis. (10) However, the present results differ somewhat from those reported by Sami ul Haq et al., who found nearly equivalent effectiveness between the two drugs. (11) Given that both treatment groups in the present study received a three-day course of their respective medications, the superior effectiveness observed with nitazoxanide (85.3%) compared to metronidazole (72.4%) indicates that nitazoxanide is the more efficacious agent when treatment duration is standardised to three days.

Conclusion

In conclusion, the present study demonstrated that oral nitazoxanide is significantly more effective than oral metronidazole in pediatric Giardia lamblia-induced diarrhea (85.3% versus 72.4%). It is recommended that a three-day course of oral nitazoxanide be preferred over a three-day course of oral metronidazole for the treatment of pediatric Giardia lamblia-induced diarrhea, given its superior clinical effectiveness and comparable treatment duration. Further large-scale multicenter studies with longer follow-up periods are needed to confirm these findings.

Declarations

Data Availability statement
All data generated or analysed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department concerned. (IRBEC-563/DME/KMC)
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Conflict of interest

The authors declared no conflict of interest.

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SA (Postgraduate Resident)
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Review of Literature, Conception of Study and Critical Guidance
RS (Postgraduate Resident)
Literature search
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Critical input.
IH (Postgraduate Resident)
Helps in Data Analysis
GK (Postgraduate Resident)
Literature Search and Referencing

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the study's integrity.

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