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Comparison of milk containing A1A2 beta casein and milk containing A2A2 beta casein among students of the Faculty of Public Health, Universitas Indonesia

Submission date 24/05/2018	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol
Registration date 25/06/2018	**Overall study status** Completed	[ ] Statistical analysis plan [ ] Results
Last Edited 29/05/2018	**Condition category** Signs and Symptoms	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol

Background and study aims

The symptoms of digestive discomfort after consuming dairy products are the main reasons for somebody to avoid commercial dairy products. Most suspect that post-dairy digestive discomfort is caused by lactose intolerance, but in fact some cases are because of a reaction to several types of milk proteins. Cow's milk contains two types of beta casein, A1 beta casein and A2 beta casein. The A1 beta casein type commonly found in commercial milk is broken down into beta-casomorphin-7 (BCM-7) in the digestive system and causes digestive discomfort. In contrast to A1 beta casein type, A2 beta casein type does not produce BCM-7 so it does not show similar symptoms. The aim of this study is to compare the effects of milk with different types of beta casein - i.e. milk containing beta casein combination A1 type and A2 type (A1A2 beta casein) and milk containing only A2 beta casein type (A2A2 beta casein) - on the symptoms of post-dairy digestive discomfort, stool frequency and consistency and also immune response.

Who can participate?

Undergraduate students of Faculty of Public Health, Universitas Indonesia, aged 17-25, who have symptoms of digestive discomfort after consuming dairy or cow’s milk products

What does the study involve?

Participants are assessed regarding symptoms of post-dairy digestive discomfort, diet, nutritional status and blood pressure. All participants receive both milk containing A1A2 beta casein and milk containing A2A2 beta casein. They are randomly allocated to receive the milk containing A1A1 beta casein then milk containing A2A2 beta casein (sequence 1) or milk containing A2A2 beta casein then milk containing A1A2 beta casein (sequence 2). Each participant consumes two bottles of 200 ml of milk daily for 2 weeks. Both types of milk are provided by ABC KOGEN. To ensure that the sample is actually consumed by participants, they have to consume the milk at the Center for Nutrition and Health room on weekdays and at weekdays the milk is taken home by the participants then they return the used bottle. There is a two-week break between consuming the two types of milk where the participants are not

allowed to consume cow’s milk products in order to remove or clear the effects of the previous milk. Participants fill out two weekdays and one weekend food diary to monitor their diet. Participants are also given a list of foods as a substitute for the source of nutrition from dairy products. Participants fill out forms about the symptoms of post-dairy digestive discomfort and stool frequency and consistency, and provide blood samples before and after the intervention to measure their immune response.

What are the possible benefits and risks of participating?
Participants will get some benefit such as knowing their body's immune response to dairy products. Overall data collection has no risks. However, an error of the screening procedure may occur so that poses a risk to this research. To minimize the risk, all data are collected by trained personnel according to the standard procedures. In addition, all of the participants are insured and receive treatment if there are any health complaints during this study.

Where is the study run from?
Universitas Indonesia

When is the study starting and how long is it expected to run for?
August 2017 to April 2018

Who is funding the study?
ABC Kogen

Who is the main contact?
Dr Ahmad Syafiq

Contact information

Type(s)
Scientific

Contact name
Dr Ahmad Syafiq

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

No.021/SP/AKD/2017

Study information

Scientific Title
Comparison of milk containing A1A2 beta casein and milk containing A2A2 beta casein to the symptoms of post dairy digestive discomfort and milk-specific IgE among students of the Faculty of Public Health, Universitas Indonesia Depok (a double-blind randomized two-way cross-over study)

Study objectives
Milk containing A2A2 beta casein decreases the symptoms of post-dairy digestive discomfort and improves immune response more than milk containing A1A2 beta casein.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Committee of Ethics Research and Public Health Service, Faculty of Public Health, Universitas Indonesia, 13/10/2017, ref: 529/UN2.F10/PPM.00.02/2017

Study design
Interventional double-blind randomized two-way cross-over single-centre study

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Other

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
Post-diary digestive discomfort

Interventions
All participants selected in this study received two interventions, that is milk containing A1A2 beta casein and milk containing A2A2 beta casein. Participants were randomized to decide who received the milk containing A1A2 then milk containing A2A2 (sequence 1) or milk containing A2A2 then milk containing A1A2 beta casein (sequence 2). Each participant consumed 200 ml milk twice a day for 2 weeks of intervention. Both types of milk were provided by ABC KOGEN. Before entering second intervention, there are a washout period (intervention-free). In this

period, the participants will not get any intervention for 2 weeks to remove or clear the effects of previous intervention. The participants were not allowed to consume dairy products on the washout period during this study. Participants will be given a list of foods as a substitute for the sources of nutrition from dairy products. On intervention period, participants were asked to fill out the form of symptoms of post-dairy digestive discomfort and Bristol Stool Scale as well as taking blood samples. Blood samples were taken within a range of 12 hours before or after the intervention.

Intervention Type
Other

Primary outcome measure
1. Symptoms of post-diary digestive discomfort, measured by questionnaire that asked the participants how they felt after milk consumption, such as bloating, abdominal pain, flatulence, heavy stomach and borborygmi (stomach rumbling). The participants were asked to fill out each questionnaire after milk consumption (twice a day) during the intervention period. Each symptom was ranked on Likert scale, as never (score =0), rarely (score=1), moderate (score=2) and severe (score=3)
2. Immune response (milk-specific IgE antibodies), assessed by milk-specific IgE blood serum test. Blood serum sample was performed by the laboratory assistant as follows: blood samples were taken within a range of 12 hours before starting the intervention and after the intervention; laboratory assistant takes 5 ml of venous blood; samples were analyzed by ELISA (enzyme-linked immunosorbent assay) technique in the laboratory

Secondary outcome measures
Stool consistency and frequency, measured using The Bristol Stool Scale every day during the intervention. Stool consistency was rated on 7 type Likert scale:
Type 1: Separate hard lumps, like nuts (hard to pass)
Type 2: Sausage-shaped but lumpy
Type 3: Like a sausage but with cracks on its surface
Type 4: like a sausage or snake, smooth and soft
Type 5: Soft blobs with clear-cut edges (passed easily)
Type 6: Fluffy pieces with ragged edges, a mushy stool
Type 7: Watery, no solid pieces, entirely liquid

Overall study start date
01/08/2017

Completion date
19/04/2018

Eligibility

Key inclusion criteria
1. Students of Faculty of Public Health, Universitas Indonesia
2. Male or female, aged 17-25 years
3. Irregular milk consumption (FFQ screening)
4. Felt the symptoms of digestive discomfort after consume commercial dairy products
5. Have a normal blood pressure

6. BMI 19-27.5 kg/m2
7. Willing to follow all of the requirements and procedures of this study and agree to sign informed consent

Participant type(s)
Healthy volunteer

Age group
Adult

Sex
Both

Target number of participants
60 participants: 30 participants for sequence 1 and 30 participants for sequence 2

Key exclusion criteria
1. Woman in pregnancy and breastfeeding
2. Consume anti inflammatory or immunosuppressive drugs within 4 weeks before screening
3. Have an allergy

Date of first enrolment
20/10/2017

Date of final enrolment
09/12/2017

Locations

Countries of recruitment
Indonesia

Study participating centre
Universitas Indonesia
Centers for Nutrition and Health
Faculty of Public Health
Room 204, F Building, 2nd floor
Depok, West Java
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Sponsor information

Organisation
Universitas Indonesia

Sponsor details
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Sponsor type
University/education

ROR
https://ror.org/03xqzzq44

Funder(s)

Funder type
Industry

Funder Name
ABC Kogen

Results and Publications

Publication and dissemination plan
American Journal of Clinical Trial; British Journal of Nutrition; Malaysian Journal of Nutrition

Intention to publish date
01/01/2019

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available.

IPD sharing plan summary
Not expected to be made available