Effects of nutritional supplementation on children with HIV/AIDS in China

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ABSTRACT

The purpose of the review was to explore the effects of nutritional supplements in children with HIV/AIDS. Nutritional supplements were found to have both positive and negative effects in HIV/AIDS children. It was found that selenium helps to boost immunity. Vitamin D supplementation was found to delay mother to child transmission (MTCT) of HIV and to reduce stunted growth associated with persistent diarrhea. Vitamins B, C, and E were found to delay HIV disease progression, reduce oxidative stress and HIV viral load. Multivitamin supplementation was found to be more effective in delaying HIV disease progression. Protein nutrition was found to improve cognitive and motor developments of children as well as helping HIV-positive children achieve 100% weight for height. Some nutrient supplements, however, were found to have negative effects on HIV/AIDS children. Vitamin A was found to double the risk of mortality of HIV/AIDS in infants exposed to HIV via breastfeeding. Zinc was found to have a positive effect on production of infectious virus through its action on reverse transcriptase. Some micronutrional interact with each other leading to harmful side effects such as diarrhea. Some nutritional supplements interact with antiretroviral drugs leading to treatment failure. It is important for children to be given right doses of nutritional supplements and that their immune system should be closely monitored.

KEY WORDS nutritional supplements; HIV/AIDS; children

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营养补充对中国艾滋病儿童的影响

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【摘要】本综述旨在探讨补充营养素对中国艾滋病儿童的影响。补充营养素对艾滋病儿童有正负两方面的影响。研究表明，微量元素硒有助于增强免疫力；补充维生素 D 可延缓艾滋病的母婴传播，有助于减少因持续性腹泻而产生的发育迟缓；维生素 B, C 和 E 可减少氧化和病毒载量，最终延缓艾滋病病程的进展；蛋白质能促进儿童认知和运动功能的发育，同时有助于艾滋病儿童的身高和体质量达标。然而也有研究显示，补充营养素对艾滋病儿童同样具有消极作用。锌可作用于病毒的逆转录过程从而增加病毒的繁殖。维生素 A 可使得因母乳喂养而暴露于艾滋病的新生儿的病死率增加一倍。许多微量元素之间相互作用，可出现腹泻等不良反应。补充的营养素与抗逆转录病毒药物间相互作用，导致药物疗效不佳。因此，为艾滋病儿童补充营养时应注意合理的剂量并严密监测其免疫状况。

【关键词】营养补充；艾滋病；儿童

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1 Introduction

Acquired immune deficiency syndrome (AIDS) is a disease of the human immune system caused by infection of a virus called human immunodeficiency virus (HIV). This condition gradually compromises one’s immune system and leaves him/her prone to opportunistic infections. HIV infection has largely contributed to the increasing rates of morbidity and mortality in children, since the report of sentinel cases of HIV in people was issued. HIV children suffer from malnutrition and a lot of opportunistic infections. Malnutrition and growth failure are among the most frequent clinical consequences of HIV/AIDS in children.

AIDS is threatening children as never before. Currently it is reported that globally 2.5 million children were living with HIV. Children under 15 years account for one in six global AIDS-related deaths and one in seven new global HIV infections[1]. China has not been spared on the impact of HIV in Children. In 2001, report indicated that 2000 children here were infected with HIV[2]. There are often inconsistencies in reports of data for people infected with HIV in China and little on children. By the end of 2009 it was estimated that 740000 adults and children were living with HIV/AIDS[3]. However it is believed that the figures are higher than these reported estimates. The National Intelligence Council in 2002 estimated that the number of infections in China would reach 10 to 15 million by 2010[4].

The world has responded to HIV complications in many ways, including the complication of malnutrition. Poor nutrition and HIV-related health outcomes form a vicious cycle that can be broken with nutritional intervention or support[5]. In case of HIV/AIDS children, these interventions which aim to prevent and reduce severe childhood malnutrition in high HIV prevalence settings need to involve many disciplines such as nutrition, economy and social, to address the prevention and treatment of HIV/AIDS. Medical nutrition protocols for children with HIV disease have been developed which facilitate nutritional support interventions.

Several nutritional supplements come into consideration: antioxidants, amino acids, carbohydrates, essential fatty acids, fats, minerals, plant extracts, proteins, trace elements and vitamins. These may be combined to produce different formulations administered to malnourished children parenterally, systematically or otherwise as prescribed. This paper is a review of both positive and negative effects of nutritional supplements on HIV infected children.

Malnutrition is the cellular imbalance between supply of nutrients and the body’s demand for energy and components to ensure growth, maintenance and other specific functions[6]. Malnutrition in HIV infected children is exacerbated by many factors resulting from a decline in body’s natural immunity. Opportunistic infections of the gastrointestinal tract can cause diarrhea and fever. These infections may also affect the body by increasing metabolic demands, by escalating feeding problems (like loss of appetite) or by decreasing intake, thus contributing to the onset of malnutrition. These problems in turn predispose children to mal-absorption and further infection. However poverty, food insecurity, poor child-feeding habits, lack of exposure and knowledge level of the parent or guardian can also contribute to the onset of malnutrition in HIV-infected children.

2 Effects of nutritional supplements on immune system

2.1 Micronutrients

These are nutrients that are required by the body in small amounts to support its physiological functions. Micronutrient supplementation has also been commonly used in nutritional therapy for children infected with HIV. It has been well established that deficiencies and sometimes excesses of micronutrients adversely affect immune and other normal body processes. A higher intake of micronutrients has been associated with a reduced risk of low CD4+ cell count[7]. In addition, there is increasing evidence that micronutrient supplementation is associated with the absence and reduction of deficiencies of micronutrients which promotes clinical stability. A study[8] done in Botswana demonstrated that long-term micronutrient supplementation was safe and significantly prolonged time to CD4+ count declining to < 250 cells/mm³. This study was conducted in adults, and it is not known whether the results would apply to children too.

According to a systematic review by Irlam et al[9], multiple micronutrient supplements reduced morbidity and mortality in HIV-infected pregnant women, as well as in their offspring as results from randomized clinical
trials. The commonly supplemented micronutrients include zinc, selenium, magnesium, iron, copper, iodine, biotin, pantothenic acid, and folic acid. Some of these micronutrients have controversial effects. For instance, zinc is important for a healthy immune system; it has been reported to facilitate wound healing and delay HIV progression by boosting immunity. On contrary, it has also been related to facilitating the replication of HIV cycle. Zinc is a component of both structural and catalytic proteins of HIV which can facilitate disease progression\textsuperscript{[10]}. The association between zinc intake and increased progression to AIDS and death was found in one cohort study in U.S. patients with a high intake of highly bio-available zinc\textsuperscript{[11]}. In addition, in several studies\textsuperscript{[12–14]}, selenium supplementation has been seen to improve CD4\textsuperscript{+} cell counts and suppress HIV-1 viral load. But, again, these studies have been conducted in adults, and, to our knowledge, these reported effects of zinc, selenium pertain also to children with HIV/AIDS is unclear.

2.2 Vitamins

Vitamin A is well known for its role in boosting immunity of individuals, along with its many other functions. WHO recommends that 6- to 59-month-old children born to HIV-infected mothers living in resource-limited settings should receive periodic (every 4–6 months) Vitamin A supplements (100000 U for infants 6 to 12 months and 200000 U for children >12 months)\textsuperscript{[15]}. Evidence is available that Vitamin A plays a role in affecting immunity of HIV children in one way or the other. In one observational study that was conducted, Vitamin A was found to reduce HIV transmission from mother to child\textsuperscript{[16]}. On the contrary, Vitamin A supplementation, a low-cost intervention, does not appear to be effective in reducing overall mother-to-child transmission (MTCT) of HIV, as least based on a large randomized clinical trial with a large sample of 1078 subjects\textsuperscript{[17]}. In this study, they assessed the impact of Vitamin A and multivitamins excluding Vitamin A on vertical transmission of HIV-1 and child mortality on pregnant women in Dar es Salaam, Tanzania. HIV women presenting at antenatal clinics between 12 and 27 weeks of pregnancy were randomized to receive 1) Vitamin A alone or matching placebo and 2) multivitamins excluding Vitamin A or matching placebo. Altogether 985 children were born alive; 896 were tested for HIV; and 268 were tested positive for HIV-1 at 6 weeks of age. Multivitamins significantly reduced death and prolonged HIV-free survival among children born to women with low maternal immunological or nutritional status. Vitamin A alone increased breastfeeding transmission but had no effect on mortality by 24 months. Another study\textsuperscript{[18]} done in Durban (South Africa) concluded that Vitamin A may actually promote transmission. In this study it was found that Vitamin A supplementation possibly increased HIV transmission and/or infant mortality in some groups of participants. It was also found that Vitamin A doubled the risk of mortality in the subset of infants exposed to HIV via breastfeeding. Obviously, additional studies are required to resolve these contradictions.

There is evidence that Vitamin D has an active role in AIDS progression in HIV infected individuals. In a cohort study\textsuperscript{[19]} done in Tanzania (enrolled pregnant women and followed them up for 69 months), low maternal Vitamin D was associated with risk of MTCT of HIV. Another clinical trial in Tanzania revealed that Vitamin D status had a protective association with HIV disease progression. These authors have suggested that Vitamin D supplementation can be a relatively simple and inexpensive method to lower mortality among children and to help prevent MTCT as an adjunct to antiretroviral therapy\textsuperscript{[20]}. However another clinical trial\textsuperscript{[21]} found that, in children infected with HIV but still with relatively preserved immune function, Vitamin D supplementation in doses as high as 1600 U/day did not impact CD4 count. This study also included single trials of Vitamin D supplements in children, which demonstrated that, while safe, there was no clinical benefit.

Other vitamins tested have been B, C, and E. Some of these have been known to have a direct association with delaying the progression of HIV disease and to provide an effective, low-cost means of delaying the initiation of antiretroviral therapy in HIV-infected children. Several of the B vitamins, as well as Vitamins C and E, have been associated with reduced risk of HIV progression. A randomized clinical trial\textsuperscript{[22]} done in Canada found that supplementation with Vitamins E and C reduced oxidative stress and HIV viral load. To our knowledge, however, these results have not been explicitly shown to be relevant to children. Generally no vitamin supplied singularly has been shown to be associated with a reduction in CD4\textsuperscript{+} T-cell counts, but there is evidence that daily use of multivitamin supplement is associated with a reduced risk of AIDS, a significant risk of low CD4\textsuperscript{+} T-cell
count, and delays the progression of HIV disease and provides an effective, low-cost means of delaying the initiation of antiretroviral therapy\textsuperscript{6,17,23}.

2.3 Proteins

A high-protein diet is well known to boost and maintain the health of one's immune system, but there are few studies done directly on the association of proteins and immunity of HIV children. Research teams have long attempted to isolate antiretroviral agents from a wide variety of plants. Soya bean glycoside isolates have been identified as promising anti-HIV agents\textsuperscript{24}. In vitro studies however have demonstrated no effect on replication, and this line of research seems not to have progressed. There is no suggestion that consuming soya products confers any protection against HIV infection or limits viral replication\textsuperscript{24}. In a study done by Berkhout et al\textsuperscript{25}, some peptides were found to inhibit the process of virus entry into cells. In fact, HIV-1 replication was elevated in the presence of β-casein or amphiphilic fragments thereof. Proteins may suppress HIV replication.

Spirulina is blue green alga that has caught the attention of researchers and nutritionist due to its unusually high amounts of protein. It contains vitamins, minerals, fats, and proteins. Spirulina is composed of proteins between 55 and 70 percent by dry weight. Spiruline has also been recently introduced in the nutritional therapy of HIV patients. Taking spiruline has been found to facilitate recovery of precarious immune system as it contains an antiretroviral activity and to inhibit HIV-1 replication in a human T-cell line\textsuperscript{26}.

One important type of protein commonly used by children is erythropoietin found in breast milk which has been shown to have positive effect on prevention of MTCT of HIV. In a cohort study\textsuperscript{27} in Tanzania, 59 MTCT cases and 116 controls nested within a cohort of antiretroviral-naïve HIV-infected women were matched from birth when breast milk sample was collected. Women were recruited during pregnancy and followed throughout the lactation period. Results showed that the risk of MTCT was inversely related to erythropoietin concentration of breast milk, suggesting that erythropoietin protects against MTCT\textsuperscript{27}. Pasha et al\textsuperscript{28} adds that erythropoietin might also have a modest beneficial effect on the production of infant's red cells.

3 Effects of nutritional supplements on development and growth

In one longitudinal, randomized and controlled trial\textsuperscript{29} found that a home stimulation program taught to the caregiver can significantly improve cognitive and motor development in young children infected with HIV. Basically, malnutrition is well known to delay neural development in children.

From animal experiments and observational studies in humans, it has been suggested that Vitamin A plays a fundamental role in physical growth. Vitamin A supplementation improves linear growth in infants who are infected with HIV and decreases the risk of stunting associated with persistent diarrhea. Its supplementation could constitute a low-cost, effective intervention to decrease the burden of growth retardation in settings where infectious diseases are highly prevalent\textsuperscript{30}. A randomized, controlled placebo trial\textsuperscript{31} in Tanzania found that supplementations of HIV-infected women with multivitamins (B complex, Vitamin C, and Vitamin E) during pregnancy and lactation is an effective intervention for facilitating ponderal growth in children. Multivitamin supplementation improved early child growth\textsuperscript{9}, but it is not clear if such supplementation has the same effect in Chinese children with HIV/AIDS.

Limited high-fat and low-fiber diets are fairly common in people with HIV infection, as well as in the general population. Recommendations have been made for increasing fiber intake (toward the levels suggested in general nutrition guidelines) because fiber is associated with a lower prevalence of lipodystrophy. In addition, lower soluble fiber intake is associated with dyslipidemia in individuals with lipodystrophy\textsuperscript{32}. It is known that there is a relationship between low dietary fiber and high glycemic index diets with increased risk of fat deposition, putting one at risk for obesity. There are scanty data regarding carbohydrates in people with HIV, not to mention of HIV children.

Adding proteins to diets may be beneficial, as proteins are known to maintain body cell mass. Development of Ready-to-Use Foods (RUTF) is an area of interest of particular importance where water supplies are at risk of contamination, for instance, in emergency situations. Soya-containing RUTF has been shown to have better outcomes in HIV-negative children in terms of reversing malnutrition.
and preventing death, than either supplements of maize/soya flour mix used for fortification at home[31]. The same authors subsequently showed that provision of soya-based RUTF resulted in many HIV-positive children achieving 100% weight-for-height despite not being treated with antiretroviral drugs[34].

One randomized controlled study[33] was done on Chinese preschool children and concluded that daily micronutrient supplement can improve growth of preschool children. Weekly iron supplement is as effective as daily supplement in improving iron status and reducing the prevalence of iron deficiency in the preschool children. Another cohort study[34] on Chinese school children revealed a significant probability of complex nutrient supplement improving growth, development, intelligence, and bone mass increment. But it is not known whether the findings in these two studies pertain to children living with HIV/AIDS as well.

4 Potential harm from nutritional supplementation

Some HIV-positive people take a lot of supplements in the hope that at least some of them might be beneficial. This is not necessarily a sensible idea because supplements can do harm as well as good. Different doses may have different and even opposite effects and the effect of the same dose may depend on baseline micronutrient intake or disease status. Furthermore, micronutrients often interact, so that the effect of a micronutrient supplement depends on the intake of other micronutrients[12]. Some foods, herbs and supplements interact with antiretroviral drugs, potentially increasing the risk of treatment failure or side effects. Certain drugs have been observed to interact, so that the effect of a micronutrient supplement or disease status. Furthermore, micronutrients often interact, so that the effect of a micronutrient supplement can improve growth, development, intelligence, and bone mass increment. But it is not known whether the findings in these two studies pertain to children living with HIV/AIDS as well.

5 Conclusion

In one way or the other, there is a strong relationship between nutritional supplementation and immune system health, and between normal growth and development in children living with HIV/AIDS. However there isn’t enough evidence about these relationships, especially in regards to the individual nutrients used food supplementation. Further investigation is required on the effects of micronutrients, vitamins, proteins, and carbohydrates on immunity, growth, and development in children living with HIV/AIDS. Most studies on any of these issues have been carried out on adults, fewer on children, and fewer still on children living with HIV/AIDS. Virtually none have been done on Chinese children living with HIV. It is therefore recommended to do further studies on effects of nutritional supplementations on Chinese children living with HIV/AIDS.

References


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