

M I R A J a n a k p u r

Multiple Micronutrient Supplementation Study

The effects of antenatal multiple micronutrient supplementation on birthweight, gestation and infection

Annual report year 1



Painting by Asha Mandal

MIRA Janakpur

Brief summary of the study

Objective

Does antenatal multiple micronutrient supplementation for pregnant women have beneficial effects on birthweight, gestation and perinatal infection?

Hypotheses

Second and third trimester maternal supplementation with multiple micronutrients at one RDA will:
Increase birth weight of infants,
Prolong gestation at birth,
Reduce indices of maternal infection.

Design

Double-blind, randomised controlled trial.

Inclusion criteria

Pregnancy at gestations up to and including 20 weeks.
No pre-existing maternal illness of a nature likely to affect pregnancy.
Single live pregnancy with no major fetal anomalies detected by obstetric ultrasound at enrollment.
Residence potentially accessible for home follow-up.

Duration

Supplements from a maximum of 20 weeks gestation until delivery.

Key outcomes

Birthweight and gestational duration.

Micronutritional outcomes

Maternal plasma vitamins A, C and E and ferritin at enrollment and 32 weeks' gestation.

Immunological outcomes

Maternal plasma acute phase proteins at 32 weeks' gestation.
Maternal urine neopterin at 32 weeks gestation.
Breastmilk sodium/potassium ratio at one month postpartum.

Ethical approval

The study has approval from the Nepal Health Research Council and the Institute of Child Health, London. It is being carried out in collaboration with His Majesty's Government, Nepal, Ministry of Health and Janakpur Zonal Hospital.

Supplement composition

Intervention group (n=600)

Vitamin A	800 mcg	Folic acid	400 mcg
Vitamin E	10 mg	Vitamin C	70 mg
Vitamin D	5 mcg	Iron	30 mg
Vitamin B1	1.4 mg	Zinc	15 mg
Vitamin B2	1.4 mg	Copper	2 mg
Niacin	18 mg	Selenium	65 mcg
Vitamin B6	1.9 mg	Iodine	150 mcg
Vitamin B12	2.6 mcg		

Control group (n=600)

Iron	60 mg	Folic acid	400 mcg
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Summary of activities for year one

Overview

There was some delay in starting the study, as a result of a combination of the Maoist insurrection, the aftermath of the palace assassination and delayed clearance by His Majesty's Government Ministry of Health. The latter is mandatory for all MIRA studies since we view collaboration with the government as crucial for both capacity building and advocacy.

The inception phase included arrangement of space within and outside Janakpur Zonal Hospital, development of partnerships with medical and paramedical cadres, recruitment and training of staff, and development of study protocols and materials.

Enrollment commenced on 11 August 2002. As expected, the first six months of recruitment presented a series of opportunities for refining the trial process. The localities from which women attending for antenatal care could be enrolled were refined on the basis of the experience of the field team in tracing and visiting participants.

The counselling process has also developed with enrollment. Apart from explaining and answering questions about the study, the counselling team emphasise the need to communicate when women experience problems or deliver their babies at home. This is particularly exigent since the study

undertakes to measure birth weight within 72 hours of delivery, as decided at the 2002 Multiple Micronutrient Trial Steering Group meeting at the Institute of Child Health, London. This meeting also developed a series of best practice outputs - to increase the potential for pooled or meta-analysis - and the study protocols have been refined to meet them.

The recording and tracking systems have required intensive development in order to follow participants up for antenatal care, home visits, delivery and postnatal checks. Data on all completing participants are concurrently available in a relational database management system.

In terms of meeting the dictates of the study protocol, we are pleased to report that there have been no shortfalls in quality or deviations from the design. The rate of enrollment has increased steadily, and we expect that the study will not overrun its proposed timeframe. Our current projection is that we will complete enrolment in February 2004.

Early outputs

Costello AM de L, Osrin D. Micronutrient status during pregnancy and outcomes for newborn infants in developing countries. *J Nutr* 2003;133(Suppl):S1757-64.

Trial progress to end April 2003

Enrolled in study	562
Completed study	100
Voluntarily dropped out or lost to follow-up	20

MIRA Janakpur

Brief reports by section

Administration

The study is coordinated from a head office close to the hospital. Facilities include computing, email, telephone, fax and printers. Equipment for study activities is stored securely. Laboratory samples are stored deep frozen with backup generator. Data entry is carried out for both the study proper and ancillary activities.

Antenatal care

Antenatal care is provided from a clinic at the hospital, according to government protocols and with the assistance of the District Public Health Office. Referral is coordinated with collaborating obstetricians. The clinic is the point of identification of potential participants in the study. It refers them on for assessment, provides follow-up care and collects and coordinates data over the course of pregnancy. Postnatal checks, urine and breastmilk sampling are also carried out.

Enrollment

Obstetric ultrasound is carried out in accordance with the inclusion criteria. It is followed by counselling, consent, collection of enrollment data and supply of supplements. Allocation has been randomised off-site and supplements are prepacked in Kathmandu by enrollment number. All study staff are therefore blind to allocation. Participants are followed up monthly and referred for obstetric opinion when necessary. Data collation, filing and tracking are also performed. The tracking system involves the division of the study into four-weekly rotational blocks alternating between home and clinic.

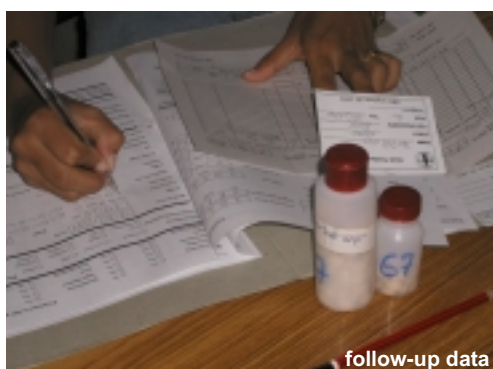
Laboratory

The laboratory is a designated, rewired and equipped room in the hospital pathology department. The following activities are performed: blood haemoglobin level, group and Rhesus status; rapid plasma reagin test for syphilis; preparation of plasma for vitamin A, C and E and acute phase protein assays; preparation of urine for neopterin assay; preparation of milk for sodium-potassium assay.



Follow-up

Participants are seen every two weeks, alternately at home and at the clinic. Supplements are provided monthly and adherence assessed fortnightly using a discrepancy estimate method of capsule counting. Visits are also made in the event of home delivery, and in the event of tracking problems. All visits are used as opportunities for counselling and checking for adverse events.



Antenatal care strengthening

Antenatal care services at Janakpur Zonal Hospital have been routinised and brought into compliance with the National Maternity Care Guidelines. MIRA has supported this process by developing protocols for current best practice, seconding staff and providing equipment.

Delivery care strengthening

Extensive collaboration has resulted in the improvement of hospital delivery services. MIRA support includes equipment, staff secondment and training, especially in essential newborn care.

Hospital birth audit

Since December 2002, data are collected on every birth at the hospital using a pro forma developed by MIRA, and entered into an electronic database for extraction of indicators such as rates of low birth weight, operative delivery, episiotomy, stillbirth and eclampsia.

Data safety monitoring

A Data Safety Monitoring Board (DSMB) will assess the interim findings at the halfway point.

Quality monitoring

The supplements have been manufactured by DK Pharma, Denmark, who were responsible for the manufacture of the UNICEF supplement. Interim compositional analysis will be carried out in mid-2003. Ultrasound scan quality is regularly assessed from recordings by the Superintendent Ultrasonographer, UCL Hospitals, London.

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M e m b e r s o f t h e s t u d y t e a m

Janakpur

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Programme Manager

Anjana Vaidya

Clinical Coordinator

Yagya Shrestha

Senior Technical Officer

Pusker Manandhar

Administrative Officer

Shiv Shankar Chaube

Bechan Chaudhary

Binaya Karki

Field Officers

Durna Thapa

Antenatal Care Coordinator

Puspa Baniya

Antenatal Care Provider

Sushila Karki

Nain Tara Sah

Chandra Thapa

Maternity Care Providers

Gunanand Sah

Syam Jha

Laboratory Officers

Phulo Kapar

Heena Chaudhary

Housekeepers

Badri Gyawale

Driver

Steering group

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Mithila Sharma Adhikari

Ram Naresh Pandit

Kalpna Bachhar

Obstetricians

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Pathologist

KP Yadav

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enrollment and follow-up



one month postpartum

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