EFFICACY OF ORAL ZINC AND PROBIOTIC ON ACUTE DIARRHEA IN INFANCY

By

Mostafa Abd El-Azeem Hassan, Mohammed Mahmoud Sayed Younis, Hadeer Abd El-Rahman Mohamed

Department of Pediatrics, Faculty of Medicine, Al-Azhar University (Assuit)

ABSTRACT

Background: *Diarrheal disease in childhood account for a large proportion (18%) of childhood deaths, with an estimated 1.5 million deaths per year globally, making it the second most common cause of child deaths worldwide. The World Health Organization (WHO) and UNICEF estimate that almost 2.5 billion episodes of diarrhea occur annually in children <5 year of age in developing countries, with more than80% of the episodes occurring in Africa and South Asia (46% and 38%, respectively).*

Objective: *To compare effect of zinc and probiotic alone or in combination in pediatric acute diarrhea (on the basis of decrease in frequency of stool and change of consistency).*

Patients and Method: *This comparative analytical study that was conducted at Sohag Teaching Hospital from 1st of March 2020 to 1st November 2020 on 150 children aged between six months to ten years was presented with acute diarrhea for 24 hours. There were divided into groups classified by simple random method into three groups:*

Group I: *included 50 patients received oral zinc for 5 days as per WHO protocol along with ORS and/ or IV fluids if required (20mg/day per oral).*

Group II: *included 50 patients received probiotic therapy orally for 5 days along with ORS and /or IV fluid if required (Saccharomyces boulardii – 1sachet (250mg = 5billion CFU). 1 sachet dissolved in 4tsp of water, to be given twice daily for five days.).*

Group III: *included 50 patients received combination zinc and probiotic for 5 days along with ORS and /or IV fluid if required.*

All studied groups subjected to complete history, clinical and laboratory examination.

Results: *In the current study we found that frequency of stool after treatment were decreased in all groups and more lower frequency founded in combined group but with insignificant differences In the current study we found that as regard diarrhea duration after treatment there were more decrease in duration in combined groups versus zinc and probiotic but with no significant differences In the current study we found that there was increase in weight after treatment with more increase in combined group but with insignificant differences In the current study we found that there was lower* *hospital stay in combined group versus zinc and probiotic group but with insignificant differences*

Conclusion: *In children with acute nonbacterial watery diarrhea, Zinc or Probiotic supplementation reduced the duration of diarrhea. In our study children receiving combined therapy were more likely to be diarrhea-free after five days, with better outcomes along with improvement in consistency and reducing the duration of hospital stay. We conclude that, combination of probiotics & zinc therapy is more effective in reducing the severity of acute diarrhea.*

Keywords: *Zinc, Probiotic, Diarrhea.*

INTRODUCTION

Diarrhea is one of the main causes of childhood disability and death worldwide, resulting in 5–10 million deaths annually. Diarrhea causes millions of deaths in Asia, Africa, and Latin America in the age group of 0–4 years **(Kliegman & Nelson, 2016)**.

The risk factors include contaminated water, poor health, or conditions such as malnutrition and factors like high-level contact with pathogens and reduced breast milk safety **(Ahmed et al., 2014)**.

Diarrhea is one of the most common clinical signs of infection associated with the lower parts of the digestive tract, and is defined as a watery stool occurring at least 3 times in a 24-hour period. Diarrhea can be divided into acute and chronic categories, acute diarrhea is the most severe type caused by viral, bacterial, fungal, and parasitic infections. Rotaviruses and Escherichia coli are the main causes of diarrhea **(Andrade et al., 2014)**.

According to the guidelines of World Health Organization, antibacterial, antiamoebic and antidiarrhoeal agents have a little role in the management of diarrhea **(Rehan et al., 2003)**.

In developing countries, duration and severity of diarrhoea is more among younger age groups with malnutrition and impaired immune status which may be associated with zinc deficiency. Diarrhoea is more common in children with zinc deficiency and responds quickly to zinc supplementation **(Zulfiqar et al., 2000)**.

World Health Organization incorporated oral rehydration solution (ORS) in the diarrhoea management guidelines thereby decreasing deaths in children by a great proportion5. Still acute gastroenteritis poses alarming contribution to paediatric mortality rate in spite of gains with oral rehydration therapy (ORS). Reason for this may be that ORS though improves the hydration status it has no effect on modulation of diarrheal episodes and their total extent, so other modalities of treatment to augment the role of ORS have been desired. Many advances have been made in this regard with the inclusion of zinc and probiotics to the pediatric diarrhea management guidelines **(Lazzerini & Ronfani, 2012)**.

The role of zinc in human nutrition has increased significantly. It is one of the micronutrients that are very effective in human health, especially in children **(Mitra et al., 2012)**. Several reports correlate diarrhea with abnormal zinc levels. The duration of diarrhea depends on several factors, among which age-related weight loss and reduced cellular immunity are established **(Walker et al., 2013)**.

Zinc therapy improves the absorption of water and electrolytes from the intestine, stimulates epithelialization, increases the level of intestinal enzymes, and enhances the immune response, resulting in rapid clearance of diarrhea.

Zinc is a fundamental part of nutrition which prevents oxidative damage to the cell. It does not get stored in the body so its deficiency may develop in diarrhea affected children due to losses from the damaged gut **(Berni et al., 2011)**.

Therapeutics of probiotics has been studied in different trials in which the beneficial use in pediatric acute diarrhea is prominent, so European Society for Pediatric Infectious Diseases has incorporated use of probiotics in the guidelines for management of gastroenteritis in children **(Dinliyici et al., 2015)**.

Probiotics are vital microorganisms, which support the intestinal flora, and reduce bacterial invasion of the intestinal wall. Thus, they prevent the growth of pathogens; enhance the production of antimicrobial substances and changes in the acidity of the intestinal environment, thereby minimizing the chances of infection by producing short-chain fatty acids **(Gibson et al., 2017)**.

Probiotics, such as Lactobacillus acidophilus and Enterococcus faecium SF68, are used to prevent or treat diarrhea. Probiotics have also been evaluated for the control of rotaviral diarrhea in children and travelers' diarrhea. Probiotics are important in controlling and reducing the symptoms of acute gastroenteritis, poisoning, irritable bowel syndrome and food allergies **(Gill & Prasad, 2008)**.

Aims of the Work

To study efficiency of Zinc and Probiotic alone or in combination in pediatric acute diarrhea (on the basis of decrease in frequency of stool and change of consistency).

MATERIALS AND METHODS

Type of study: Comparative analytical study.

Sample size: 150 children aged between 6 months to 10 years presenting with acute diarrhea for 24 hours divided by simple randomization into three groups.

Group I: 50 patients received zinc therapy orally for five days as per WHO protocol along with ORS and/ or IV fluids if required (20mg/day per oral)

Group II: 50 patients received probiotic therapy orally for five days along with ORS and /or IV fluid if required (Saccharomyces boulardii – 1sachet (250mg = 5billion CFU). 1 sachet dissolved in 4tsp of water, to be given twice daily for five days).

Group III: 50 patients received combination zinc and probiotics for five days along with ORS and /or IV fluid if required.

Study population: The included study population was children with acute diarrhea in Suhag teaching hospital.

Inclusion criteria: Age; from 6 months to 10 years of age presenting with acute diarrhea for 24 hours having stool frequency more than five semi liquid stools per day, both gender were included.

Exclusion criteria: Severely dehydrated children. Presence of blood in stool. Uses of antibiotic and probiotics in last week. RBCs in stool. Bacterial diarrhea. Presence of other chronic diseases. Sever under nutrition. Persistent and chronic diarrhea more than 14 days.

Method:

The clinical data of patients fulfilling the inclusion criteria were evaluated as follow:

1. Clinical data:

Careful history was taken from patients relatives including age, diarrheal details (onset, frequency, consistency, duration and associated symptoms vomiting, fever). History of antibiotic or probiotic intake in last week.

Clinical examination: A thorough clinical examination was done for all children including weight, temperature, pulse rate, and respiratory rate. Status of vomiting, dehydration, stool frequency, stool consistency, and mean duration of diarrhea with mean duration of hospital stay was studied and compared in all the three groups. Those who were well hydrated, improved consistency and had well-formed stools were discharged accordingly and were not included in the study thereafter.

2. Laboratory investigation:

Complete blood count Celltac MEK6510K.

C reactive protein Latex agglutination method using SPINREACT vial lot no #CR341B.

Stool analysis Olympus light microscopy.

Monitoring of the duration and frequency of diarrhea was done during hospitalization on daily follow up, number of stool passed with consistency was recorded and sign of dehydration was assessed. Presence of fever, vomiting toxicity and side effects relating to the administration of zinc and probiotic were also observed. We defined recovery from diarrhea as stool passed <3 times with normal consistency. Home monitoring was done by contacting the parents or caregiver by mobile phone.

Ethical consideration:

1. A written informed consent was obtained from parents or the legal guardians before the study.
2. An approval by the local ethical committee was obtained before the study.
3. The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.
4. All the data of the patients and results of the study are confidential & the patients have the right to keep it.
5. The authors received no financial support for the research, authorship and/ or publications of this article.

Statistical analysis of the data:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Significance of the obtained results was judged at the 5% level.

The used tests were:

1. **Chi-square test:** For categorical variables, to compare between different groups.
2. **Student t-test:** For normally distributed quantitative variables, to compare between two studied groups.
3. **Mann Whitney test:** For abnormally distributed quantitative variables, to compare between two studied groups.

RESULTS

Table (1): Comparison between the three studied groups regarding to demographic data

	Zinc (Group I) (n = 50)		Probiotic (Group II) (n = 50)		Combined (Group III) (n = 50)		Test of sig.	p
	No.	**%**	**No.**	**%**	**No.**	**%**		
Sex								
Male	25	50.0	20	40.0	20	40.0	χ^2=1.357	0.507
Female	25	50.0	30	60.0	30	60.0		
Age (months)								
Mean ± SD.	20.90 ± 10.12		20.80 ± 9.95		21.40 ± 9.39		U=1250.0	1.000
Residence								
Rural	20	40.0	15	30.0	10	20.0	χ^2=4.762	0.092
Urban	30	60.0	35	70.0	40	80.0		
Mean weight (Kg)								
Mean ± SD.	9.31 ± 1.69		9.62 ± 1.60		9.60 ± 1.59		t=0.942	0.348

χ2: Chi square test   t: Student t-test, U: Mann Whitney test.
p: p value for comparing between the studied groups.
IQR: Inter quartile range.

This table shows that there were insignificant differences between the three studied groups regarding demographic data.

Table (2): Comparison between the three studied groups regarding to feeding history

Feeding history	Zinc (Group I) (n = 50)		Probiotic (Group II) (n = 50)		Combined (Group III) (n = 50)		χ^2	p
	No.	%	No.	%	No.	%		
Breast feeding only	20	40.0	20	40.0	20	40.0	2.250	0.690
Formula feeding	15	30.0	10	20.0	15	30.0		
Complimentary food	15	30.0	20	40.0	15	30.0		

$\chi 2$: Chi square test
p: p value for comparing between the studied groups

This table shows that there were insignificant differences between the three studied groups regarding feeding history.

Table (3): Comparison between the three studied groups regarding to mean frequency of diarrhea before and after treatment

Mean frequency of diarrhea	Zinc (Group I) (n = 50)	Probiotic (Group II) (n = 50)	Combined (Group III) (n = 50)
Before treatment (times/day) Mean ± SD.	10.90 ± 1.82	11.16 ± 1.99	10.94 ± 1.634
After treatment (times/day) Mean ± SD.	4.74 ± 1.07	4.84 ± 0.817	4.44 ± 0.501
P Value	<0.0008	<0.0001	<0.0001

p: p value for comparing between the studied groups
IQR: Inter quartile range

This table shows that there were significant differences between the studied groups regarding Mean frequency of diarrhea before and after treatment (times/day).

Table (4): Comparison between the three studied groups regarding to mean duration of diarrhea before and after onset of treatment (recovery)

Mean duration of diarrhea (hours)	Zinc (Group I) (n = 50)	Probiotic (Group II) (n = 50)	Combined (Group III) (n = 50)
Before treatment (hours) Mean ± SD.	21.22 ± 4.17	21.10 ± 4.487	20.82 ± 4.217
After treatment recovery (hours) Mean ± SD	12.36 ± 1.8	12.34 ± 1.780	10.96 ± 0.947
P Value	<0.0008	<0.0003	<0.0001

p: p value for comparing between the studied groups
IQR: Inter quartile range

This table shows diarrhea duration after treatment there were more decrease in duration in combined groups versus zinc and probiotic but with significant differences.

Table (5): Comparison between the three studied groups regarding to stool consistency before treatment but after show high significant difference between group three and the other two groups

Stool consistency	Zinc (Group I) (n = 50)		Probiotic (Group II) (n = 50)		Combined (Group III) (n = 50)		χ^2	p
	No.	%	No.	%	No.	%		
Before treatment								
Watery	30	60.0	35	70.0	35	70.0	3.0	0.809
Soft	5	10.0	5	10.0	5	10.0		
Semisolid	10	20.0	5	10.0	5	10.0		
Well-formed	5	10.0	5	10.0	5	10.0		
After treatment								
Watery	10	20.0	10	20.0	0	0.0	21.50*	<0.001*
Soft	0	0.0	0	0.0	0	0.0		
Semisolid	15	30.0	10	20.0	5	10.0		
Well-formed	25	50.0	30	60.0	45	90.0		

$\chi 2$: Chi square test
p: p value for comparing between the studied groups
*: Statistically significant at $p \leq 0.05$

This table shows that there was insignificant differences between the three studied groups as regard before treatment stool consistency but after treatment combined group showed more semisolid and well-formed stool.

Table (6): Comparison between the three studied groups regarding to dehydration and weight gain

Dehydration before treatment (%)	Zinc (Group I) (n = 50)		Probiotic (Group II) (n = 50)		Combined (Group III) (n = 50)		χ^2
	No.	%	No.	%	No.	%	
No dehydration	15	30.0	20	40.0	15	30.0	1.500
Some dehydration	35	70.0	30	60.0	35	70.0	
Dehydration after treatment (%)							
No dehydration	48	99	49	99.5	50	100	
Some dehydration	2	1	1	0.5	0	0	
Mean Weight before and after treatment	**Zinc (n = 50)**		**Probiotic (n = 50)**		**Combined (n = 50)**		
Weight before treatment	9.37 ± 1.65		9.55 ± 1.53		9.5 ± 1.6		
Weight after treatment	9.74 ± 1.68		9.43 ± 1.51		9.7 ± 1.5		
P Value	<0.0005		0.2		0.025		

$\chi 2$: Chi square test
p: p value for comparing between the studied groups

This table shows that there were insignificant differences between the three studied groups regarding dehydration before treatment. There was increase in weight after treatment with more increase in combined group but with insignificant differences

Table (7): Comparison between the three studied groups regarding to hospital stay

Discharge from hospital (hours)	Zinc (Group I) (n = 50)	Probiotic (Group II) (n = 50)	Combined (Group III) (n = 50)	U	p
Min. – Max.	20.0 – 66.0	20.0 – 65.0	20.0 – 40.0	1162.5	0.545
Mean ± SD.	43.40 ± 16.57	42.20 ± 15.87	31.70 ± 7.21		
Median (IQR)	45.0 (25.0 – 60.0)	42.50 (25.0 – 56.0)	32.50 (25.0 – 40.0)		

U: Mann Whitney test
p: p value for comparing between the studied groups
IQR: Inter quartile range

This table shows that there was lower hospital stay in combined group versus zinc and probiotic group but with insignificant differences.

DISCUSSION

In the current study we found that there were insignificant differences between the three studied groups regarding demographic data.

In agreement with our result **Ahmadipour S et al.,** showed that a total of 96 children (50 treated with probiotics and 46 with zinc) were studied. The mean age of the children in PRG group was 11.8±5.95 months and that of the ZRG was 11.15±5.51 months, which was not statistically significant (p=0.586) based on the independent t-test. Also, no significant differences existed between the grounds based on sex distribution **(Ahmadipour et al., 2019)**.

Farhat A et al., also found that Amongst the total study population of 150 patients, male patients predominate with a total of 87 (58%) while 63 (42%) were female; giving male to female ratio 1.38:1. Gender wise, there was no significant difference amongst the patients Moreover, 66 out of 150 (44%) patients were 6-12 months old while 84 (56%) patients were between 12 to 120 months old **(Farhat et al., 2018)**.

In the current study we found that there were insignificant differences between two groups as regard feeding history, nutritional status.

In agreement with our result **Ahmadipour S et al.,** showed that there was insignificant differences between cases received probiotics or zinc as regard type of nutrition **(Ahmadipour et al., 2019)**.

In the current study we found that there were insignificant differences between groups as regard Mean frequency of diarrhea before treatment (times/day).

In consistent with our result **Ahmadipour S et al.,** showed that frequency of bowel habits (p=0.334) in the 2 groups was not statistically significant before the administration of probiotics and zinc supplements **(Ahmadipour et al., 2019)**.

In the current study we found that there was insignificant differences between groups as regard Mean duration of diarrhea before treatment (hours), there was insignificant differences between groups as regard before treatment stool consistency but after treatment combined group showed more semisolid and well-formed stool.

Similar studies conducted by **Billoo et al., Aggarwal et al., and Azim et al.,** also reported that probiotics improved consistency of stool **(Billoo et al., 2006** and **Aggarwal et al., 2014)**.

Htwe et al., shown that stools had a normal consistency on day 3 in 38 (76%) of 50 patients in the probiotic (S. boulardii) group compared with only 12 (24%) of 50 in the control group (P=0.019) **(Htwe et al., 2008)**.

In a study by **Abraham et al.,** the combination of zinc supplements and probiotic therapy was superior to probiotics alone in terms of alleviation of vomiting and diarrhea symptoms in children **(Abraham et al., 2016)**.

In the current study we found that there were insignificant differences between groups as regard dehydration before treatment.

In the current study we found that frequency of stool after treatment were decreased in all groups and more lower frequency founded in combined group but with insignificant differences.

Ahmadipour S et al., showed that the frequency of daily bowel habits in children under each group over time was statistically significant ($p<0.001$). However, the difference in frequency of bowel habits between the 2 groups was not statistically significant ($p=0.824$) **(Ahmadipour et al., 2019)**.

In a randomized controlled trial conducted in India by **Sachdev et al.,** involving infants with watery diarrhea, it was found that the duration of diarrhea and the frequency of bowel habits after zinc therapy were significantly reduced only in patients with severe zinc deficiency, and the results of diarrheal duration were consistent with our study findings **(Sachdev et al., 1988)**.

In a randomized double-blind study conducted in India, 287 boys (3 to 36 months) with a maximum of 72h lapse since the onset of diarrhea, showed significant changes in bowel habits following zinc therapy., which was consistent with our findings **(Bhatnagar et al., 2004)**.

Farhat A et al., showed that It has been shown in this study that by the end of 3rd day, nearly all patients in group C who were given combination of zinc suspension and probiotic showed decrease in frequency to less than three stools/day as well as improvement in consistency of stools. In Group A patients who received oral zinc suspension thirty nine patients responded to monotherapy while eleven patients continued passing watery stools even after 72 hours of starting the therapy. While in Group B patients who were given probiotics alone no significant improvement was seen even after 72 hours of therapy **(Farhat et al., 2018)**.

In the current study we found that as regard diarrhea duration after treatment there were more decrease in duration in combined groups versus zinc and probiotic but with no significant differences.

Ahmadipour S et al., showed that there was a significant difference between the duration of diarrhea, the length of hospitalization and the reduction of complications after treatment with Zn **(Ahmadipour et al., 2019)**.

In a study conducted by **Boran et al.,** in 280 children aged 6 to 60 months, the intervention group received zinc supplements for 14 days. The subsequent plasma levels of zinc were higher than in the control group, and the duration and frequency of diarrhea was lower in the treatment group compared with the control group, without any significant differences **(Boran et al., 2006)**.

In the current study we found that there was lower hospital stay in combined group versus zinc and probiotic group but with insignificant differences.

Ahmadipour S et al., showed that in the PRG group, diarrhea persisted in 80% of cases until day 4 of admission, whereas in the ZRG group, it was only in 47.8% of children until day 4 of hospitalization, and this difference was significant ($p<0.001$). The relative persistence of diarrhea until day 4 in the PRG was 36.4 times higher than in the ZRG **(Ahmadipour et al., 2019)**.

CONCLUSION

In children with acute noninfectious watery diarrhea, Zinc or Probiotic supplementation reduced the duration of diarrhea. In our study children receiving combined therapy were more likely to be diarrhea-free after five days, with better outcomes along with improvement in consistency and reducing the duration of hospital stay. We conclude that, combination of probiotics & zinc therapy is more effective in reducing the severity of acute diarrhea than zinc therapy alone.

RECOMMENDATION

- Probiotic can be effectively used with Zinc to treat acute watery diarrhea in children
- This study was not powered for mortality or the number of complications so larger trials are also needed to detect a significant difference in diarrheal duration and its morbidity in different types and severity of acute diarrhea.

REFERENCES

1. **Abraham AA, Amritha SR, Selvin CD (2016):** A comparative evaluation on the effect of zinc-probiotic and probiotic therapy in paediatric acute diarrhoea and the impact of counselling of mothers. Int J Pharm Pharm Sci;8:241-3.
2. **Aggarwal S, Upadhyay A, Shah D, Teotia N, Agarwal A & JaiswalV. (2014):** Lactobacillus GG for treatment of acute childhood diarrhea: An open labelled, randomized controlled trial. Indian J Med Res.; 139: 379-385.
3. **Ahmadipour S, Mohsenzadeh A, Alimadadi H, et al. (2019):** Treating Viral Diarrhea in Children by Probiotic and Zinc Supplements. Pediatr Gastroenterol Hepatol Nutr.; 22(2):162-170
4. **Ahmed SM, Hall AJ, Robinson AE, Verhoef L, Premkumar P, Parashar UD, et al. (2014):** Global prevalence of norovirus in cases of gastroenteritis: a systematic review and meta-analysis. Lancet Infect Dis.;14:725-30.
5. **Andradef B, Gomes TA, Elias WP. (2014):** A sensitive and specific molecular tool fodetectir on of both typical and atypical enteroaggregative Escherichiacoli J Microbiol Methods.;106:16-8.
6. **Berni CR, Buccigrossi V, Passariello A. (2011):** Mechanisms of action of zinc in acute diarrhea. Curr Opin Gastroenterol.;27:8-12.
7. **BerniCanani R, Buccigrossi V, Passariello A. (2011):** Mechanisms of action of zinc in acute diarrhoea. CurrOpinGastroenterol.;27:8-12.
8. **Bhatnagar S, Bahl R, Sharma PK, Kumar GT, Saxena SK, Bhan MK. (2004):** Zinc with oral rehydration therapy reduces stool output and duration of diarrhea in hospitalized children: a randomized controlled trial. J Pediatr Gastroenterol Nutr;38:34-40.
9. **Billoo AG, Memon MA, Khaskheli SA, Murtaza G, Iqbal K, Shekhani M S, Siddiqi A Q. (2006):** Role of a probiotic (Saccharomyces boulardii) in management and prevention of diarrhoea. World J Gastroenterol.; 12(28): 4557-4560.
10. **Boran P, Tokuc G, Vagas E, Oktem S, Gokduman MK. (2006):** Impact of zinc supplementation in children with acute diarrhoea in Turkey. Arch Dis Child;91:296-9.
11. **Dinliyici EC, Kara A, Dalgic N, KurugolZ,Arica V et al. (2015):** Saccharomyces boulardii CNCM I-745 reduces the duration of diarrhoea, length of emergency care and hospital stay in children with acute diarrhea. Beneficial Microbes.; 6(4):415 – 421.
12. **Farhat A, Shaukat A, Sadiq N. (2018):** Comparison Of Clinical Efficacy Of Combined Versus Monotherapy Of Oral Zinc And Probiotic In Pediatric Acute Diarrhoea At Benazir Bhutto Shaheed Teaching Hospital, Abbottabad. JBUMDC.; 8(4):210-213.
13. **Gibson GR, Hutkins R, Sanders ME, Prescott SL, Reimer RA, Salminen SJ, et al. (2017):** Expert consensus document: the International Scientific Association for Probiotics and Prebiotics

(ISAPP) consensus statement on the definition and scope of prebiotics. Nat Rev Gastroenterol Hepatol.; 14:491-502.

14. **Gill H, Prasad J. (2008):** Probiotics, Immunomodulation, and Health Benefits. In: Bösze Z, ed. Bioactive Components of Milk. New York (NY): Springer.; 423-54.
15. **Htwe K, Yee KS, Tin M, (2008):** et al. Effect of Saccharomyces boulardii in the treatment of acute watery diarrhea in Myanmar children: a randomized controlled study. Am J Trop Med Hyg.; 78 (2): 214-6.
16. **Kliegman RM, Nelson WE. (2016):** Nelson textbook of pediatrics. 20th ed. Philadelphia (PA): Elsevier.
17. **Lazzerini M, Ronfani L. (2009):** Cochrane review: Oral zinc for treating diarrhoea in children. Evidence-Based Child Health: A Cochrane Review Journal. 2009 Dec;4(4):1351-417.
18. **Mitra H, Shokoufeh A, Homa B, Azam M. (2003):** The effect of oral zinc sulfate on hepatitis b vaccine immunogenicity in premature infants. Life Sci J.; 9:3359-61.
19. **Rehan HS, Gautam K, Gurung K. (2003):** Mothres needs to know more regarding management of acute childhood diarrhoea. Indian J PrevSoc Med.; 34:40-5.
20. **Sachdev HP, Mittal NK, Mittal SK, Yadav HS. (1988):** A controlled trial on utility of oral zinc supplementation in acute dehydrating diarrhea in infants. J Pediatr Gastroenterol Nutr;7:877-81.
21. **Walker CL, Rudan I, Liu L, (2013):** Nair H, Theodoratou E, Bhutta ZA, et al. Global burden of childhood pneumonia and diarrhoea. Lancet.; 381:1405-16.
22. **Yazar AS, Guven S, Dinleyici EC. (2016):** Effects of zinc or symbiotic on the duration of diarrhoea in children with acute infectious diarrhoea. Turk J Gastroenterol; 27:537-40
23. **Zulfiqar AB, Sheila MB, Robert EB, Kenneth HB, Julie MG, et al. (2000):** Therapeutic effects of oral zinc in acute and persistent diarrhoea in children in developing countries: pooled analysis of randomized controlled trials. Am J ClinNutr.; 72:1516-22.

مقارنة الكفاءة السريرية فى معالجة الاسهال الحاد عند الأطفال بين الزنك والبروبيوتيك والجمع بينهما

مصطفى عبد العظيم حسن، محمد محمود سيد يونس، هدير عبد الرحمن محمد

قسم الأطفال، كلية الطب، جامعة الأزهر بأسيوط

خلفية البحث: تمثل اضطرابات الإسهال في الطفولة نسبة كبيرة (18٪) من وفيات الأطفال، مع ما يقدر بنحو 1.5 مليون حالة وفاة سنويًا على مستوى العالم، مما يجعلها السبب الثاني الأكثر شيوعًا لوفيات الأطفال في جميع أنحاء العالم. تقدر منظمة الصحة العالمية (WHO) واليونيسيف أن ما يقرب من 2.5 مليار نوبة إسهال تحدث سنويًا في الأطفال أقل من 5 سنوات من العمر في البلدان النامية، مع حدوث أكثر من 80٪ من النوبات في إفريقيا وجنوب آسيا (46٪ و38٪، على التوالى).

الهدف: المقارنة بين استخدام الزنك والبروبيوتيك معا واستخدام كل منهم على حدة في الإسهال الحاد عند الأطفال (على أساس انخفاض وتيرة البراز وتغيير الاتساق).

المرضى: أجريت هذه الدراسة على 150 حالة تم تقسيمها إلى ثلاث مجموعات: المجموعة أ - 50 مريضًا سيتلقون علاجًا بالزنك عن طريق الفم لمدة خمسة أيام وفقًا لبروتوكول منظمة الصحة العالمية جنبًا إلى جنب مع محلول معالجة الجفاف الفموي أو مع المحاليل الوريدية إذا لزم الأمر. سيتلقى مرضى المجموعة ب 50 مريضا بروبيوتيك مع محلول معالجة

الجفـــاف الفمـــوي أو مـــع المحاليـــل الوريديـــة إذا لـــزم الأمـــر. ســـيتلقى مرضـــــى المجموعـــــة ج 50 مريضـــــا علاجـــــا مـــــن الزنـــــك والبروبيوتيـــك معـــا لمـــدة خمســـة أيـــام مـــع محلـــول معالجـــة الجفـــاف الفموي أو مع المحاليل الوريدية إذا لزم الأمر.

النتـــائج: وجـــدنا فـــي الدراســـة الحاليـــة أن معـــدل تكـــرار البـــراز بعـــد العـــلاج انخفـــض فـــي جميـــع المجموعـــات وأقـــل تكـــرارا بشـــكل كبيـــر فـــي المجموعـــة المشـــتركة ولكـــن مـــع وجـــود اختلافـــات طفيفـــة فـــي الدراســـة الحاليـــة وجـــدنا أنـــه فيمـــا يتعلـــق بمـــدة الإســـهال بعـــد العـــلاج كـــان هنـــاك انخفـــاض أكبـــر فـــي المجموعـــة المشـــتركة مقابـــل الزنـــك والبروبيوتيـــك ولكـــن مـــع عـــدم وجـــود فـــروق ذات دلالـــة إحصـــائية فـــي الدراســـة الحاليـــة وجـــدنا أن هنـــاك زيـــادة فـــي الـــوزن بعـــد العـــلاج مـــع زيـــادة أكبـــر فـــي المجموعـــة المشـــتركة ولكـــن مـــع وجـــود اختلافـــات طفيفـــة فـــي الدراســـة الحاليـــة وجـــدنا أن هنـــاك إقامـــة أقـــل فـــي المستشـــفى فـــي المجموعـــة المشـــتركة مقابـــل مجموعـــة الزنـــك والبروبيوتيك ولكن مع اختلافات طفيفة.

الخلاصـــة: فـــي الأطفـــال الـــذين يعـــانون مـــن الإســـهال الحـــاد غيـــر المعـــدي، تقلـــل مكمـــلات الزنـــك أو البروبيوتيـــك مـــن مـــدة الإســـهال. فـــي دراســـتنا، كـــان الأطفـــال الـــذين يتلقـــون علاجًـــا مشـــتركًا أكثـــر عرضـــة لقلـــة الإســـهال بعـــد ذلـــك، مـــع نتـــائج أفضـــل جنبًـــا إلـــى جنـــب مـــع تحســـن قـــوام الاســـهال وتقليـــل مـــدة الإقامـــة فـــي المستشـــفى. نســـتنتج أن الجمـــع بـــين البروبيوتيـــك والعـــلاج بالزنـــك أكثـــر فعاليـــة في الحد من شدة الإسهال الحاد من العلاج بالزنك وحده.