Sahera Dirajlal-Fargo, MS, DO
Assistant Professor of Pediatrics
Division of Pediatric Infectious Diseases
11100 Euclid Avenue
Cleveland, OH 44106
Phone: (216)844-3644
Sahera.dirajlal-fargo @uhhospitals.org

Zinc Supplementation and Inflammation in Treated HIV

Sahera Dirajlal-Fargo DO, MS[1,2], Jiao Yu[1], Abdus Sattar PhD[1], Manjusha Kulkarni PhD[3], Nicholas Funderburg PhD[1], Grace A McComsey MD[1,2]

1 Case Western Reserve University, Cleveland, OH, 2Rainbow Babies and Children's Hospital, Cleveland, OH,

3Ohio States University, Columbus, OH

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BACKGROUND

The WHO estimates that nearly two billion subjects may be zinc deficient in resource limited settings. This is due to the fact that most of these populations consume mainly bread made of whole wheat flour, which is high in phosphate compound that decreases the absorption of zinc. In higher income settings, In HIV, the prevalence of zinc deficiency appears to be high and low plasma zinc levels have been linked with disease progression and an increased risk of death.

OBJECTIVES

1) To evaluate the efficacy and safety of zinc supplementation in HIV

2) To evaluate the effect of zinc supplementation on inflammation and monocyte activation in ART-treated HIV infection

MATERIALS AND METHODS

Study design: open labeled randomized double arm study

Subjects:

Inclusion criteria:

- >18 years of age
- Stable ART for at least 12 weeks
- Zinc ≤75 µg/dL in the last 60 days

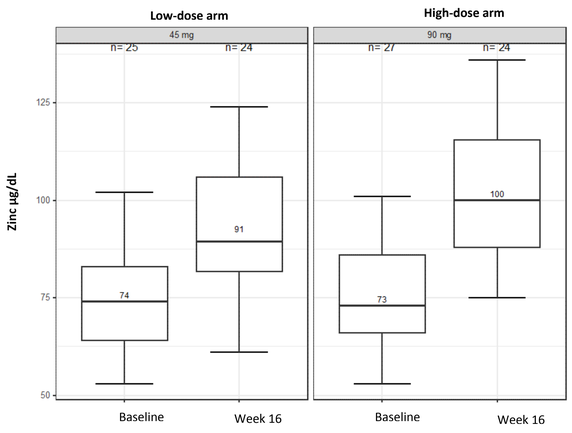
Exclusion criteria:

- Pregnancy
- Active infectious or inflammatory condition
- Uncontrolled diabetes or known Cardiovascular disease

intervention

Patients were randomized 1:1 to zinc gluconate capsules at a dose of 45mg (low-dose), or 90mg (high-dose) elemental zinc daily for 16 weeks.

FIGURE 1: BOX PLOTS OF THE CHANGE IN ZINC LEVELS AT 16 WEEKS



RESULTS

TABLE 1: BASELINE CHARACTERISTICS

	Low-dose (45 mg) arm	High-dose (90mg) arm	p value
No. of subjects (n)	25	27	
Age	54	47	**0.01**
Male (%)	20 (80%)	20 (74%)	0.75
African American (%)	18	20 (74%)	1.00
Current smoking (%)	11 (44%)	16 (59%)	0.41
Alcohol (%)	15 (60%)	20 (77%)	0.24
BMI (kg/m²)	25	27	0.36
CD4 cell count (cells/µL)	685	681	0.71
HIV RNA(<20 copies) (%)	19 (76%)	24 (89%)	0.28
ART duration (months)	1139	104	**0.01**
Protease inhibitor use (%)	7 (28%)	4 (15%)	0.32
hsCRP (ng/mL)	2433	2324	0.43
sCD14 (pg/mL)	1829	1568	0.08
sTNF-RI (pg/mL)	1048	1026	0.28
sTNF-RII (pg/mL)	3349	3053	0.13
LBP (µg/mL)	15026	15483	0.50
IFABP (pg/mL)	3445	3314	0.43
Zinc (µg/dL)	74	73	0.96

SUMMARY

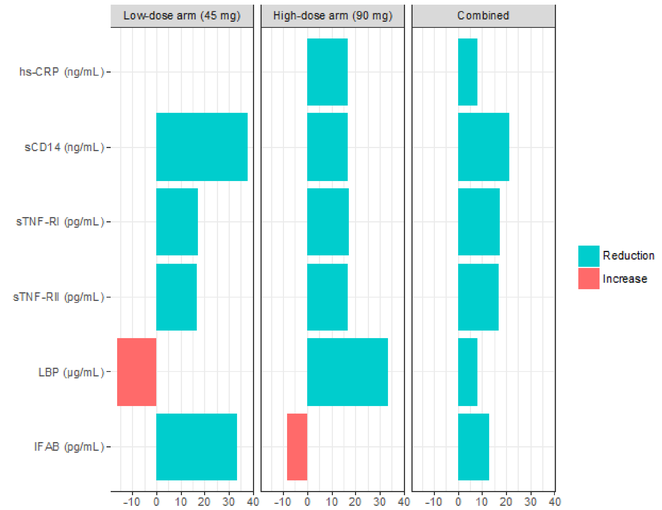
- Participants in the low dose arm were significantly older
- After 16 weeks, loss to follow up was minimal with 94% retention and one possible study related adverse event
- 92% of participants reached zinc levels >75µg/dL after 16 weeks
- Overall, all biomarkers decreased when the arms were combined.
- Biomarker reductions were meaningful with large effect size.

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FIGURE 2: THE MARGIN OF CHANGES (EFFECT SIZES) FOR EACH ZINC TREATMENT ARMS OVER 16 WEEKS



Margin of changes calculated as percent of positive change – percent of negative change. Reductions in biomarkers are shown in blue, increases in red.

TABLE 2: CHANGES IN BIOMARKERS FOR ZINC TREATMENT (ARMS COMBINED) OVER 16 WEEKS

	Week 1 N=52	Week 16 N=48	Week1-Week16 N=48	Cohen's D[c]
	Median	Median	+Δ (%) [a]	
hs-CRP (ng/mL)	2378.52	2251.36	54.17	5.25
sCD14 (pg/mL)	1746.99	1613.64	60.42	13.46
sTNF-RI (pg/mL)	1037.17	1017.03	58.33	10.79
sTNF-RII (pg/mL)	1037.17	1017.03	58.3	14.66
LBP (µg/mL)	15358.15	13968.18	54.17	8.92
IFAB (pg/mL)	3429.87	2224.22	56.25	19.44

a. + Δ (%) indicates the percentages of subjects experienced decrease in the biomarker.
b. The Cohen's d is calculated after Box-Cox transformation. Small effect ≤ 0.2; Medium Effect [0.3, 0.8]; Large Effect > 0.8.

CONCLUSION

- Zinc supplementation is safe and effective at increasing zinc levels in HIV+ participants on effective ART.
- Zinc supplementation decreases biomarkers known to be abnormally elevated in this population.
- Zinc supplementation in treated HIV has the potential to be an effective agent in decreasing microbial translocation and improving gut epithelial barrier dysfunction.