The effect of taurolidine on human blood cells

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To investigate the effects of taurolidine on human blood cells by identification of gene expression, protein production and immune response.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON50878

Source
ToetsingOnline

Brief title
The effect of taurolidine on human blood cells

Condition

- Other condition
- Bacterial infectious disorders

Synonym
bloodstream infection, Catheter-related bloodstream infection

Health condition

Catheter-related bloodstream infection

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Blood cells, Taurolidine

Outcome measures

Primary outcome

To investigate the effects of taurolidine on human blood cells by

identification of gene expression, protein production and immune response.

Secondary outcome

Not applicable

Study description

Background summary

Intestinal failure and home parenteral nutrition:
Over the last decade, the number of patients with severe intestinal failure (IF) in the Netherlands has exponentially increased up to 400 cases. Causes are mainly extensive intestinal resections following inflammatory or vascular bowel diseases that lead to short bowel syndrome, and motility disorders. IF patients depend on life-long home parenteral nutrition (HPN). This is a complex treatment that centers on the self-management of central venous catheters (CVCs) at home. The challenge here is to prevent the most daunting complications of this treatment, i.e. catheter-related bloodstream infection (CRBSI) [1, 2].

Catheter-related bloodstream infections:
Despite all preventive measures, CRBSIs remain a frequent complication, with a reported incidence in expert centers that ranges from 0.38 to 2.99 CRBSIs per 1000 catheter days, and accounts for approximately 70% of all HPN related hospital admissions [1-3]. CRBSIs are a threat to both catheter- and patient survival and may lead to permanent loss of vascular access in case of repeated catheter loss, and hence provide an indication for small bowel transplantation. This is a highly complex therapy with a worse prognosis compared to HPN

treatment [1, 2].
There are various risk factors of developing an CRBSI. One of the risks is the formation of a biofilm inside the catheter.

Taurolidine
In patients with IF taurolidine is often used to reduce the incidence of CRBSI. The working mechanism of taurolidine is based on a chemical reaction, in which during the metabolism of taurolidine methyl groups are released. First, those methyl groups induce cell death by destroying the cell wall. Second, they adhere to the microorganism wall and thereby inhibit adhesion to the catheter surface[4].
Resistance to taurolidine is rare in microorganisms, since the mechanism of action depends on active methylol group generation [5]. All these characteristics of taurolidine provides a high potency for broad use in the clinic. Yet, the exact mechanism of action is not elucidated to date.

Several studies have shown a reduction in CRBSI*s [4, 6, 7]. Wouters et al. showed a significant reduction in CRBSIs in the group of patients with new catheters [4]. However despite administration of taurolidine to more than 13.000 patients, overall data on the effects of taurolidine on gene expression, protein production and immune function remain surprisingly scarce [8]. Taurolidine is eventually metabolized into taurine, which modulates intracellular calcium activity, a critical component in the priming and activation of phagocytes. In a murine sepsis model, taurolidine increased the functional activity of peritoneal macrophages[9]. Also, taurolidine seems to prevent the depression of cellular immunity after an operative trauma, with a maintained delayed-type hypersensitivity response and increased Kupffer cell numbers after intraperitoneal administration in a rat model[10]. Other cellular effects of taurolidine include the induction of cancer cell death through a variety of mechanisms that in part remain unclear but at least comprise enhanced apoptosis, inhibition of angiogenesis, reduced tumor cell adherence and down-regulation of inflammatory cytokine release[11].

Taken together these notions above urged us to design a study protocol to characterize the effects of taurolidine on gene expression, protein production and various immune system functions in vitro and the mechanism of action.

Study objective

To investigate the effects of taurolidine on human blood cells by identification of gene expression, protein production and immune response.

Study design

Cohort study of healthy volunteers

Study burden and risks

Incidental findings (knowledge of being at risk for the development of diseases), however the discovery of these incidental findings is extremely small

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Healthy volunteers

Exclusion criteria

Age under 18 year

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-08-2021
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	22-07-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL77571.091.21