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OPTIMIZING NUTRIENT SUPPLEMENTATION AMONG PREGNANT AND REPRODUCTIVE AGE WOMEN IN KENYA (VIRUTUBISHO)

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BACKGROUND AND OBJECTIVES

Micronutrient deficiencies are common and result in poor health and pregnancy outcomes. WHO recommends multiple micronutrients supplements (UNIMMAP formulation) over iron and folate (IFA). Dosage in UNIMMAP is based on studies among healthy populations in North American women. Emerging data from Gambia & Bangladesh indicates that the current dose may not be adequate for women in LMIC with inadequate diets.

The Virutubisho study objectives are:
Primary : to determine optimal dosing of multiple micronutrient supplements (MMS) to correct micronutrient deficiencies among pregnant and non-pregnant women of reproductive age in Kilifi County, Kenya

Secondary: to describe tolerability and safety of micronutrients at different doses, including birth outcomes.

STUDY ACTIVITIES

In each cohort, the first 36 women will undergo "rich" PK sampling with more frequent sampling visits and more samples taken than the following 72 women in the "sparse" PK sampling regime as shown in the study flow chart below. Birth outcomes including anthropometry will be recorded as well as health of mother and infant until 1 month postpartum.

STUDY DESIGN

A Phase 2b dose-finding pharmacokinetic (PK) trial, recruiting 2 cohorts: 108 non-pregnant and 108 pregnant women, aged 18 to 35 years from 2 locations of Kilifi North sub-county. Each cohort is randomized into 3 intervention arms: control, test dose 1 and test dose 2 containing 15 or 24 micronutrients (MN)- see table 1. Non-pregnant women will receive MN for 3 months, and pregnant, enrolled at 14-20 weeks' gestation, will receive MN until delivery. Fieldworkers will administer the MNs daily to women at their homes.

Table 1 Contents of micronutrient supplements in mg

Nutrient	Control	Test dose 1	Test dose 2
Vitamin A	0.8	1.6	2
Vitamin D	0.005	0.01	0.02
Vitamin E	10	100	300
Thiamine	1.4	2.8	5.6
Riboflavin	1.4	2.8	5.6
Nicotinamide	18	35	70
Vitamin B12	0.0026	0.125	0.25
Vitamin B6	1.9	3.8	7.6
Folate	0.4	0.6	0.78
Vitamin C	70	140	280
Iron	60	60	60
Zinc	15	20	30
Iodine	0.15	0.22	0.26
Selenium	0.065	0.13	0.26
Copper	2	2	2
Calcium	-	500	500
Phosphorus	-	500	500
Vitamin K	-	0.09	0.09
Pantothenic acid	-	7	7
Biotin	-	0.035	0.035
Choline	-	550	900
Potassium	-	1,000	1,000
Manganese	-	2.6	2.6
Magnesium	-	350	350

Study Flow chart

Community Mobilization & DSS records

Screening for eligibility *All: Anthropometry, full blood count, biochemistry & urine pregnancy; If pregnant: ultrasound & ANC profile*

Information and Consent *(Demography, SEE &GPS)*

Non-pregnant, non-lactating women 18-35yrs old (N=108)

Baseline tests *(HIV, helminths, malaria, biochemistry, inflammatory markers, FBC)*

Randomization into three arms

- Control (N=36) Fortified BEP +Placebo tablet
- Test dose 1 (N=36) Expanded fortified BEP+MMS tablet
- Test dose 2 (N=36) Larger fortified BEP+MMS tablet

All: Daily supplementation for 3 months (Observed by FW)

Systematically allocate sampling into 2 cohorts (Rich & Sparse)

Rich N=36: (8 blood, 5 urines, 2 stool)

Day 1: Blood predose, 1hr, 2hrs, 4hrs.
Urine: predose & post-dose & stool

Days, 7, 14, week 6:
Predose blood & urine

Month 3:Predose Blood, Urine & Stool

Sparse N=72: (3 blood, 2 urine, 2 stool)

Day 1: Blood: predose, 2hrs.
Urine: predose & postdose & stool

Month 3: Predose Blood, Urine, Stool

Study conclusion

Pregnant women <20 weeks gestation (N=108)

Baseline tests *(HIV, helminths, malaria, biochemistry, inflammatory markers, FBC)*

Randomization into three arms

- Control (N=36) Fortified BEP +Placebo tablet
- Test dose 1 (N=36) Expanded fortified BEP+MMS tablet
- Test dose 2 (N=36) Larger fortified BEP+MMS tablet

All: Daily supplementation to birth (Observed by FW)

Systematically allocate sampling into 2 cohorts (Rich & Sparse)

Rich N=36: (8 blood, 5 urine, 2 stool)

Day 1: Blood predose, 1hr, 2hrs, 4hrs.
Urine predose & postdose & stool

Days, 7, 14, week 6:
Predose blood & Predose urine

Month 3: Predose Blood, Urine & Stool

Month 5:Predose Blood, Urine

Birth: Blood, Urine & cord blood

1 month post-delivery: Breastmilk

sparse N=72: (3 blood, 2 urine, 2 stool)

Day 1: Blood: predose , 2hrs.
Urine predose & postdose & stool

Month 3: Predose Blood, Urine & Stool

Birth: Blood, Urine & cord blood

1 month post-delivery: Breastmilk

Study conclusion

EXPECTED RESULTS

Optimal doses of multiple micronutrient supplements for correction of deficiencies in the study population will be calculated from PK modelling

DISCUSSION

The identified multiple micronutrient supplement doses will be tested in future Phase 3 trials to assess safety, birth, and developmental outcomes.

ETHICS STATEMENT

The study has received ethics approval from the KEMRI Scientific and Ethics Review Unit (SERU) 4609 and Oxford University Tropical Research Ethics Committee (OxTREC) 37-22

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