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Research Article

### STUDY TO DETERMINE THE CLINICAL EFFECTIVENESS OF NITAZOXANIDE IN TREATMENT OF GIARDIASIS AMONG CHILDREN

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**Abstract:**

*Giardia lamblia* intestinal infection is a common cause of diarrhea not only in Pakistan but around the world. It is believed to be a significant cause of morbidity and mortality in the pediatric age group.

**Aim:** The aim of the study was to test the effectiveness of Nitazoxanide treatment in children with diarrhea caused by *G. lamblia*.

**Methods:** A total of 50 children with diarrhea caused by *G. intestinalis* received a 3-day nitazoxanide therapy (10 mg / kg / day in 2 doses for 3 days). Patients were monitored for clinical response 7 days after initiation of treatment, and then a stool sample was collected for parasitology and lamblia antigen testing.

**Results:** Diarrhea resolved in all 50 (100%) children treated with nitazoxanide prior to the 7-day follow-up visit. Most diarrhea resolved within 4 days. The *Giardia* antigen turned negative in 96.0% of the population after 3 days of treatment. Whereas the giardia and / or oocytes / cysts became negative in 86.0% of the patient population.

**Conclusions:** The 3-day cycle of nitazoxanide suspension is as effective as the treatment of lamblia in children. It is well tolerated and has no significant side effects.

**Key words:** nitazoxanide, Giardiasis.

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**INTRODUCTION:**

According to the World Health Organization (WHO), diarrheal diseases in children remain the second leading cause of death in children under 5 years of age. It is estimated that 1.7 billion cases of diarrhea in children are reported annually [1-2]. Among these reported cases, 760,000 cases die each year. Countries in Africa and Southeast Asia collectively account for about 78% of diarrhea-related child deaths. Most of these cases are concentrated in only 15 developing countries, and Pakistan is one of those fifteen. Child mortality in Pakistan is a major concern, as one in 10 children die before the age of five and one in 30 just after birth [3-4]. The disease causes over 2.5 billion disease episodes and 1.5 million deaths annually worldwide (500 deaths a day in Pakistan). Most of these deaths occur in developing countries. In Pakistan, on average, every child suffers from 5-6 episodes of diarrhea each year [5-6]. The reported incidence of diarrhea in Punjab is 7.8%. *Giardia lamblia* is an intestinal parasitic protozoan that infects many host species, including humans and domestic mammals. The incidence of *G. lamblia* infections varies in different parts of the world, but is generally higher in developing countries, where the reported incidence ranges from 3% to 38%. *Giardia lamblia* (also known as *Lambia intestinalis* and *Giardia duodenalis*) is a parasitic protozoan that occurs all over the world [7-8]. The incidence of infections varies greatly in different regions of the world, ranging from 3% to 38%. In underdeveloped countries, *Giardia* Infection is more likely to occur due to contaminated water or food. Patients with giardiasis may be asymptomatic or have mild to severe gastrointestinal symptoms, including explosive diarrhea, abdominal pain, fatty diarrhea, flatulence, flatulence, nausea and vomiting. Treatment varies by geography, preferences, and preferences. physician, and availability and cost of drugs Various treatment regimens with varying degrees of efficacy have been tried Nitazoxanide (2-acetyloxy-N-benzamide) is a synthetic oral antiprotozoal agent for the treatment of diarrhea caused by *Cryptosporidium parvum* and *Giardia lamblia*. The study was conducted to see clinical efficacy and safety of nitazoxanide in children suffering from *Giardia* sister

**METHODOLOGY:**

This experimental study was conducted at the Pediatric department of Bahawal Victoria Hospital Bahawalpur for one-year duration from June 2019 to June 2020. A total of fifty pediatric patients presenting with acute watery diarrhea who tested positive for *Giardia* stool or *Giardia* antigen were included in the study. The study excluded patients

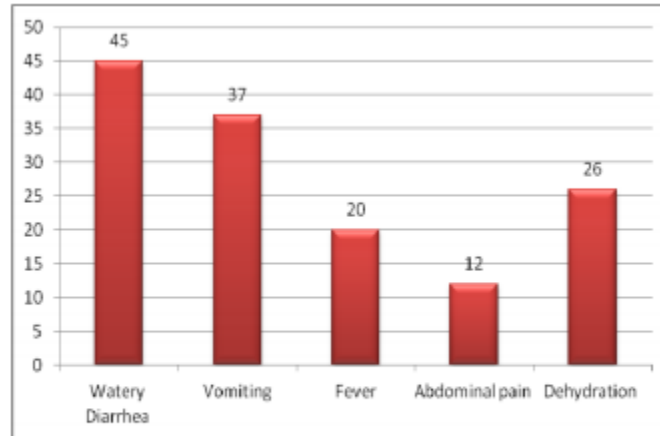
who had blood in their stools, patients who had received metronidazole in the last 3 days on an antibiotic, and with other infections such as otitis media and respiratory infections. Patients with watery diarrhea and symptoms such as abdominal pain, vomiting and degree of dehydration were also registered. All patients underwent a stool test for abscesses, red blood cells, oocytes / cysts, trophozoite and lamblia. After giardiasis conformation, the patient was administered Nitazoxanide at a dose of 10 mg / kg / day in 2 doses for 3 days as the cause of diarrhea. After 3 days, the stool was re-examined for purulent cells, red blood cells, oocytes / cysts, trophozoite and *Giardia* antigen. The data was analyzed for variables such as age, gender, symptoms and signs. The results were compiled using SPSS v.16. Variables are described as mean  $\pm$  standard deviation. The frequency was described as the percentages in each group. Response to treatment was measured by paired Student's t-test with 95% confidence intervals.

**RESULTS:**

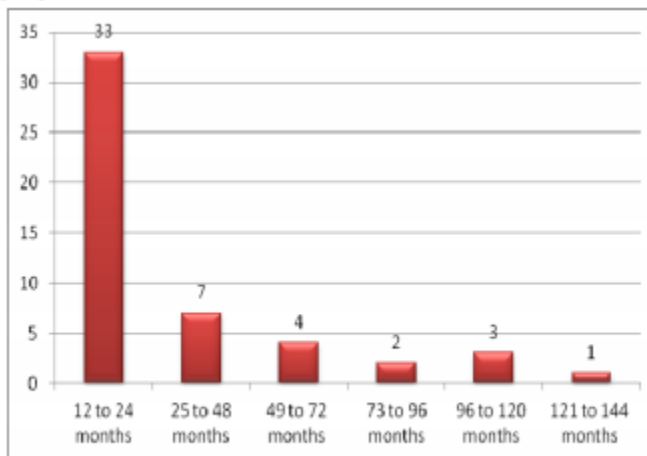
A total of 50 patients presented to the pediatric emergency room with symptoms of acute watery diarrhea. The mean age was  $33.48 \pm 34.42$  months. The age range of the selected population was 6 to 132 months. The mean body weight of the patients was  $6.46 \pm 5.45$  kg. The weight range of patients is 4.2 to 30 kg. Of the total study population of 50 people, 22 were men and the rest were women. The most frequently reported complaint was watery diarrhea (100%). The mean duration of diarrhea was  $1.45 \pm 1.1$  days. Out of the entire study population, 78.0% (n = 39) had accompanying vomiting as symptoms of ailments. Pyrexia was also one of the main complaints in 44.0% (n = 22) of patients. 24.0% (n = 12) also suffered from abdominal pain. Mild dehydration occurred in 44.0% of patients (n = 22), while 12.0% (n = 6) had severe dehydration. A stool test was performed on the entire study population to confirm the presence of *Giardia* *Lambia*, and 90.0% (n = 45) of the study population had *Giardia* *lamblia* cysts / ova in their feces. *Giardia* *lamblia* was tested for stool in 96.0% (n = 48) of patients. In addition, a test for *Giardia* antigen was also performed in the study population and 100% of patients had the *Giardia* antigen present. The patient was orally administered nitazoxanide at a dose of 10 mg / kg / day twice a day for three days and repeated stool testing. Of the total population studied, 86.0% (n = 43) of patients were negative for *Giardia* oocytes / cysts, however the remaining six patients had a *Giardia* cyst / cyst in the stool. The *Giardia* antigen was negative in 96.0% (n = 48) of the patients in the control stool test. Student's t-test was used on the

results of the stool test of the study population before and after treatment with a confidence interval of 95%, and the p-value was <0.0001, which was statistically significant, which proves that

Nitazoxanide eliminated *Giardia lamblia* from the study population and after treatment. In the test no trophozoite, egg, cyst or lamblia antigen was found in 98.0% of patients.



**Fig 1: Presenting complaints in study population**



**Fig 2: Age wise prevalence of the Giardiasis in**

### DISCUSSION:

Diarrhea is one of the leading causes of death in children worldwide. Children with a single episode of mild to severe (MSD) diarrhea had an almost 8.5-fold increased risk of death over the two-month follow-up period compared with children in the control group without MSD [9-11]. A large study of around 22,000 children in a developing country found that 61% of deaths occurred more than one week after MSD was diagnosed, when children may no longer be in care. This study also identified 40 pathogens responsible for mild to severe diarrhea in children under 5 years of age. Walker et al estimated that 15% of the estimated 8.8 million deaths in children under the age of 5 were due to diarrhea. This study found that Pakistan, with an estimated 465,000 child deaths per year in 2008, is the fourth largest contributor to the

global child mortality pie, with 5% or 1 in 20 child deaths [12-13]. The severity of diarrheal disease in Pakistan has been shown to have a huge impact on children's survival due to the acute and chronic complications of diarrhea. *Giardia lamblia* (intestinalis) is not a common pathogen of diarrhea infection among children in developed countries and has been found to be around 2–5%, but is up to 20–30% in developing countries. Various treatment regimens are available to treat *Giardia lamblia* infection. The Centers for Disease Control and Prevention recommends tinidazole, metronidazole, quinacrine, albendazole, or nitazoxanide for the treatment of lamblia; however, there are no specific guidelines to favor one or the other treatment. Stanford's guidelines recommend a single dose of tinidazole or nitazoxanide for three days to treat

Giardiasis [14]. This study was undertaken to test the effectiveness of nitazoxanide treatment in children suffering from Giardiasis. Our test population consists of 22 men and 28 women. It seems that the incidence of lamblia-induced diarrhea in the study population is higher in women (44.0% of men and 56.0% of women). On the other hand, a study by Younas et al. Showed the advantage of men in the studied population. A possible reason for this difference may be the lower number of patients in our study (n = 50) compared to the study by Younas et al. (N = 239). In the studied population, the distribution of the age vice was also noted, and it was found that approximately 68% of patients were under 2 years of age. In a study by Mehmood et al. 72% of patients were under the age of 5. If we divide our study population in a similar way into more and less than 5 years, 82% of our study population will be less than 5 years old. This higher prevalence has also been reported in many other published studies from developing countries. Various studies have found nitazoxanide to be effective in treating gastrointestinal infections. Ortiz and all compared the effectiveness of the 3-day nitazoxanide treatment regimen versus the 5-day metronidazole treatment regimen for glial diarrhea in children and concluded that nitazoxamide was well tolerated, more effective and had fewer side effects. In another double-blind, randomized, controlled trial, Nitazoxanide was as effective as metronidazole in children with lamblia. Nitazoxanide has been compared with various treatment regimens and found to be equally effective in treating and controlling symptoms. One such study by Escobedo et al. Compared nitazoxanide with tinidazole and found that the frequency of parasitological cures with tinidazole was higher than with nitazoxanide (90.5% vs. 78.4%; P <0.05). However, both drugs were well accepted and well tolerated, with only mild, transient and self-limiting side effects reported. The author stated that "although apparently less effective than tinidazole, nitazoxanide remains a good candidate for the treatment of children with G. lamblia infection." It should also be noted that nitazoxanide eliminated trophozoite and oocytes / cysts in 86.0% of patients and the lamblia antigen in 98.0% of patients was negative. Ortiz et al. In their study showed that in 71% of the studied population, oocytes and cysts became negative after treatment with nitazoxanide. Our study, compared to that of Ortiz et al., Shows better results, possibly due to the difference in dosing schedule in both studies. Ortix et al. Used a fixed dose regimen and administered 5 ml of suspension at 1-4 years of age and 10 ml at 4-11 years of age. For comparison, the dose used depends on the patient's weight. This optimal dosing regimen may result in increased

efficacy in our study population. Moreover, our results confirm the lamblia antigen, which is a more sensitive and specific test compared to the identification of oocytes / cyst in stool examination<sup>15</sup>. The lamblia antigen in our study population became negative in 96.0% of patients, which confirms the high efficacy of nitazoxanide in the treatment of children with lamblia-induced diarrhea. The study population was also analyzed and found that 66.0% (N = 33) of the population were under 2 years of age. The age distribution of the patient population is shown in Figure 2.

### CONCLUSION:

Acute and chronic diarrhea are a serious cause of increased morbidity and mortality in the pediatric population in Pakistan. Timely treatment not only prevents short- and long-term complications, but also reduces mortality from diarrhea. Nitazoxanide has been recognized worldwide as a very effective agent for treating diarrhea caused by giardia lamblia. The study conducted on our patient cohort in Pakistan mirrors the results published worldwide.

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