The Effect of Zinc (Sulfate & Gluconate) on the Most Common Infectious Diseases (Acute, Persistent Diarrhea and Pneumonia)

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Abstract

Background: In children of developing countries, zinc deficiency is common and associated with immune impairment and increased risk of serious infectious diseases such as diarrhea and pneumonia.

Objective: Evaluation of Zinc therapy (sulfate and gluconate) on the most common infectious diseases (pneumonia and diarrhea) with comparison of effectiveness between them.

Patients and Method: - In this study of 390 cases, age ranging from 1 month to 10 years old children from AL- Kadhymia Teaching Hospital and Child Central Teaching Hospital in Al-Eskan, 240 cases having diarrhea (150 cases having acute diarrhea, 90 cases having protracted diarrhea), and other 150 cases having pneumonia (diagnosed by clinical presentation, duration and X- ray findings in the diagnosis of pneumonia). We divided them in to 3 groups the 1st one we gave them zinc sulfate and 2nd group we gave them zinc gluconate for 5 days and 3rd one not put on zinc as control, and we observed the reduction in frequency of passing stool in day1, day3 and day5 and reduction in duration of diarrhea. We also observed improvement in the most important clinical features of pneumonia these are: respiratory rate, chest indrawing, temperature in day1, day3 and day5.

Results: We found that both of zinc sulfate and gluconate having effect on decrease of frequency and duration of diarrhea with more significant effect of gluconate over than sulfate in 1-5 months, 4-10 yrs age groups, similar effect in 1-3yrs age, and more effect of sulfate over gluconate in 6-11 months age group, with equal effect of both Zinc sulfate and gluconate in reduction of duration of chronic diarrhea. Significant improvement of respiratory rate, temperature and chest indrawing in the 1st 72 hrs after administration of zinc gluconate over zinc sulfate in all age groups in cases of pneumonia.

Conclusions & Recommendations: Zinc supplementation reduces the duration and severity of acute, persistent diarrhea and pneumonia; however, the mechanism by which zinc exerts its antidiarrheal effect has not been fully elucidated. So Zinc sulfate and zinc gluconate should be added in the treatment of diarrhea and pneumonia.

Key words: - Zinc supplementation, diarrhea, lower respiratory infection & children.

Introduction:-

Diarrheal diseases pose a significant public health problem on a global scale and especially in developing countries.

It is estimated that there are _1.5 billion episodes of diarrhea per year and that diarrheal disease accounted for 21% of all deaths in children who were younger than 5 years. This is equivalent to 2.5 million deaths in the same age group [1,2].

The efficacy of zinc in the treatment of diarrhea is supported by several randomized, controlled trials that showed reduction of diarrhea duration, stool output, and stool frequency. Meta-analyses on the therapeutic effects [3] of zinc in acute and persistent diarrhea as well as prevention [4] of diarrhea with zinc supplementation have been previously published. The published data so far have shown the efficacy of zinc in the treatment of acute and chronic diarrhea.

Pneumonia is a leading cause of morbidity and mortality in children less than 5 years old.

About 20% of deaths in such children are attributable to pneumonia (1·9 million deaths per year) [5]. Two-thirds of these deaths happen during infancy, and more than 90% are in developing countries.

Zinc is reported to prevent pneumonia [4,6,7], prevents and treats diarrhea [3,4,8-10]. It might act in the acute phase response to infection [11,12] helping to boost the body's immune response through a defense cascade, beginning with mobilization and sequestration of zinc to metallothionein-rich tissue, rapid up regulation of immune defense-specific protein synthesis, activation of immune defense activity such as macrophages, lymphocytes, and natural killer cells, and antibody-dependent cytotoxicity [13].

Children with good zinc status may have a more robust immune response than those with poor zinc status [14, 15]. Thus, our aim was to see whether zinc, along with antibiotics, would improve the outcome of severe pneumonia and diarrheal disease (acute and persistent).

Patients and Methods:-

This prospective study include 150 cases of acute diarrhea (As an increase in the frequency, fluidity and volume of feces, more than three times per day and duration less than 14 days) and 90 cases of persistent diarrhea (If the diarrhea persists for more than 14 days) and 150 cases of pneumonia (we depend on the clinical presentation, duration and X-ray finding in the diagnosis of pneumonia) from Al-Kadhymia Teaching Hospital and Child Central Teaching Hospital in Al-Eskan, during the period from 20th October 2008 to 20th April 2010.

In acute diarrhea we divided the patients into 3 groups, first group controlled (not put on zinc), second group (taking zinc sulfate), and third group (taking zinc gluconate) each group consisted of 50 patients, with three major age groups selection, (1-12 months, >1-4 years, > 4-10 years). In protracted diarrhea we divided the patients into 3 groups, first group controlled (not put on zinc), second group (taking zinc sulfate) and third group (taking zinc gluconate) each group consisted of 30 patients, with

three major age groups selection, (1-12 months, >1-4 years, >4-10 years).

In pneumonia we divided the patients into 3 groups, first group controlled (not put on zinc), second group (taking zinc sulfate) and third group (taking zinc gluconate) each group consisted of 50 patients, also the three major age groups selection, (1-12 months, >1-4 years, >4-10 years). Children less than 6 months we gave them 10 mg Zn sulfate and those more than 6 months we gave them 20 mg daily tablet for 5 days, and 12.5mg daily tablet of Zn gluconate for children<6 months and 25 mg daily tablet for children>6 months and we see the response by reduction of frequency of passing stool in day 1, day3 and day 5 for every one of them and reduction in duration of diarrhea, and compare the results with control group, all of them received intra venous fluid and some of them received antimicrobial therapy according to the general stool examination, and response in respiratory rate, chest indrawing and temperature day1,day3 and day5 and compare the results with control group by using paired T-test in which P-value< 0.05 is significant and Chi square in which P-value < 0.05 is significant.

All cases of pneumonia involved in this study were severe types(The severe pneumonia indicators, including chest indrawing, raised respiratory rate and hypoxia, indicating a consistency between these specific signs and the diagnosis of severe pneumonia) because all of them were admitted to the hospital, all of them received empirical antibiotics.

The measurement of improvement made concerning the frequency and duration of acute diarrhea by Mean: summation of frequencies and duration for 3 days (day 1, day 3& day 5) divided by 50, and for persistent diarrhea made by *mean: summation of frequencies and duration for 3 days (day 1, day 3& day 5) divided by 30. The measurement of improvement made concerning the temperatures and respiratory rates in cases of pneumonia by *mean: summation of temperatures & respiratory rates for 3 days (day 1, day 3& day 5) divided by 50.

Results:-

During the study period of 240 children with diarrhea (acute & persistent), No. of cases of acute diarrhea was 150 patients, No. of cases of persistent diarrhea was 90 patients, 140 (58%) were males and 100 (42%) were females.

Number of cases under 1 year of age was 130 (54%) while number of cases above 1 year was 110 (46%).

All patients received zinc sulfate or gluconate tablets and showed reduced frequency and duration of diarrhea in day 1, day 3, and day 5 with good response to gluconate, and control group not put on zinc as shown in table 1, 2 .

The pneumonia involved in this study was about 150 cases at different age groups which mostly at age 5-10 years 80 cases (53%). We show the response in signs and symptoms of pneumonia (which include respiratory rate, chest indrawing and temperature) in day1, day3 ,day5 in different age groups after administration of Zinc sulfate and Zinc gluconate tablets, with more benefit of gluconate in the improvement of these signs and symptoms over sulfate and control group not put on zinc as shown in table 3,4.

Table 1:- Distribution of patients according to frequency and duration of acute diarrhea (AD) in control group patients, patients taking zinc sulfate and patients taking zinc gluconate.

Parameters	Sample size	Age (Mean±SD) year	*Mean± SD	P-value
Frequency of **AD in control group patients	50	2.9±3.40 year	46.26±7.811 motions/day	-
Duration of AD in control group patients			42.66±7.179 days	-
Frequency of AD in patients taking zinc sulfate	50	3±3.38 year	36.90±7.229 motions/day	0.03***
Duration of AD in patients taking zinc sulfate			34.14±5.417 days	0.014
Frequency of AD in patients taking zinc gluconate	50	3±3.8 year	28.20±5.522 motions/day	0.01
Duration of AD in patients taking zinc gluconate			22.02±5.305 days	0.006

***Mean:** summation of frequencies and duration for 3 days (day 1, day 3& day 5) divided by 50.
****AD:** Acute Diarrhea, ****P-value < 0.05** is significant

Table 2:- Distribution of patients according to frequency and duration of persistent diarrhea in control group patients, patients taking zinc sulfate and patients taking zinc gluconate.

Parameters	Sample size	Age (Mean±SD) year	*Mean± SD	P-value
Frequency of **PD in control group patients	30	1.6±0.534 year	45.50±8.266	-
Duration of PD in control group patients			25.97±5.623	-
Frequency of PD in patients taking zinc sulfate	30	1.8±0.533 year	41.80±7.554	0.04***
Duration of PD in patients taking zinc sulfate			18.53±3.866	0.03
Frequency of PD in patients taking zinc gluconate	30	1.5±0.443 year	36.00±7.432	0.024
Duration of PD in patients taking zinc gluconate			12.47±1.756	0.034

***Mean:** summation of frequencies and duration for 3 days (day 1, day 3& day 5) divided by 30.
****PD:** Persistent Diarrhea. ****P-value < 0.05** is significant.

Table 3:- Distribution of the studied sample with pneumonia according to symptoms in control group patients, patients taking zinc sulfate and patients taking zinc gluconate.

Parameters	Sample size	Age (Mean±SD) year	*Mean± SD	P-value
Temperatures of pneumonia in control group patients	50	3±3.22 year	122.0046±2.98636 Cº	-
RR of pneumonia in control group patients			136.92±19.898 breaths/minute	-
Temperatures of pneumonia in patients taking zinc sulfate	50	3±3.22 year	113.1060±1.92188 Cº	0.03***
RR of pneumonia in patients taking zinc sulfate			100.08±12.012 breaths/minute	0.02
Temperatures of pneumonia in patients taking zinc gluconate	50	3.1±3.23 year	110.3220±1.47818 Cº	0.024
RR of pneumonia in patients taking zinc gluconate			85.74±12.259 breaths/minute	0.022

***Mean:** summation of temperatures & respiratory rates for 3 days (day 1, day 3& day 5) divided by 50.
****RR:** Respiratory Rate. ****P-value < 0.05** is significant.

Table 4:- The number and percentage of patients presented with chest indrawing in control group patients, patients on zinc sulphate and patients on zinc gluconate.

Group	Sample size	Number & percentage of patients with chest indrawing	Number & percentage of patients without chest indrawing	P-value
Control group patients	50	50(100%)	Zero	-
Patients on zinc sulfate	50	25(50%)	25(50%)	0.003*
Patients on zinc gluconate	50	22(44%)	28(56%)	< 0.001

***P-value < 0.05** is significant.

Discussion:-

On the basis of these findings, zinc therapy is useful for treating both acute and persistent diarrhea. Still, as extensively addressed in a recent systematic review [16], much information is lacking relative to the mechanisms by which zinc physiologically exerts its antidiarrheal effect. In this study all age groups of patients taking zinc sulfate was significant in reducing the frequency & duration of acute diarrhea, and more significant in reducing the frequency & duration of acute diarrhea in patients taking zinc gluconate. These finding agree with other studies done in India (17,18), Bangladesh (19) and Indonesia (AHidayat, personal communication, 1997), also found that acute diarrheal episodes in zinc- supplemented children were less likely to last >5 days (20).

In all age groups the patients taking zinc sulfate was significant in reducing the frequency & duration of persistent diarrhea, and more significant in reducing the frequency & duration of persistent diarrhea in patients taking zinc gluconate.

As a comparison with other results, several studies studied the therapeutic effects of zinc on persistent diarrhea. The first study on this topic was conducted by Sachdev et al in India (21).

Other studies in Mexico(22), Guatemala(23), Bangladesh, Papua New Guinea and Peru found lower diarrheal frequency and duration in the zinc-supplemented group, with statistical significance depending in large part on the sample size. Children in the zinc-supplemented group had a significant 22% lower incidence of diarrhea during the period of surveillance than unsupplemented children.

We have shown clinically and statistically significant reductions in recovery time from severe pneumonia (signs and symptoms) and overall hospital stay in children from 1 month to 10 years old given zinc with standard antimicrobial therapy.

This improvement seems to result from substantial reductions in the resolution times of each of the severe pneumonia indicators, including chest indrawing, raised respiratory rate and hypoxia, indicating a consistency between these specific signs and the diagnosis of severe pneumonia. The reductions in the duration of severe pneumonia and its components and overall hospitalization might be mediated by the role of zinc in the acute phase response [5,6,14].

We have shown clinically and statistically significant reductions in recovery time from severe pneumonia (by improvement of their symptoms) in children of all age groups involved in this study given zinc with standard antimicrobial therapy.

In all age groups with pneumonia included in this study the number & percentage of patients presented with chest indrawing taking zinc sulfate were 25(50%), P value 0.003, those patients with chest indrawing taking zinc gluconate were 22(44%), P value < 0.001.

These results are coincident with study conducted in India with a reduction of 45% in the signs and symptoms of severe pneumonia in zinc-supplemented children compared with control children (6).

The study from Vietnam reported a 2.5-fold decrease in respiratory infections (7). Other study in Bangladesh has likewise found reductions in all respiratory diseases, but did not have sufficient numbers of severe pneumonia to evaluate this outcome (18).

This improvement seems to result from substantial reductions in the resolution times of each of the severe pneumonia indicators, including, severely raised respiratory rate, temperature and cough, indicating a consistency between these specific signs and the diagnosis of severe pneumonia.

The zinc gluconate supplement was safe and improved the reductions in components of severe pneumonia might be thus, zinc may reduce inflammation, and lower airway obstruction, in supplemented children and contribute to faster inflammation resolution time, manifested by shorter duration of high respiratory rate, temperature and hypoxia(24).

With more significant effect of zinc gluconate over zinc sulfate in the improvement if these symptoms in the 1st few hrs after administration of zinc gluconate.

Conclusions and recommendations:-

Children appear to benefit from zinc supplementation during acute diarrhea, with a reduction in episode duration and severity. The effect on illness duration is also seen in the reduction in the proportion of acute diarrheal episodes that last > 7 days.

The therapeutic effect of zinc supplementation on persistent diarrhea appears to be of a magnitude similar to that found in acute diarrhea.

Routine zinc supplementation in children also appears to reduce the incidence of acute diarrhea and possibly also the incidence of persistent diarrhea and dysentery, at least in some subgroups. Zinc supplementation may also reduce the incidence of acute lower respiratory infections.

There is very significant effect of Zinc gluconate than Zinc sulfate in improvement of symptoms (respiratory rate, temperature and chest indrawing), also there is significant effect of Zinc gluconate than Zinc sulfate in improvement of acute and persistent diarrhea.

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