

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

Protocol

Registration date
30/04/2009

Overall study status
Completed

Statistical analysis plan

Results

Last Edited
19/10/2017

Condition category
Nutritional, Metabolic, Endocrine

Individual participant data

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

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Additional identifiers

Protocol serial number

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

Study type(s)

Quality of life

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%, $\alpha = 0.05$), 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%, $\alpha = 0.05$) 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%, $\alpha = 0.05$) 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(s)

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

Key secondary outcome(s)

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

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

Healthy volunteers allowed

No

Age group

Senior

Sex

All

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 mIU/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)

ROR

<https://ror.org/047gc3g35>

Funder(s)

Funder type

Government

Funder Name

Fondo Nacional de Desarrollo Científico y Tecnológico (ref: FONDECYT N° 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

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?
Results article	results	01/01/2016		Yes	No
Results article	results	24/07/2017		Yes	No
Results article	results	01/10/2017		Yes	No
Protocol article	protocol	27/09/2011		Yes	No