Short-course aminoglycosides as adjunctive treatment in adults with sepsis

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON29602

Source
NTR

Brief title
SAGA

Health condition

Sepsis

Sponsors and support

Primary sponsor: University Medical Center Utrecht
Source(s) of monetary or material Support: ZonMw

Intervention

Outcome measures

Primary outcome

30-day all-cause mortality

Secondary outcome

Secondary outcomes include duration of IC and hospital admission, quality of life, nephrotoxicity, ototoxicity and costs. In a cost-effectiveness analysis we will determine the costs per quality-adjusted life year gained.

Study description

Background summary

In the Netherlands, there is a large variation in the empirical treatment of sepsis, especially regarding the use of adjunctive short-term treatment with aminoglycosides on top of beta-lactam antibiotics. However, there is no convincing evidence that combination treatment is associated with a better outcome. Therefore, a randomized trial is necessary to determine the effect of adding aminoglycosides to a beta-lactam antibiotic on patient-relevant outcomes and cost-effectiveness in sepsis patients.
Objective: To determine the effectiveness, safety, quality of life, pharmacokinetics/pharmacodynamics targets and cost-effectiveness of a strategy of cefuroxime combined with short-course treatment with aminoglycosides compared to a strategy of ceftriaxone or cefuroxime monotherapy in patients with sepsis presenting to the emergency department (ED) and admitted to the hospital.
This study will be performed as a cluster-randomized cross-over trial. During two consecutive periods of 12 months, hospitals will be randomized to alternating antibiotic policies for patients admitted with sepsis of unknown origin, suspected urinary origin or suspected abdominal origin. For the Active Follow-up Subset (AFS), patients will be followed up to an additional 12 months after initial presentation to the ED.

Study objective

We hypothesize that the ceftriaxone monotherapy strategy is non-inferior for mortality and for nephrotoxicity a strategy of ceftriaxone monotherapy is superior to a strategy of cefuroxime combined with short course aminoglycosides.

Study design

Admission at the hospital: baseline values
During hospitalization: specific data will be collected

For the Active Follow-up Subset:
-A questionnaire after 2, 6 and 12 months.
-A bloodsample to determine the kidney function at day 7 and, if applicable, at day 90

To determine the pharmacokinetic/pharmacokinetic characteristics, waste material of the routinely collected blood samples will be used to measure the free and/or total plasma concentrations of the antibiotics, as well as albumin and creatine if these are not already measured in regular care.

Intervention

Ceftriaxon monotherapy vs cefuroxime with short-course aminoglycoside (gentamicin or tobramycin)

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Eligibility criteria

Inclusion criteria

1) Age >= 18 years
2) Presenting to the ER
3) Suspicion of bacterial infection of unknown origin, primary suspected urinary origin or primary suspected abdominal origin.
4) National Early Warning Score (NEWS) or Modified Early Warning Score (MEWS) ≥ 5.
5) Requiring intravenous antibiotic treatment and hospitalization.

Exclusion criteria

1) Working diagnosis at the ER of pneumonia.
2) Chemotherapy induced neutropenia as this is considered a separate entity in the guidelines.
3) Pre-existing renal failure defined as a GFR < 30, due to a relative contra-indication for aminoglycosides.
4) Allergy for cephalosporins or aminoglycosides, known prior to the start of treatment.
5) Indication for empirical coverage of ESBL-producing gram-negative bacteria according to the Dutch sepsis guidelines, i.e. known colonization or infection with ESBL-producing gram-negative bacteria in the prior year.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2021
Enrollment:	3140
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL9429
Other	METC Utrecht : N/A (not yet submitted)

Study results