Rifampicine vermindert de ontstekingsreactie bij patienten met een (matig) ernstige longontsteking.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON22991

Source
Nationaal Trial Register

Brief title
PRISTINE

Health condition

Community Acquired Pneumonia
Rifampicin
Lipoteichoid Acid
Pneumolysin
inflammatory respons
clinical outcome
prognosis
pneumonia
Emergency medicine
hospital

Spoedeisende hulp
ziekenhuis
Thuis opgelopen longontsteking
CURB-65 score
rifampicine
lipoteichoidzuur
pneumolysine

inflammatoire respons
prognose
klinische uitkomst
pneumonie

Sponsors and support

Primary sponsor: Prof. dr. J.T. van Dissel
LUMC
Source(s) of monetary or material Support: This study was supported by the Virgo consortium, funded by the Dutch government project number FES0908, and by the Netherlands Genomics Initiative (NGI) project number 050-060-452.

Intervention

Outcome measures

Primary outcome

To primary objective is to demonstrate a reduction in lipoteichoic acid release in patients with pneumococcal pneumonia treated with rifampicin and standard treatment as compared to those given standard treatment only. Lipoteichoic acid release will be quantified by measuring lipoteichoic acid in serum and urine. Evaluable patients for Intention-to-Treat analysis are those who met the following criteria: (1) enrollment criteria of pneumonia, with 2 or more points in the CURB65 score, for which a patient is admitted to the hospital, (2) Streptococcus pneumonia is identified as the cause of pneumonia, (3) received at least one dose of study drugs and (4) outcome is measured at 30 days.

Evaluable patients for Per-Protocol analysis are those who meet the following criteria: (1) enrollment criteria of pneumonia, with 2 or more points in the CURB65 score, for which a patient is admitted to the hospital, (2) Streptococcus pneumonia is identified as the cause of pneumonia, (3) received the study drug for 48 hours and (4) outcome is measured at 30 days.

Secondary outcome

The secondary objectives of this study are to determine:

1. Duration of symptoms;

2. Length of hospital stay;

3. 30 Day all cause mortality;

4. Length of ICU stay;

5. (Multiple) organ failure on ICU;

6. Adverse events;

7. Serum biomarkers: C-reactive protein (CRP), Procalcitonin (PCT), Plasma secretory leukocyte protease inhibitor (SLPI), Soluble triggering receptor expressed on myeloid cells (sTREM)-1, IP-10, vitamin D and antimicrobial peptides like Cathelicidin and Beta-defensin-2, lipopolysaccharide;

8. Microbiological diagnosis;

9. Evaluation of empirical coverage of the microbiological diagnosis (with this, we can determine whether the empirical treatment was appropriate or not);

10. Emerging of resistant microorganism carriage.

Study description

Background summary

N/A

Study objective

In vitro studies have shown that – in the presence of identical bacterial kill – rifampicin causes reduced release of proinflammatory components of Streptococcus pneumoniae cell wall, lipoteichoic acid (LTA), as compared with other antibiotics including benzylpenicillin. Because the inflammatory response to these proinflammatory components determines the intensity of the host immune reaction and, by consequence, collateral tissue damage in infection, a reduced inflammatory response in pneumococcal infection, e.g., community acquired pneumonia, may reduce damage to the lungs and severity of disease in pneumonia.
We will try to demonstrate a reduction in lipoteichoic acid release in patients with pneumococcal pneumonia treated with rifampicin and standard treatment as compared to those given standard treatment only.

Study design

Assessments of clinical response will be performed continuously during the treatment period by the attending physician, 1-3 days after admission by the clinical researchers, 30 days after start of therapy by a visit of the clinical researchers and 90 days post therapy by a telephone call.
Besides normal diagnostic procedures (sputum culture, blood culture, routine laboratory tests), extra samples are taken:

1. At inclusion: 1 throat swabs, 1 rectum swabs, a urine sample and 4 ml of EDTA blood for biomarker assay and 4 ml of Natriumheparin blood for LTA measurement and 2 ml of blood
(in PAXgene RNA tubes);

2. At 2, 4, 8, 16, 24 and 48 hours after inclusion: 8 ml of blood and a urine sample (10ml); at 24 hours we'll also collect 2ml of blood in PAXgene tubes;

3. At day 30: 10 ml of blood, a urine sample (10 ml) and a rectum swab.

Intervention

After informed consent, patients will be randomized (2:1) on the emergency department.

The intervention group (2/3) receives rifampicin 600 mg b.i.d. in the first 48 hours + a beta-lactam antibiotic (mostly penicillin) with or without ciprofloxacin.

The control group (1/3) receives a beta-lactam antibiotic (mostly penicillin) with or without ciprofloxacin.

The choice whether or not to add ciprofloxacin is described in the Dutch SWAB guidelines (http://www.swab.nl/richtlijnen).

Contacts

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Eligibility criteria

Inclusion criteria

1. Patient aged 18 years or above;

2. Hospitalization for community acquired pneumonia with CURB65 score ≥ 2.

Exclusion criteria

1. Known allergy to rifampicin or other rifamycins;

2. Haemolytic anaemia or thrombopenia as side effect of rifampicin in medical history;

3. Liver failure;

4. Use of voriconazol or protease inhibitors.

Note: Patients using other drugs that influence cytochrome P450 3A4 are not excluded. This is an open label trial, all doctors are aware when their patient is treated with rifampicin (or not). If necessary, proper adjustments of concomitant medications can be
made (e.g. with oral anticoagulants, ciclosporin). A short period of lower levels of drugs that are prescribed for long-term effects (e.g. antihypertensive drugs or glucose lower medication) will not
interfere with long term outcome. In case female patients in reproductive age use oral anticontraceptives, other contraceptive
measures will be advised after discharge from hospital.
Treatment with rifampicin is for maximum of 48 hours. The enzyme

inducing effect is only limited.
The College ter Beoordeling van Geneesmiddelen indicates only voriconazol and protease inhibitors as a real contra-indication.

5. Female patients who are pregnant

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-01-2013
Enrollment:	40
Type:	Actual

Ethics review

Positive opinion

Date:	14-12-2012
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 39089
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL3586
NTR-old	NTR3751
CCMO	NL40521.058.12
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON39089

Study results

Summary results
N/A