Evaluation of Nitazoxanide versus Metronidazole in Pediatric Giardia lamblia-Induced Diarrhea: A Comparative Efficacy Analysis

Muhammad Irfan¹, Sara Najeeb², Muhammad Kaleem Raza Shah³, Muhammad Shahid Jamil⁴, Nosheen Iftikhar⁵, Allah Nawaz Sultan⁶

ABSTRACT

Background: The choice between shorter-duration Nitazoxanide and longer-duration Metronidazole regimens for treating Giardia lamblia-induced diarrhea in children requires careful consideration of efficacy, safety, and treatment adherence. Objective: The objective of this study is to compare the efficacy of a 3-day treatment regimen with Nitazoxanide to a 5-day treatment regimen with Metronidazole in children with diarrhea caused by Giardia lamblia. Study Design: Randomized controlled trial (RCT). Settings: Department of Paediatric, Shahida Islam Medical College, Lodhran Pakistan. Duration: From 1st September, 2022 to February 2023. Methods: Pediatric patients aged 1 to 12 years diagnosed with diarrhea attributed to Giardia lamblia infection. Exclusion criteria were children suffering from chronic gastrointestinal diseases, immunodeficiency disorders, or those who had undergone anti-parasitic medication in the last month. Subjects were randomised to one of two treatment groups in a random manner: Nitazoxanide Group: The patients were administered a 3-day regimen of Nitazoxanide at a dosage of 15 mg/kg/day, split into two separate doses. Metronidazole Group: Patients were administered a 5-day regimen of Metronidazole at a dosage of 30 mg/kg/day, which was divided into three equal doses. The primary outcome measure was the resolution of diarrhea, assessed by the absence of loose or watery stools for at least 24 hours. Statistical analysis was performed using SPSS to compare outcomes between the two treatment groups. Results: The mean age of patients in the Nitazoxanide group was 6.7 ± 2.3 years, while in the Metronidazole group, it was slightly lower at 6.3±2.1 years. In terms of gender distribution, there were 40 males (53.3%) and 35 females (46.7%) in the Nitazoxanide group, whereas in the Metronidazole group, there were 35 males (46.7%) and 40 females (53.3%). In the Nitazoxanide group, 90% of patients achieved resolution, with 68 patients. In contrast, 85% of patients in the Metronidazole group had resolved diarrhea, totaling 64 patients. Conclusion: In conclusion, our study found comparable efficacy between nitazoxanide and metronidazole for treating Giardia lamblia-induced diarrhea with 95% parasite clearance in nitazoxanide and 90% in metronidazole. However, nitazoxanide exhibits superior parasite clearance, suggesting its potential as a promising alternative in pediatric clinical practice.

Keywords: Children, Diarrhea, Giardia lamblia, Metronidazole, Nitazoxanide, Pediatric, Treatment.

INTRODUCTION

Diarrhea remains one of the leading causes of morbidity and mortality worldwide, particularly among children in resource-limited settings. Among the myriad of pathogens responsible for diarrheal illness, Giardia lamblia stands out as a significant contributor, imposing a considerable burden on global public health. Giardia lamblia, a flagellated protozoan parasite, is responsible for a substantial portion of diarrheal disease burden globally. It is estimated that...
Giardia infects over 200 million individuals annually, with endemicity particularly prevalent in low and middle-income countries where inadequate sanitation and water contamination are common. The transmission of Giardia lamblia occurs primarily through the fecal-oral route, facilitated by ingestion of contaminated food or water sources. Additionally, person-to-person transmission can occur, particularly in settings with poor hygiene practices. The resilience of Giardia cysts in the environment contributes to its persistence, enabling prolonged survival in various ecological niches. Following ingestion, Giardia lamblia cysts undergo excystation in the duodenum, releasing trophozoites that attach to the intestinal mucosa. The trophozoites then undergo replication and colonization, leading to malabsorption, inflammation, and disruption of normal gut physiology. Mechanisms underlying Giardia-induced diarrhea include interference with epithelial barrier function, alteration of host immune responses, and induction of secretory diarrhea via toxin release.

Giardia lamblia-induced diarrhea typically manifests as acute or chronic watery diarrhea, often accompanied by abdominal pain, bloating, flatulence, and weight loss. While self-limiting in some cases, persistent infection can lead to malnutrition, growth stunting, and impaired cognitive development, particularly in pediatric populations.

The management of diarrhea, particularly in pediatric populations, remains a critical aspect of public health interventions worldwide. Nitazoxanide and Metronidazole are both recommended agents for the treatment of Giardia lamblia infection, albeit with different dosing regimens and durations. Nitazoxanide, a broad-spectrum antiparasitic agent, has demonstrated efficacy in treating various gastrointestinal infections, including Giardia lamblia, with shorter treatment duration of 3 days. On the other hand, Metronidazole, a nitroimidazole antibiotic, is commonly prescribed for Giardia lamblia infection with a longer treatment course typically spanning 5 to 7 days.

The rationale for this study lies in the necessity to optimize treatment protocols for Giardia lamblia-induced diarrhea in pediatric patients. Given the significant burden of this parasitic infection globally, it is essential to identify the most effective and efficient treatment regimen to alleviate symptoms and prevent complications.

METHODS

The study was carried out after obtaining clearance from the institutional ethics committee. The study employed a randomized controlled trial (RCT) design. Consent was gained from the parents or legal guardians of all participating children after providing them with relevant information.

Pediatric patients aged 1 to 12 years diagnosed with diarrhea attributed to Giardia lamblia infection. Participants were required to have a positive stool examination confirming the presence of Giardia lamblia cysts or trophozoites. Children with severe dehydration requiring immediate medical intervention, those with a history of hypersensitivity or contraindications to Nitazoxanide or Metronidazole, as well as those with concurrent infections requiring antibiotic therapy were excluded. Additionally, patients with chronic gastrointestinal conditions, immunodeficiency disorders, or recent history of anti-parasitic treatment within the past month were excluded from the study.

The participants were assigned to one of two treatment groups in a random manner. Nitazoxanide Group: Patients were administered a 3-day regimen of Nitazoxanide at a dosage of 15 mg/kg/day, split into two separate doses. Metronidazole Group: Participants were administered Metronidazole for duration of 5 days, at a dosage of 30 mg/kg/day, divided into three separate doses. The main criterion for evaluating the effectiveness was the cessation of diarrhoea, determined by the absence of loose or watery bowel movements for a minimum of 24 consecutive hours. Secondary outcome measures included treatment adherence, adverse effects, and stool examination results (parasite clearance). Baseline demographic and clinical characteristics were recorded for all participants. Clinical assessments were conducted at baseline and at specified follow-up intervals. Stool samples were collected pre- and post-treatment for microscopic examination to confirm Giardia lamblia infection and assess treatment response.

The outcomes between the two therapy groups were compared using SPSS for statistical analysis. Demographic and clinical data were summarised using descriptive statistics. Statistical methods, such as chi-square tests or t-tests, were used to analyse primary and secondary outcome measures. A p-value less than 0.05 was deemed to be statistically significant.

RESULTS

The average age of patients in the Nitazoxanide group was 6.7 ± 2.3 years, but in the Metronidazole group, it was somewhat lower at 6.3 ± 2.1 years. The Nitazoxanide group consisted of 40 males (53.3%) and 35 females (46.7%), while the Metronidazole group had 35 males (46.7%) and 40 females (53.3%) in terms of gender distribution. In terms of stool frequency, the majority of patients in both groups saw less than 10 bowel movements within a 24-hour period. Specifically, 49 patients (65%) in the Nitazoxanide group and 45 patients...
(60%) in the Metronidazole group fell into this category. In contrast, a lesser percentage of patients experienced over 10 bowel movements over a 24-hour period, with 26 (35%) in the Nitazoxanide group and 30 (40%) in the Metronidazole group, as indicated in table 1.

Table 1: Baseline demographic and clinical characteristics between the Nitazoxanide and Metronidazole groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Demographic Variables</th>
<th>Nitazoxanide Group (n=75)</th>
<th>Metronidazole Group (n=75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>Mean ± SD</td>
<td>6.7 ± 2.3</td>
<td>6.3 ± 2.1</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>40 (53.3%)</td>
<td>35 (46.7%)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>35 (46.7%)</td>
<td>40 (53.3%)</td>
</tr>
<tr>
<td>Stool Frequency</td>
<td>&lt;10 per 24 hours</td>
<td>49 (65%)</td>
<td>45 (60%)</td>
</tr>
<tr>
<td></td>
<td>&gt;10 per 24 hours</td>
<td>26 (35%)</td>
<td>30 (40%)</td>
</tr>
</tbody>
</table>

Table 2, in the Nitazoxanide group, 90% of patients achieved resolution, with 68 patients. In contrast, 85% of patients in the Metronidazole group had resolved diarrhea, totaling 64 patients.

Table 2: The resolution of diarrhea in the Nitazoxanide group compared to Metronidazole group

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Resolution of Diarrhea (%)</th>
<th>Number of Patients</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitazoxanide</td>
<td>90%</td>
<td>68</td>
<td>0.9</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>85%</td>
<td>64</td>
<td>0.302</td>
</tr>
</tbody>
</table>

Table 3, in both treatment groups, high adherence rates were observed, with 95% of patients adhering to Nitazoxanide treatment and 93% adhering to Metronidazole treatment, comprising 71 and 70 patients, respectively. Adverse effects were reported in 10% of patients receiving Nitazoxanide, involving 7 patients, while in the Metronidazole group, adverse effects were noted in 15% of patients, affecting 11 individuals.

Table 3: Treatment adherence in both groups with adverse effects

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Treatment Adherence (%)</th>
<th>Number of Patients</th>
<th>Adverse Effects (%)</th>
<th>Number of Patients</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitazoxanide</td>
<td>95%</td>
<td>71</td>
<td>10%</td>
<td>7</td>
<td>0.054</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>93%</td>
<td>70</td>
<td>15%</td>
<td>11</td>
<td></td>
</tr>
</tbody>
</table>

Table 4, in both the Nitazoxanide and Metronidazole groups, microscopic examination of stool samples revealed parasite clearance. Specifically, 95% of patients in the Nitazoxanide group achieved parasite clearance, totaling 71 patients, while in the Metronidazole group, 90% of patients had clearance, comprising 68 individuals. The difference in parasite clearance rates between the two groups was statistically significant, with a p-value of 0.031.

Table 4: Microscopic examination of stool samples

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Parasite Clearance (%)</th>
<th>Patients with Clearance</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitazoxanide</td>
<td>95%</td>
<td>71</td>
<td>0.031</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>90%</td>
<td>68</td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION

Giardia lamblia is a common cause of diarrheal illness in children worldwide, posing significant health burdens, particularly in resource-limited settings. Treatment options typically include Nitazoxanide and Metronidazole, yet the optimal duration of therapy remains uncertain. Understanding the comparative effectiveness of these treatments is essential for guiding clinical decision-making and optimizing patient outcomes.11,12

Our study observed a mean age of 6.7±2.3 years in the Nitazoxanide group and 6.3±2.1 years in the Metronidazole group, with a relatively balanced gender distribution. The majority of patients in both treatment groups had less than 10 stools per 24 hours. Fallah et al. (2007) reported higher parasitological cure rates with tinidazole compared to metronidazole (88.1% vs. 67.2%, p < 0.01). Minimal side effects were observed with both tinidazole and metronidazole, including mild headache, abdominal pain, metallic taste, nausea, dizziness, and headache.13 González et al. (2010) reported comparable cure rates between nitazoxanide and secnidazole (NTZ: 95.2%, SNZ: 93.7%, p > 0.05). Specific side effects associated with nitazoxanide and secnidazole included bitter taste, urinary coloration, rash, nausea, and headache.14 Maryiam et al. (2021) found that diarrhea resolved in all children treated with nitazoxanide prior to the 7-day follow-up visit, with 96.0% achieving Giardia antigen negativity after 3 days of treatment and 86.0% achieving parasite clearance.15

When comparing the treatment efficacy and side effects of nitazoxanide (NTZ) and metronidazole across multiple studies, several key observations emerge. Ortiz et al. (2001) reported that both nitazoxanide and metronidazole were effective in resolving diarrhea, with nitazoxanide showing a slightly lower but comparable efficacy (85% vs. 80%, respectively).16 Similarly, Mehdood et al. (2022) found high effectiveness with both nitazoxanide (90%) and metronidazole (92%).17 Pasupuleti et al. (2014) conducted a comprehensive analysis across multiple studies, indicating slightly higher response rates with 5-nitroimidazoles (including nitazoxanide) compared to controls, albeit with high heterogeneity.18 Regarding side effects, Ortiz et al. (2001)
reported only mild, transient adverse events with both nitazoxanide and metronidazole, aligning with the findings of Mehmood et al. (2022). However, Pasupuleti et al. (2014) highlighted that while harmful outcomes were uncommon with 5-nitroimidazoles, there was a slightly higher risk of bitter or metallic taste and headache compared to controls.\textsuperscript{16,17,18}

Ahmed et al. (2023) reported significantly higher cure rates with nitazoxanide compared to metronidazole, mirroring our study’s efficacy outcomes. These results collectively emphasize the importance of timely and effective treatment in managing parasitic diarrhea.\textsuperscript{19} Our study’s strength lies in its rigorous comparison of nitazoxanide and metronidazole efficacy in pediatric parasitic diarrhea, supported by comprehensive demographic and clinical data and adherence to standardized protocols, enhancing reliability and generalizability for clinical practice.

CONCLUSION

In conclusion, our study found comparable efficacy between nitazoxanide and metronidazole for treating Giardia lamblia-induced diarrhea with 95% parasite clearance in nitazoxanide and 90% in metronidazole. However, nitazoxanide exhibits superior parasite clearance, suggesting its potential as a promising alternative in pediatric clinical practice.

LIMITATIONS

Limitations of our study include a short follow-up period, potentially hindering long-term outcome assessment, and its single-center design, which may limit the generalizability of findings.

SUGGESTIONS / RECOMMENDATIONS

Further multicenter studies with extended follow-up periods are recommended to validate the findings and enhance generalizability.

CONFLICT OF INTEREST / DISCLOSURE

None.

ACKNOWLEDGEMENTS

None.

REFERENCES