The effects of ethanol on gut wall integrity as measured by I-FABP and LBP

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The aim of this study is to determine the immediate effects of oral alcohol consumption in healthy volunteers on gut wall integrity as measured by Intestinal Fatty Acid Binding Protein (I-FABP) and Lipopolysaccharide Binding Protein (LBP) These...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal conditions NEC
Study type	Observational invasive

Summary

ID

NL-OMON36207

Source
ToetsingOnline

Brief title
Effects of ethanol on gut wall integrity

Condition

- Gastrointestinal conditions NEC
- Exposures, chemical injuries and poisoning

Synonym
alcohol consumption

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,Aanvraag voor De Cock fonds wordt ingediend

Intervention

Keyword: alcohol, gut wall integrity, LBP, L-FABP

Outcome measures

Primary outcome

The aim of this study is to determine the immediate effects of oral alcohol

consumption in healthy volunteers on gut wall integrity as measured by I-FABP

and LBP.

Secondary outcome

L-FABP will be used as a marker for liver damage

Study description

Background summary

A common finding in trauma patients admitted to the ER with serious injuries is the presence of alcohol abuse. Alcohol is involved in up to 40% of deaths from motor vehicle crashes, 60% of deaths from intentional injuries, and 50% of hospital admissions for injuries.
Chronic alcohol consumption leads to a decrease in gut wall integrity in actively drinking alcoholics and patients with alcohol induced liver disease. Animal studies show that the mucosal damage caused by alcohol consumption increases the permeability of the gut to macromolecules. This facilitates the translocation of endotoxin and other bacterial toxins from the gut lumen to the portal circulation. In addition to increased endotoxemia other studies show that the initial event in response to alcohol is an increased influx of leukocytes leading to an enhanced release of noxious mediators, such as reactive oxygen species, leukotrienes and histamine by mast cells. Alcohol consumption thus leads to a decrease in gut wall integrity with increased endotoxemia and as a result induces an inflammatory response. Data on the effects of acute alcohol consumption on gut wall integrity in non-alcoholics is still scarce.
In patients exposed to severe trauma, loss of gut wall integrity has been implicated as an important contributor to the development of excessive inflammation. Intestinal mucosal damage develops early after trauma leading to loss of gut wall integrity and resulting in translocation of luminal bacteria and toxins into the gut wall. This has been associated with the development of

an inflammatory response. This excessive inflammation can in turn lead to the systemic inflammatory response syndrome (SIRS) which can ultimately lead to multiple organ failure (MOF) and death. Up to 20% of the deaths in trauma patients are due to the consequences of SIRS and MOF.
When assessing the effects of alcohol and severe trauma on gut wall integrity combined with the fact that the two co-exist frequently one can hypothesize that the outcome for trauma patients under the influence of alcohol is detrimental. Literature regarding this issue is unequivocal, consisting only of relatively small retrospective series.

Study objective

The aim of this study is to determine the immediate effects of oral alcohol consumption in healthy volunteers on gut wall integrity as measured by Intestinal Fatty Acid Binding Protein (I-FABP) and Lipopolysaccharide Binding Protein (LBP) These proteins enter the systemic circulation within minutes of mucosal damage to the gut resp translocation.
Furthermore, the effect of alcohol on gut wall integrity markers per se is assessed by artificially adding alcohol to blood and comparing it to non-alcoholised blood.

Study design

Randomized crossover design. After informed consent fifteen healthy adult male volunteers, aged 18-60, will be randomized into two groups. One will drink alcohol, the other group will drink water according to the protocol. The next week, groups will be switched.

Volunteers with a medical history of alcohol abuse or bowel disease or subjects using any medication will be excluded from the study. Volunteers will be fasting for 6 hours before sampling to obtain a reproducible alcohol uptake. To avoid dehydration or hypoglycaemia, volunteers will be allowed to drink tea, water or clear fruit juices until 2 hours before sampling.
Blood sampling: from each volunteer two samples of blood will be collected without additives after discarding the first 3 ml of blood to avoid sample contamination. The first sample (S1) of 19 ml blood will be divided in two halves: 8 ml blood for analyzing the gut wall integrity without addition of ethanol, the other 8 ml will be analyzed after addition of 10 µl of 96% pure ethanol to obtain a blood concentration of 1* ethanol. After the first sample 15 volunteers will drink 1 g/kg ethanol in wine (Pinot noir 12%, 12 gr/100 ml) to obtain a blood alcohol level of 1 * and 2 volunteers will drink three 200 ml glasses of water. The beverages will be consumed in maximal 45 minutes. Thirty minutes after the last glass of beverage is consumed, the second sample (S2) of 11 ml blood will be collected. The next 4 samples are taken with one hour intervals (S3, S4, S5 and S6 respectively). The last sample is taken in a second visit at 17:00 the day after.

In each sample I-FABP, L-FABP and LBP will be measured as well as the alcohol promillage.
The first 19 ml blood sample (S1) drawn from the sober participants is divided in two halves:
The first 8 ml for analyzing native blood and the second 8 ml for analyzing artificially alcoholised blood.
After ingestion of water or wine 5 samples are drawn with one hour intervals.
From the 11 ml drawn blood: 3 ml is used for blood alcohol concentration
5 ml is used for I-FABP, L-FABP and LBP
Artificially alcoholised sample:
10 µl 96 % pure ethanol is added to 8 ml blood to obtain an alcohol blood level of 1 *
Naturally alcoholised:
8 volunteers drink 1 g/kg ethanol in wine (12%) = 8.3 ml wine/kg (average 600 ml per person)
Non alcoholised:
7 volunteers drink 600ml of water

Healthy male volunteers (ASA I) will be included between 18 and 60 years old after they have given their informed consent. Exclusion criteria are the use of medicine as well as a medical history of alcohol abuse or bowel disease.

Study burden and risks

Subjects consume 1g of alcohol per kg bodyweight. One blood sample of 19 ml followed by 5 samples of 11 ml and one of 8ml will be drawn between 16.45 hours and 17:00 hours the day after. The first 6 observations take place in a single visit followed by one observation in short visit the next day. It is unlikely that subjects will experience any physical or psychological discomfort from the withdrawal of a total of 82 ml of blood in 24 hours or the consumption of the amounts alcohol or water mentioned above.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
9700RB
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1

9700RB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy males between the ages of 18-60 years old that sign a written informed consent.

Exclusion criteria

Medical history of alcohol abuse
Use of any medication
Medical history of bowel disease

Study design

Design

Study type:	Observational invasive
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-01-2012
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO

Date:	04-01-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL37376.042.11