APA12/PANTER* study: ""PTM202 and modulation of host resistance to diarrheagenic Escherichia coli in a randomized placebo-controlled trial in healthy human subjects"

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To study whether PTM202, a dietary formula containing a proprietary mixture of dried bovine colostrum and dried whole egg, improves the resistance of humans to traveller*s diarrhea as caused by diarrheagenic E. coli. PTM202 contains specific...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON44640

Source
ToetsingOnline

Brief title
APA12/PANTER

Condition

- Bacterial infectious disorders

Synonym
Gastroenteritis, Traveler's diarrhea

Research involving
Human

Sponsors and support

Primary sponsor: PanTheryx, Inc.
Source(s) of monetary or material Support: PanTheryx;Inc. 5480 Valmont Road |Suite 325 Boulder Colorado 80301

Intervention

Keyword: Colostrum, Diarrhea, ETEC

Outcome measures

Primary outcome

The main study parameters are Stool consistency (Bristol Stool Scale reported by the subjects in the online diary, and Percentage of fecal wet weight (% determined by freeze-drying).

Secondary outcome

Secondary study parameters are: Stool frequency (Stools per day reported by the subjects in the online diary), Total fecal wet weight (fecal weight in g/day), and the incidence and severity of Gastro-intestinal symptoms (Gastro-intestinal Symptom Rating Scale reported by the subjects in the online diary).

Study description

Background summary

Diarrhea is an important cause of morbidity and mortality in all regions of the world and among all ages. The annual number of enterotoxigenic Escherichia coli (ETEC) cases in the developing world was estimated at 840 million, with another 50 million asymptomatic carriers in children aged <5 years. Food-borne infections are also frequently encountered by travelers to tropical countries, with incidences up to 80%. Travelers* diarrhea is the most common health impairment in persons visiting developing countries, affecting up to 50-90% of travelers in high risk areas. Antibiotics can be a form of treatment, but the growing resistances of pathogens against antibiotics is a drawback. Enhancement of human resistance to food-borne infections by functional food ingredients is

therefore an attractive option.

Study objective

To study whether PTM202, a dietary formula containing a proprietary mixture of dried bovine colostrum and dried whole egg, improves the resistance of humans to traveller*s diarrhea as caused by diarrheagenic E. coli. PTM202 contains specific immunoglobulins that target rotavirus, enterotoxigenic E. coli, shigatoxin-producing E. coli and Salmonella.

Study design

The APA12/PANTER study is a parallel 3-weeks intervention study. Subjects will be randomly assigned to one of two treatment groups; placebo or PTM202 (n=36 per group). Subjects will be instructed to maintain their usual pattern of physical activity and their habitual food intake, but to standardize their dietary calcium intake. After a standardized evening meal and an overnight fast, subjects will be orally infected with a live, but attenuated, diarrheagenic E. coli (strain E1392-75-2A; collection NIZO food research; dose 1E10 CFU at study day 14. At various time points before and after diarrheagenic E. coli challenge an online diary will be kept to record information on stool consistency, frequency and severity of symptoms and stool samples will be collected.

Intervention

During the entire study, subjects will be instructed to maintain their habitual diet, except for their dairy intake. Dairy has a high calcium content and contributes significantly to total daily calcium intake. These dietary guidelines will limit calcium intake on average to 500 mg/day. At study day 14, after an overnight fast, all subjects will receive an inoculation of the diarrheagenic E. coli (1E10 CFU (n=72) at study day 14). At study day 14, 15 and 16, subjects will receive either placebo or PTM202, a dietary formula containing a proprietary mixture of dried bovine colostrum and dried whole egg.

Study burden and risks

Diarrheagenic E. coli strain E1392-75-2A
The strain used at NIZO food research, the diarrheagenic E. coli strain E1392-75-2A, is a spontaneous mutant with deletion of the genes encoding the LT and ST toxins, and can therefore not produce any toxins.
NIZO food research has previously performed 7 nutritional intervention studies (n=305 subjects) in humans with E. coli strain E1392/75(2A). In the previous studies, the diarrheagenic E. coli strain transiently induced symptoms of a food borne infection increasing infectious diarrhea, fecal pathogen excretion, stool frequency, Bristol Stool Score, and reported symptoms. All recorded

disease episodes were self-limiting and did not require early antibiotic treatment. No treatment-related serious adverse events were reported during these studies. The diarrheagenic E. coli strain E1392-75-2A strain is sensitive to Ciprofloxacin which is a commonly used antibiotic in case of treatment of this kind of E. coli infections.

PTM202
Both dairy and egg ingredients of PTM202 & soy protein based isonitrogenous placebo have the potential to cause allergic responses in sensitive individuals, including severe and anaphylactic reactions. Individuals with known sensitization to either milk, egg or soy protein will be excluded, and we anticipate that the majority of subjects will have had prior exposure to both as part of normal diet. PTM202 should be avoided by those with intolerance to lactose. Most clinical studies report no adverse effects from bovine colostrum although minor side effects including nausea and flatulence have been rarely reported. Soy protein may have allergic symptoms like skin redness (rash), hives, itching, abdominal pain, diarrhea, nausea or vomiting, wheezing, runny nose etc. For most people, soy allergy is uncomfortable but not serious. Rarely, an allergic reaction to soy can be life-threatening.

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

1. Age between 18 and 55 years.
2. BMI *18 and *27 kg/m2.
3. Healthy as assessed by the NIZO food research medical questionnaire.

Exclusion criteria

1. Any confirmed or suspected immunosuppressive or immunodeficient condition including human immunodeficiency virus infection (HIV).
2. Disease of the GI tract, liver, bile bladder, kidney, thyroid gland (self-reported).
3. Diarrheagenic E. coli strain (as used in the study) detected in fecal sample at screening.
4. Evidence of current excessive alcohol consumption or non-therapeutic drug (ab)use).
5. High titer serum antibodies against CFA-II diarrheagenic E. coli strain (as used in the study) at screening.
6. History of microbiologically confirmed ETEC or cholera infection in last 3 years.
7. Known allergy to the following antibiotics: ciprofloxacin, trimethoprim-sulfamethoxazole, and penicillins.
8. Known allergy to soy, milk- and/or egg.
9. Mental status that is incompatible with the proper conduct of the study.
10. Occupation involving handling of ETEC or Vibrio cholerae currently, or in the past 3 years.
11. Reported average stool frequency of <1 or >3 per day.
12. Symptoms consistent with Travelers' Diarrhea concurrent with travel to countries where ETEC infection is endemic (most of the developing world) within 3 years prior to dosing, OR planned travel to endemic countries during the length of the study.
13. Use of antibiotics, norit, laxatives (up till 6 months prior to inclusion), cholesterol lowering agents, antacids, proton pump inhibitors and immune suppressive agents (up till 3 months prior to inclusion)
14. Vaccination for or ingestion of ETEC, cholera, or E coli heat labile toxin within 3 years prior to inclusion.
15. Vegans.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-12-2017
Enrollment:	72
Type:	Actual

Ethics review

Approved WMO Date:	14-09-2017
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	16-11-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	20-12-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	NL62453.028.17