

# Prevention of vitamin A deficiency by supplementation alongside routine vaccinations: a randomised controlled trial in Tanzanian infants

**Submission date**

03/08/2004

**Recruitment status**

No longer recruiting

**Registration date**

22/09/2004

**Overall study status**

Completed

**Last Edited**

26/10/2007

**Condition category**

Nutritional, Metabolic, Endocrine

☐ Prospectively registered

☐ Protocol

☐ Statistical analysis plan

☐ Results

☐ Individual participant data

☐ Record updated in last year

**Plain English summary of protocol**

Not provided at time of registration

## Contact information

**Type(s)**

Scientific

**Contact name**

Dr Tracey Goodman

**Contact details**

World Health Organization

20 Avenue Appia

Geneva-27

Switzerland

CH-1211

goodmant@who.int

## Additional identifiers

**Protocol serial number**

WHO/RPC005

## Study information

Scientific Title

## Study objectives

The primary objectives of the trial are to:

1. Measure the effect of 400,000 IU of vitamin A given in two divided doses of 200,000 to mothers, and 3 doses of 50,000 IU of vitamin A given to their infants concurrently with Diphtheria, Pertussis and Tetanus (DPT)/Polio immunisations, on vitamin A status of the infants at 26 weeks of age
2. Compare the effect of such a regimen to that of the previously recommended regimen of 200,000 IU of vitamin A given to mothers and 3 doses of 25,000 IU of vitamin A given to their infants concurrently with DPT/Polio immunisations
3. Measure the short-term side effects of each of the two doses of 200,000 IU given to mothers, and of the 50,000 IU of vitamin A administered with each of the three DPT/Polio immunisations

The secondary objectives are to:

1. Measure the relative effect of the two different maternal dosing regimens on the breast milk retinol concentration up to at 6 and 9 months post partum
2. Measure the effect of the maternal doses of vitamin A on the relative incidence of short-term side effects in the mother over the 48-hour period after the first and second 200,000 IU maternal doses of vitamin A
3. Measure the effect of the maternal doses of vitamin A on the breast milk retinoic acid concentration 3 hours after the first and second 200,000 IU maternal doses of vitamin A
4. Examine if any relative impacts on vitamin A status are sustained at 9 months of age

Related to the main objectives, the following hypotheses will be tested:

HYPOTHESIS 1: Giving 400,000 IU of vitamin A to mothers within 6 weeks of delivery, plus 50,000 IU given to their infants with their DPT/Polio immunisations, will improve infants' vitamin A status to a significantly greater degree than giving 200,000 IU of vitamin A within 6 weeks of delivery, plus 25,000 IU given to their infants with each of their three DPT/Polio immunisations. This will be measured by mean serum retinol concentration, or by proportions below 20ug/dl, or proportions with abnormal modified Retinol Dose Response (mRDR) at 6 months of age. The proportion of infants with serum retinol concentration below 20ug/dl at 6 months of age will be approximately 37% in the comparison group infants and 27% or less in the group of infants allocated to receive the higher dose regimen.

HYPOTHESIS 2: Giving 50,000 IU of vitamin A to infants with their DPT/Polio immunisations will produce no significant increase in the incidence of short-term side effects, relative to 25,000IU.

The outcomes to be monitored for the above objectives include serum retinol concentrations, mRDR tests, and incidence of side effects such as bulging of anterior fontanelle and vomiting, and incidence of severe morbidity.

HYPOTHESIS 3: Giving 400,000 IU of vitamin A to mothers in the post partum period will result in a greater improvement in breast milk retinol concentrations at 6 months post partum than that achieved with 200,000IU, and that this improvement will be sustained up to 9 months.

HYPOTHESIS 4: Giving a second 200,000 IU dose of vitamin A to mothers in the post partum period will result in no significant increase in the incidence of short-term side effects, relative to no second dose.

HYPOTHESIS 5: Giving a second 200,000IU dose of vitamin A to mothers in the post partum period will result in no significant increase in the prevalence of potentially toxic breast milk retinoic acid concentrations 3 hours after the second maternal dose, relative to no second dose.

**HYPOTHESIS 6:** At 9 months of age, the vitamin A status of infants who were allocated to receive the higher dose regimen will be significantly better than the status of infants who were allocated to receive the lower dose regimen.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Ethics approval received from the Research Ethics Committees (REC) of:

1. National Institute for Medical Research, Ministry of Health (Tanzania) on the 1st October 2001
2. Second year of trial approved by the London School of Hygiene and Tropical Medicine on the 5th August 2003
3. World Health Organization (WHO) Secretariat Committee on Research Involving Human Subjects (SCRIHS) - conditional approval on 11th April 2003, amendments approved on 8th October 2003

### **Study design**

Randomised controlled trial

### **Primary study design**

Interventional

### **Study type(s)**

Prevention

### **Health condition(s) or problem(s) studied**

Vitamin A deficiency

### **Interventions**

1st Group:

1. Mothers 200,000 IU Vitamin A shortly after delivery
2. Infants: 25,000 IU Vitamin A with each Diphtheria, Pertussis, Tetanus (DPT) vaccine 1, 2 and 3

2nd Group:

1. Mothers 200,000 IU Vitamin A at infant's Bacillus Calmette-Guerin (BCG) vaccine and another 200,000 IU Vitamin A at infant's 1st DPT
2. Infants: 50,000 IU Vitamin A with each DPT 1, 2 and 3

Time Frame:

Recruitment should start in December 2001 and is expected to last for approximately 9 months. Hence the data required to address the primary endpoint will be available 15 months after the start of recruitment. Data required to address the secondary endpoints will be available 21 months after the start of recruitment. Assuming that the WHO-appointed micronutrient laboratory will be able to report the results of vitamin A-related analyses within six weeks of the completion of specimen collection, all laboratory and statistical analyses will be completed within 4 months of finishing field activities.

### **Intervention Type**

Supplement

### **Phase**

Not Specified

**Drug/device/biological/vaccine name(s)**

Vitamin A supplementation

**Primary outcome(s)**

1. Prevalence of Vitamin A Deficiency (VAD) (any: less than 20 mg/dL and severe: less than 10 mg/dL) at 6 months of age
2. Incidence of each of the following:
  - 2.1. Bulging fontanelle
  - 2.2. Temperature greater than 37.5°C
  - 2.3. Vomiting
  - 2.4. Diarrhoea
  - 2.5. Inability to suck/feed during the two days following each vitamin A supplementation

**Key secondary outcome(s)**

1. Mean serum retinol concentration at 6 months of age
2. Prevalence of VAD (any and severe) at 9 months of age
3. Mean retinol concentration at 9 months of age

**Completion date**

01/09/2003

## **Eligibility**

**Key inclusion criteria**

1. Mothers normally resident in the study area
2. Informed consent obtained from the mother

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Child

**Sex**

All

**Key exclusion criteria**

1. Mothers unable to give informed consent
2. Mothers considered to be at high risk of adverse outcome in puerperal period
3. Multiple deliveries
4. Severe adverse reaction to vitamin A supplementation

**Date of first enrolment**

01/12/2001

**Date of final enrolment**

01/09/2003

## **Locations**

**Countries of recruitment**

Switzerland

Tanzania

**Study participating centre**

**World Health Organization**

Geneva-27

Switzerland

CH-1211

## **Sponsor information**

**Organisation**

World Health Organization (WHO)/Department of Immunisation, Vaccines and Biologicals (IVB)  
(Switzerland)

**ROR**

<https://ror.org/01f80g185>

## **Funder(s)**

**Funder type**

Research organisation

**Funder Name**

World Health Organization (WHO)/Department of Immunisation, Vaccines and Biologicals (IVB)  
(Switzerland)

## **Results and Publications**

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration