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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	[ ] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 22/09/2004	**Overall study status** Completed	
Last Edited 26/10/2007	**Condition category** Nutritional, Metabolic, Endocrine	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

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

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Prevention

Participant information sheet

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 measure
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

Secondary outcome measures
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

Overall study start date
01/12/2001

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

Age group

Child

Sex
Both

Target number of participants
770 infants

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)

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Sponsor type
Research organisation

Website
http://www.who.int

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

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration