The efficacy of a lock solution containing taurolidine, citrate and heparin for the prevention of tunneled central line-associated bloodstream infections in pediatric oncology patients, a randomized controlled, mono-center trial.

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To determine wheter the use of the taurolidine 1.35%, citrate 4%, and heparin 100 IU/ml lock solution (TauroLock*-Hep100) reduces the incidence of first tunneled central line associated bloodstream inections (CLABSI) compared to the heparin 100 IU/...

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

Summary

ID

NL-OMON55586

Source
ToetsingOnline

Brief title
CATERPILLAR

Condition

- Other condition
- Hepatobiliary neoplasms malignant and unspecified
- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
central line infections, central line-associated bloodstream infections

Health condition

centraal veneuze toegang

Research involving
Human

Sponsors and support

Primary sponsor: Prinses Máxima Centrum voor Kinderoncologie
Source(s) of monetary or material Support: Cablon Medical BV, distributeur in NL van TauroLock-Hep100, de TauroLock-Hep100 ampullen zullen belangeloos gesponsord worden door de fabrikant. ,Koningin Wilhelmina Fonds (KWF)

Intervention

Keyword: central venous access device, central-line associated bloodstream infection prevention, pediatric oncology

Outcome measures

Primary outcome

The incidence of first tunneled central line associated bloodstream infections

(CLABSI) since the insertion of the central venous access device (CVAD). All

data-points that are needed for the evaluation of the occurrence of a CLABSI

will be collected by the local data-manager. Three experts will blindly and

independently judge if a CLABSI or no-CLABSI occurred in all patient based on

the collected data and the CLABSI definition. All non unanimous judgements

will be discussed between the experts until they all agree. If the experts

still disagree, the final judgement will be based on the judgement of the

majority.

Secondary outcome

Time to first tunneled central line associated bloodstream infections (CLABSI)

since the insertion of the central line (CVAD)

CLABSI incidence per 1,000 CVAD-days

Incidence of symptomatic central venous thrombosis (CVT)

Incidence of bacteremia

Incidence of local infections

Dispense of thrombolysis/systemic antibiotic treatment due to CLABSI/CVT

Incidence of and reasons for CVAD-removal

Cultured microorganisms causing CLABSIs

Days of hospital admission due to CLABSIs/CVTs

Safety of the taurolidine-citrate-heparin/heparin lock in terms of known side effects, severe adverse events (SAEs), intensive care unit admission, and mortality rate due to CLABSIs/CVTs

Study description

Background summary

Tunneled central venous access devices (CVAD) are fundamental in pediatric oncology for long-term venous access. The incidence of central line-associated bloodstream infections (CLABSI) is high and ranges between 0.1-2.3 per 1,000 CVAD-days. In the Princess Máxima Center for pediatric oncology, the incidence rate of CLABSI was 1.51 per 1,000 CVAD-days. Of all CVADs inserted, 17% were removed and 5% of the patients were admitted at an intensive care unit due to CLABSIs. Central venous thrombosis (CVT) is another severe complication of the CVAD, with an incidence rate of 0.02-0.24 per 1,000 CVAD-days. Different lock solutions are available to prevent the CVAD from CLABSIs and CVAD-related CVTs. In the Netherlands, the heparin lock (HL) is the standard of care. The HL however, does not have an antimicrobial activity and its use is barely supported by literature. Locks containing taurolidine and citrate, which have anticoagulant and antimicrobial activities without reported resistance to taurolidine, appear to be promising in the prevention of CLABSIs. The taurolidine-citrate(-heparin) lock solution (TCHL) was shown to decrease the CVAD-infection incidence in haemodialysis patients, total parenteral nutrition

patients, and adult oncology patients compared to heparin, citrate and saline locks (Rate Ratios (RRs) ranged from 0.00-0.77). In pediatric oncology patients, six studies have been performed which only included a small number of patients (n<=180). Therefore, these studies did not deliver enough evidence to implement the TCHL in pediatric oncology patients. Due to the centralization of the pediatric oncology care in the Netherlands we are now able to perform an open labelled randomized controlled trial and include a large number of patients (n=462), so that we can finally draw conclusions on the efficacy and safety of the TCHL in pediatric oncology patients. Our goal is to reduce the CLABSI-rate, CVAD-removal rate, dispense of antibiotics, days of hospital/intensive care admission, and mortality rate due to CLABSI.

Study objective

To determine wheter the use of the taurolidine 1.35%, citrate 4%, and heparin 100 IU/ml lock solution (TauroLock*-Hep100) reduces the incidence of first tunneled central line associated bloodstream inections (CLABSI) compared to the heparin 100 IU/ml lock solution, in pediatric oncology patients, with a maximum follow-up of 90 days.

Study design

The CATERPILLAR study is designed as a mono-centre, investigator initiated, open labelled randomized controlled trial (RCT). Patients who receive their first CVAD or patients who receive a second, third, fourth etc. CVAD after a CVAD-free interval of more than 12 months, will be asked to participate in this study. Patients will be randomized into the HL study arm (n=231) or TCHL study arm (n=231). The lock will be instilled in the Princess Maxima Center with a maximum of once weekly (if admitted at the hospital or regulary visiting the hospital) and a minimum of once every three weeks (instillation before going home or to a different hospital for >1 week). In between, all patients will receive heparin 100 IU/ml. All patients will be followed up from CVAD insertion until the first CLABSI episode, CVAD-removal, second CVAD insertion or death with a maximum study period of 90 days. The maximum study period of 90 days was chosen since a great deal of the CLABSI episodes occur within the first 90 days after insertion. All data (incl. shared care hospital data as this is standard of practice) will be collected in the Princess Máxima Center for Pediatric Oncology.

Intervention

One group will receive the TauroLock-Hep100 locks (taurolidine 1.35%, citrate 4.0%, and heparin 100 IU/ml) with a maximum of once weekly and a minimum of once every three weeks. The other group will receive Heparin locks (heparin 100IU/ml) with a maximum of once weekly and a minimum of once every three weeks. The locks will be instilled in the central line and will fill the

complete lumen, the lock will stay in situ until the central line is manipulated again.

Study burden and risks

Hypothetically, the taurolidine-citrate-heparin lock (TCHL) will reduce the central line associated bloodstream infection (CLABSI) rate compared to the heparin lock (HL). Therefore, the TCHL may reduce the administration of antibiotics, result in lower rates of central venous access device (CVAD) removal, fewer days of hospital/intensive care unit admission, and a reduced mortality rate due to CLABSI compared to the HL. Additionally, patients will benefit directly from reduced and more appropriate antibiotic use, without the risk of antibiotic resistance development.

The expected side effects are temporarily, caused by a spill-over of citrate, described if the TCHL is instilled to fast, and if the TCHL is accidentally flushed instead of aspirated: perioral dysesthesia, discomfort of neck and chest, dygeusia, nausea and vomiting. Hypocalcaemia events causing arrhythmias have only been associated with much higher concentrations of citrate, which are not used in this study. Additionally, hypersensitivity reactions, and heparin induced thrombocytopenia are possible side-effects, but only in one patient an anaphylactic-like reaction was observed. Liver-injury is associated with high-concentrations of systemic taurolidine in mouse-models. The TCHL contains low-dose taurolidine, which is not associated with liver-injury. A more frequent dispense of thrombolytics has been associated with lock solutions containing taurolidine and citrate in haemodialysis patients. However, this was only observed without the addition of heparin and has not been observed in pediatric oncology patients. In this study, the lock volumina are adjusted to the lumen of the CVAD that is inserted, the locks will be aspirated before instillation of a new lock, the locks will be instilled slowly (<1 ml per second), heparin is added to the solution for the prevention of the more frequent dispense of thrombolytics, and an ultrasound of the insertion veins to detect central venous thrombosis (CVT) will be performed if CVT related symptoms are observed during the study. The locks will be instilled with a maximum of once weekly and a minimum of once every three weeks. For a small number of patients this means that they have to visit the Princess Máxima Center for Pediatric Oncology 1-2 times more compared to patients that do not participate in the study. After every study-lock instillation, the patients will be asked to answer a questionnaire about the experience of possible side effects.

In conclusion, we think the possible positive effects of the TCHL outweigh the remaining minimal and rare side effects of the TCHL. We hope to prove that the TCHL will reduce the CLABSI rate, CVAD-removal rate, dispense of antibiotics, days of hospital/intensive care unit admission, and mortality rate due to CLABSI.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)
Babies and toddlers (28 days-23 months)
Newborns

Inclusion criteria

1. Age between 0 - <19 years
2. Radiological, cytological or histological proven paediatric malignancy (hematologic, solid, and neurologic malignancies)
3. Hickman/powerline or totally implantable venous access port to be inserted at the Princess Maxima Center
4. Planned central venous access device insertion of >90 days
5. Written consent signed according to local law and regulations
6. Parents/guardians or patient willing and able to comply with the trial

procedure

Exclusion criteria

1. A previous CVAD removed <12 months ago.
2. Expected treatment for a majority of the time in a different hospital than the Princess Maxima Center for pediatric oncology in the first 90 days of inclusion resulting in difficulties/an inability to visit the Princess Maxima Center at least once every 3 weeks.
3. Primary immunological disorder
4. Contra indications: hypersensitivity to taurolidine, citrate or heparin, and a history of heparin-induced thrombocytopenia
5. Documented bacteremia in the period from 24h before catheter insertion until inclusion.
6. Insertion of the central venous access device at the same site as a previously confirmed central venous thrombosis
7. Pregnant, not willing to use adequate contraceptives, or breast feeding.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	27-10-2020
Enrollment:	462
Type:	Actual

Medical products/devices used

Generic name:	TauroLock-Hep100
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	03-08-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	03-05-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-09-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-09-2022
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 20136
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
Other	Nederlands Trial Register;NL6500/NTR6688
CCMO	NL67388.041.20
OMON	NL-OMON20136