Zinc Supplementation in Treatment of Children With Urinary Tract Infection

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Introduction. Urinary tract infection (UTI) is very common in children. Precocious diagnosis and appropriate treatment are important because of the permanent disease complications. Zinc increases the response to treatment in many infections. In this study, we explored the effect of zinc in treating UTI.
Materials and Methods. Two hundred children with UTI were divided into 2 groups of 100 who were comparable in terms of age, sex, urine laboratory profiles, and clinical signs and symptoms. The control group received a standard treatment protocol for UTI and the intervention group received oral zinc sulfate syrup plus routine treatment of UTI.
Results. A faster recovery was observed in the patients receiving zinc, but abdominal pain was exacerbated by zinc and lasted longer. Three months after the treatment, there was no significant difference between the two groups in the time of fever stop and negative urine culture.
Conclusions. In children with UTI, zinc supplementation has a positive effect in ameliorating severe dysuria and urinary frequency while the use of this medication is not recommended in the presence of abdominal pain.

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INTRODUCTION

Urinary tract infection (UTI) is the most common disease of the urinary tract system and the 2nd prevalent infection in children after viral flu.[1] Unlike in adults, UTI in children does not have characteristic symptoms and sometimes occurs with atypical presentations such as weight loss, growth failure and anorexia, jaundice, and fever of unknown origin.[2-7] Precocious diagnosis and appropriate treatment are important because of the disease complications, including precocious complications such as sepsis and bacteremia, and late complications such as hypertension, chronic kidney failure, and nephropathy reflux.[8-12]

Zinc is the 2nd most abundant mineral in the body and its existence is important to synthesis and metabolism of proteins and nucleic acids, as well as the stability of cell membranes.[13] Zinc acts as a cofactor for over 200 enzymes, and it is essential for many metabolic functions of a cell. In general, physiological functions are dynamically linked to zinc, including growth, cell division, puberty, reproduction, and regulation of host's immune system .The immune system function is impaired even in cases of moderate zinc deficiency.[14,15] Severe zinc deficiency reduces immune system function. Zinc is one of the body's protective mechanisms against rare diseases. This mineral is necessary for the development and activity of T lymphocytes. Zinc deficiency causes a reduction in cellular immunity and duration of some diseases such as diarrhea. Zinc plays a role in the production of interferon-γ, inerleukin-2, and tumor necrosis factor-α.[16,17]

Unfortunately, to our knowledge, there is no study on the effectiveness of zinc in treating UTI

in children. Appropriate treatment is crucial in a way that it can prevent permanent kidney damage (kidney scar). Therefore the use of medicinal and nonmedicinal substances which can help us to prevent kidney damage is necessary and useful. Given that zinc is a nutrient that plays a role in the regulation and improvement of the immune system, this study aimed to evaluate the use of zinc for boosting the immune system function, and thus its effectiveness in the treatment of pyelonephritis.

MATERIALS AND METHODS

This clinical trial was conducted on the children with UTI who were hospitalized in Amirkabir Hospital. The study protocol was approved by the Ethics Committee of Arak University of Medical Sciences. Indications for hospitalization included absence of a previous UTI history, dehydration (moderate to severe), inability to drink fluids and medications (oral drug intolerance), vomiting, and suspected blood infection and UTI at the same time.[18] The inclusion criteria was existence of UTI, an age of 3 to 12 years old, and indications for hospitalization to receive intravenous medication. Patients who were not willing to participate or to take medication were excluded from the study. Other exclusion criteria were a diagnosis of renal scarring based on the results of dimercaptosuccinic acid scan; history of any form of UTI; vesicoureteral reflux, symptoms of renal abscess, renal and urinary tract calculus, urinary tract obstruction, emphysematous pyelonephritis, renal hypoplasia, ectopic kidney, and any unilateral or bilateral renal anomaly based on ultrasonography, computed tomography scan, and voiding cystourethrography findings; neurogenic bladder; history of voiding dysfunctions; anatomical problems of the genitalia such as labial adhesion, trauma, surgery, and congenital anomalies; history of diabetes mellitus, immunodeficiency, and organ transplantation; severe sepsis and bacteremia; and severe dehydration.

Two hundred eligible children were enrolled in the study after explaining the study to their parents and obtaining written consent. Using random assignment, they were divided into 2 experimental and control groups (each comprising of 100 children). On admission, all of the children received intravenous ceftriaxone (Jabir Ibn Hayyan, Tehrna, Iran) at a dose of 50 mg/kg/d to75 mg/kg/day, and the treatment was continued after discharge using cefixime suspension (Farabi, Tehran, Iran). The total duration of treatment was 14 days. In the study group, in addition to the standard treatment, all of the patients received zinc syrup (1 mg/kg/d) for 14 days (Razak, Tehran, Iran).

Data were collected during hospitalization and after discharge on the time of becoming fever free, dysuria, abdominal pain, urinary frequency, time of negative urine culture, dribbling, and the time of improving urinary incontinence. The method of measuring dysuria, abdominal pain, and urinary frequency was that children reported their parents each of the above symptoms during urination at every turn and during the treatment period, based on which the rate of dysuria reduction, urinary frequency, and abdominal pain was calculated.

Laboratory tests included complete blood count; measurement of serum levels of urea, creatinine, sodium, and potassium; and urinalysis and urine culture, 48 hours and 7 to 10 days after the start of the treatment, and then every month for 3 months.

Comparisons between the two groups were performed using the chi-square test, Fisher exact test, and independent *t* test.

RESULTS

There was no significant difference between the study (zinc) and control groups in terms of the time of fever stop or the frequency of negative urine culture (none of the measurements), urinary incontinence, and dribbling (Tables 1 and 2). In the zinc group, the number of days with dysuria, urinary frequency, and urgency were significantly less, and the recovery time was reported faster (Table 2). Abdominal pain and dysuria, however,

Table1. Positive Urine Culture for Microorganisms in Children With Urinary Tract Infection

Urine Culture Time	Positive Urine Culture		*P*
	Zinc Group (n = 100)	Control Group (n = 100)	
48 hours after starting treatment	7	11	.23
7 to 10 days after starting treatment	3	6	.25
1 month after starting treatment	1	2	.56
2 months after starting treatment	0	1	.32
3 months after starting treatment	0	0	> .99

Table 2. Symptoms in Children With Urinary Tract Infection

Symptoms	Patients With Symptom (%)		
	Zinc Group	Control Group	*P*
Days with fever			
1	37 (50.0)	37 (50.0)	
2	28 (52.8)	25 (47.2)	
3	27 (51.9)	25 (48.1)	
4	1 (33.3)	2 (66.7)	.92
Days with dysuria			
1	29 (64.4)	16 (35.6)	
2	18 (42.9)	24 (57.1)	
3	12 (30.0)	28 (70.0)	
4	0 (0.0)	1 (100.0)	.01
Days with frequency			
1	35 (79.5)	9 (20.5)	
2	21 (52.5)	19 (47.5)	
3	14 (48.3)	15 (51.7)	
4	0 (0.0)	3 (100.0)	
5	0 (0.0)	1 (100.0)	.004
Days with incontinency			
1	36 (63.2)	21 (36.8)	
2	21 (48.8)	22 (51.2)	
3	12 (46.2)	14 (53.8)	
4	0	1 (100)	
5	0	2 (100)	.16
Days with dribbling			
1	27 (58.7)	19 (41.3)	
2	20 (48.8)	21 (51.2)	
3	11 (52.4)	10 (47.6)	.65
Days with urgency			
1	36 (60.0)	24 (40.0)	
2	23 (48.9)	24 (51.1)	
3	15 (55.6)	12 (44.4)	
4	0	2 (100)	.03

were longer in the zinc group, which was likely due to the abdominal pain after taking zinc (Table 2).

DISCUSSION

The aim of this study was to determine the effect of zinc on treatment of UTI in children. The two groups were comparable in terms of age, sex, urine laboratory characteristics, and clinical condition and symptoms such as fever, dysuria, and urinary frequency. The results showed that in UTI with severe dysuria and urinary frequency, zinc is an effective medication in reducing the symptoms, but it was associated with more abdominal pain.

Zinc deficiency with an immunodeficiency and increase in creating background of infections are common in developing countries such as Iran, in which children are susceptible to viral and bacterial infections. In these areas, the use of zinc as a supplement or treatment can significantly improve the immune system and help to deal with infections.[19] Previous studies have shown that the use of zinc can help to improve symptoms in patients with lower respiratory tract infections.[20,21] Zinc spray has also been used successfully in the treatment of upper respiratory disease.[21] Other studies suggest that zinc sulfate is useful in the prevention of diarrhea and pneumonia.[22-24] It has been shown that the use of zinc for 14 days improves the immune response to Shigella infections in developing countries where malnutrition is common.[25,26] Zinc also reduces the burden of disease in children under 5 years of age and increases the body resistance to infectious diseases such as influenza.[27,28]

According to the results of previous studies, there is no organized report on the effects of zinc sulfate in the treatment of UTI, and given the fact that UTI is a major risk factor for kidney injury in children that leads to many complications, the use of suitable therapeutic methods which facilitate more rapid recovery of the patients and prevent other complications is highly recommended. Our results showed that zinc could be effective for reducing dysuria and frequent urination, but not other symptoms; in addition, it increased abdominal pain as a side effect.

As mentioned above, zinc is useful in improving frequent urination and dysuria, but it may increase abdominal pain; thus, we conclude that zinc as an adjunct medication can be used to treat the symptoms in children who suffer from dysuria and frequent urination; however, its use is not recommended for children who experience abdominal pain.

One challenge of the study was nonadherence of the parents to the treatment and follow-up protocol. There was also concerns about reliability of self-report and expression of symptoms by the children, in order to make a proper evaluation of the treatment process. The results might have been affected by the patterns of bringing the children for hospitalization by the parents, early hospital discharge, and oral zinc intolerance by children.

CONCLUSIONS

According to the obtained results, zinc can be used for clinical improvement in cases of severe dysuria and frequent urination among children with UTI. More investigation with larger samples are required to confirm these findings.

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CONFLICT OF INTEREST

None declared.

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