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The effect of a micronutrient-fortified complementary food on micronutrient status, growth and development of 6- to 12-month-old disadvantaged urban South African infants

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The study was conducted to look at the effectiveness of a multimicronutrient-fortified complementary food on the micronutrient status, linear growth and psychomotor development of 6- to 12-month-old infants from a black urban disadvantaged community in the Western Cape, South Africa. The study was designed as an intervention study. In both the experimental and control groups, serum retinol concentration showed a decline over the intervention period of 6 months. The decline was less pronounced in the experimental group. This resulted in a significantly ($P < 0.05$) higher serum retinol concentration at 12 months in the experimental group (26.8 ± 5.8 $\mu\text{g/dl}$) compared with the control group (21.4 ± 5 $\mu\text{g/dl}$). Serum iron concentration also declined over the intervention period. The decline was less pronounced in the experimental group. No difference was observed in haemoglobin levels between the groups at 12 months. Serum zinc concentration did not differ significantly between the two groups at follow up. Weight gain over the 6 months period did not differ significantly between the experimental (2.1 ± 0.9 kg) and control groups (2.1 ± 1.2 kg). There was no difference in linear growth between the experimental (10.0 ± 1.5 cm) and control group (10.1 ± 2.1 cm) at the end of the follow-up period. Weight and length at 6 months significantly predicted weight and length at 12 months. No difference was observed in psychomotor developmental scores between the two groups after 6 months of intervention. Introducing a multimicronutrient-fortified complementary food into the diet of 6- to 12-month-old infants seemed to have an arresting effect on declining serum retinol and iron concentration in the experimental group. No benefit was observed in serum zinc concentration, linear growth and psychomotor development.

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Introduction

Research has shown that the development of stunting occurs in a relatively narrow age window. Because of the fact that stunting is most often a sign of chronic nutritional deficiencies, the problem usually has its origin at an earlier age, mostly from the age of 2–4 months. This is generally associated with the age of introduction of complementary feeding (Brown *et al.*, 1995). Once present, stunting could remain for life and there may be no catch-up growth as many believe. If stunting is not reversed or addressed at an early stage it could lock children in a lower growth trajectory with a lower potential for future growth. This will inevitably go together with the associated detrimental consequences of stunting including impaired psychomotor development (Martorell *et al.*, 1990; Schroeder *et al.*, 1995). This emphasises the importance of addressing the problem at an age when nutritional deficiencies are most likely to start.

Children suffering from stunting as a consequence of micronutrient deficiencies often present with below normal psychomotor development (Grantham-McGregor & Walker, 1996). A more serious consequence is the long term deficits in mental performance (Grantham-McGregor, 1993; Grantham-McGregor *et al.*, 2000; Walker *et al.*, 2000). These children are also usually at a higher risk of morbidity and often have impaired immune function (Chandra, 1991; Pelletier, 1994).

It is often not the availability or accessibility of food, but poor infant feeding practices that contribute mostly to deficiencies seen in these children (Gulden *et al.*, 2000). Introducing single or multi-micronutrients to the diet of young children has been proven successful in addressing linear growth retardation and morbidity (Sazawal *et al.*, 1998; Williams *et al.*, 1999; Umeta *et al.*, 2000). In this study we introduced a multi-micronutrient-fortified complementary food into the diet of 6- to 12-month-old disadvantaged South African infants and studied the effect on micronutrient status, linear growth and psychomotor development.

Subjects and methods

Study area

The study sample came from an urban disadvantaged black community, Kaya-mandi, in the Western Cape, South Africa with approximately 12,000 inhabitants. This community has a low socio-economic status as indicated by type of housing, possession of household appliances and access to basic amenities. More than 30% of the population have either low or no formal education. Most of the inhabitants work in the industries in the city or as domestic workers in private homes. Hence, many infants are in the care of grandparents or other family members.

Subjects and design

From this community, 60 children aged approximately 6 months were randomly selected from all mothers visiting the local clinic with their infants. The study was designed as an intervention study to establish the effectiveness of a micronutrient-fortified complementary food in the diet of 6- to 12-month-old black South African infants on their micronutrient status, linear growth and psychomotor development. The study was performed between March 1999 and June 2000. Selection criteria included infants with birth weight ≥ 2.5 kg and no congenital abnormalities.

Appointments were made with the mothers to visit the local day clinic in the community. Each mother visited the clinic on three occasions when the infants were approximately 6 months old and again when the infants were approximately 12 months old. These three visits at 6 and again at 12 months had to be completed within a period of 2 weeks for each infant. The purpose of the three visits at both 6 and 12 months was for the repeat measurements of the psychomotor test, as well as the collection of the questionnaire, anthropometric and biochemical data. A minimum of 1 week was needed between repeat measures of the psychomotor test to minimise a learning effect (Cools & Hermanns, 1976). Participants who defaulted were followed-up and accommodated during

another session. If a mother-child pair did not default they would complete their three baseline visits within a period of 2 weeks. The same would hold true at 12 months. In between baseline and follow-up, research assistants visited participants weekly at home. Some infants were lost to the study due to leaving the study area. Three research assistants were trained in the aspects of methodology used and data collection. The research assistants interviewed each mother or caretaker accompanying the infant in an enclosed room to ensure no distraction during data collection.

Intervention

Each infant was randomly allocated to either an experimental or a control group. The experimental group received a micronutrient-fortified complementary food throughout the 6-month period, while the control group did not receive any complementary food, but continued their normal diet. Prior to the intervention, information on consumption of complementary food was collected by means of a questionnaire. From this information it was clear that the majority of infants (90%) received commercially prepared complementary foods on a regular basis. For this reason the complementary food given to the experimental group was similar to what was well known and used in the community. However, the quantity prescribed for use per day during the intervention was 60 g dry cereal and would ensure consumption of 100% of the recommended daily allowance for vitamin A, 80% for iron, and more than 100% for zinc. The composition of the test porridge is presented in Table 1. Zinc was in the form of zinc sulphate and iron as ferric pyrophosphate.

After the third visit during the baseline study the mothers with infants in the experimental group received sufficient infant cereal to last approximately 1.5 weeks. They received demonstrations on how to prepare the porridge and a measuring spoon to ensure the correct amount of porridge to be consumed. Each child was expected to consume 60 g dry porridge mixed with cooled boiled water per day for six months.

At intervals of 1 week, the research assistants paid home visits to deliver the next batch of infant cereal to the experimental group. These visits were also used to check cereal consumption by the infant. Before commencement of the study mothers gave informed consent. The Ethics Committee of the Medical Research Council approved the study.

Methods

Blood analyses

A 5 ml venous blood sample was collected from each infant from the ante-cubital vein for the analyses of serum retinol, iron and zinc concentration. Serum retinol was determined using a slightly modified version of the reversed-phase high performance liquid chromatography method described by Catignani and Bieri (1983). Whole blood was analysed on a Coulter Counter for haemoglobin values. Total iron was analysed using a Boehringer Mannheim kit (Catalogue number 125806, GmbH, Mannheim, Germany). Serum zinc concentration was determined by atomic absorption. Blood samples could not be obtained from all infants. Reasons for failure to obtain blood samples included refusal by the mother, unsuccessful blood collection and collection of too small amounts of blood for analyses.

Weight and length measurements

The weight of infants was measured without clothing to the nearest 0.1 kg using a calibrated electronic load cell digital scale (UC-300 Precision Health Scale, Huntsville, AL). The length of infants was measured three times in the recumbent position on a baby board to the nearest 0.1 cm. The average of the three readings was used. Height-for-age (HAZ), weight-for-age (WAZ) and weight-for-height (WHZ) Z scores were calculated using the Epi Info computer program version 6.04 (Dean *et al.*, 1993).

Baseline infant food intake

Daily dietary intake was measured on three non-consecutive days by 24-h dietary recall

Table 1. Composition of fortified infant cereal consumed by experimental group

Nutrient	Per 60 g dry product	% Recommended daily allowance*
Energy (kJ)	1304	42
Protein (g)	12	86
Fat (g)	6	–
Carbohydrate (g)	54.8	–
Vitamin A (iu)	1200 (420)**	96
Vitamin C (mg)	40	114
Vitamin B ₁ (mg)	0.64	160
Vitamin B ₂ (mg)	0.24	128
Niacin (mg)	3.2	53
Calcium (mg)	368	61
Iron (mg)	8 (8.8)**	80
Vitamin D (iu)	160	40
Vitamin E (iu)	4	72
Biotin (µg)	20	40
Folic acid (µg)	17.6	50
Pantothenic acid (mg)	0.6	40
Vitamin B ₁₂ (µg)	0.6	120
Vitamin B ₆ (mg)	0.24	40
Phosphorous (mg)	232	46
Iodine (µg)	26	52
Zinc (mg)	5.6 (0)**	112
Potassium (mg)	632	50
Sodium (mg)	272	36
Chloride (mg)	440	36

*Subcommittee on the Tenth Edition of the RDAs 1989.

**Values in brackets are of the comparable cereal consumed by the control group.

at 6 months of age (Cameron and Van Staveren, 1988). To obtain information on breast feeding and weaning practices, data on breast feeding and use of complementary food were collected by questionnaire.

Psychomotor test

The Denver Developmental Screening Test (DDST) was used to establish psychomotor development. A questionnaire determining the level of mental and motor development of each child was completed for all children at 6 months and again at 12 months according to the guidelines set out in the DDST manual (Cools & Hermanns, 1976). The test was done twice at both 6 and 12 months. For every age group specific items were selected. This would include easy and more difficult items to accommodate children of all levels of development. There were four categories in the test; namely, social adaptive, language, gross motor and fine motor. The DDST score of each child was calculated by expressing the number of positive observations as a percen-

tage of the maximum possible positive observations. Research assistants conducted the psychomotor test. The test took place in an enclosed room to ensure no distraction. It also ensured a consistent environment for repeat measurements. Research assistants had been thoroughly trained to ensure correct and consistent execution of the test items. A senior research worker supervised the execution of the test.

Statistical analyses

Anthropometric indices for HAZ, WAZ and WHZ were calculated using the Epi Info version 6.04 computer program (Dean *et al.*, 1993). This program uses the National Center for Health Statistics reference population data (Hamill *et al.*, 1979) for calculating anthropometric indices. In normally distributed data, comparison of means between groups was carried out with the unpaired *t*-test. In data not normally distributed, the Wilcoxon sign rank test was used. For measures of association between numerical

variables the Spearman's rho correlation coefficient was used. For categorical data, the chi-square test or Fisher's exact test for cell sizes less than five was used. Data was analysed using SPSS version 10.04 for windows (SPSS 10.04 for Windows; SPSS Inc, Chicago, IL, USA). The significance level was taken at $\alpha = 0.05$.

Results

Micronutrient status

Table 2 presents the serum retinol, iron and zinc concentration at 6 and 12 months for both the experimental and control groups. In both groups serum retinol concentration declined over the 6-month intervention period. The decline was greater in the control group. This resulted in serum retinol concentration at 12 months being significantly ($P < 0.05$) higher in the experimental group (26.8 ± 5.8 $\mu\text{g/dl}$) when compared with the control group (21.4 ± 5.7 $\mu\text{g/dl}$). The haemoglobin concentration remained similar from baseline to follow-up in both groups. During the 6 months follow-up, the total serum iron levels declined in both groups. The decline was more pronounced in the control group; however, no significant difference was observed. Serum zinc levels differed greatly at baseline and at follow-up between both experimental and control groups. There was no significant difference in increase in serum zinc concentration between groups over the intervention period.

At baseline the serum retinol concentration showed a positive significant association (0.56 ; $P < 0.01$) with serum iron concentration, which disappeared after 6 months. At 12 months serum retinol concentration

showed a significant association ($r = 0.54$; $P < 0.01$) with haemoglobin concentration.

Anthropometry

The age, weight and total length were similar for both experimental and control groups at 6 months (Table 3). After the intervention period at 12 months no significant difference was observed in weight or length between the experimental and control groups. Weight gain did not differ between the experimental group (2.1 ± 0.9 kg) and the control group (2.1 ± 1.2 kg) after 6 months of intervention. No difference was observed in linear growth between the experimental (10.0 ± 1.5 cm) and the control group (10.1 ± 2.1 cm) after intervention.

The mean Z -scores for HAZ, WAZ and WHZ were similar between the two groups at both 6 and 12 months. The mean Z -scores for all three indices decreased over the 6-month intervention period. No difference was observed in magnitude of difference in Z -scores after the intervention in any of the three indices between the experimental and control groups.

At baseline the psychomotor test results did not differ between the experimental group (67.8 ± 8.3) and the control group (64.3 ± 10.3). Neither was any significant difference in test scores observed between the experimental group (83.0 ± 10.9) and the control group (88.2 ± 9.0) at 12 months.

The composition of the test differed for baseline and follow-up due to age difference, thus no comparison was made for the difference between baseline and follow-up, but only between groups at both 6 and 12 months.

Table 2. Micronutrient status of experimental and control group at the age of 6 months and at 12 months

	At 6 months		At 12 months	
	Experimental ($n = 25$)	Control ($n = 21$)	Experimental ($n = 16$)	Control ($n = 14$)
Serum retinol ($\mu\text{g/dl}$)	30.5 (7.4)	28.8 (6.6)	26.8 (5.8)	21.4 (5.7)*
Total iron ($\mu\text{mol/l}$)	10.6 (4.4)	9.6 (4.0)	8.0 (3.2)	6.5 (3.9)
Hb (g/dl)	10.8 (1.0)	10.3 (1.0)	10.8 (0.9)	10.6 (1.3)
Zinc ($\mu\text{g/dl}$)	79.3 (12.1)	69.1 (15.8)	85.0 (9.1)	73.6 (12.1)

Data presented as mean (standard deviation).

*Significant difference at 0.05 level.

Table 3. Anthropometric variables of the experimental and control groups at the age of 6 months and at 12 months

	At 6 months		At 12 months	
	Experimental (n = 25)	Control (n = 21)	Experimental (n = 16)	Control (n = 14)
Age (months)	6.2 (0.4)	6.1 (0.4)	13.7 (0.6)	13.4 (0.6)
Weight (kg)	7.6 (0.6)	7.8 (1.2)	9.6 (1.0)	9.9 (1.8)
Length (cm)	64.4 (1.5)	64.6 (3.1)	74.4 (1.8)	74.5 (3.1)
Weight-for-age Z score	0.71 (1.10)	0.46 (1.21)	-0.55 (0.99)	-0.52 (1.60)
Height-for-age Z score	-0.68 (1.35)	-0.57 (0.87)	-0.94 (0.70)	-0.72 (1.10)
Weight-for-height Z score	1.58 (1.10)	1.11 (1.10)	0.11 (1.10)	0.42 (1.60)

Discussion

In this study, consumption of a fortified complementary food appeared to have a positive effect on serum retinol and, to a lesser extent, iron concentration. No effect was observed on serum zinc concentration, linear growth and psychomotor development. Mean serum retinol concentration was significantly higher in the experimental group; however, the difference between groups in change in retinol concentration from baseline to follow-up did not reach significance. The significantly higher serum retinol concentration in the experimental group may have been due to the higher intake of dietary vitamin A preventing a similar decline in serum retinol levels as seen in the control group over the 6-month period. The level of fortification with vitamin A was 96% of the recommended daily allowance. Other intervention studies using fortified complementary food also found a positive association of dietary vitamin A with serum retinol in the experimental group (Lartey *et al.*, 1999). In the latter study the control groups had a decline in vitamin A status similar to what was observed in the control group of the current study. In the aforementioned study, a slight increase in serum retinol in the experimental group was observed. In the present study, a decline in serum retinol was observed in both groups. The consequences of the potential prevention of decline in serum retinol would positively impact on morbidity (Dudley, 1997; Fawzi *et al.*, 1999; Lartey *et al.*, 2000) and the efficacy of immunisation (Bhaskaram & Rao, 1997), especially in this age group.

The lack of significant differences in serum iron concentration between the two groups at the end of intervention could possibly be ascribed to the type of iron fortification. Iron in the fortified cereal was in the form of ferric pyrophosphate, a form of iron less bio-available than, for example, iron in the form of ferrous fumarate (Davidsson *et al.*, 2000).

At baseline the mean serum zinc concentration was visibly higher in the experimental group. This could possibly explain the higher levels of serum zinc in the experimental group at follow-up. Although some studies showed a significant positive association between serum zinc and anthropometric measurements, it was not observed in our study (Umeta *et al.*, 2000). However, a lack of association was found in other zinc supplementation studies (Friis *et al.*, 1997; Kikafunda *et al.*, 1998). The low prevalence of stunting may have contributed to this lack of association. Stunted children respond better than non-stunted children to zinc supplementation with regard to linear growth (Umeta *et al.*, 2000).

In the present study we found no significant difference in linear growth between infants receiving a fortified weaning food and infants in the control group. The prevalence of stunting in our population was low compared with neighbouring African countries where the prevalence can vary from 36% in Mozambique to 44% in Lesotho (Hiadar and Demisse, 1999; Hautvast *et al.*, 2000; World Health Organisation, 2000). The absence of significant changes in any of the anthropometric parameters may be explained by the short follow-up period of 6 months. However, the mean difference in weight and height from baseline to follow-up (2.1 ± 0.9

kg and 10.0 ± 1.8 cm) seemed great enough to have shown a difference if there was a true difference. With the current sample size, a difference between groups of an increase of more than 2 cm in height between baseline and follow-up would have been detected in this study at a power of 80%. In a zinc supplementation study of similar duration in the same age group by Umeta *et al.* (2000), differences in increase in height over the intervention period between stunted groups of more than 4 cm and between non-stunted groups of 1.6 cm were observed.

Breast-feeding and complementary feeding practices could also have contributed towards explaining the lack of a pronounced effect of fortification on the outcome measures. The average age of cessation of breast-feeding was 3 months. At this age the introduction of complementary food was common. This may have influenced the actual intake of the fortified cereal. Infants may have been used to a greater variety, eventually resulting in reports of infants refusing the cereal due to being tired of it. However, data collected on type of weaning food consumed revealed that a large proportion of the diet of these infants consisted of commercially fortified infant cereal eaten on a regular basis; hence the decision to have the control group maintain their habitual diet (Morley *et al.*, 1999).

The lack of a significant difference in psychomotor development scores at follow-up is difficult to explain. Many studies have shown a significant association of iron-deficiency anaemia with impaired psychomotor development (Pollit, 1995; Morley *et al.*, 1999; Williams *et al.*, 1999). It has also been shown that infants consuming an iron-fortified milk had a less pronounced decline in psychomotor development (Williams *et al.*, 1999). One would expect higher DDST scores for the experimental group. However, some iron fortification studies have found no difference in psychomotor developmental performance between infants receiving an iron-fortified food and infants in a control group (Morley *et al.*, 1999). The relatively low prevalence of undernutrition may also explain the lack of difference between the experimental and control groups (Benefice *et*

al., 1999). The relatively high scores observed in both groups after 6 months suggest that, at least for this age group, psychomotor development seems not to have been impaired a great deal.

The high percentage of default may be explained by a few possible factors. Perceptions of better health care in the city attract thousands of prospective mothers. They come to the city and stay with relatives or friends during the antenatal period. Often incorrect addresses are given for fear of being persecuted. During this time the local health clinics are frequented for antenatal care. After delivery these mothers continue their clinic visits with the newborn for a varying period of time, but many return to their home area after the infant has reached the age of 6 months and has completed the immunisation schedule. This complicates the recruitment and follow-up of infants. In addition to this primary cause of default, another important contributory factor is the annual migration. Over the Christmas and New Year period many people visit their home areas, and some return only after a few months. To only include those remaining would contribute to bias. In planning the study we considered these aspects and planned accordingly, but never envisaged the extent of these issues. The recruiting also posed difficulties not anticipated. Finding participants based on given addresses often ended in hours of searching due to incorrect and non-existing addresses. Intervention studies in urban populations, especially among the very young will always remain problematic with respect to defaulting. In order to address these difficulties one would need to increase the time allocated to recruitment and follow-up as well as the initial sample size to compensate for any loss of participants due to the reasons given earlier.

In conclusion, the significantly higher serum retinol levels observed in the fortified group may hold promise for further studies on food fortification. The associated higher levels of serum iron may reach significance in larger studies. In the intervention study no difference in anthropometric indices between the experimental and control groups was

observed. This study suggests the necessity of further effectiveness studies on food fortification in infants.

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