Global Livestock CRSP

Intervention with Animal Source Foods to Improve Vitamin A Status

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Research Brief 05-02-CNP January 2005

Vitamin A deficiency is common among African children, largely caused by low intake of retinol from animal source foods (ASF), infections, malaria and intestinal parasites. The effect of supplemental ASF on plasma and liver retinol was evaluated in rural Kenyan children. Twelve schools were randomly assigned to one of four groups: Beef, Milk, or the usual vegetable dish with added oil providing an additional 17, 44 and 21% RDA of vitamin A respectively, or Control. Children consumed the foods as a daily snack for two years. Plasma retinol, C-reactive protein (CRP), and malaria antigens were measured at baseline and after one and two years of intervention, and liver retinol stores assessed by the Modified Relative Dose Response (MRDR) after year 2. Mean plasma retinol (umol/L) and % severely deficient (<0.35 umol/L) plus deficient (0.35-0.70 umol/L) values were: baseline, 0.48 ± 0.17 and 91%; 1 y, 0.76 ± 0.22 and 43% (P<0.001 compared to baseline); and two years, 0.33 ± 0.14 and 98% (P<0.0001 compared to baseline). Children with malaria or high CRP had lower plasma retinol at all times (p<0.001). The MRDR confirmed that the majority of children had depleted liver retinol after two years, which was unaffected by dietary treatment.

Background

Vitamin A deficiency is a public health problem of immense significance in developing countries, especially among pregnant and lactating women, children and adolescents. The main causes of vitamin A deficiency are an inadequate intake of vitamin A-rich foods, and increased requirements due to infectious and parasitic diseases. In addition to causing higher risk of blindness and other ocular lesions, deficiency of the vitamin is associated with an augmented susceptibility to infections, and increased morbidity and mortality from infectious disease especially in children. Randomized trials reveal that supplementation of deficient populations with vitamin A reduces infectious disease morbidity and mortality.

Infections increase the apparent prevalence of vitamin A deficiency when it is estimated on the basis of low serum or plasma retinol concentrations, because infectious episodes (detected by elevated CRP) and malaria lower serum retinol. For the same reason these conditions may obscure improvements in vitamin A status resulting from small increases in intake of the vitamin, such as may occur in food-based interventions. Infection could also affect the usual relationship between serum levels and liver stores of the vitamin. Acute phase reactants can reduce the liver synthesis of retinol binding protein, with less delivery of retinol from the liver to the plasma. If this occurs, infected individuals would be less depleted of the vitamin than would appear from their serum retinol levels. Theoretically, interpretation of the impact of infection and malaria on liver retinol stores can be evaluated with the relative dose response (RDR) test. However, the only reported evaluation of the effect of infection on this test showed that the prevalence of low liver retinol may be underestimated in Peruvian children with an elevated acute phase response but few of those children had elevated CRP concentrations and none had malaria.

African children consume low amounts of ASF, and malaria and other infections are common. The present study was part of a larger investigation of the effects of supplemental ASF on the micronutrient status, growth and development of rural Kenyan schoolers over a two-year period. This study describes the response of plasma retinol to the intervention over the two-year period, taking into account the potential influence of chronic infection (elevated CRP) and malaria. In addition, liver stores of retinol were estimated post-intervention using the Modified Relative Dose Response (MRDR) assay, to confirm vitamin A status and explore associations between malaria, infection, and mobilization of the vitamin to or from the liver.

Major Findings

Age and gender did not differ among groups at baseline. Across all groups, the initial mean plasma retinol

concentration was 0.48 +/- 0.17 umol/L; at the end of year 1 it increased to 0.76 +/- 0.22 umol/L (p<0.000); and after two years it fell to 0.33 umol/L +/- 0.14 (p =0.000). The prevalence of deficient and marginal values was 69% and 22% at baseline, indicating that virtually all of the children had poor vitamin A status. By the end of the first year the situation was better, with 43% being deficient and only 1% severe cases. However, by the end of year two, vitamin A status had apparently deteriorated, with the prevalence of deficiency remaining similar to that at the end of year one (35%), while 63% of children had become severely deficient - a significantly higher proportion than at baseline or at the end of the first year. (Table 1).

A drought in Kenya during year two, and lower vitamin A intakes from the usual diet, may have been the cause of the increased prevalence of vitamin A deficiency, confounding any effects of the dietary intervention. The mean MRDR ratio at the end of year 2 was 0.08 +/- 0.03. 67% of children had a ratio indicating deficient liver stores (> 0.06) (Table 1).

There were no differences in plasma retinol among groups in the same year. Virtually all children were deficient or severely deficient, and had abnormal MRDR values (depleted liver retinol stores) at the end of the study.

The prevalence of malaria antigens and high CRP values respectively was 32% and 18% at baseline, 27% and 8% at the end of Year 1, and 31% and 9% in Year 2. The prevalence of malaria was significantly different between baseline and the end of Year 1 ($p < 0.05$). Based on elevated CRP, infections were more common at baseline than at the end of Year one or Year two ($p < 0.005$) (Table 1).

Children with malaria had significantly lower plasma retinol concentrations compared to those without malaria, in the first and second year after intervention ($P < 0.05$) but not at baseline (Table 2). Children with elevated CRP also had significantly lower plasma retinol concentrations at baseline and at both time points after intervention ($P < 0.05$) (Table 2).

The presence of malaria did not affect the prevalence of MRDR ratios >0.06. However, in children with malaria there was a difference in the relationship between plasma retinol category and MRDR. Specifically, malaria was associated with a higher proportion of children in the lowest plasma retinol category (severe deficiency, <0.35 umol/L) having elevated MRDR values ($p<0.004$). Controlling for treatment group and elevated CRP, the interaction between malaria, and the prevalence of children classified with depleted liver retinol stores by plasma retinol category, was highly significant ($p<0.004$). MRDR ratios were also significantly different in children who had elevated CRP values. In children with normal CRP concentrations, 56% had MRDR values indicating vitamin A depletion. This proportion increased to 78% in cases with elevated

Table 1: Mean plasma retinol and prevalence of retinol deficiency, malaria and CRP, by year of study[1].

	1998	1999	2000
Mean plasma retinol	**0.48[b]**	**0.76[a]**	**0.33[c]**
(µmol/L, S.D.)	**(0.17)**	**(0.22)**	**(0.14)**
% deficient[2]	**69[a]**	**42[b]**	**35[b]**
% severely deficient[3]	**22[b]**	**1.3[c]**	**63[a]**
Malaria (%)	**32[a]**	**27[a]**	**31[a]**
Elevated CRP (%)	**18[a]**	**8[b]**	**9[b]**
Mean MRDR	**--**	**--**	**0.08±0.03**
% depleted liver stores[4]	**--**	**--**	**67**

[1]Means and proportions in the same row with different superscripts denote statistically significant differences ($p<0.001$). Significance test: Generalized Linear Models.
[2] 0.35-0.70 µmol/L.
[3] <0.35 µmol/L.
[4] MRDR >0.06.

Table 2: Mean plasma retinol (_mol/L) for children with malaria, and with elevated C-reactive protein.

Year	Malaria[1]		P[2]	CRP		P[1,3]
	+	-		+	-	
1998	0.42	0.43	0.99	0.40	0.45	0.05
1999	0.59	0.66	0.05	0.57	0.68	0.05
2000	0.23	0.27	0.05	0.21	0.30	0.0001

[1] Children with malaria and normal CRP (78% of malaria cases) had serum retinol 0.06 µmol/L lower than those who had malaria (P<0.05).
[2] ANOVA for repeated measurements of the natural log (ln) for serum retinol.
[3] Malaria did not affect the negative association between elevated CRP and serum retinol.

CRP, and controlling for malaria and plasma retinol, was significantly different from values in non-infected children (p=0.001, logistic regression model).

Practical Implications

The rural Kenyan school children in this study were severely depleted of vitamin A, assessed by plasma retinol concentrations and/or on the basis of low liver retinol stores. Plasma retinol improved during the first year of intervention but fell to even lower values than baseline by the end of the second year. Drought and food shortages occurred in both years of the study, but were worse during year 2. The poor food situation probably explained the lower retinol concentrations at the end of year 2, as the prevalence of malaria and elevated CRP was not higher at the time when these final blood samples were drawn.

It is not yet clear whether vitamin A supplementation of vitamin A deficient children in
regions where malaria is endemic, such as in this study, would improve resistance to the
infection. Although the interactions between malaria, infections and vitamin A status are complex, there can be little doubt of the high prevalence and severe level of vitamin A deficiency in these children. Infection, and to a lesser extent malaria, lowered serum retinol. This did not result from a shift in retinol from serum to liver; rather it appeared that liver stores were even further depleted by these conditions.

Further Reading

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About the Project: The GL-CRSP Child Nutrition Project (CNP) was established in 1997 and was built on a decade of research conducted by the Nutrition CRSP (USAID) in the 1980s. CNP research addresses food-based approaches to micronutrient deficiencies, particularly of children, with respect to both the quantity and quality of food intake. The Child Nutrition Project was centered on a controlled intervention feeding trial of school children in Embu, Kenya. The Child Survival Study of toddlers was supported by funds from USAID as a follow-up to the study of school children. The project is directed by Dr. Charlotte Neumann, Dr. Suzanne Murphy, and Dr. Nimrod Bwibo as Principal Investigators and Dr. Marian Sigman, Dr. Lindsay Allen, and Dr. Shannon Whaley as Co-Investigators. Jonathan H. Siekmann, Ph.D., Ana Zubieta, Ph.D. former doctoral students and Erin Ried, a doctoral candidate, made significant contributions to the nutrition biochemical analyses. Email contact for Dr. C. Neumann is: cneumann@mednet.ucla.edu.

The Global Livestock CRSP is comprised of multidisciplinary, collaborative projects focused on human nutrition, economic growth, environment and policy related to animal agriculture and linked by a global theme of risk in a changing environment. The program is active in East Africa, Central Asia and Latin America.

This publication was made possible through support provided by the Office of Agriculture, Bureau of Economic Growth, Agriculture and Trade, under Grant No. PCE-G-00-98-00036-00 to University of California, Davis. The opinions expressed herein are those of the authors and do not necessarily reflect the views of USAID.

Design by Susan L. Johnson