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Original Article

Effect of beta-carotene supplementation on health and growth of vitamin A deficient children in China rural villages: A randomized controlled trial

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SUMMARY

Aims: To examine whether beta-carotene supplementation had a similar effect on vitamin A deficient children as retinol supplementation.

Methods: The study was a randomized, double-blind, placebo-controlled, clinical trial. It was divided into two parts including surveying and intervening stages. 225 children in two villages in rural China were surveyed and 132 vitamin A deficient children included were randomly divided into retinol intervening group, beta-carotene intervening group and placebo group. Detailed dietary assessment and physical examination were evaluated. The baseline and follow-up serum vitamin A level of the children in the three intervention groups were compared.

Results: The total proportion of severe and marginal vitamin A deficient children was 23.1% and 44.4%, respectively. After intervention, children with retinol and beta-carotene supplementation significantly increased serum vitamin A level ($p < 0.001$). The morbidity days of children with retinol and beta-carotene supplementation were significantly less than of children given placebo ($p < 0.05$). The mean increased value of weight of vitamin A and beta-carotene intervening groups was both significantly higher than placebo group ($p < 0.05$). No significant difference in increased value of height was observed between the three intervening groups.

Conclusions: We found that beta-carotene supplementation had a similar effect on correcting childhood vitamin A deficiency as retinol supplementation. Considering the health risk of vitamin A supplementation and the easier acquisition and antioxidant value of dietary beta-carotene, we recommended dietary beta-carotene supplementation for intervening high prevalent of children vitamin A deficiency in China rural areas.

1. Introduction

Vitamin A deficiency (VAD), seriously affecting children health and growth, has long been a public health problem in many developing countries. It is estimated that there are approximately 127 million and 4.4 million preschool children with vitamin A deficiency and xerophthalmia, respectively.[1] Sommer et al. observed that mortality rate among children with mild xerophthalmia (night blindness and/or Bitot's spots) was on average 4 times the rate among children without xerophthalmia.[2]

Considering the severe health risk of vitamin A deficiency, a lot of trials about vitamin A supplementation were carried out later. A randomized trial launched by Sommer et al. showed that large-dose vitamin A supplementation reduced preschool-age mortality by >30%.[3] Another small hospital-based randomized study by Sommer et al. also showed that large-dose vitamin A supplementation resulted in a 50% reduction in the rate of severe measles complications and in measles case fatalities.[4] As evidence grew, the idea of decreasing children morbidity by high-dose vitamin A supplementation was widely accepted. UNICEF and the WHO both recommended large-dose vitamin A supplementation for the routine treatment of measles under conditions existing in most developing countries.[5] A lot of subsequent studies have proved the validity of the strategy with vitamin A supplementation.[6–8]

Beta-carotene is a commonly consumed plant pigment that is a biological antioxidant and a nutritional precursor of vitamin A.[5]

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Beta-carotene is currently under intense scrutiny regarding their potential to modulate chronic disease risk and prevent vitamin A deficiency. Fruits and vegetables that are a rich source of carotenoids are thought to provide health benefits by decreasing the risk of various diseases, including cardiovascular disease and certain cancers.[9–11] The beneficial effects of consumed beta-carotene are thought to be due to its ability to be converted to vitamin A and its role as antioxidants.[15]

However, though beta-carotene is a major natural source of dietary vitamin A, there have been little published reports that investigated the effect of dietary beta-carotene supplementation on vitamin A deficient children. Furthermore, many epidemiological and experimental studies have found that excess vitamin A supplementation and high accumulation of its metabolite had potential adverse health effects.[12–14] For beta-carotene is abundantly present in vegetables and fruits, we then hypothesized that whether beta-carotene supplementation could be used as an alternative or an additional source for vitamin A supplementation.

The aim of the present study was to determine whether beta-carotene supplementation had a similar effect on vitamin A deficient children as retinol supplementation. We conducted a supplemental trial by retinol and beta-carotene supplementation to evaluate their effects on health and growth of vitamin A deficient children.

2. Materials and methods

2.1. Study grouping

The study was a randomized, placebo-controlled, clinical trial. It was divided into two parts including surveying and intervening stages. The study was carried out in Jiangchong and Xiongwan villages, Xincheng town, Dawu, Hubei province, which was a poor rural community in the center area of China. Most inhabitants were low-income farmers. The purpose, methods, and risks of the study were explained during a parent–teacher meeting and informed consent was obtained from parents before their children participated. The Ethics Committee of Tongji Medical College approved the study.

2.2. Surveying stage

We contacted all the 246 children (6 months to 7 years) in the two villages. 21 children without informed consent or with acute and chronic diseases were excluded and we only enrolled 225 children (female 111, male 114) in the study. Data on demographic, lifestyle, socioeconomic, and health-related variables were collected by use of a validated questionnaire. Physicians at examination centers performed a standardized physical examination. Mothers were proxy respondents for children.

According to Chinese young children investigational regulation of physical capacity, we evaluated the health state of the children. A study physician also recorded weights and heights of the 225 children during a physical examination. Weight of children in light, indoor clothing was measured to the nearest 0.1 kg with a beam balance scale. Height of children without shoes was measured to the nearest 0.1 cm by using a portable stadiometer. *Z* scores of the indicators weight-for-age, length-for-age, and weight-for-length were calculated by using the growth charts of American National Center for Health Statistics (NCHS)/Centers for Disease Control and Prevention (CDC) 2000 as a reference, because similar Chinese growth charts are not available.

2.3. Intervening stage

2.3.1. Grouping

The diagnostic standard of VAD used[16] considered children, whose serum vitamin A concentration < 20 μg/dl (<0.70 μmol/l) to have severe VAD, whose serum vitamin A concentration between 20 and 30 μg/dl (0.70–1.1 μmol/l) to have marginal VAD, whose serum vitamin A concentration between 30 and 70 μg/dl (>1.1 μmol/l) to normal. According to serum vitamin A level, 132 vitamin A deficient children (50 severe VAD and 82 marginal VAD) were enrolled. The 50 severe vitamin A deficient children and 82 marginal vitamin A deficient children were randomly divided into three groups respectively by using a table with randomly assorted digits: vitamin A intervening group, beta-carotene intervening group and placebo group.

2.3.2. Intervening

44 children (18 severe VAD, 26 marginal VAD) of vitamin A intervening group were administered 100,000 IU vitamin A capsules [30 mg retinol equivalent (RE)] (50,000 IU vitamin A in vegetable oil per capsule, Cod Liver Oil Factory in Xiamen, China) every month for 3 months.[17] Each child of the beta-carotene intervening group (16 severe VAD, 25 marginal VAD) was administered 4 mg purified beta-carotene [0.66 mg retinol equivalent (RE)] (Merck, Darmstadt, Germany) every day for 3 months, which was dissolved in vegetable oil and dropped into a general little biscuit (Energy 1960 kJ, Protein 7.6 g, Fat 16.5 g, Carbohydrate 71.8 g, Ca 260 mg, Fe 4.8 mg/average per 100 g).[18] All the 47 children (16 severe VAD, 31 marginal VAD) in the placebo group were just administered a general little biscuit every day for 3 months as beta-carotene intervening group.

2.3.3. Nutrition survey

The dietary intake information of the grouping children at baseline was assessed by trained postgraduate students using the 24-h recall method. Three consecutive days were randomly selected for the dietary assessment. Household food consumption of the children was determined by inquiring their parents and recorded by the trained postgraduate students from the beginning to the end of each day. Dietary intake data were converted into nutrient values by using the 1991 China Food Composition Table (Institute of Food and Nutrition Hygiene at Chinese Academy of Preventive Medicine).

2.3.4. Feedback

Physical examination on the children was carried out after 3 months' follow-up. Children mean morbidity days including diarrhea, fever and cold days were recorded. Standardized, previously validated morbidity questionnaires were used during these visits to interview mothers regarding the presence of the following symptoms in their children: diarrhea, the presence of blood and mucus in stools, fever, cough, and difficulty in breathing.[19] For children

Table 1
The age distribution of serum vitamin A levels.

Age group (year)	*N*	Mean serum vitamin A levels (μg/dl)	The proportion of severe VAD (%)	The proportion of marginal VAD (%)
0.5∼	4	24.70 ± 14.50	25.0	50.0
1∼	40	24.78 ± 12.66	37.5	32.5
2∼	49	25.77 ± 11.77	30.6	42.8
3∼	42	28.25 ± 8.63	14.3	47.6
4∼	39	28.22 ± 11.22	20.5	48.7
5∼	51	28.48 ± 9.00	13.7	49.0
Total	225	27.05 ± 10.82	23.1	44.4

N, the number of children in each age group.
Serum vitamin A levels were presented as means ± SEM.
Severe VA deficiency defined as value below 20 μg/dl (<0.70 μmol/l).
Marginal VA deficiency defined as value between 20 μg/dl (<0.70 μmol/l) and 30 μg/dl (1.1 μmol/l).
No significant difference was observed in serum VA levels between age groups.