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Investigating the effect of ORS with probiotics, zinc and vitamin A on children's diarrhea: a randomized clinical trial

Investigación del efecto de las SRO con probióticos, zinc y vitamina A en la diarrea infantil: un ensayo clínico aleatorizado

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Abstract

Background: Diarrhea is one of the leading causes of death in developing countries. Due to the interaction of diarrhea and malnutrition on each other, as well as the role of malnutrition in children's developmental and developmental disorders, improving diarrhea treatment programs plays an important role in children's health. Our aim in this study was to evaluate the effect of ORS with probiotics, zinc and vitamin A on children's diarrhea.

Methods: In this clinical trial study, children aged 9 months to 5 years were referred to Shahid Beheshti Hospital in Kashan with a complaint of acute watery diarrhea in 2017-2018. The children were randomly divided into five groups. In these groups, patients with zinc gluconate were treated with 20 mg of omental with ORS, vitamin A 20000 units with ORS, CFU probiotic with ORS, zinc gluconate, vitamin A and probiotic with ORS and finally ORS were treated only they got. Then, during the daily visit, the condition of the patients in terms of continuing diarrhea and the number of times diarrhea was asked to their mother during the last 24 hours and was recorded in the questionnaires. Then the results were entered in SPSS17 software and analyzed according to related statistical methods.

Results: All the intervention groups were similar and comparable in terms of gender characteristics ($p = 0.052$), age ($p = 0.871$) and weight ($p = 0.958$). The duration of diarrhea after intervention in the combined group decreased significantly ($P < 0.001$) and in the ORS group only increased significantly ($p = 0.013$). The frequency of diarrhea decreased significantly after intervention in all groups ($P < 0.001$). In the combined group, the number of diarrhea and the length of hospital stay decreased significantly.

Conclusion: The results of the present study showed that the group of children receiving zinc supplements, vitamin A, probiotics and ORS had a significant decrease in the number of times diarrhea and the duration of diarrhea and the duration of hospitalization.

Keywords: Children's diarrhea, probiotics, vitamin A, zinc, OR.

Resumen

Antecedentes: La diarrea es una de las principales causas de muerte en los países en desarrollo. Debido a la interacción de la diarrea y la malnutrición entre sí, así como el papel de la malnutrición en los trastornos del desarrollo de los niños, la mejora de los programas de tratamiento de la diarrea de la diarrea desempeña un papel importante en la salud de los niños. Nuestro objetivo en este estudio era evaluar el efecto de las SRO con probióticos, zinc y vitamina A en la diarrea infantil.

Métodos: En este estudio de ensayo clínico, los niños de 9 meses a 5 años fueron remitidos al Hospital Shahid Beheshti de Kashan con una queja de diarrea acuosa aguda en 2017-2018. Los niños fueron divididos aleatoriamente en cinco grupos. En estos grupos, los pacientes con gluconato de zinc fueron tratados con 20 mg de omental con SRO, vitamina A 20000 unidades con SRO, probiótico UFC con SRO, gluconato de zinc vitamina A y probiótico con SRO y, por último, sólo se trató con SRO. Luego, durante la visita diaria, se evaluó el estado de los pacientes en diarrea continua y el número de veces que tuvieron diarrea durante las últimas 24 horas y se registró en los cuestionarios. A continuación, los resultados se introdujeron en el programa informático SPSS17 y se analizaron según los métodos estadísticos correspondientes.

Resultados: Todos los grupos de intervención fueron similares y comparables en cuanto a las características de género ($p = 0,052$), edad ($p = 0,871$) y peso ($p = 0,958$). La duración de la diarrea tras la intervención en el grupo combinado disminuyó significativamente ($p < 0,001$) y en el grupo de SRO sólo aumentó significativamente ($p = 0,013$). La frecuencia de la diarrea disminuyó significativamente después de la intervención en todos los grupos ($p < 0,001$). En el grupo combinado, el número de diarreas y la duración de la estancia hospitalaria disminuyeron significativamente.

Conclusiones: Los resultados del presente estudio mostraron que el grupo de niños que recibió suplementos de zinc, vitamina A, probióticos y SRO tuvo una disminución significativa del número de veces de diarrea y de la duración de la misma, así como de la duración de la hospitalización.

Palabras clave: Diarrea infantil, probióticos, vitamina A, zinc, SRO.

Introduction

Diarrhea is one of the leading causes of death in developing countries, killing more than three million children a year[1,2]. Most of these deaths are related to dehydration[3]. About 63% of all diarrhea in the world occurs in children under the age of five[4]. This is more common in disadvantaged areas and in children with malnutrition[5]. There are 70,000 deaths from diarrhea in the world each year[6]. According to statistics provided by the World Health Organization, the number of deaths due to diarrhea in children is much higher than deaths from AIDS and malaria[7]. According to the Department of Health, diarrhea is the second leading cause of death and disability among children. Most of the signs and symptoms of diarrhea syndrome are related to the pathology of the infection and the extent of the infection. Other symptoms depend on the complications (such as dehydration and electrolyte disturbance) and the nature of the infectious pathogen. The most common manifestations of gastrointestinal gastro intestinal infection in children are diarrhea, abdominal cramps, and vomiting. Fever is common in patients with inflammatory diarrhea[8].

Due to the interaction of diarrhea and malnutrition on each other, as well as the role of malnutrition in children's developmental and developmental disorders, improving diarrhea treatment programs has an important role in children's health[8]. The duration of diarrhea depends on several factors, two of which are important and proven: malnutrition[8] and decreased immunity[9], and vitamin A deficiency can be associated with both factors. Vitamin A plays an important role in the visual process. But other roles have been mentioned, such as increasing the immune system and reducing the severity of infections, stopping some cancers, and linking some diseases such as visual impairment, skin diseases, increasing the severity of infections such as measles and diarrhea, respiratory and parasitic diseases to deficiency. It has been proposed[10]. Vitamin A deficiency is one of the most important problems in developing countries, so the World Health Organization recommends vitamin A supplements for children, and some researchers have suggested continuing to prescribe vitamin A supplements until the age of five[11]. Despite the use of ORS, micronutrient deficiencies are still one of the leading causes of death in patients with diarrhea. In addition, micronutrient deficiencies increase the severity, duration, and chronicity of diarrhea in patients[12]. Zinc is one of the most important micronutrients that is involved in neutralizing free radicals, the antioxidant system, and the proper functioning of the immune system[13]. It has been observed that serum zinc levels decrease in acute diarrhea[14]. Some studies have reported that zinc supplementation accelerates recovery, reduces the duration and severity of diarrhea, and reduces mortality in patients[15]. Oral zinc supplementation reduces the amount, frequency of bowel movements and the duration of diarrhea. This practice is associated with safety, efficiency and cost-effectiveness. Therefore, supplementation is a simple and effective treatment for acute diarrhea control[16]. Co-administration of zinc and ORS simultaneously reduces treatment costs and the duration of acute diarrhea in children[17]. Probiotics are now used in various areas of prevention and treatment, especially in acute infectious diarrhea. The results of a systematic review of 56 studies in infants and children showed that probiotic use was safe and had a significant effect on reducing the duration and frequency of acute infectious diarrhea[18]. Yogurt has been known to be effective in treating diarrhea since ancient times, and many studies today have reported beneficial effects in the treatment of diarrhea[19]. In recent years, the use of probiotics to reduce the duration of treatment and the severity of infectious diarrhea in the clinical field has been proposed, and most studies have found the effects of lactobacilli and sucrose to be useful in the treatment of acute diarrhea[20]. The aim of this study was to investigate the effect of ORS with probiotics, zinc and vitamin A on children's diarrhea.

Materials and methods

Study design

This study is an intervention and is a two-course clinical trial. The study population of all children with diarrhea with an age range of 9 months to 5 years referred to the children's subspecialty clinic of Shahid Beheshti Hospital in Kashan and the specialized clinic in 2017-2018 were studied with complaints of acute watery diarrhea.

Input and output criteria

The criteria for entering the study include children with acute gastroenteritis hospitalized in the pediatric ward of Shahid Beheshti Hospital and the age range of 9 months to 5 years. Criteria for withdrawal include bloody and infectious diarrhea, fever equal to or above 38 C, known chronic disease (cystic fibrosis, inflammatory bowel disease, and malabsorption), severe malnutrition (less than 3%), severe dehydration, or severe dehydration. Resistant vomiting, a history of taking supplements containing zinc in the past month, a history of taking supplements containing vitamin A and probiotics in the past month, and drug intolerance were excluded.

Sample size

The sample size was calculated using the sample size formula with 5% error parameters and 80% statistical power to compare a small variable in 5 groups independent of the previous study. The minimum sample size of 27 patients were obtained, including the loss of 20 percent in each of the study was 30.

The non-probabilistic sampling method was easy. And after applying entry and exit criteria, they were randomly divided into five groups. Group 1: This group received 20 mg of gluconate zinc in combination with ORS in 4

sachets, each of which could be dissolved in 250 ml of water, for 24 hours, Group 2: This group received vitamin A powder in the amount of 20,000 units with ORS in 4 sachets, each of which could be dissolved in 250 ml of water, for 24 hours. Group 3: The CFU 109 probiotic group received ORS with 4 sachets, each capable of dissolving in 250 ml of water, for 24 hours. Group 4: This group received 20 mg of gluconate zinc, 20,000 units of powdered vitamin A and 4 tablets of CFU 109 probiotic with ORS in 4 sachets, each of which can be dissolved in 250 ml of water, for 24 hours. Group 5: This control group, as the control group, received only ORS in 4 sachets, each of which could be dissolved in 250 ml of water, for 24 hours.

Gather information

Data collection was a questionnaire. A questionnaire containing demographic characteristics, nutritional status, history of zinc supplementation, vitamin A and probiotics was asked of the patient's parents, and since the follow-up period was up to three days, parents were asked to do so. According to the doctor's prescription, no additional supplement should be given to the patient. Water shortage and daily progression of the disease for each patient is completed by the pediatric assistant. and recorded in questionnaires.

Data analysis

After collecting the data, the data was entered into SPSS v17 software, Kolmogorov-Smir Now tests were used to check the normality of the data and to compare the mean between all groups, One Way ANOVA test was used for statistical analysis. ANCOVA statistical test was used to control the variable variables.

Moral considerations

The code of the ethics committee of this study is IR.KAUMS.REC.1395.114 of Kashan University of Medical Sciences and the registration number of IRCT20170101031212437N2.

Results

In this study, which was performed on 150 children hospitalized with diarrhea complaints, the frequency of sex included 59 males (39.3%) and 91 females (60.7%). The present findings, according to **table I**, showed that there was no significant relationship between gender and the groups studied and all groups were gender-equal and comparable (p=0.052). According to the One way ANOVA test, there was no significant difference in age in the studied groups and all groups were identical

Table I: Mean and standard deviation of treatment groups.

Therapeutic groups	Number	Average age group	The standard deviation of the age group	Average weight group	The standard deviation of the weight group	The average duration of diarrhea before the intervention	Critical deviation of the duration of diarrhea before the intervention	The average number of diarrhea times before the intervention	Critical deviation of the number of times diarrhea before the intervention	The average duration of diarrhea after the intervention	Critical deviation of the duration of diarrhea after the intervention
ORS * Zinc	30	2.80	1.23	14.77	3.71	2.30	0.92	5.93	1.05	0.65	0.12
ORS * Vitamin A.	30	2.48	1.15	14.20	3.69	2.47	0.82	6.23	1.07	0.50	0.09
ORS * Probiotics	30	2.58	1.15	14.13	3.43	2.52	0.82	5.93	1.01	0.57	0.10
ORS * Zinc * Vitamin A * Probiotic	30	2.62	1.19	14.53	3.36	2.83	0.65	6.00	1.02	0.35	0.06
ORS	30	2.53	1.24	14.47	3.39	2.33	0.71	5.80	1.03	0.73	0.13
Total	150	2.60	1.18	14.42	3.48	2.40	0.83	5.98	1.03	0.81	0.07

Table II: Frequency of duration and number of diarrhea before and after intervention according to treatment groups.

Therapeutic groups		Number	The average duration of diarrhea before and after the intervention	Standard criteria for the duration of diarrhea before and after the intervention	The average number of diarrhea times before and after the intervention	Critical deviation of the number of times diarrhea before and after the intervention
ORS * Zinc	Before intervention	30	2.30	0.92	5.93	1.05
	After the intervention	30	2.30	0.65	3.03	0.76
ORS * Vitamin A.	Before intervention	30	2.47	0.82	6.23	1.07
	After the intervention	30	2.43	0.50	3.03	0.76
ORS * Probiotics	Before intervention	30	2.07	0.87	5.93	1.01
	After the intervention	30	2.23	0.57	2.93	0.69
ORS * Zinc * Vitamin A * Probiotic	Before intervention	30	2.83	0.65	6.00	1.01
	After the intervention	30	2.13	0.35	2.40	0.77
ORS	Before intervention	30	2.33	0.71	5.93	1.03
	After the intervention	30	2.87	0.73	3.03	0.91

and comparable in terms of age (p=0.871). According to the One way ANOVA test, there was no significant relationship between weight and the studied groups and all groups were similar and comparable in terms of weight (p=0.958). According to the One Way ANOVA test, there was a significant difference between the duration of diarrhea before the intervention and the groups studied, so that the combined group had the highest dose of all substances and the probiotic group had the lowest duration of diarrhea before the intervention. (p=0.006). The present findings, according to the One way ANOVA test, showed that there was no significant difference in the number of diarrhea periods before the intervention in the studied groups and the number of diarrhea times before the intervention in the groups was similar and comparable (p=0.588). The present findings, according to the One way ANOVA test, showed a significant relationship between the duration of diarrhea after the intervention and the treatment groups studied, and in the combined group, the lowest duration of diarrhea was achieved after the intervention (p<0.001). Findings in **table II** showed that the duration of diarrhea after the intervention was significantly reduced (P<0.001) in the combined group and only significantly increased in the ORS group (p = 0.013) before the intervention. Findings in **table III** showed that the number of times diarrhea after the intervention decreased significantly compared to before the intervention in all groups. (P<0.001). The present findings indicate that there is a significant relationship between the length of hospital stay and the treatment groups studied, so that the combined group had the lowest and the vitamin A group had the longest hospital stay (p<0.001). The duration of diarrhea in both males and females in the ORS group is only the highest and in the combined group the lowest. According to **table IV**, it can be shown that by eliminating the effect of age, sex and disruptive factors, a significant relationship remained between the duration of diarrhea after intervention with groups. (p <0.001). The frequency of diarrhea in both males and females in the ORS group is only the highest and in the combined group the lowest. According to **table V**, the significant relationship between the number of diarrhea recurrences after intervention with groups remained with the elimination of the effect of age on sex and disruptive factors. (p <0.001).

Discussion

Infectious diseases are considered the most important human threat in the last 10 days[21-25]. The results of the present study showed that all the intervention groups were identical and comparable in terms of demographic characteristics of sex, age, weight and clinical characteristics, the number of times and duration of diarrhea before the intervention. The duration of diarrhea after the intervention decreased compared to before the intervention in the combined group and increased only in the ORS group. The frequency of diarrhea decreased after the intervention compared to before the intervention in all groups. In the variables after the intervention, including the duration of diarrhea, the number of times diarrhea and the duration of hospitalization, there is a significant relationship with the treatment groups studied. The combined group showed the shortest duration of diarrhea after the intervention, the lowest number of diarrhea times after the intervention, and the shortest duration of hospitalization. The ORS group alone had the longest duration of diarrhea after the intervention and the highest number of diarrhea times, and the vitamin

Table III: Comparison of different treatment groups with each other in terms of the duration of diarrhea and the frequency of diarrhea after the intervention.

Group	Groups	Significant duration of diarrhea after intervention	Significant frequency of diarrhea after the intervention
ORS * Zinc ORS * Vitamin A.	ORS * Vitamin A ORS * Probiotics ORS * Zinc * Vitamin A * Probiotic ORS	0.9 0.99 0.001> 0.001>	1 0.99 0.02 0.001>
ORS * Probiotics ORS * Zinc * Vitamin A * Probiotic	ORS * Zinc ORS * Probiotics ORS * Zinc * Vitamin A * Probiotic ORS	0.90 0.66 0.001> 0.03	1 0.99 0.02 0.001>
ORS ORS * Zinc	ORS * Roy ORS * Vitamin A ORS * Zinc * Vitamin A * Probiotic ORS	0.99 0.66 0.001> 0.001>	0.99 0.99 0.07 0.001>
ORS * Vitamin A. ORS * Probiotics	ORS * Zinc ORS * Vitamin A. ORS * Probiotics ORS	0.001> 0.001> 0.001> <0.001	0.02 0.02 0.07 0.001>
ORS * Zinc * Vitamin A * Probiotic	ORS * Roy ORS * Vitamin A. ORS * Probiotics ORS * Zinc * Vitamin A * Probiotic	<0.001 0.03 <0.001 <0.001	0.001> 0.001> 0.001> 0.001>

Table IV: Duration of diarrhea after intervention according to contextual variables.

References	Sum of squares	Degrees of freedom	Average of squares	F	Significant	Partial Eta Squared
Corrected model	52.790	12	4.399	13.512	0.001>	0.542
Intercept	10.843	1	10.843	33.305	0.001>	0.196
The duration of diarrhea before the intervention	0.528	1	0.528	1.621	0.205	0.012
Age	1.297	1	1.297	3.985	0.048	0.028
Weight	1.187	1	1.187	3.647	0.058	0.026
Gender	1.194	1	1.194	3.667	0.058	0.026
Group	48.946	4	12.237	37.585	0.001>	0.523

Table V: Number of diarrhea times after intervention according to contextual variables.

References	Sum of squares	Degrees of freedom	Average of squares	F	Significant	Partial Eta Squared
Corrected model	103.606	12	8.634	15.032	0.001>	0.568
Intercept	11.561	1	11.561	20.129	0.001>	0.128
The duration of diarrhea before the intervention	3.914	1	3.914	6.814	0.010	0.047
Age	0.790	1	0.790	1.376	0.243	0.010
Weight	0.253	1	0.253	0.440	0.508	0.003
Gender	3.474	1	3.474	6.049	0.015	0.042
Group	90.608	4	22.652	39.438	0.001>	0.535

A group had the longest hospital stay. Acute infectious diarrhea is still a major cause of morbiditis in children. Additionally, the source of anxiety in affected families and children involved and because of the relative high cost to society and the family. Drugs used to treat diarrhea affect intestinal motility, ion transport, and intestinal bacteria to reduce the length of diarrhea[26,27]. Probiotics have improved their reputation for treating diarrhea. But in most countries, microorganisms are still more of a food additive than a drug. For this reason, its safety and harmlessness aspects have been preferred in food industry research due to its effectiveness on clinical efficacy. In addition, the word "probiotic" is often incorrectly applied to certain categories of products that are used in most products[28]. Probiotics are prescribed for diarrhea in many countries without specific indications. In this study, we did not conduct a quantitative or qualitative study of the amount and type of microbial probiotics, but because we intended to evaluate the effectiveness of probiotics on the clinical symptoms of diarrhea, we used probiotics available and prescribed by pediatricians. Other supplements included in the present study include vitamin A and zinc, which, in addition to some reports of therapeutic effects, were also a response to children's malnutrition. According to the National Food Administration in Mexico, 34% of children under the age of 5 are deficient in zinc and less than 5% are deficient in vitamin A, but children in urban areas are less at risk for nutritional deficiencies than children in rural areas[29]. The findings of the study in the probiotic group with ORS showed a significant reduction in the number of times and a significant increase in the duration of diarrhea after the intervention. In the probiotic group, along with zinc and vitamin A, the effect of both duration and number of diarrhea was improved. In contrast to the present finding, Lactobacillus probiotics are less associated with the length of diarrhea, and this effect has been reported in cocaine admitted to a hospital or clinic in both developed and developing countries[30]. Another effective probiotic is the combination of ST thermophilus and B bifidum, which is effective in chronic diarrhea in the buttocks under 24 months. On the other hand, previous studies in streptococcal probiotic Fecium have shown an improvement in children's diarrhea and ineffectiveness in adult diarrhea[31]. It is noteworthy that most of the children involved had acute viral diarrhea. Some factors were distorted in similar studies but were not eliminated in their study. The results of the present study in the group treated with vitamin A or zinc with ORS showed a significant reduction in the number of times and no significant change in the duration of diarrhea after the intervention compared to before. In the probiotic group, along with zinc and vitamin A, the effect of both duration and number of diarrhea was improved. In addition to the present study, previous studies on the effect of vitamin A in different parts of the world showed an ineffective effect on diarrhea and increased risk of respiratory infections[32]. Our current study also showed a significant increase in hospital stay length in the vitamin A-only intervention group. A large number of previous trials that reported positive or negative effects of vitamin supplementation on diarrhea varied according to age, diet, and diet, and did not show any clear and definite effect on the overall prognosis of diarrhea[33]. However, in the present study, we measured the effect of vitamin A in combination with ORS alone or with zinc and probiotics according to the main components of diarrhea assessment, ie duration and number of times. In contrast, in combination with the present results, it has been shown that zinc supplementation has a positive and effective effect on the prognosis of diarrhea[34]. A study by Long et al.[35] found

that vitamin A supplementation was associated with an overall increase in acute diarrhea, fever, and infection among children living on the outskirts of Mexico City. However, it had no effect on diarrhea, fever or infection. However, in the present study, zinc had a significant effect on reducing the number of times diarrhea[36]. Vitamin A supplementation, on the other hand, increases Th2 self-regulation. In contrast, zinc deficiency is associated with a decrease in Th1 immune response, and this is offset by a supplement that helps increase Th1[37]. Deficiency of a significant effect of zinc supplementation in long-term study may be due to the reduction of diarrhea pathogens such as Salmonella and Typhoid after health education programs as well as the elimination of major microorganisms and their susceptible growth medium[38]. Increased zinc self-regulation leads to Th1 stimulation and subsequent protection against these pathogens[39]. Increased diarrhea indicates a relatively higher prevalence of gastrointestinal pathogens such as rotavirus.

Conclusion

The results of the present study showed that the group of children receiving zinc supplements, vitamin A, probiotics and ORS had a positive effect on reducing the number and duration of diarrhea. All groups also had a reduced effect on the number of times diarrhea.

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Interests conflict

The researchers declare that they have no conflict of interest.

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