

## Micronutrient supplementation in addition to antiprotozoal therapy for reducing morbidity and possibly mortality

### CITATION

Kelly P, Musonda R, Kafwembe E et al. Micronutrient supplementation in the AIDS diarrhoea-wasting syndrome in Zambia: A randomized controlled trial. *AIDS* 1999;13:495-500

### RESEARCH QUESTION

Does micronutrient supplements in addition to antiprotozoal therapy reduce morbidity and possibly mortality?

### THE STUDY DESIGN

Randomized placebo controlled trial

### STUDY SETTING

Home care service of Ndola Central Hospital in Zambia

Ethics approval obtained.

Written informed consent was obtained.

### PARTICIPANTS

Included: HIV-seropositive patients with persistent diarrhoea (over one month duration)

Excluded: Patients under the age of 18; received antibiotics in the week prior to recruitment; pregnant women; had Karnofsky<sup>1</sup> scores of over 80 or under 50.

### INTERVENTIONS

All participants received oral rehydration therapy and 5mg of folic acid daily and the use of antidiarrhoeal agents was permitted.

Intervention Group: 800 mg of albendazole twice daily for 14 days plus 10500 U of vitamin A, 300 mg of vitamin C, 300 mg of vitamin E, 150 µg of selenium, 200 mg of zinc and 1 tablet of zinc sulphate daily for 14 days.

Control: 800 mg of albendazole twice daily for 14 days plus placebo for 14 days  
Placebo was not identical but was not identifiable by any markings.  
Patients were followed up to 3 months.

### OUTCOMES

Primary: Recovery from diarrhoea during the first 12 weeks; Change in Body Mass Index (BMI), change in mid-upper arm circumference (MUAC) and death during the first 4 weeks

Secondary: Change in vitamin A and E concentrations in serum after 4 weeks; Change in CD4 and CD8 cell counts at 4 weeks

**RISK OF BIAS** (Risk Scale: Low – Moderate – High)

### SELECTION BIAS: Moderate

Patients were randomly allocated. Method of allocation sequence generation was not specified (under Acknowledgements, it is mentioned that the micronutrient supplements were pre-randomized). Allocation concealment not reported. Demographic and clinical characteristics of the patients were similar in both intervention and control groups at initial treatment allocation.

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<sup>1</sup> Karnofsky score is a subjective measure of how well the patient is doing. Karnofsky score is measured from 0 to 100 for e.g. 0: Dead, 50: Requires considerable assistance and frequent medical care, 100: Normal, no complaints or evidence of disease.

**PERFORMANCE BIAS: Moderate**

(I.e what else happened that may have affected the result?)

All participants received oral rehydration therapy and folic acid daily and the use of antidiarrhoeal agents was permitted. No blinding reported. Placebo was not identical but was not identifiable by any markings.

**DETECTION BIAS: Moderate**

No blinding reported. Initial investigations included full blood count, CD4 and CD8 cell counts and serum vitamin A and E concentrations. Diarrhoea was defined as three or more loose stools per 24 hours. Weight, height, MUAC and BMI were measured and reported.

**ATTRITION BIAS: Moderate**

	Intervention	Placebo
Started	66	69
Completed trial	32	43
Loss to follow-up	34 (51.5%)	26 (37.7%)

No intention to treat analyses was carried out.

**STUDY FINDINGS**Recovery from Diarrhoea

Weeks	Treatment	Event Rate	RRR	ARR	NNT
1-2	I	85/126	1%	0.009	111
	P	93/136	-15%;18%	-0.104;0.122	NNT 8;Inf to NNH 10;Inf
3-4	I	30/85	17%	0.072	14
	P	45/106	-16%;50%	-0.066;0.210	NNT 5;Inf to NNH 15;Inf
5-8	I	44/146	9%	0.026	38
	P	50/182	-4.5%;26%	-0.125;0.073	NNT 14;Inf to NNH 8;Inf
9-12	I	29/130	28%	0.049	20
	P	30/172	-81%;24%	-0.140;0.042	NNT 24;Inf to NNH 7;Inf

Mortality

No raw data was provided. "There was no difference in mortality in the treatment groups (RR 1.06,  $P = 0.87$ )".

Change in serum vitamin A concentrations did not differ in the two treatment groups. Change in BMI and MUAC not reported. CD4 cell count did not change after 4 weeks and no mention of CD8 cell count was made.

**ADVERSE EVENTS**

No adverse events were recorded except death.

**COMMENTS**

Considering the doubtful quality of the trial, the effect of micronutrient supplements in addition to antiprotozoal therapy for reducing morbidity and mortality remains unclear.

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