UNIVERSITI PUTRA MALAYSIA

EFFECTS OF IRON AND ZINC SUPPLEMENTATION ON GROWTH AND MORBIDITY STATUS OF UNDERNOURISHED INFANTS (6-12 MONTHS OLD) FROM RURAL VILLAGES IN KELANTAN

YIM HIP SENG

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By

YIM HIP SENG

Thesis Submitted in Fulfilment of the Requirement for the Degree of Master of Science in the Faculty of Medicine and Health Sciences Universiti Putra Malaysia

April 2001

DEDICATED TO

Those mothers and children who took part in this project

For their extraordinary co-operation and commitment for the success of the project

Yim's family and Rachel Lai

For their invaluable encouragement and emotional support towards the completion of this thesis

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Master of Science.

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Chairman: **Professor Khor Geok Lin, Ph.D.**

Faculty: **Medicine and Health Sciences**

Stunting in children is a common form of undernutrition in developing countries. Deficiency of micronutrients including iron and zinc has been associated with growth faltering in young children. The aim of the study was to assess the effects of iron and zinc supplementation on the growth and morbidity status of undernourished infants from rural villages in the district of Kota Bharu, Kelantan.

A six months randomised, double-blind, placebo-controlled study was conducted on 95 undernourished (weight-for-age Z score < –1.0 SD of NCHS reference) infants aged 6–12 months. The infants were divided into 5 groups, comprising 4 supplementation and a placebo groups: Group I–Fe (20 mg/week) + Zn (17 mg/week) with vitamins A (1700 μg/week) and C (20 mg/week); Group II–Fe with vitamins A and C; Group III–Zn with vitamins A and C; Group IV–Fe + Zn only; and Group V–Placebo (plain syrup).

Length, weight and circumferences of mid-upper arm (MUAC), head and chest were measured monthly. Morbidity status as indicated by symptoms including diarrhoea, fever, cough, running nose and vomiting was recorded by interviewing the mothers fortnightly. Information on feeding practices, use of complementary foods and their nutrient intake were also obtained from the mothers.

At the beginning of the study, there were no significant differences in the anthropometric indices among the infants in all the supplementation and placebo groups. At the end of the study, among the three groups that received vitamins A and C, Group I (Fe + Zn) and Group III (Zn) showed higher gain values in weight, length and MUAC than Group II (Fe). However, there were no significant differences in the gain values among these three groups. Comparing between Group I (Fe + Zn with vitamins A and C) and Group IV (Fe + Zn without vitamins A and C), there were no significant differences in the gain values for weight, length and MUAC.

When comparing all the four supplementation groups with the placebo group, it is found that Groups I, III and IV consistently ranked higher in the gain values for weight, length and MUAC than the placebo group. Group II showed lower gain value for weight than the placebo group. However, the differences in the gain values for all the anthropometric indices were not significant among all the five groups at the end of the study.

All the four supplementation groups recorded significantly lower prevalence and shorter duration of running nose and cough episodes compared with the placebo group. The mean prevalence and duration of fever occurrences in Group I and Group III were significantly lower than in Group II and the placebo group.

During the six months study, majority of the infants (>60%) were either breastfed and given infant formula with complementary foods or given infant formula with complementary foods, while about 16% ceased breastfeeding. Insufficient breast milk and children disliking breast milk were the main reasons for cessation of breastfeeding. Solid foods including commercial cereals, rice and porridge were first introduced at the mean age of five months. Based on the 24-hour recall, intake of protein, calcium, iron,

thiamine, riboflavin and niacin were found to be below the RDA levels for Malaysians. The mean intake of calories was about one-third of the RDA level. However, intake of vitamins A and C were above the RDA level (excluding the supplements given).

In general, weekly supplementation of zinc and iron was found to produce higher gain values in weight, length and MUAC of undernourished infants than the placebo group, although the differences were not statistically significant. The gain in the anthropometric indices appeared to be better for groups that received zinc by itself or in combination with iron supplementation. Morbidity status of the supplementation groups was generally better than that of the placebo group. The supplementation groups showed significantly lower prevalence and duration of running nose, cough and fever occurrences compared to the placebo group. More studies are necessary to determine the effectiveness of iron and zinc supplementation for periods longer than six months on the nutritional and health status of undernourished infants.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains.

KESAN SUPLEMENTASI FERUM DAN ZINK KE ATAS PERTUMBUHAN DAN STATUS MORBIDITI BAYI-BAYI YANG MENGALAMI MALPEMAKANAN (6–12 BULAN) DARI KAMPUNG-KAMPUNG LUAR BANDAR DI KELANTAN

Oleh

YIM HIP SENG

April 2001

Pengerusi: **Profesor Khor Geok Lin, Ph.D.**

Fakulti: **Perubatan dan Sains Kesihatan**

Pertumbuhan terbantut di kalangan kanak-kanak merupakan masalah malpemakanan di banyak negara membangun. Kekurangan mikronutrien termasuk ferum dan zink didapati mempunyai perkaitan dengan pertumbuhan terbantut dalam kanak-kanak. Objektif kajian ini ialah untuk mengkaji kesan suplementasi ferum dan zink ke atas pertumbuhan dan status morbiditi bayi-bayi yang mengalami malpemakanan dari kampung-kampung luar bandar di Daerah Kota Bharu, Kelantan.

Satu kajian rawak, "double-blind", kawalan-plasebo selama enam bulan dijalankan ke atas 95 bayi yang mengalami malpemakanan (berat-ikut-umur Z skor < –1.0 SD daripada rujukan NCHS) berumur 6–12 bulan. Bayi-bayi ini dibahagikan kepada 5 kumpulan, dengan 4 kumpulan suplementasi dan 1 kumpulan plasebo: Kumpulan I–Fe (20 mg/minggu) + Zn (17 mg/minggu) dengan vitamin A (1700 μg/minggu) dan vitamin C (20 mg/minggu); Kumpulan II–Fe dengan vitamin A dan vitamin C; Kumpulan III–Zn dengan vitamin A dan vitamin C; Kumpulan IV–Fe + Zn sahaja; dan Kumpulan V–Plasebo (sirup)

Panjang, berat, lilitan lengan tengah atas (MUAC), dada dan kepala diukur sebulan sekali. Status morbiditi yang dicirikan sebagai simtom termasuk cirit-birit, demam, batuk, selsema, sesak nafas dan muntah direkodkan dua minggu sekali dengan menemubual ibu. Maklumat tentang penyusuan bayi, makanan tambahan dan pengambilan nutrien juga diperolehi semasa kajian dijalankan.

Pada permulaan kajian, tidak terdapat perbezaan yang signifikan dari segi indeks anthropometrik di antara kumpulan-kumpulan suplementasi dan plasebo. Pada akhir kajian, antara kumpulan-kumpulan yang menerima vitamin A dan C, Kumpulan I (Fe + Zn) dan Kumpulan III (Zn) menunjukkan pertambahan yang lebih dalam berat, panjang, dan MUAC berbanding Kumpulan II (Fe). Tetapi, tiada perbezaan signifikan dalam nilai pertambahan antara ketiga-tiga kumpulan ini. Dalam perbandingan antara Kumpulan I (Fe + Zn dengan vitamin A dan C) dengan Kumpulan IV (Fe + Zn sahaja), tiada perbezaan yang signifikan dalam pertambahan berat, panjang dan MUAC.

Dalam perbandingan antara semua kumpulan suplementasi dengan kumpulan plasebo, Kumpulan I, III dan IV menunjukkan pertambahan nilai yang lebih dalam berat, panjang dan MUAC, berbanding kumpulan plasebo. Kumpulan II menunjukkan pertambahan berat yang lebih rendah berbanding dengan kumpulan plasebo. Tetapi, tiada perbezaan yang signifikan dalam nilai pertambahan untuk semua indeks anthropometrik antara kelima-lima kumpulan pada akhir kajian.

Kesemua 4 kumpulan suplementasi menunjukkan penurunan prevalens dan jangka masa untuk selsema dan batuk berbanding dengan Kumpulan plasebo. Min prevalens dan jangka masa untuk demam dalam Kumpulan I dan III menunjukkan penurunan signifikan berbanding Kumpulan II dan Kumpulan Plasebo.

Semasa enam bulan kajian, kebanyakan daripada bayi-bayi (>60%) menerima samada penyusuan ibu dan diberi susu formula dengan makanan tambahan atau diberi susu formula dengan makanan tambahan, manakala lebih kurang 16% sudah berhenti penyusuan ibu. Kekurangan susu ibu dan bayi tidak suka susu ibu adalah antara sebab berhenti penyusuan ibu. Makanan pejal termasuk bijirin komersil, nasi dan bubur pertama kali diberi kepada bayi pada min umur lima bulan. Berdasarkan "ingatan 24 jam", pengambilan protein, kalsium, ferum, thiamin, riboflavin dan niasin didapati berada di bawah paras RDA untuk Malaysia. Pengambilan kalori adalah lebih-kurang satu-pertiga daripada paras RDA. Tetapi, pengambilan vitamin A dan C berada lebih daripada paras RDA (tidak termasuk suplemen yang diberikan).

Umumnya, mingguan suplementasi dengan zink dan ferum menghasilkan pertambahan berat, panjang dan MUAC dalam bayi-bayi yang mengalami malpemakanan berbanding kumpulan plasebo, tetapi perbezaan adalah tidak signifikan secara statistik. Pertambahan indeks anthropometrik ini menampakkan nilai yang lebih baik dalam kumpulan yang menerima zink atau dengan ferum suplementasi. Status morbiditi dalam kumpulan suplementasi secara umumnya lebih baik berbanding kumpulan plasebo. Kumpulan suplementasi menunjukkan penurunan prevalens dan jangka masa bagi selsema, batuk dan demam berbanding kumpulan plasebo. Lebih banyak kajian diperlukan untuk menentukan kesan ferum dan zink suplementasi untuk jangka waktu yang lebih daripada enam bulan ke atas taraf pemakanan dan kesihatan bayi-bayi yang yang mengalami malpemakanan.

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Yim Hip Seng

April 2001

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I certify that an Examination Committee met on 20th April 2001 to conduct the final examination of Yim Hip Seng on his Master of Science thesis entitled "Effects of Iron and Zinc Supplementation on Growth and Morbidity Status of Undernourished Infants (6–12 Months Old) from Rural Villages in Kelantan" in accordance with Universiti Pertanian Malaysia (Higher Degree) Act 1980 and Universiti Pertanian Malaysia (Higher Degree) Regulations 1981. The Committee recommends that the candidate be awarded the relevant degree. Members of the Examination Committee are as follows:

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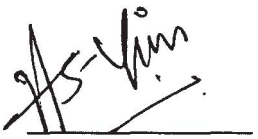
Date: 12 JUL 2001

DECLARATION

I hereby declare that the thesis is based on my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously or concurrently submitted for any other degree at UPM or other institutions.



YIM HIP SENG

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GLOSSARY OF TERMS

Definitions used in the WHO Global Data Bank on Breastfeeding

Exclusive breastfeeding refers to all children less than 2 years who are exclusively breast fed before the age of 4 months [<120 days]. This includes breast feeding from a wet nurse and feeding on expressed breast milk. However, it also includes children who were given vitamins, minerals, medicines, holy water, drops or syrups in addition to breast milk.

Ever breastfed is defined as all children less than 2 years who were ever given breast milk at any time.

Predominant breastfeeding is defined as all children less than 2 years who are given breast milk as the predominant source of nourishment before the age of 4 months [<120 days]. This indicator includes children who were fed on breast milk (including breastfeeding from wet nurse and feeding on expressed breast milk), as well as given other liquids (such as water, glucose water and fruit juice) except other non-human milk and food-based fluids.

Complementary feeding refers to children less than 2 years who were given breast milk and complementary foods including other non-human milk, solid or semi-solid foods before the age of 4 months [<120 days].

Bottle-feeding includes all children less than 2 years given any liquid or semi-solid food from a bottle with teat including expressed breast milk.

(Source: WHO, 1996a)

Anthropometric Indicators of Nutritional Status

Underweight defined as weight-for-age below minus 2 SD from the United States National Center for Health Statistics (NCHS) median.

Stunted defined as height-for-age below minus 2 SD from the NCHS median.

Wasted defined as weight-for-height below minus 2 SD from the NCHS median.

(Source: WHO, 1986)

CHAPTER ONE

INTRODUCTION

Background

Nutritional deficiencies including micronutrient deficiency prevail as a significant public health problem in most developing countries. It is estimated that at least 20% of the world population is at risk for micronutrient deficiency, primarily in developing regions (Trowbridge et al., 1993). Among the micronutrients, iron, iodine, and vitamin A deficiencies are the most prevalent in the at risk groups, which include young children and women of childbearing age.

Iron deficiency and anaemia affect more than 3.5 billion people in the developing countries (UNICEF/UNU/WHO/MI, 1999). The affected population groups in these countries are pregnant women (56%), school-age children (53%), non-pregnant women (44%) and pre-school children (42%) (United Nations ACC/SCN, 2000). As for iodine deficiency, globally about 740 million people are affected by goitre, and more than two billion (or over 38% of the population living in 130 countries) are estimated to be at risk of iodine deficiency disorders (United Nations ACC/SCN, 2000). The magnitude of clinical and sub-clinical vitamin A deficiency among children under five years is estimated as three million children and 250 million respectively (WHO, 1995a).

Young children aged 6–24 months old are at greatest risk for micronutrient deficiency, including iron and zinc. Young children require iron and other micronutrients for rapid growth and normal body physiological needs that breast

milk alone cannot meet. Low bioavailability of iron, vitamin A and zinc in complementary foods, aggravates micronutrient deficiency condition in young children (Gibson, 1994).

Micronutrient deficiencies alter physiological functions well before the clinically manifestation of the deficiency appears, and the true consequences of diet that is deficient in multiple micronutrients are often underestimated (Underwood, 1999). The consequential effects of micronutrient deficiencies include overall poor health, growth retardation, increased morbidity and mortality related to diarrhoea and respiratory diseases, psychomotor and learning disabilities, and reduced scholastic and work performance.

The primary effects of iron and zinc deficiencies in young children can be profound. Iron deficiency decreases physical capacity and growth, impairs motor and mental development and scholastic achievement (Aukett et al., 1986; Lozoff et al., 1987; Idjradinata and Pollitt, 1993). Iron supplementation has been reported to decrease stunting rate among anaemic pre-school children in Indonesia (Angeles et al., 1993).

The impact of zinc deficiency on human health has received increasingly more recognition world-wide. Zinc deficiency has been postulated to be as common as iron deficiency in the developing region owing to the nature of the staple diets that are predominantly plant-based and intakes of animal tissues are low (Gibson and Ferguson, 1998). Growth retardation and increased morbidity in young children have been shown to be associated with zinc deficiency in several studies (Chen

et al., 1985; Smit-Vanderkooy and Gibson, 1987; Cavan et al., 1993a). Zinc supplementation trials have shown to reduce the incidence, duration and severity of diarrhoea in Indian children (Sazawal et al., 1995; 1996; 1997).

In Malaysia, protein-energy malnutrition and micronutrient deficiency particularly iron and iodine in children still persist as a public health concern (Khor, 1997). Based on the Malaysian National Surveillance System in 1995, underweight (weight-for-age < –2.0 SD) among young children aged below five year was reported as 20.7% (Ministry of Health Malaysia, 1996). Meanwhile, the prevalence of stunting of infants in rural communities has been reported as 13.8% in boys and 10.8% in girls (Khor and Tee, 1997).

The prevalence of anaemia among young children between six and 24 months has been reported between 15% and 60% amongst different rural community groups (Tee et al., 1998). Whereby, a goitre prevalence of about 46% was found in population aged 15 years and above in an inland Iban community in Sarawak (Yap, 1985), and in Kelantan, a goitre rate of 37% in the same age group has been reported (Mafauzy et al., 1993).

Statement of Problem

Growth retardation prevails at moderate to high levels among children especially from low socio-economic families in developing countries. Approximately 43% of the children under five years of age in these countries are stunted (De Onis et al., 1993), as defined by height-for-age less than –2.0 SD of the WHO/NCHS reference median (WHO, 1986). Low dietary intake particularly energy and protein is

a major factor associated with poor linear growth. Low dietary intake often includes inadequacy in micronutrient intake as well (Allen, 1994).

In the early years of life, growth in length is on one part influenced by nutritional and environmental factors, such as poor diets and high infection rates, which in turn are the basic cause of stunting (Lei et al., 1999). Marginal zinc status is likely in children in developing countries, generally as a result of low quality diets that are often low in iron and zinc but high in fibre and phytates (Bates et al., 1993; Ferguson et al., 1993). Iron deficiency anaemia and reduced growth rate among pre-school children are two important nutrition-related problems in the developing countries (United Nations ACC/SCN, 1987; De Maeyer, 1989). Therefore, iron and zinc deficiencies have an important role in the overall growth and health status of young children, and should be of great concern to health authorities.

A number of community trials testing the effects of zinc supplementation on the growth of the children have been conducted world-wide with contradictory results. Positive effects of zinc supplementation on growth were documented in two major studies in the 1970's involving infants from low-economic families in the United States (Walravens and Hambidge, 1976), and school-aged boys and girls from Iran (Ronaghy et al., 1974).

Studies in the late 1980's and early 1990's on school-aged boys with low height-for-age in Canada (Gibson et al., 1989), infants from low-economic in France (Walravens et al., 1992), children recovering from malnutrition in Bangladesh (Khanum et al., 1988) and in Chile (Schlesinger et al., 1992) also showed

beneficial effects of zinc supplementation on growth. Growth of stunted infants was shown to improve with zinc supplementation in two recent studies, in Guatemala (Rivera et al., 1998) and Ethiopia (Umeta et al., 2000).

However, there were other studies that did not find positive effects of zinc on growth. These include studies involving pre-school and school-aged children from the United States (Hambidge et al., 1979), school-aged children in Guatemala (Cavan et al., 1993b), and pre-school children with suspected zinc deficiency in The Gambia (Bates et al., 1993) and Mexico (Rosado et al., 1997).

Iron deficiency has been shown to impair motor and mental development in young children (Lozoff et al., 1991; Idjradinata et al., 1993). Programmes such as mass supplementation and food fortification of iron have been advocated in many countries to combat iron deficiency (Yip, 1994). Iron supplementation have been shown to promote growth and reduced infectious disease morbidity in children (Chwang et al., 1988; Angeles et al., 1993).

As for studies that investigated the combined effects of iron and zinc, both iron and zinc deficiency were found to cause impaired immune response (Dallman, 1987; Keen and Gershwin, 1990). In Mexico, Rosado and colleagues (1997) found a significant reduction in morbidity related to diarrhoea in a group of Mexican pre-school children who received zinc and iron supplements. They also found a reduction in morbidity related to respiratory disease but this was not statistically significant from that for the placebo group.