

Effects of A2 milk (compared to regular milk) on asthma symptoms, inflammation and exercise performance in athletes with asthma-related conditions

Submission date 07/08/2017	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 22/08/2017	Overall study status Stopped	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 08/07/2020	Condition category Respiratory	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Asthma and exercise-induced bronchoconstriction (EIB) are obstructive airway diseases that may be caused (in part) by inflammation in the cells that line the small airways. They are more common in athletes than in the general population. Inflammation in the gut may influence inflammation in the small airways, which may impact on asthma severity. Regular cow's milk contains a mix of A1 and A2 protein (beta-caseins). Previous research has shown that the A1 type of protein may affect gut transit and inflammation. It has also been shown to pass into the body and affect other organs e.g. skin and it is possible that regular cow's milk (containing A1 protein) may be linked to EIB/asthma symptoms via this mechanism. Previous research has shown that when individuals switch to using milk containing only A2 protein (beta-caseins) gut transit and inflammation are improved. It is also possible that replacing regular cow's milk with A2 milk may help to improve immune function and balance, which is another possible pathway linked to inflammation. The aim of this study is to find out whether switching to using milk that contains no A1 protein (A2 only) causes decreases in gut inflammation/damage, reduced airway inflammation and asthma symptoms, and improved immune function and exercise performance in active people with asthma.

Who can participate?

People aged 18 – 45 years with asthma who engage in regular endurance training (at least three times per week)

What does the study involve?

Each participant is required to swap their usual milk with milk provided by the researchers over two 2-week periods. In one period this is regular cow's milk and in the other period it is A2 milk. Before and after each 2-week period participants complete assessments of asthma severity and undertake exercise and provide blood, saliva and urine samples before and after each test to measure gut inflammation/damage, airway inflammation, immune function, asthma symptoms and lung function.

What are the possible benefits and risks of participating?

There are no direct benefits other than receiving results and feedback from several breathing and exercise tests. The asthma challenges may cause airway narrowing, which may feel uncomfortable. Participants may feel like it is more difficult to breathe air out, or the chest may feel tight. The dry air used in the test may make them feel like they want to cough for a little while after the challenge. Drinking water relieves this. To reduce risks participants are not be able to take part in the study if their resting lung function appears obstructed (if it is less than 80% of predicted value). Lung function is closely monitored during all tests. If lung function falls below 10% of baseline participants should take their asthma medication to reverse this (e.g. salbutamol). Participants are advised to remain in the laboratory for observation until lung function is within 10% of its resting value. The risks associated with the exercise tests are fatigue, muscle soreness, chest pain, cardiac (heart) symptoms and sudden heart attack. There is also a risk of picking up a musculoskeletal injury (e.g. sprain or strain). These risks are present during any physical activity or exercise (e.g. normal daily activity or training). For those without underlying heart disease, the risks to health are extremely low. Participants are regular exercisers so the risks of adverse or unusual effects are reduced. They are also required to complete a health/physical activity readiness questionnaire to assess their suitability and this further reduces the risk. It is common to experience muscle aches and soreness in the days (usually 12-72 hours) after the exercise tests. During the exercise tests, the test is stopped at any point if it appears that the participant is either having difficulty breathing, is in any other form of distress or if they become injured. There is a small risk of infection at the site where the blood sample is taken but the likelihood is low when following standard health and safety procedures (including sterilising the area before taking a sample). Some bruising may occur and the site may be sore for a day or two afterwards.

Where is the study run from?

University of Kent (UK)

When is the study starting and how long is it expected to run for?

March 2017 to January 2019

Who is funding the study?

The a2 Milk Company Ltd (New Zealand)

Who is the main contact?

1. Dr John Dickinson

J.W.Dickinson@kent.ac.uk

2. Dr Glen Davison

Contact information

Type(s)

Scientific

Contact name

Dr John Dickinson

Contact details

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Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number**ClinicalTrials.gov number**

Nil known

Secondary identifying numbers

UoK REAG (Sciences) Ref No. 0281617

Study information

Scientific Title

The effect of A2 milk on exercise performance, inflammation and severity of exercise induced bronchospasm (EIB) in athletes with asthma-related conditions: a randomised crossover study

Study objectives

Purpose: To investigate the effect on airway health, inflammatory and immune markers, and exercise performance in athletes with asthma related conditions who switch to using A2 milk from standard (regular) cow's milk.

Hypothesis: markers of airway health, inflammatory and immune markers, and exercise performance will be improved in the A2 milk arm, compared to the regular milk arm.

Ethics approval required

Old ethics approval format

Ethics approval(s)

University of Kent, Faculty of Science Research Ethics Advisory Group for Human Participants, 12/05/2017, ref: 0281617

Study design

Single-centre randomised crossover double-blind study

Primary study design

Interventional

Secondary study design

Randomised cross over trial

Study setting(s)

Other

Study type(s)

Other

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

Exercise performance and airway health in athletes/physically active adults with asthma/asthma-related conditions or exercise-induced bronchospasm (EIB)

Interventions

Each participant will be required to swap their usual milk with milk provided by the trialists over two 2-week periods. On one occasion this will be regular cow's milk (control condition) and on another it will be A2 milk. The order will be randomised using computer randomisation software and neither the researchers nor participants will know which was which until after the study is complete. Before and after each two-week period of using regular cow's milk or A2 milk participants will complete assessments of asthma severity and undertake exercise and provide blood, saliva and urine samples before and after each test to measure gut inflammation /damage, airway inflammation, immune function, asthma symptoms and lung function.

Intervention Type

Other

Primary outcome measure

All of the following measures will be assessed on 3 separate occasions over the study period - once at baseline and once after each 2-week period:

1. Eucapnic Voluntary Hyperpnea (EVH) challenge with lung function testing (maximal flow-volume loop method) before and after EVH challenge test. The lung function test will be performed before and at 3, 5, 7, 10, and 15 min post-EVH challenge
2. Urine levels of 9 α ,11 β -prostaglandin and Clara cell protein (CC16) will be assessed in samples collected before and after (~1 h) EVH challenge by enzyme-linked immunosorbent assay (ELISA) method

3. Exhaled Nitric Oxide levels before and after (1 h) EVH challenge using a exhaled breath gas analyser

Secondary outcome measures

1. To determine whether switching to A2 milk improves markers of inflammation, immune function and intestinal barrier integrity/intestinal epithelial cell damage markers:

On the day after the EVH challenge participants will undertake an exercise trial (treadmill running) consisting of 20 min at ~60% maximal aerobic capacity followed by a 3 km performance time-trial in which they must cover this distance as quickly as possible. The following will be assessed before, immediately-post and up to 1h post-exercise:

1. Blood markers of intestinal barrier integrity/cell damage (e.g. iFABP), immune markers and systemic inflammatory, stress and oxidative stress markers (e.g. differential white blood cell count (by automated haematology analyser), phagocyte oxidative burst (stimulated and unstimulated) (by chemiluminescence assay), plasma CRP, inflammatory cytokines, and saliva secretory IgA (by ELISA), glutathione, and lipid peroxidation markers (by ELISA and photometric assay methods)

2. Self-report gut symptoms logged in a questionnaire immediately post-exercise using a visual analogue scale (VAS)

3. Self-report gut symptoms logged in a questionnaire for one rest day and one normal exercise training day (in their normal training schedule), using a VAS, at the beginning and end of each 2-week study period. The Bristol stool scale (self-report) and a frequency log will also be recorded on these days

4. Plasma levels of dipeptidyl peptidase 4 (DPP4) and beta-casomorphin-7 may also be analysed by ELISA and HPLC methods (depending on equipment availability and access)

2. To determine whether switching to A2 milk improves exercise performance and/or physiological responses to exercise, the following measures will be used:

1. 3 km time-trial performance (completion time)

2. Gas exchange (VO₂, VCO₂) during exercise using a respiratory gas analyser

3. Perceptual responses (using the Borg rating of Perceived Exertion, RPE, scale) during exercise

4. Heart rate during exercise using short range telemetry

5. Blood lactate concentration before and after exercise using an automated blood lactate /glucose analyser

Overall study start date

01/03/2017

Completion date

31/12/2019

Reason abandoned (if study stopped)

Participant recruitment issue

Eligibility

Key inclusion criteria

1. Ability to consent to the research

2. Prior clinician-based diagnosis of asthma

3. Males and females

4. 18 – 45 years

5. Engage in regular endurance training (at least three times per week)

6. Normal resting Forced Expiratory Volume in One Second (FEV1); defined as greater than 80% of predicted value

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

24

Total final enrolment

9

Key exclusion criteria

1. Chest infection within the past 4 weeks, or any other illness within the past 2 weeks
2. Fall in FEV1 >50% from baseline following exercise challenge
3. Baseline FEV1 of < 80% of predicted
4. Respiratory conditions (other than asthma/EIB) e.g. COPD
5. Cardiovascular conditions:
 - 5.1. Coronary artery disease
 - 5.2. High blood pressure
 - 5.3. Heart failure
 - 5.4. Diagnosed abnormality of heart rhythm
6. Metabolic diseases:
 - 6.1. Type 1 diabetes
 - 6.2. Type 2 diabetes
 - 6.3. Pre-diabetes
7. Daily use of oral corticosteroids
8. Hospitalisation due to asthma in the six months prior to study commencement
9. Injury or conditions that limit mobility
10. Pregnancy
11. Known allergy or intolerance to milk or dairy
12. Does not regularly consume milk

Date of first enrolment

01/09/2017

Date of final enrolment

31/08/2019

Locations

Countries of recruitment

England

United Kingdom

Study participating centre

University of Kent

School of Sport and Exercise Sciences

Medway

United Kingdom

ME4 4AG

Sponsor information**Organisation**

University of Kent

Sponsor details

-

Canterbury

England

United Kingdom

CT2 7NZ

Sponsor type

University/education

ROR

<https://ror.org/00xkeyj56>

Funder(s)**Funder type**

Industry

Funder Name

The a2 Milk Company Ltd

Results and Publications

Publication and dissemination plan

Intention to submit to peer-reviewed journal(s) by September 2019 (sooner if desired sample size is achieved and study completed earlier).

Intention to publish date

31/07/2020

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Dr John Dickinson (J.W.Dickinson@kent.ac.uk) or Dr Glen Davison after completion and publication of study results (de-identified participant data).

IPD sharing plan summary

Available on request