ISRCTN02694183 https://doi.org/10.1186/ISRCTN02694183

Impact of different modes of vitamin B12 supplementation on subclinical vitamin B12 deficiency on sensory, motor and cognitive function among older people

Submission date 31/03/2009	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 30/04/2009	**Overall study status** Completed	
Last Edited 19/10/2017	**Condition category** Nutritional, Metabolic, Endocrine	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Ricardo Uauy

Contact details
El Libano 5540
Santiago
Chile
7830489

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Impact of different modes of vitamin B12 supplementation on subclinical vitamin B12 deficiency on sensory, motor and cognitive function among older people: a community based prospective cluster randomised controlled double blind interventional trial

Study objectives
1. Unrecognised subclinical vitamin B12 deficiency is associated to impaired cognitive and/or nerve conduction in Chilean older people (70 - 79 years)
2. Vitamin B12 intake provided by the National Complementary Food Program (PACAM) to older people in Chile based on existing recommendations, is potentially insufficient to prevent poor cognition, neuroconduction and sensory functions related to vitamin B12 intake
3. High dose (1 mg/day) vitamin B12 intake will correct subclinical vitamin B12 deficiency, will modify biomarkers of vitamin B12 status and will improve impaired cognitive, sensory and nerve conduction in older people
4. Vitamin B12 supplementation through an existing nutrition program for older people will be more effective than vitamin B12 administered as a pill over an 18-month intervention

Ethics approval required
Old ethics approval format

Ethics approval(s)
University of Chile, Institute of Nutrition and Food Technology (INTA), 19/07/2006, ref: IRB00001493

Study design
Community-based prospective cluster randomised controlled double-blind interventional trial

Primary study design
Interventional

Secondary study design
Cluster randomised trial

Study setting(s)
Community

Study type(s)
Quality of life

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Vitamin B12 deficiency

Interventions

A routine fortified food program provided monthly is delivered by the Ministry of Health under the PACAM programme through the health centres. The nutritional products are 1 kg of Años Dorados (a cereal-legume and vegetable powdered food) which provides 400 kcal/100 g and multiple micronutrients (including B12 1.4 µg/100 g) and 1 kg of Bebida Láctea, a micronutrient fortified milk-based drink (including B12 2.8 µg/100 g). The recommended serving size of these supplements provides daily 1.4 µg or 58.3% of the daily B12 recommended intake (World Health Organization [WHO] 2002) and 20% of daily energy needed by older people.

Potential study subjects will be identified from the registry of older people participating in the PACAM in 15 health centres; 20 subjects per centre/cluster will be included in three arms. Each subject will be included in the study after assessing inclusion and exclusion criteria and will be followed for 18 months.

All subjects in the three study arms will receive both a pill and the food supplement in order to maintain the double blind nature of the study. Each centre/cluster was randomly assigned to one of three arms:
1. 1 mg B12 pill taken daily and a routine PACAM food
2. Placebo pill and the PACAM food fortified to provide 1 mg of B12 as consumed on a daily basis
3. Routine PACAM food and a placebo pill

Compliance with the nutrition intervention is defined for this study as collecting more than 1 kg per month of the fortified food as documented by the health centres. Compliance for the pill intervention will be monitored based on collection of the pills supplement from the health centre, 12 out of 18 months will be considered compliant. Sample size calculation 20 subjects per each of 5 clusters in each study arm was calculated based on the capacity to detect biochemical changes in serum vitamin B12 markers, neuroconduction velocity, and mini-mental test as the main outcomes of this study.

Sample size was calculated based on the capacity to detect biochemical changes in serum vitamin B12 markers, neuroconduction velocity, and mini-mental test as the main outcomes of this study. The intra-cluster coefficient (ICC) of the serum B12 values across the study clusters was assumed to be 0.00001 which is consistent with the Aberdeen database (http://www.abdn.ac.uk/hsru/epp/iccs-web.xls) of reported ICCs for interventions in primary care (range: 0.00001 to 0.28). 17 subjects per cluster, a total of 85 per arm were found to be necessary to detect a 25% drop in the number of marginal vitamin B12 deficiency at 18 months based on serum B12 less than 221 mg/dl (power = 95%, a = 0.05), using a non-parametric comparison of treatment arms. Similar sample size estimates were considered for the mini-mental test score assessment. 40 per arm a total of 120 were found to be necessary to detect an 8% modification in neuroconduction velocity (power = 90%, a = 0.05) considering a repeated measure double sided parametric test and a similar number of subjects were considered necessary to detect an 8% modification increase in nerve conduction velocity (power = 80%, a = 0.05) using single sided parametric testing. It was estimated a 15% loss of subjects over the 18 months study, thus final sample size was 100 subjects per arm (20 subjects per each of the 5 health centres/cluster in each study arm) for vitamin B12 status and mini-mental studies. For neuroconduction study 40 subjects were considered sufficient, thus a subsample of the 8 per cluster or 40 per arm per arm were randomly selected for nerve conduction studies and subtle functional neurophysiologic tests on entry and at 18 months (end of study).

Intervention Type
Supplement

Phase

Not Applicable

Drug/device/biological/vaccine name(s)
Vitamin B12 supplementation

Primary outcome measure
1. Serum vitamin B12 status, assessed at initial visit and 3, 9 and 18 months
2. Haematological and biochemical parameters, assessed at initial visit and 3, 9 and 18 months
3. Peripheral nerve conduction, assessed at initial visit, 3 and 18 months
4. Compound muscle action potential (CMAP) amplitude, distal motor latency and F-wave latency (a measure of conduction time from the distal stimulation site to the spinal cord), assessed at initial visit, 3 and 18 months
5. Mini-mental score: Mini Mental State Examination (MMSE), assessed at initial visit and 18 months

Secondary outcome measures
1. Serum folate, homocysteine, methyl malonic acid, holo-transcobalamin, assessed at initial visit and 3, 9 and 18 months
2. Neurological battery evaluation include sensory pathways of conduction of afferent sensory pathways of small diameter, quantitative thermal and somatosensory responses, specific neurosensory pathways and visual evoked potential. All techniques will use surface electrodes and limb temperature will be controlled to be above 30°C by suitable heating and blankets. Assessed at initial visit, 3 and 18 months.
3. Cognitive function: Test Wechsler, Consortium to Establish a Registry for Alzheimer's Disease (CERAD), Test Hamilton and Trail Making Test, assessed at initial visit and 18 months

Overall study start date
01/09/2008

Completion date
31/03/2010

Eligibility

Key inclusion criteria
1. Men and women between 70 to 79 years of age
2. Participate in the National Health Service Nutrition Program for Older People (PACAM) targeted to the elderly (70 years or older)

Participant type(s)
Patient

Age group
Senior

Sex
Both

Target number of participants
300 participants from 15 health centres (clusters)

Key exclusion criteria
1. Diabetes (fasting blood glucose greater than or equal to 126 mg/dl)
2. Hypothyroidism (thyroid stimulating hormone [TSH] greater than 6 mlU/l)
3. Serum creatinine greater than or equal to 30 mg/ml
4. Serum vitamin B12 level less than 120 or greater than 700 pmol/l or vitamin B12 supplemented
5. Cerebrovascular disease
6. Previous gastrointestinal surgery
7. Unexplained weight lost greater than or equal to 3 kg in the previous 3 months
8. Low cognitive development (Mini-mental test less than 20, and Pfeffer test greater than 5)

Date of first enrolment
01/09/2008

Date of final enrolment
31/03/2010

Locations

Countries of recruitment
Chile

Study participating centre
El Libano 5540
Santiago
Chile
7830489

Sponsor information

Organisation
University of Chile, Institute of Nutrition and Food Technology (INTA) (Chile)

Sponsor details
E Libano 5540
Santiago
Chile
7830489

Sponsor type
University/education

Website
http://www.inta.cl

ROR
https://ror.org/047gc3g35

Funder(s)

Funder type
Government

Funder Name
Fondo Nacional de Desarrollo Científico y Tecnológico (ref: FONDECYT Nº 1070592)

Alternative Name(s)
National Fund for Scientific and Technological Development, El Fondo Nacional de Desarrollo Científico y Tecnológico, FONDECYT

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Chile

Funder Name
Ministry of Health (Chile)

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	27/09/2011		Yes	No

Results article	results	01/01/2016	Yes	No
Results article	results	24/07/2017	Yes	No
Results article	results	01/10/2017	Yes	No