Taurolidine 2% catheter locking to prevent catheter-related bloodstream infections in patients on home parenteral nutrition with a high infection risk and those with a new central venous access device:
A double-blind multicenter randomized controlled trial under guidance of the Home Artificial Nutrition & Chronic Intestinal Failure Special Interest Group of ESPEN

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Primary objectiveThe primary objective of this trial is to compare TauroSept® (taurolidine 2% solution) with saline solution 0.9% as catheter lock solutions to prevent catheter-related bloodstream infections (CRBSI) in patients on home parenteral...

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON36907

Source
ToetsingOnline

Brief title
Research with catheter lock TauroSept® (taurolidine 2%) or saline 0,9%

Condition

- Other condition
- Bacterial infectious disorders

Synonym
catheter-related bloodstream infections (CRBSI)

Health condition

intestinal failure, home parenteral nutrition

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Geistlich Pharma AG;Bahnhofstrasse 40;CH-6110 Wolhusen;Switzerland

Intervention

Keyword: catheter lock, catheter-related bloodstream infection, home parenteral nutition, taurolidine

Outcome measures

Primary outcome

Primary endpoint

Mean number of CRBSI/1*000 catheter days

(Note: Patients without infection after 1 year will have a value of 0.)

Secondary outcome

Secondary endpoints

1. Median time to CRBSI

2. Number and frequency of catheter removals due to catheter-related infections

3. Median time to catheter removal due to catheter-related infections

4. Number and frequency of exit site infections

5. Number and frequency of catheter occlusions

6. Patient satisfaction with the assigned catheter lock solution

7. Costs of catheter lock solution plus costs of hospitalizations, unscheduled outpatient-clinic consultations, drug treatment costs of infections and catheter changes

8. Number and frequency of patients having serious adverse events and adverse events

Study description

Background summary

The most recent guideline by the European Society for Nutrition and Metabolism (ESPEN) states that CRBSI are the most frequent complication of HPN treatment and that it remains unclear what the optimal agent is to lock catheters and prevent infections (Staun 2009). While bacteria in the catheter biofilm are considered to be the major source of CRBSI (Allon 2008), there is evidence suggesting that heparin, a heterogeneous glycosaminoglycan that is most commonly used as catheter lock, promotes the formation of bacterial biofilm. (Shanks 2005). Since antibiotics are less successful than hoped for as catheter locking solution and because the associated risk for the development of bacterial resistance, alternatives are urgently needed. While saline solution 0.9% is increasingly being used as catheter lock as alternative for heparin, well-powered studies comparing both catheter locking solutions are eagerly awaited.

A recent single-centre open-label trial (Bisseling 2010) on 14 controls (heparin) and 16 cases (taurolidine 2%) showed a dramatic (> 90%) decrease in recurrence of catheter-related bloodstream infections (CRBSI) in HPN patients who presented with a proven episode of CRBSI and who continued HPN using either

taurolidine 2% (TauroSept®) or low-dose heparin (150 IU/ml) as a catheter lock. After crossing over patients of patients who developed CRBSI while on heparin to taurolidine, none of these patients developed another episode of CRBSI. Also important, there were no catheter occlusions in either group. However, limitations of this trial were the open design and the small sample size.
At this point, data from a larger double-blind randomized multi-centre trial in patients with old and new CVAD are needed to confirm the efficacy of taurolidine 2% in the prevention of CRBSI in HPN patients with CVADs. Moreover, a comparison of taurolidine 2% with saline solution 0.9% instead of heparin should be made because of reasons outlined above.

Study objective

Primary objective

The primary objective of this trial is to compare TauroSept® (taurolidine 2% solution) with saline solution 0.9% as catheter lock solutions to prevent catheter-related bloodstream infections (CRBSI) in patients on home parenteral nutrition (HPN).

Secondary objectives
Secondary objectives are to compare the two devices with respect to further efficacy parameters, treatment costs and resource utilization, patient-rated willingness to continue treatment, tolerability and safety.

Primary hypothesis
The primary working hypothesis states that the TauroSept® treatment arm differs from the saline solution 0.9% treatment arm with respect to the mean number of CRBSI/1*000 catheter days.

Secondary hypothesis
The secondary working hypotheses state that the TauroSept® treatment arm differs in further efficacy parameters (e.g. median time to CRBSI, number and frequency of catheter removals due to catheter-related infections, number and frequency of exit site infections, number and frequency of catheter occlusions etc.).

Study design

This is a double-blind, randomized multi-centre controlled trial investigating the efficacy of TauroSept® and saline solution 0.9% as catheter lock solutions on the prevention of CRBSI in HPN patients.
Patients will be stratified in two groups according to their risk of developing CRBSI prior to randomization. Patients receiving a new single lumen central vascular access device for HPN (new patient starting HPN or patient already on HPN) will be allocated to the new catheter group (Group I). These patients

therefore have a catheter without any biofim when they enter the trial.
Patient who are already on HPN for at least 1 year prior to trial inclusion who had a CRBSI rate (bacterial and/or yeast infections) of >0.3/year and have a catheter in place for at least 6 months will be allocated to the high risk group (Group II). These patients therefore have a catheter where biofilm formation may have occurred
Groups I and II will separately be randomized to the two treatment arms (TauroSept® or saline solution 0.9%).

Intervention

After randomisation the patient wil draw the catheter lock solution (containing TauroSept® or physiological saline 0,9%) from a blinded vial and fill the catheter in between TPN administrations and if possible withdraw the catheter lock siolution before the next use of the catheter.

The content of the blinded vial will be instilled in the catheter by the patient or his/her caregiver. All patients will receive instructions and will be trained how to do this in accordance will local treatment protocols of the participating clinics

Instructions for use:
• Flush the catheter with 10 ml sterile saline 0,9% before instillation of the catheter lock from the blinded vial
• Draw the catheter lock from the blinded vial and fill the lumen of the catheter
• Withdraw the catheter locking solution from the catheter and discard this before use of the catheter for a new infusion

Study burden and risks

The burden and risks associated with participation in this trial are limited to:

- the extension of a regular outpatient clinic visit by 30 minutes to receive instructions on the instillation and withdrawing of the catheter locking solution, instructions on storing of the catheter lock vials and the instruction on how to report any side effects.

- as mentioned in section E9 there is a theoretical risk associated in the form of allergic or immunogenic reactions to the device or its components

Contacts

Public

Universitair Medisch Centrum Sint Radboud

Philips van Leydenlaan 15
6525 EX Nijmegen
NL
Scientific
Universitair Medisch Centrum Sint Radboud

Philips van Leydenlaan 15
6525 EX Nijmegen
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Inclusion criteria:
1. Benign underlying disease leading to long-term intestinal failure who will receive HPN and/or fluids (saline and/or glucose) at least 2 times /week over a subcutaneously tunnelled single-lumen central venous catheter (Hickman/Broviac or subcutaneous port) for at least one year ;2. a) Patient receives a new single lumen central vascular access device for HPN (new patient starting HPN or patient already on HPN) [allocation to Group I = new catheter group] or
b) Patient is already on HPN for >=1 year prior to trial inclusion and has a CRBSI rate (bacterial and/or yeast infections) of >0.3/year and a catheter that has been in place for >=6 months (allocation to Group II = high risk group).
(Previous salvage of this catheter by line-lock antibiotics or other therapeutic interventions is not an exclusion criterion as long as this has been performed at least two months before enrolment in the trial)
3. Estimated life expectancy >=1 year
4. Male or female patient aged 18 - 80 years
5. Patient is fully able to understand the nature of the proposed intervention and gives

written informed consent before entering the trial.

Exclusion criteria

Exclusion criteria:
Patient who:
1. cannot be expected to comply with the trial plan (substance abuse, mental condition)
2. has significant cardiovascular disease such as unstable angina, acute myocardial infarction or recent cerebral vascular accident (within 6 weeks); a cardiac rhythm which in the investigators judgment may result in significant hemodynamic effects
3. has a known hypersensitivity/allergy to taurolidine 2% or saline solution 0.9%
4. is pregnant, lactating, or nursing.
5. has a current bloodstream infection
6. has any clinically significant abnormalities in PT or PTT requiring intervention
7. has received thrombolytic therapy in the 6 weeks prior to insertion (aspirin 80-325 mg daily is acceptable).
8. has received an investigational drug within 30 days of trial entry
9. has an antibiotic coated, silver impregnated or antimicrobial cuff catheter
10. has compromised skin integrity, including any infection at the insertion site
11. has received parenteral or oral antibiotic therapy < 2 months prior trial inclusion

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2013
Enrollment:	20
Type:	Anticipated

Ethics review

Approved WMO Date:	18-06-2013
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	NL40910.091.12