

Effects of Zinc (Zn) and Micronutrient (M) Repletion on Chinese Children*

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Zn deficiency was suspected 50 years ago among malnourished adult Chinese (Eggleton 1940). Chen et al. (1985) suggested Zn deficiency is common among Chinese children. Therefore we conducted a 10 week double-blind treatment (Rx) trial of Zn, during the spring of 1994 in urban first grade children, from Chongqing (CQ), and Qingdao (QD) and Shanghai (SH), to ascertain effects on growth, cognition and lead (Pb) status.

Methods

The Rx's were: (1) 20 mg Zn, (2) 20 mg Zn with selected M, and (3) selected M alone. The M mixture provided 50% of the 1989 US NRC RDA or mean ESADDI, except that folate was included at 25% of the RDA, and iron, calcium, magnesium and phosphate were excluded. Classes of about 40 children each were assigned an Rx. Here we report height (Ht), knee height (KH) (Cronk et al. 1989), hemoglobin (HB), serum and hair Zn (s Zn, h Zn), and whole blood and hair lead (b Pb, h Pb). Data were assessed by ANOVA and two tailed t-test.

Results and Discussion

Data are summarized in Table 1. Ages (years) were CQ 6–7; QD, 7–8; SH, 8–9. Mean Hts (cm) were: CQ, 116.5; QD, 121; and SH, 119.0. Rx 2 and 3 significantly increased Ht in CQ and SH compared to Rx1, but changes after Rx 2 and Rx3 were similar. Changes in Ht were similar across Rx's in QD. Changes in KH reflected Rx in subjects from CQ and QD. Growth after Rx2 > Rx3 > Rx1 (all Rx comparisons: $p < 0.001$). KH findings from SH appeared technically compromised.

Laboratory analysis found mean base HB was normal in CQ and SH. After Rx changes occurred at all locations. The significance of the changes in HB is unclear. Base s Zn was similar in CQ and QD, as were responses to Rx. Increases occurred after Rx 2 and 3, with Rx2 > Rx3. The base s Zn levels suggested many subjects had low Zn status, an impression confirmed by the increases in KH after Rx. Base s Zn was higher in SH. Small and similar (to CQ and QD) increases occurred after Rx 2 and 3. The lack of a substantial increase in s Zn in SH after Rx may indicate subjects did not receive Rx consistently. Base h Zn was also consistent with many subjects low in Zn. Decreases in h Zn after Rx were without a clear pattern; they may reflect the limited Zn available to the growing hair follicle. A similar decrease in h Zn after Zn Rx was reported in a subject with low cellular immunity from Zn deficiency (Pekarek et al. 1979).

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Table 1. KH (mm), HB (g/L), s Zn ($\mu\text{mol/L}$), h Zn ($\mu\text{g/g}$), b Pb ($\mu\text{mol/L}$) and h Pb ($\mu\text{g/g}$).

City	Inde	n	base	CV	delta	CV	p <	Rx1	Rx2	Rx3
CQ	KH	123	340.4	5	8.4	19	0.001	5.4 ^a	10.9 ^b	9.1 ^c
QD	KH	120	375.2	5	6.6	35	0.002	5.5 ^a	7.5 ^b	6.7 ^c
CQ	HB	118	145	7	-14	-75	0.04	-13 ^{abc}	-17 ^{ab}	-10 ^c
QD	HB	121	113	6	6	98	0.001	2 ^a	9 ^b	6 ^c
SH	HB	117	124	11	-16	-122	0.003	-20 ^{ab}	-20 ^{ab}	-7 ^c
CQ	s Zn	110	12.15	32	6.92	46	0.001	2.00 ^a	11.69 ^b	7.84 ^c
QD	s Zn	114	12.15	32	7.07	49	0.001	2.31 ^a	11.07 ^b	8.46 ^c
SH	s Zn	111	15.75	16	1.38	235	0.001	-0.45 ^a	2.32 ^{bc}	2.25 ^{bc}
CQ	h Zn	113	128	25	-29	-109	0.3	-33.1	-32.1	-21.6
QD	h Zn	119	109	30	-29	-93	0.2	-26	-37	-26
SH	h Zn	119	107	26	-44	-71	0.02	-50 ^{ab}	-51 ^{ab}	-32 ^c
CQ	b Pb	100	0.487	27	0.024	509	0.06	0.042 ^{abc}	-0.017 ^b	0.063 ^c
QD	b Pb	116	0.462	36	-0.023	-737	0.06	-0.024	-0.030	-0.021
SH	b Pb	117	0.433	31	0.084	132	0.001	-0.057 ^a	0.055 ^b	0.295 ^c
CQ	h Pb	112	0.77	99	4.32	116	0.2	3.07 ^a	5.45 ^{bc}	4.68 ^{bc}
QD	h Pb	118	0.43	133	1.14	160	0.06	0.68 ^a	1.56 ^{bc}	1.54 ^{bc}
SH	h Pb	112	0.31	187	2.55	123	0.05	3.26 ^{ac}	1.59 ^b	2.95 ^{ac}

Different superscripts in the same row indicate significant differences ($p < 0.05$).

Base b Pb concentrations were > USPHS CDC safe guidelines in nearly half of the subjects. Changes in b Pb after Rx were inconsistent across locations. Mean base h Pb concentrations were 2x as high in CQ as SH. After Rx h Pb increased, perhaps by Pb mobilization from bone.

The efficacy of KH for measuring growth over short intervals of Rx was confirmed. The findings were consistent with the Chen et al. (1985) hypothesis. KH changes after M Rx indicated the presence of multiple deficiencies. The findings also suggest many children were exposed to increased environmental lead.

Literature Cited

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Discussion

Q1. Bob Smith, Great Smokies Diagnostics Lab., Asheville, NC, USA: I've done segmented hair analyses on people who use chelators, EDTA, DMPS and so on. Without question, the level of lead goes up when you give a chelating agent. I've also seen many times with supplementation, if you take a hair sample, the level of lead goes up in hair. Also, the levels of zinc do go down when you have someone who has had long-term zinc deprivation. Zinc goes down, and then goes back up.

A. Thank you.

Q2. Les Klevay, USDA-ARS, Grand Forks, ND, USA: There is known sex difference between males and females in hair lead, and I can't remember for sure, but I think females have higher leads. Did you find this as well?

A. We haven't yet looked at this as the results have only just been completed.

Q3. John Sorenson, University of Arkansas, Little Rock, AR, USA: Did you say where you sampled the hair?

A. We asked for the proximal 2 cm from the occipital area of the scalp. Sometimes the hair sample was a little longer than 2 cm, however. The duration of the intervention was 10 weeks and the sample was taken right at the end of the treatment.

Q4. Janet King, USDA, San Francisco, CA, USA: Did you make any observations on the morbidity of the children?

A. We have collected the data, and we have finally received the forms, but it is not yet analyzed.

Q5. Noel Solomons, Guatemala: There is a message here for those of us who do field supplementation and try to draw conclusions. I'd like to try to draw some conclusions from the results you've presented us with. It seems to me that you had two important deltas to look at: nothing versus zinc alone, and zinc on top of micronutrients. The hypothesis then should be that there would be a greater response to zinc than to its control. That is, that zinc should be better than nothing, and micronutrients plus zinc should be better than micronutrients. The conclusion that I could draw statistically is that you should accept both of null hypotheses that there is no independent effect of zinc, either on top of micronutrients, or on top of nothing. I think that is consistent with many other studies. Changes in knee height are very small.

Zinc is better than nothing and zinc plus micronutrients is better than micronutrients. Micronutrients are better than anything.

A. Well, our statistics didn't agree with your analysis. In fact, if you looked at the figures, you'd conclude that these effects were very highly significant. We used an ANOVA, which was very highly significant, and then everything else was compared with a two-tailed t-test which is very conservative. And those were also extremely significant. That was presented to you. And in fact, our statistician at our place told me I shouldn't put any more information on these charts, because anybody who knows anything could observe the changes. (Please, everyone understand that Noel and I are very good friends). We conclude that Zn is better than nothing and that zinc plus micronutrients is better than micronutrients alone. You are absolutely right that micronutrients are best of all. The conclusion is that if you're going to treat people, you've got to give them micronutrients and zinc.

Q6. Susan Kaup, Wyeth-Ayerst Research, Philadelphia, PA, USA: To follow up on that, if I remember right from Penland's abstract on cognitive development, zinc seemed to stand out markedly, whereas micronutrients did not. Yet you've demonstrated that growth responded great to micronutrients, and zinc didn't do to well, so which do we rely on, growth, or cognitive performance?

A. Well, that's an interesting thing for us to think about. Our current hypothesis is that neuropsychological indices may be better than growth to evaluate but growth is easier to measure. You do get different sorts of answers, that's exactly right.

Q7. Barbara Golden, University of Aberdeen, Scotland: I am impressed with the micronutrients but not necessarily with zinc. I would like you to speculate on what micronutrients might have affected growth?

A. Okay, it will be a wild speculation. There are data from Central America. Jim Smith has done a randomized trial down there, and one of his groups was vitamin A, one of his groups was vitamin A plus zinc and so forth. He found a substantial growth response to vitamin A in children. So one wonders, there's probably a whole bunch of things in there, but probably the vitamin A was important here, because they were all given vitamin A.