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EFFECT OF ZINC SUPPLEMENTATION ON INCIDENCE OF ACUTE RESPIRATORY INFECTIONS AMONG UNDER-FIVE CHILDREN IN RURAL COMMUNITIES OF EKITI STATE.

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Abstract

Background: Children more than adults are more vulnerable to acute respiratory infections (ARI). Evidence has shown that there is a causal relationship between zinc deficiency and childhood infections. The objective of this study was to determine the effect of zinc supplementation on incidence of ARI among under-five children in rural communities of Ekiti State.

Methods: Study design was interventional. Multistage sampling technique was used to select a total of 281 healthy under-five with their care giver for the study, 157 respondents and 124 respondents for study and control group respectively. Zinc tablet (20mg) was given daily to the study group for 2 weeks to determine the difference in ARI incidence between the study and control group. The questionnaire was validated, pretested and interviewer administered. Data was analysed using SPSS version 20. Descriptive statistics was done using percentages and mean while inferential statistics was generated using chi square and independent t test.

Results: The incidence of ARI in study group was 2.45 per child/year while in the control group it was 9.75 per child/year (IRR = 0.25, 95% CI 0.20 – 0.31)). There was 75% reduction in incidence of ARI and 41% reduction in the duration of ARI among under-five in the study group.

Conclusion: The study showed that zinc supplementation reduces incidence and duration of episodes of ARI in under-five children. Formulating policy that will incorporate the use of zinc into the child survival strategy will reduce under-five morbidity and mortality from ARI.

Word count: 242

Key words: ARI, Incidence, duration, Zinc and Under-five

Introduction

An infection of any part of respiratory tract or its related structures including para-nasal sinuses, middle ear and pleural cavity is referred to as ARI.[1] According to World Health Organization (WHO) working group on case management of ARIs, case definition of ARI is a clinical state presenting with rapid breathing more than expected upper limit for age with or

without chest in drawing, too sick to feed, nasal discharge, cough, fever with or without auscultatory findings of less than 2 weeks.[2]

ARI can be classified into two groups depending on the main organ affected, acute upper respiratory tract infections (AURIs) and acute lower respiratory infections (ALRIs). The upper respiratory tract consists of the airways from the nostrils to the vocal cords in the larynx, including the paranasal sinuses and the middle ear. The lower respiratory tract covers the continuation of the airways from the trachea and bronchi to the bronchioles and the alveoli.[3]

Children more than adults are more vulnerable to acute respiratory infections because their lungs are still developing and the airways are narrower than the adults'. Due to the fact that their oxygen demand is higher, they are more exposed to air pollution. The irritation as a result of these pollutants in their narrow airways leads to more significant obstruction in children compared to that of the adults.[4] According to WHO, indoor smoke and zinc deficiency are some of the major contributors to the poor health of the world's children.[5]

Most ARIs in children on their own can be self limiting but the risk of recurrence infection in developing countries due to repeated exposure to respiratory pathogens, environmental pollution and defects in immune system bear substantial limits hence preventive measures should become priority.[6, 7] One of the preventive strategies is adequate nutrition in both macro and micronutrient. Micronutrient supplements like zinc can be introduced which will boost the immune system because strong evidence has been discovered about the causal relationship between zinc deficiency and childhood infections.[8] Globally there is increasing interest in the role of zinc in the prevention and treatment of ARI. Meta-analyses result demonstrated that both therapeutic and prophylactic zinc supplementation reduce the duration, severity and incidence of ARIs.[8, 9]

Zinc deficiency is wide spread in developing countries and most vulnerable are the under-five children.[10, 11] As a consequence of the large number of zinc-dependent metabolic functions, the clinical morbidities associated with zinc deficiency are considerable.[12] The spectrum of clinical effects of zinc deficiency depends on the serum level, age, stage of development, deficiencies of related metals and other micronutrients, and individual susceptibility. It includes: (i) primary T-cell lymphocyte immune system dysfunction (leading to failure to terminate bacterial, viral and fungal infections); (ii) frequent opportunistic infections (due to inability to protect cell membranes from viruses, toxins, complement, and venoms); (iii) respiratory and skin allergies, (iv) asthma; and (v) chronic diarrhoea.[12]

In children, appropriate level of plasma zinc in the mother is essential for normal development in utero whilst exclusive breastfeeding will guarantee that a child zinc requirement is met in the first six months of life. Afterwards complementary foods should meet such demand, but in most cases this demand is not met especially in the second and third years of life.[13] During these periods of rapid growth, zinc demand is usually high.[11]

Viral and bacterial agents play various causal roles in the epidemiology of ARI according to age, the immunological status of the population, and the degree of exposure of individuals. Thus in infants, for instance, during the first 1-2 months of life, persisting maternal antibodies may provide a certain amount of protection against some viral infections. However, with the loss of maternal antibodies, the number of susceptible individual within the community increases until the new antibodies are formed to different antigens, bringing about a certain degree of protection. Good nutritional status will enhance normal growth and development of the under-five and subsequently the learning ability of the child.[1]

Low cost promotional interventions like micronutrient supplementation with zinc, hand washing, exclusive breast feeding, introduction of pentavalent vaccine with heamophilus influenza vaccine component are necessary for reduction of the burden of ARI.[14] Therefore,

The effect of short term zinc supplementation on ARI morbidity among under-five children in rural communities of Ekiti was evaluated in this study.

Definition of terms

ARI in this study is defined as any child between 6 – 59 months with history of fever, with all or one of these: cough, running/blocked nose, difficulty in breathing and chest in drawing in the past two weeks

It includes a new episode occurring in an individual who has been free of symptoms for at least 72 hours.[15]

AURI: any child between 6 – 59 months with any of these symptoms: cough, running/blocked nose with or without fever in the past two weeks

ALRI: any child between 6 – 59 months with history of fever, with all difficulty in breathing and chest in drawing with or without cough or/and running/blocked nose in the past two weeks.

Mild: cough, blocked or running nose, sore throat requiring home management and supportive management only in the past two weeks.

Moderate: cough and fast breathing requiring home management with antibiotics and supportive measures only in the past two weeks.

Severe: cough, fast breathing, chest in-drawing, stridor at rest requiring hospital admission in the past two weeks

Materials and Methods

Study Area: The study was carried out in rural communities where majorly cooking was done with fire wood and roads were not tarred. They had few existing health centres where only

Community Health Extension Workers were attending to their health needs. The rural dwellers were of low socio economic status with poor health seeking behaviour.

Study population and design: It was an interventional study design. The study population were a caregiver and an under-five pair. A caregiver is anyone who is 18 years old or above and has been with the child since birth or for the past 12 months and has been involved in taking care of the child. Only under-five without ARI with their caregivers were selected for this study. Two hundred and eighty one caregiver/child pairs were selected.

Sampling technique: Multistage sampling technique was used in selecting two rural local government areas by simple random sampling by balloting out of the four predominantly rural local governments. One local government area was selected as study (zinc) group and the other as control group. Ekiti State has 16 Local Government Areas (LGAs), comprising of four urban LGAs, four rural LGAs and eight semi urban LGAs. Three communities were selected from each of the two local government areas through simple random sampling. Since a community (settlement) was taken as a cluster, using cluster sampling method, all houses where there were eligible under-five children were selected. Household selection was from one household to the other i.e. from one door to the next. Caregiver/child pair was selected from each household. Where there was more than one care-giver/child pair, one of them was selected using simple random sampling by balloting. Where there was more than one child, one was selected by balloting. Where there was no care giver/ child pair the next household was automatically selected.

Sample size determination

Sample size was determined with the formula for calculating minimal sample size using a test of difference in proportions and considering Alpha and Beta Error (α of 0.05 and β of 0.84). Difference of 20% in incidence rate of ARI and Attrition rate of 10% was adjusted for,

minimum sample size required was 220 caregiver/under-five pair (110 in each group). The final sample size was 281 (157 in study (zinc) group and 127 in control group).

Intervention and follow up

Short course supplementation of dispersible zinc tablet of 20 mg daily for two weeks was given to all the respondents in the study group. The researcher administered the first dose of dispersible zinc tablet after educating the caregiver on the purpose of the study and benefit of zinc. Caregiver was then instructed to give 20 mg (one tablet) to the child daily for the next 14 days. Follow up visit was made on the 7^{th} and 14^{th} day after the zinc tablet has been commenced to ensure compliance. In cases where the tablet was not given regularly one additional week was added for the dose to be completed and those that still did not comply were dropped from the cohort. No zinc was given in the control group.

Follow up for ARIs episodes began on the 15^{th} day post intervention and all healthy respondents (study and control groups) were followed up every two weeks for a period of four (4) months to determine episodes (incidence) of ARIs, duration and severity of ARI and for possible symptoms suggestive of zinc side effect.

Administration of zinc supplementation in the study group

Zinc supplementation was given to 157 respondents from the study group. Seven of the respondents did not comply and were given additional 1 week to use the zinc supplement. At the end of the 3^{rd} week, 3 respondents still did not comply; these three were dropped from the cohort. There was no adverse effect from the zinc supplementation except for 2 of the respondents that complained of nausea. Six of the respondents were lost to follow up. Only

148 respondents completed the study. In the control group 7 of the respondents were lost to follow up, only 117 completed. Each episode signified new case of ARI.

Data Collection

An interviewer administered semi structured pre tested questionnaire was used. The questionnaire was pre-tested in another rural community contiguous to the communities used in the research. Questionnaires were administered before and after the zinc tablet administration. Research assistants were trained to collect data and their proficiency was verified through role play.

Statistical Analysis

Analysis was done using Statistical Package for Social Sciences (SPSS) version 20.

Descriptive statistics: Categorical variables were expressed as frequencies, percentages, mean and standard deviation to get the general description of the study respondents and their parents, socio-demographic characteristics.

Inferential statistics: independent t test statistics was used to determine the association between two independent groups, and chi square for association between independent and dependent variables. Level of significance was put at p value < 0.05.

Independent variable

Zinc

Dependent (Outcome) variables

Incidence of ARI

Number of episodes per child year was determined during the four months follow up after the zinc supplementation for both study and control group and relative risk at 95% confidence interval was calculated.

Duration of ARI

Duration was assessed as the number of days with ARI in both study and control group, also the mean duration an ARI episode lasted.

Severity of ARI

Severity of ARI was assessed with the presence of cough, fast breathing, chest in-drawing and stridor at rest requiring hospital admission. Relative risk was calculated to compare incidence of ALRI in exposed (zinc) and unexposed group.

Ethical Approval

Research approval was obtained from the Ethics and Research Review Committee of the Ekiti State University Teaching Hospital Ado Ekiti. Permission was obtained from the community heads and written informed consent from the care givers of the study respondents after giving adequate information on the study objectives including the risks and benefits.

Results

Response rate and socio demographic characteristics

The response rate in the study group was 94.9% and 94.4% in the control group. Overall response rate in the study was 94.6%. The socio demographic characteristics of the respondents in the study and control groups are similar, this is evidence by the fact that the differences between the groups were not statistically significance with p values > 0.05 as shown in table 1.

Incidence of ARI

The episodes of ARI in eight visits for the period of 4 months among the respondents in the study (zinc) and control groups 111 and 349 episodes. Each episode signified new case of ARI. There was a significant reduction of 68.2% in episodes of Acute Upper Respiratory Infection (AURI) in the study group compared to the control group. The difference was

statistically significant ($p<0.05$). This gives an incidence rate of 2.44 and 9.72 respectively in study and control groups.

Effect of zinc on incidence of ARI

Zinc supplementation brought 74.9% reduction in incidence of ARI. It reduces the risk of ARI about 4 times in the study group (IRR 0.25, 95% CI: 0.21 – 0.31). Table 3

Duration of ARI

The mean duration (no of days) of ARI in the study group was 3.01 days with standard deviation of 0.69 while the duration in the control group was 5.10 days with standard deviation of 1.11 (t test = 18.78, p = 0.001) as shown in tab 3. This gives about 40% reduction in the duration of ARI in the study group as a result of zinc supplementation.

Severity of ARI

Throughout out the follow up period, only a case of Acute Lower Respiratory Infection (ALRI) and 459 cases of AURI occurred. Out of the Acute Upper Respiratory Infection (AURI), 111 cases were from the study (zinc) group while 348 were from the control group. The case of ALRI was found in the control group. See tab 4.

Discussion

Zinc is known to exhibit powerful anti-oxidant activity in several organ systems including the lungs.[16, 17] Increase in the level of zinc has been proven to be very effective in fighting against pneumonia, diarrhoea and other infections. It has a role in improving the immune system and reducing morbidity and mortality among under-five children.[7] Effect of zinc on incidence duration and severity of ARI in this study is quite remarkable.

One of the major findings in the current study was a 75% reduction in incidence of ARI among the under-fives in the study (zinc) group compared with the control group where there was no intervention with zinc supplementation. There is dearth of study locally where zinc

supplementation as an intervention was used either for preventing or treating ARI. This makes local comparison difficult. This is similar to the findings from Strands where a 26% reduction in acute lower respiratory infections was reported with daily zinc supplementation for 4 months.[18] Strand's study was a hospital based and mostly the cases that report in the hospital are the serious cases unlike in this present study which is community based and almost all the cases were that of acute upper respiratory infections. Community based studies give the true picture of the burden of diseases. In similar study a 23% reduction was observed by Martha in Indonesia[18] and 9% reduction by Malik in India.[8] Though Martha study was a hospital based between children age 2 – 5 years. Malik's study was a community based among infants only with more episodes of ALRI which is not surprising among this age group because they are more prone to severe infection due to their immature lung and immune system.

Shaker et al equally documented a significant different in the incident of respiratory tract infection after treating with zinc in combination with antibiotic prescribed by the managing Physician.[20] Zinc if given as daily supplement or for treatment strategy appear to provide protection against future occurrence of respiratory infection for 3-5 month after treatment or cessation of supplementation from the studies documented above.

Sunil Sazawal et al in India documented 45% reduction in the incidence of ARI which is lower compared to the 68% reduction in the incidence of ARI observed in this study. Sunil Sazawal worked on the effect of daily zinc supplementation for three months on pnemonia whereas in this study, zinc was given for only two weeks and 99.7 % of the cases were AURI.[21] With the result we can possibly say that the short term effect is more compare to the long term effect. If zinc is given for duration of two weeks twice a year, cost effectiveness will be more in an economically challenged environment.

In a hospital based study conducted in India by Nair et al among children age 2 – 60 months, it was reported that there was no difference in the outcome of the participants in both the study and control group. This is contrasting to the current study and other similar studies that had been documented, the outcome in Bindu study might be as a result of the small sample size.[22]

There was a reduction of 40% in the duration of ARI in this study as a result of zinc supplementation. Mahalanbis et al discovered in their work that zinc reduced the duration of illness where the subjects were zinc deficient.[23] Shahid Mahmood documented 33% reduction in duration of ARI in the group where supplemented zinc was given. This is slightly lower than the outcome in this study most likely because 20 mg of zinc was given to the participant in this study compare with 10 mg of zinc given in Shahid work.[24]

Anuradha Bansal documented no significant effect of zinc on duration of stay in the hospital among children with severe acute respiratory tract infection in a triple-blind randomized placebo controlled trial conducted in India.[25] Kumar Bagri also documented no effect of zinc on radiologically confirmed cases of pneumonia. These studies are different from ours in the sense that participants in our study were mostly having upper respiratory tract infection and it was a community based intervention.[26] This study shows that with short term zinc supplementation ARI can be prevented in under-five children and if they will develop it at all, most likely it will be a mild infection.

In this study during the follow up, the ratio of cases of acute respiratory infection seen in the control group compared to the study group was 3:1 and a case of acute lower respiratory infection was seen in the control group while none was seen in the study group. Inferably this showed that zinc might prevent ARI and if it occurs, it can prevent the severe form. The

reason for reduction in the episode of ARI in the study group most likely is as a result of the effect of short term supplementation of zinc. It has been documented by Tahsin Somuk that low concentration of zinc in the tissue can lead to recurrent tonsillitis.[27]

Furthermore, Abdullah in Bangladesh reported 30% lower risk of infection in infants who were malnourished compared to 19 % lower risk of infection in infants who were not malnourished with both having zinc supplementation.[28] This may indicate that effect of zinc is more pronounced with malnutrition. The effect of zinc observed in this study may be as a result of possible coexisting malnutrition in the respondents which was not tested for. This will be very appropriate in our environment where malnutrition among the under five is still prevalent. For future research on the effect of zinc on acute respiratory infection, measuring the anthropometric parameters to determine the nutritional status and measuring the serum zinc level to determine the level of zinc deficiency will be necessary. This will enable comparison in nutritional status and serum zinc before and after zinc supplement is given.

Conclusion: The study showed that zinc supplementation reduces incidence, duration and severity of ARI in under-five children, thereby reducing morbidity and mortality due to ARI in children in the community. Formulating policy that will incorporate the use of zinc into the management algorithm of ARI and child survival strategy will reduce under-five morbidity and mortality from ARI.

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Table 1: Socio-Demographic Characteristics of Respondents

Variables	Study N = 157 (%)	Control N = 124 (%)	Statistical Indices
Age in months			
6 - 11	18 (11.5%)	12 (9.7%)	**$\chi 2$** = 0.355
12 -23	45 (28.7%)	36 (29.0%)	**p** = 0.986
24 - 35	31 (19.7%)	27 (21.8%)	
36 - 47	36 (22.9%)	28 (22.6%)	
48 - 59	27 (17.2%)	21 (16.9%)	
Gender			
Male	89 (56.7%)	72 (58.1%)	**$\chi 2$** = 0.054
Female	68 (43.3%)	52 (41.9%)	**p** = 0.817
Ethnicity			
Yoruba	127 (80.9%)	93 (75.0%)	**$\chi 2$** = 3.083
Igbo	8 (5.1%)	13 (10.5%)	**p** = 0.379
Hausa	3 (1.9%)	3 (2.4%)	
others	19 (12.1%)	15 (12.1%)	
Religion			
Christianity	128 (81.5%)	98 (79.0%)	**$\chi 2$** = 0.274
Islam	29 (18.5%)	26 (21.0%)	**p** = 0.600
SES			
Upper class	6 (3.8%)	4 (3.3%)	**$\chi 2$** = 2.823
Middle class	82 (52.3%)	53 (42.7%)	**p** = 0.244
Lower class	69 (43.9%)	67 (54.0%)	

SES – Socio Economic Status, level of significant ≤ 0.0

Table 2: Incidence of ARI among the Under-fives in study (zinc) and control groups post-intervention

Variables	Control N= 117	Study (zinc) N = 148	Total N = 265
Total no. of episodes of ARI	349	111	460
Total no of days at follow up	13104	16576	29680
Child year observed	35.9	45.4	81.3
Incidence rate (episodes/child-year*)	9.72	2.44	5.67

*Child-year: 365 days/year

Table 3: Effect of Zinc on Incidence and Duration of ARI

Variable	Study	Control	Statistical indices
Days per episode of ARI (Duration)	3.01 (0.69)	5.10 (1.11)	*t = 18.641, p <**0.001**
Incidence rate (episodes/child-year*)	2.44	9.72	IRR = 0.25 (0.20 – 0.31)

IRR incidence rate ratio; level of significance p<0.05; null value is 1; *t t test

Tab 4: Effect of Zinc on Severity of ARI

	No of cases with AURI	**No of cases with ALRI**	**Total**	**Chi square**	**p-value**
Study communities	111	None	111		
Controlled communities	347	1	348		
Total	458	1	**459**	**119370.25**	<**0.001***

*Yate's chi-square