MOSAIC study:
MOdel to Study upper Airway Immunity upon Cholera vaccination

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To investigate whether raw milk is able to enhance the upper airway immune response as induced by oral cholera vaccination.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory tract infections
Study type	Interventional

Summary

ID

NL-OMON41015

Source
ToetsingOnline

Brief title
MOSAIC

Condition

- Respiratory tract infections

Synonym
airway infection, upper respiratory tract infection

Research involving
Human

Sponsors and support

Primary sponsor: FrieslandCampina Innovation
Source(s) of monetary or material Support: FrieslandCampina Innovation

Intervention

Keyword: immunity, milk, upper airways, vaccination

Outcome measures

Primary outcome

Primary outcome is the increase in vaccine-specific secretory IgA or IgG levels detectable in nasal washes, as a measure for upper airway immunity.

Secondary outcome

Secondary outcomes are:

- Vaccine-specific secretory IgA (and IgG) levels in saliva, serum and feces

- Percentage of antigen-specific IgA or IgG positive B cells with airway-homing potential

- Antigen-specific T cell proliferation.

In case of positive outcomes on the primary and/or secondary outcome parameters, stored serum, saliva, nasal wash or fecal material may also be explored by analysis of markers of inflammation or gut permeability (such as calprotectin, CRP, cytokines/chemokines, I-FABP).

Study description

Background summary

Airway infections are an important worldwide cause of death, both in elderly and young children. Upper airway infections are a risk factor for the development of lower airway infections, which are often more severe. Therefore, support of upper airway immunity could help to reduce the incidence of lower airway infection.
To screen the potential of specific foods or food ingredients to support airway

immunity in young children is not feasible. Therefore, an alternative human model was identified. Oral vaccination is known to induce a weak immune response in the upper airways, and can therefore serve as a model to study upper airway immunity. The oral cholera vaccine Dukoral® was chosen as model vaccine, for 3 reasons: its availability as registered vaccine, its safety, and the availability of information on the kinetics of the immune response. In this study, oral cholera vaccination will be applied in human adult volunteers, and used as a model to study the support of upper airway immunity by raw milk. Milk, and especially raw milk, is known to contain many different bioactive compounds. Several of these compounds have been shown to be involved in the protection against infection and in the support of immunity. Notably, raw milk consumption is inversely associated with the occurrence of asthma, upper respiratory tract infection and otitis media. Pasteurization and homogenization can harm these compounds and reduce the bioactivity of milk. Therefore, in this study, the effect of raw milk will be evaluated on the immune response to oral cholera vaccination.

Study objective

To investigate whether raw milk is able to enhance the upper airway immune response as induced by oral cholera vaccination.

Study design

Three groups of 14 healthy adult volunteers (total n=42) will be vaccinated with the oral cholera vaccine Dukoral®. The vaccine is given on day 0 and day 14 of the study. One group will receive the vaccine in the regular sodium carbonate buffer. One group will receive the vaccine in a matrix of raw milk. One group will receive the vaccine in a matrix of raw milk and keep every sip in the mouth for 30 seconds, to have prolonged exposure to raw milk and to the vaccine. At baseline, and 7, 14, 18 and 28 days after start of the vaccination, the immune response will be measured in blood, saliva, nasal wash and feces.

Intervention

Raw milk, obtained from farms that comply to the high quality requirements for production of raw milk, and that has been screened according to the safety criteria for raw milk (a.o. presence of specific pathogens).

Study burden and risks

The participants will visit the study location 6 times. At 5 time points, 40-60 mL of blood will be drawn (total amount 260 mL). At 6 time points, a nasal wash will be performed. At 10 time points, saliva will be collected. At 5 time points, fecal samples will be collected.
At 2 time points, the participants will receive a dosage of the vaccine.

Dukoral® is a registered vaccine, consisting of heat-killed and formalin-killed Vibrio cholerae plus recombinant cholera toxin subunit B. The vaccine can be safely used for adults and for children above the age of 2 yr. The vaccination has a low risk of side effects, and the side effects are mainly mild. Two groups will receive the vaccine in a matrix of raw milk. Raw milk has a potential risk of containing pathogens that can result in gastrointestinal disease. By selecting farms that comply to strict quality criteria, and by screening the milk for specific pathogens, the risk of subsequent infection is considered very limited.
Side effects occurring during the study will be registered by a short daily online survey. If serious side effects occur, the study doctor will be consulted.
The study participants will have no direct benefit from the study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Age 18-50 yr
Signed informed consent
Availability of internet connection
Male or female
Willing to stop blood donation at the blood bank during the study period

Exclusion criteria

Currently participating in another clinical trial
Previous cholera, Salmonella, or E. coli vaccination
Tonsillectomy
Acute gastroenteritis in the past 2 months
Use of antibiotics in the past 2 months
Hypersensitivity to the vaccine, to formaldehyde or to any of the excipients (sodium salts)
Pregnancy or lactating (pregnancy test will be performed on the vaccination days)
Not willing to drink raw milk
Allergic to milk or lactose-intolerant
Disease of GI tract, liver, gall bladder, kidneys, thyroid gland
Immune-compromised
Use of immunosuppressive drugs
Drug abuse, and not willing/able to stop this during the study
Excessive alcohol usage (men: >4 consumptions/day or >20 consumptions/week; women: >3 consumptions/day or >15 consumptions/week)

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-10-2014
Enrollment:	42
Type:	Actual

Ethics review

Approved WMO

Date:	15-07-2014
Application type:	First submission
Review commission:	METC Wageningen Universiteit (Wageningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL49042.081.14