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ORIGINAL ARTICLE

To compare the efficacy of 3 days treatment with Nitazoxanide vs 5 days treatment with Metronidazole in treating children with diarrhea caused by Giardia-lamblia.

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ABSTRACT… Objective: To compare the efficacy of 3 days treatment with Nitazoxanide vs 5 days treatment with Metronidazole in treating children with diarrhea caused by Giardia-lamblia. **Study Design:** Randomized Controlled Trial Study. **Setting:** Department of Pediatric, Women & Children Hospital MTI Bannu. **Period:** December 15, 2019 to May 15, 2020. **Material & Methods:** All 230 children meeting inclusion criteria were enrolled in the study through OPD or emergency. Written informed consent was taken and questionnaire was filled from parents. Complete history and physical examination were done for all included children upon arrival. The patients were divided into two groups. All the children were randomly assigned to either group by lottery method. Group-A was the experimental group and had received Nitazoxanide. Group-B was the control group and had received Metronidazole. The children had received 15 mg/kg/day of Nitazoxanide twice daily for 3 days; or 30 mg/kg/day of Metronidazole thrice daily for 5 days as per group. On follow-up patients were assessed for clinical improvement that is for resolution of diarrhea & Stool sample was collected for the presence of Giardia cysts or trophozoites. **Results:** Two groups were analyzed after two days of completion of therapy as in Group-A 104 children had resolution of diarrhea while 11 didn't had resolution. Whereas in Group-B 107 children had resolution of diarrhea while 8 children didn't had resolution. **Conclusion:** Nitazoxanide (90%) & Metronidazole (92%) were almost equally effective in treating diarrhea caused by Giardia-lamblia.

Key words: Children, Diarrhea, Giardia-lamblia, Metronidazole, Nitazoxanide.

INTRODUCTION

Giardiasis is a main diarrheal illness found across the globe. The Giardia intestinalis (formerly recognized as G lamblia), its causal organism, is frequently known intestinal organism in US and is a frequent protozoan identified globally.[1,2,3,4] Infection is greater in kids as compared to grownups.[5,6]

This organism could initiate acute or chronic diarrheal disease or asymptomatic colonization. The parasite has been isolated in Eighty percent of untreated water sources from ponds, rivers, and lakes and also in Fifteen Percent of filtered water sources.[7,8] In unindustrialized states it is a frequent etiology of growth delay and long-lasting diarrhea in kids.

Giardiasis typically signifies contamination between faunae and human beings. It is found in the excreta of rodents, cats and dogs. Rodents could be a significant pool reservoir for this protozoan.[9,10,11] Additional species include G agilis in amphibians; G psittaci and G ardeae in flying organism; G microti and G muris in rodent.[12,13,14]

Giardia types are widespread in parts of biosphere that have underprivileged hygiene. In underdeveloped states, this illness is a significant reason for illness. Food-borne and Water-borne epidemics are frequent. Ten Giardia cysts could be adequate to cause infection, giardiasis is frequent in daycare center and institutionalized patients in advanced states. It is mainly important organism for individuals having undernourishment, cystic

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fibrosis, or immunodeficiencies.

Immunocompromised persons, Some homosexual people and travelers to endemic areas, are included in high-risk groups for giardiasis. In symptomatic homosexual people the cyst transmission ratio of twenty percent has been described.[15,9]

How Giardia causes intestinal malabsorption & diarrhea is perhaps multifactorial and is not yet completely explained.[16] The straight damage is an improbable reason of the wide lessening in microvilli superficial area, the reduction in activities of disaccharidase, and extra marked abnormalities in the architecture of villi which are observed in giardiasis.[17]

The structure of the organism's cyst is oval shaped with smooth wall, gaging 7-10 μm wide and 8-12 μm long. As it ripens, nucleoli divides and prepare cyst to proclamation of two trophozoites after excystation. Trophozoites may be seen in the intestine within minutes once the human is infected.[18]

Obvious or sensible incomplete atrophic changes in villi of the small intestine may be seen in tissue segments from those peoples who are infected but have no symptoms. Moreover unsettling the epithelium, changes in the lumen of intestine could pay to development of malabsorption and diarrhea.[19,5]

Weight loss can be major side effect due to various grades of malabsorption of fat-soluble vitamins (eg, vitamins E and A) & sugars (eg, Disaccharides, Xylose). The association between symptoms and signs and histologic changes due to giardiasis is poor.[20,10]

MATERIAL AND METHODS

This Randomized controlled trial study was carried out in Pediatric Department of Women & Children Teaching Hospital, Bannu KPK, Pakistan for 6 months duration from December 15, 2019 to May 15, 2020. Sample size was 115 in each group using 78.4% efficacy of nitazoxanide and 92% efficacy of metronidazole in treating diarrhea due to giardia lamblia in kids with Confidence interval of 95% with power of test 90% and level of significance 5% by using WHO sample size calculator. The selection was through non-probability consecutive sampling.

Inclusion Criteria

1. Children aged 2 to 11 years.
2. Diarrhea of any duration and cysts or trophozoites of G. lamblia in their stool sample.

Exclusion Criteria

1. Age less than 2 yrs or more than 11 years.
2. Children with bloody diarrhea.
3. Children with stool specimen showing other parasites. e.g E. histolytica or H-Nana.

Data Collection Procedure

This study was carried out after endorsement from ethical and research committee (47-A/DIR&MJ/BMC/2019). All children meeting the inclusion criteria were enrolled in the study through OPD and / or emergency. Informed consent and filled questionnaire were filled from parents of all included children and they were elucidated the aim of study and was counseled regarding safety profile of drugs. All the included children had detailed history and underwent physical examination upon arrival. Upon admission, the patients were divided into two groups. All the children were randomly assigned to either group by lottery method. Group A was the experimental group and had received nitazoxanide. Group B was the control group and had received metronidazole.

The children had received 15 mg per kg per day of nitazoxanide twice daily for 3 days; or 30 mg per kg per day of metronidazole thrice daily for 5 days as per group. Patients were instructed to take their medication with food. Patients were advised to have follow up on day 2 following completion of therapy for complete physical examination at which time they were assessed for clinical improvement that is for resolution of diarrhea. Stool sample was collected on day 2 following the completion of therapy for the presence of giardia cysts or trophozoites using

light microscopy.

Data Analysis

Data was entered and analyzed in SPSS version 10. Mean + SD was calculated for numerical variables like age. Frequencies and percentages were calculated for definite variables like gender and effectiveness. Effectiveness in both groups was stratified amongst gender and age. To determine the result modifications. Chi square test was applied to link the efficacy between the two groups. P-value <0.05 was well thought-out as significant. All the results were presented as tables and graphs.

RESULTS

The study was steered at Pediatric Department of Women & Children Teaching Hospital in which a total of 230 (115 in each group) patients were observed to associate the efficacy of 3 days treatment with nitazoxanide vs 5 days treatment with metronidazole in treating children with diarrhea caused by Giardia lamblia and the results were analyzed as:

Age dispersal amid two groups was analyzed as in Group A (Nitazoxanide) 48 children were in age range 2-5 years, 42 children were in age range 6-8 years and 25 children were in age range 9-11 years. Mean age was 6 years with SD ± 1.26. Whereas in Group B (metronidazole) 45 children were in age range 2-5 years, 41 children were in age range 6-8 years and 29 children were in age range 9-11 years. Mean age was 7 years with SD ± 2.11.)

Frequency of diarrhea among two groups was analyzed as in Group A (Nitazoxanide) 52 children had diarrhea < 10 stools per 24 hours and 63 children had diarrhea > 10 stools per 24 hours. Whereas in Group B (Metronidazole) 46 children had diarrhea < 10 stools per 24 hours and 69 children had diarrhea > 10 stools per 24 hours. (as shown in Table-I)

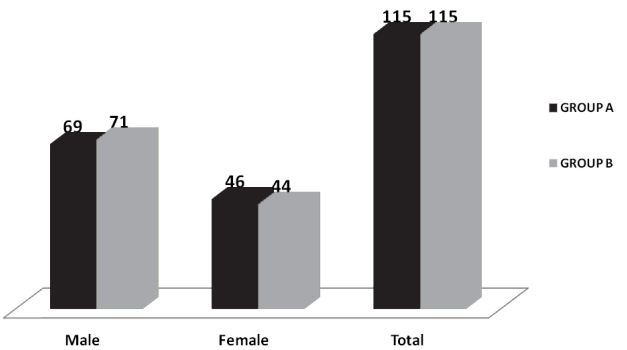
Gender distribution among two groups was analyzed as in Group A (nitazoxanide) 69 children were male and 46 children were female. Whereas in Group B (metronidazole) 71 children were male and 44 children were female. (as shown in Figure-1)

Resolution of diarrhea among two groups was analyzed after two days of completion of therapy as in Group A (nitazoxanide) 104 children had resolution of diarrhea while 11 children did not have resolution of diarrhea. Whereas in Group B (Metronidazole) 107 children had resolution of diarrhea while 8 children did not have resolution of diarrhea. (as shown in Table-II)

Giardia cyst among two groups was analyzed after two days completion of therapy as in Group A (Nitazoxanide) Giardia cyst was negative in 104 children and was positive in 11 children. Whereas in Group B (Metronidazole) Giardia cyst was negative in 107 children and was positive in 8 children.

Efficacy among two groups was analyzed as Nitazoxanide was effective in 104 children while Metronidazole was effective in 107 children. Stratification of efficacy with gender and age is given in Table-III,IV and V.

Figure. 01: Gender distribution



Frequency of Passing Stools Per 24 hrs	Group A	Group B
<10 per 24 hours	52	46
> 10 per 24hours	63	69
Total	115	115

Table-I. Frequency of diarrhea (n=230)

Resolution of Diarrhea	Group A	Group B
Yes	104	107
No	11	8
Total	115	115

Table-II. Resolution of diarrhea (n=230)

Efficacy	Group A	Group B
Effective	104	107
Not Effective	11	8
Total	115	115

Table-III. Efficacy (n=230)

Age	Efficacy	Nitazoxa-nide	Metronida-zole
2-5 years	Effective	43	42
	Not effective	5	4
Total		48	46
6-8 years	Effective	37	37
	Not effective	4	3
Total		41	40
9-11 years	Effective	24	27
	Not effective	2	2
Total		26	29

Table-IV. Stratification of efficacy with age

Gender	Efficacy	Nitazox-anide	Metroni-dazole	P-Value
Male	Effective	63	65	0.58
	Not effective	6	7	
Total		69	72	
Female	Effective	41	40	0.61
	Not effective	5	3	
Total		46	43	

Table-V. Stratification of efficacy with gender

DISSCUSSION

In developing countries, the dispersal of different varients of protozoal infections including G. lamblia, which is recognized as G. intestinalis, is a global spectacle than in industrialized states. Contamination from G. lamblia remains the major water-borne diarrhea-causing illness among people from all ages and people from all professions, either when they drink unintentionally or ingest water from polluted or untreated sources. One of the high-risk groups are children particularly those in daycare settings, orphanages and primary schools. In developing countries the occurrence of Giardia has been described 20-30% of the residents.

Our study shows that mean age in Group A (nitazoxanide) was 6 years with SD ± 1.26. Whereas mean age in Group B (metronidazole) was 7 years with SD ± 2.11. In Group A (nitazoxanide) 69 children were male and 46 children were female. Whereas in Group B (metronidazole) 72 children were male and 43 children were female. Out of these nitazoxanide was effective in 90% children while metronidazole was effective in 92% children.

For people with symptomatic giardiasis effective therapies including quinacrine, furazolidone, paromomycin, nitazoxanide, tinidazole, and metronidazole are available. The metronidazole is highly effective drug available for treating giardiasis. In literature the reported efficacy of metronidazole in treating patients with giardiasis is from 75%-100%, while the efficacy of nitazoxanide in giardiasis is 78.4%.

Our study confirmed the safety and efficacy of nitazoxanide as a 3-day treatment of giardiasis in kids. The 5-days treatment with metronidazole was equivalent to 3-days treatment regimen of nitazoxanide.

CONCLUSION

Our study concludes that Nitazoxanide (90%) and Metronidazole (92%) were almost equally effective in treating diarrhea caused by Giardia-lamblia.

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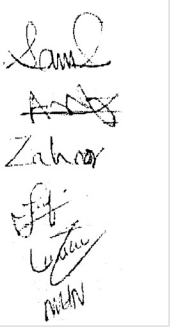
1	Sami ul haq	1st Author	
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