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THE EFFECTIVENESS OF DIOSMECTITE IN HOSPITALIZED CHILDREN WITH ACUTE WATERY DIARRHEA AND DEHYDRATION

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Abstract:

Aim: *To determine the effect of diosmectite on the reduction of diarrhea duration compared to placebo.*

Method and Material: *This randomized, open-label clinical study was conducted at Pediatric Unit-I of Sir Ganga Ram Hospital Lahore for one-year duration from December 2019 to December 2020. Children 6-24 months of age taken with acute watery diarrhea ≤ 72 hours but ≥ 24 hours and with some dehydration / severe dehydration. Patients were assigned either group A (Diosmectite group) or group B (placebo group) by lottery method. After initial rehydration, Diosmectite at a dose of 1 gram in children under 12 months of age and 1.5 grams in children aged 12-24 months three times a day after dilution in water or other semi-solid food together with zinc sulphate was orally administered 5 days to group A, while group B was given a placebo (oral zinc sulfate). All study participants were followed from initiation of therapy to normalization, defined as passing the first pre-diarrheal stool (hours) and for a maximum of six days after starting therapy in the absence of a pre-diarrheal stool.*

Results: *There were 103 children in each group who were initially recruited into the study. 99 (96.12%) children in the diosmectite group and 97 (94.17%) children in the placebo group completed the study. Both groups had similar characteristics. There were 6 of 99 cases in the diosmectite group and 7 of 97 cases in the placebo group in which no pre-diarrheal stool was expelled at the end of six days after initiation of treatment (p-value 0.782). The time required to pass the first pre-diarrheal stool (hours) for the remaining 93 diosmectites was 58.935 ± 30.482, while the transit time for the first pre-diarrheal stool (hours) for the remaining 90 placebo patients was 76.511 ± 35.323 (p-value 0.0004). This showed that the drug was moderately effective compared to the placebo.*

Conclusion: *Smectite may be a useful additive to rehydration therapy in the treatment of acute watery diarrhea in children, but cost-effective research is needed before its routine use is recommended.*

Key words: *randomized clinical trial with acute diarrhea, drug efficacy.*

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INTRODUCTION:

Diarrhea is the second most common cause of death in young children, killing more than 1.5 million children under the age of 5 each year. It is estimated that there are approximately 4 billion cases of diarrhea in children under the age of 5 each year. Oral hydration is the mainstay of treatment of acute diarrhea, but has no effect on the duration of the diarrhea or the amount of fluid loss. Diarrhea medication prescribing practices are very common among physicians in Pakistan. The ideal drug for acute diarrhea is one that reduces intestinal fluid loss, is effective regardless of etiology, is administered once, tastes good, does not interfere with nutrient absorption, has no side effects, is widely available, is stable (does not need refrigeration) and cheap, but unfortunately such a drug does not exist. The main problem with most drugs is the lack of evidence that they work, and some, such as loperamide, can even cause life-threatening side effects. Diosmectite is a natural magnesium silicate clay with a lamellar, non-fibrous crystal structure that gives it strong adsorbing properties and is often used to treat acute diarrhea. Its mechanisms of action are not yet fully understood, but are likely to be multiple. Diosmectite soothes inflammation, modifies the rheological properties of mucus, inhibits mucolysis and adsorbs bacteria, bacterial enterotoxins, viruses and other potentially diarrheal substances. As it is not absorbed from the gastrointestinal tract, it does not cause any systemic side effects. A meta-analysis by Szajewska et al. 2006 showed that diosmectite was associated with a moderate reduction in the duration of diarrhea in children with acute infectious gastroenteritis. International studies have shown that the duration of diarrhea in children treated with diosmectite was 42-96 hours and 61.3-119 hours in children receiving placebo. The WHO does not yet recommend the use of this drug for the treatment of diarrhea under five years of age. Diarrhea is a very common problem in children in Pakistan, but so far research has been conducted on this drug in any part of Pakistan. The aim of the study is to determine the effect of diosmectite on the reduction of the duration of diarrhea compared to placebo.

MATERIALS AND METHODS:

This randomized, open-label clinical study was conducted at Pediatric Unit-I of Sir Ganga Ram Hospital Lahore for one-year duration from December 2019 to December 2020. Children 6-24 months of age receiving severe watery diarrhea (passing three or more loose stools within 24 hours) time duration ≤ 72 hours but ≥ 24 hours and some dehydration (if the child has two or more of the four symptoms i.e. irritation, sunken eyes, increased desire to drink, the skin recedes slowly) or severe dehydration (if the child has two or more of the four symptoms, i.e. lethargy, sunken eyes, inability to drink, skin receding very slowly15). Children with abdominal distension, bloody diarrhea, history of taking any antibacterial / anti-diarrheal drugs in the past 72 hours, severe protein energy malnutrition (defined as body weight <60% of the reference age for age) and clinical signs of systemic infection from the study. After informed consent of parents / guardians, patients were assigned to group A (Diosmectite group) or group B (placebo group) by lottery. Their demographic data (age, gender) as well as a short history, weight and degree of dehydration were recorded. After pre-hydration with intravenous Ringer's lactate / oral rehydration salt, they were treated according to the WHO protocol for the management of acute watery diarrhea15. Diosmectite at a dose of 1 gram in children under 12 months of age and 1.5 grams in children aged 12-24 months three times a day, diluted in water or other semi-solid food together with zinc sulphate, was administered orally for 5 days in group A while group B was given a placebo (oral zinc sulfate). All study participants were followed from initiation of therapy to normalization, defined as passing the first pre-diarrheal stool (hours) and up to 6 days after starting therapy in the absence of a pre-diarrheal stool (treatment failure). Mean, range, and standard deviation (SD) were calculated for quantitative data. The Fisher test was used for qualitative comparison and the t-test for comparing quantitative data. A value of $p < 0.5$ was considered significant.

RESULTS:

There were 103 children in each group and initially recruited into the study. 4 cases in the diosmectite group (Group A) and 6 cases in the placebo group (Group B) left the study before completion. As a result, 99 (96.12%) children from the diosmectite group and 97 (94.17%) children from the placebo group completed the study. Table I

TABLE I: Comparison of Characteristics of the Children of Both Groups

Characteristic	Diosmectite Gp (Group A) (n= 99)	Placebo Gp (Group B) (n= 97)	P value
Sex Male (%)	52 (52.52%)	57 (58.76%)	0.392
Age (months)			
Mean±SD	11.081±5.104	10.753±5.498	0.665
Range	6-23 mo	6-23 mo	
Weight (Kg)			
Mean±SD	8.179 ±1.586	8.379±1.719	0.397
Range	5.8-11.9	5.7-13.7	
Breast fed	55(55.55)	59 (60.82%)	0.472
Duration of diarrhea before admission (hours)			
Mean±SD	43.515±17.157	41.268±17.048	0.359
Range	24-72	24-72	
Frequency of stool in the last 24 hours before admission			
Mean±SD	8.62±2.37	8.47±2.22	0.64
Range	5-14	5-13	
Children with severe Dehydration at the time of admission	27(27.27%)	23(23.71%)	0.624

compares the characteristics of children from both groups who completed the study. There were 6 of 99 cases in the diosmectite group and 7 of 97 cases in the placebo group in which no pre-diarrheal stool was expelled at the end of six days after initiation of treatment (p-value 0.782). The time required to pass the first pre-diarrheal stool (hours) for the remaining 93 diosmectites was 58.935 ± 30.482, while the transit time for the first pre-diarrheal stool (hours) for the remaining 90 placebo patients was 76.511 ± 35.323 (p-value 0.0004). This showed that the drug was moderately effective compared to the placebo.

DISCUSSION:

The study showed that the time from the initiation of therapy to the passage of the first pre-diarrheal stool was significantly shorter in children treated with diosmectite compared to placebo (58.93 ± 30.48 versus 76.51 ± 35.32 hours). Other studies have also found similar results. A study by Narkeviciute et al. From Lithuania showed a significantly shorter duration of diarrhea in the group of diosmectites (42.3 ± 24.7 vs 61.8 ± 33.9). Vivatvakin et al. Thailand found a significantly shorter duration of diarrhea in the diosmectite group (43.3 ± 25.1 compared with 84.7 ± 48.5). Madkour et al. From Egypt showed a significantly shorter duration of diarrhea in the group of diosmectites (54.1 ± 2.35 versus 72.9 ± 1.98). Mujawar et al. 2012 from India showed that the mean time needed to resolve diarrhea was significantly shorter in the treated group (64.34 ± 14.86 hours) compared to the control group (82.37 ± 21.43 hours). Guarino et al. From Italy showed a significantly shorter duration of diarrhea in the treated group (96 ± 21 compared with 119 ± 23). Lexomboon et al. From Thailand showed that the cure rate of diarrhea after 72 hours was significantly higher in the treatment group (71% vs 34%). In our study, children aged 6-24 months were used, and Narkeviciute et al. Children aged 6-48 months, Vivatvakin et al. Aged 1-24 months, Madkour et al. Aged 3-24 months, Mujawar et al. . 2012 aged 2-5 years. , Guarino et al. 3 months to 5 years and Lexomboon et al. 1-24 months. This study has some

limitations. This is a hospital study and only looked at children who were dehydrated. There has been no further research into the cause of diarrhea. This study does not concern the profitability analysis.

CONCLUSION:

Smectite may be a useful adjunct to rehydration therapy in the treatment of acute watery diarrhea in children. Before recommending routine pharmacological treatment with smectite, a cost-effectiveness analysis should be performed.

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