Community-Acquired Pneumonia: lytA TArgeted real-time quantitative polymerase chaIN reaction for improved detection of pneumococci.

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Primary objective: To determine the added diagnostic value of the lytA qPCR on samples of the upper respiratory tract on top of routine microbiological tests in detecting pneumococci as responsible pathogen in patients with CAP.Secondary objective (...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON50405

Source
ToetsingOnline

Brief title
qPCR in community-acquired pneumonia, CAPTAIN

Condition

- Bacterial infectious disorders
- Respiratory tract infections

Synonym
Community-acquired pneumonia, lower respiratory tract infection

Research involving
Human

Sponsors and support

Primary sponsor: Noordwest Ziekenhuisgroep
Source(s) of monetary or material Support: Pulmoscience

Intervention

Keyword: autolysin lytA, Community-acquired pneumonia (CAP), Quantitative polymerase chain reaction (qPCR), S. pneumoniae

Outcome measures

Primary outcome

A. Primary studyparameters (patients)

-Occurrence of qPCR proven pneumococcal pneumonia using the cut-off value in at

least one of the specimens;

-Occurrence of pneumococcal pneumonia proven by at least one of the routine

microbiological tests.

B. Primary studyparameters (controls)

Number of DNA copies of S. pneumoniae identified by lytA qPCR in samples of

different locations in patients with a positive qPCR test:

-Nasopharynx

-Oropharynx

-Saliva

-Sputum

Secondary outcome

A. Secondary study parameters (patients)

-Occurrence of positive lytA qPCR in the different samples: oropharynx,

nasopharynx, saliva and sputum;

-Occurrence of S. pneumoniae identified in the different samples by routine

microbiological tests;

-Number of DNA copies of S. pneumoniae in all lytA qPCR positive patients;

-Ct-values in all lytA qPCR positive study subjects;

-CURB-65 scores (or other pneumonia severity scores);

-CRP levels;

-PCT levels.

B. Secondary study parameters (controls)

-Occurrence of S. pneumoniae identified with lytA qPCR in at least one of the

specimens;

-Occurrence of S. pneumoniae identified in at least one of the specimens with

cultures (culture of oropharyngeal or nasopharyngeal swab or saliva);

-Ct-values in all lytA qPCR positive study subjects.

Study description

Background summary

Streptococcus pneumoniae (S. pneumoniae) is the leading cause of community-acquired pneumonia (CAP) but is believed to be underdiagnosed due to lack of sensitivity of used tests and inadequate specimen collection. The current diagnostic standard (composite of blood culture, sputum culture and urine antigen test (UAT)) detects S. pneumoniae as the responsible pathogen in CAP in less than 30% of the cases. Assays with increased sensitivity applied on easily obtainable specimens could improve the detection of S. pneumoniae and treatment strategies.

Real-time quantitative polymerase chain reaction (qPCR) on samples of the upper respiratory tract targeting the S. pneumoniae specific autolysin gene, lytA, could be able to improve and fasten the diagnostic process of CAP. Rapid and

correct detection of pneumococcal pneumonia provides support for initial narrow-spectrum antibiotic treatment. This targeted therapy might be able to help in preventing antibiotic resistance.

At present, the qPCR targeting lytA (lytA qPCR) is not routinely performed in the standard diagnostic process of a CAP. We recently set-up and validated a home-made lytA qPCR and tested it in a pilot study in patients with a CAP. Preliminary results were promising. Moreover, a recent study in South-Africa (Albrich 2012) found an added diagnostic value of the lytA qPCR in mostly HIV-positive patients with a CAP in nasopharyngeal specimens. The amount of pneumococcal pneumonias increased from 27.1% to 52.5% after added the results of the lytA qPCR.

In the present study we want to test this home-made qPCR prospectively in patients with CAP and determine the added diagnostic value of the qPCR on samples of the upper respiratory tract on top of the routine microbiologically tests in diagnosing S. pneumoniae as the responsible pathogen in CAP. For the differentiation between colonisation and CAP with S. pneumoniae we will determine a cut-off value with the use of test results of CAP patients and healthy subjects with colonisation. Patients with stable chronic obstructive pulmonary disease (COPD) and those with an exacerbation will be tested as well to determine the amount of copy numbers in stable and exacerbated disease. We will perform the lytA qPCR in specimens of different sites of the upper respiratory tract (oropharynx, nasopharynx, saliva and sputum) because of easy access and availability and promising results in previous studies.

Study objective

Primary objective: To determine the added diagnostic value of the lytA qPCR on samples of the upper respiratory tract on top of routine microbiological tests in detecting pneumococci as responsible pathogen in patients with CAP.

Secondary objective (most important, the rest is described in the protocol): To determine the cut-off value for the number of lytA DNA copies to differentiate between colonisation and pneumonia with S. pneumoniae.

Study design

Multicenter cross-sectional case-control study with short follow-up period (approximately 30 days) in the patient group and 4 different control groups. Two centers: Noordwest Ziekenhuisgroep and Spaarne Gasthuis.

Study burden and risks

There are no risks associated with performing the lytA qPCR. Nasopharyngeal swab collection causes a temporary unpleasant sensation. Extra blood sampling

is of negligible risk.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patients:
-Age 18 years or above;
-Presentation at the emergency department (ED);
-Working diagnosis of CAP at the ED with the presence of at least two of the following criteria:
1. New or worsened coughing;
2. Production of purulent sputum or change in sputum colour;
3. Temperature >38.0 *C or <=36.0 *C (tympanic);
4. Auscultatory findings consistent with pneumonia, including rales, evidence

of pulmonary consolidation (dullness on percussion, bronchial breath sounds, rales,
or egophony), or both;
5. White blood cell count of >10x10^9 cells/L or <4x10^9 cells/L or >15% bands;
6. C-reactive protein level >=30mg/L;
7. Dyspnea, tachypnea, (>20 breaths per minute), or hypoxemia (arterial pO2 <60mmHg or peripheral O2 saturation <90%).
-New consolidation(s) on the chest radiograph or computed tomography (CT);
-No other explanation for the signs and symptoms;Control group 1 - Related controls
-Being aged 18 years or above;
-Close relative of the patient: relative defined as living in the same house as the CAP patient or daily contact;
-Is at the hospital at the moment of inclusion of the CAP patient or is willing to come for testing within 7 days.Control group 2 - Unrelated healthy individuals
-Being aged 18 years or above;
-Subject with a preoperative appointment with the anaesthiologist for a planned surgical procedure;
-Age, gender and time matched to an included CAP patient.Control group 3 - Patients with stable COPD
-Being aged 18 years or above;
-Diagnosis of COPD confirmed with spirometry (GOLD criteria 2017)(76).Control group 4 - Patients with exacerbation of COPD
-Being aged 18 years or above;
-Diagnosis of COPD confirmed with spirometry (GOLD criteria 2017)(76);
-Diagnosis of exacerbation of COPD: defined as an acute event characterised by a worsening of the patient*s respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication (76);

Exclusion criteria

In general:
-Pneumonia in the last month or pneumococcal pneumonia (proven by usual diagnostics) in the last three months;
-Not capable of understanding information needed to sign informed consent;Patients:
-Was included in the present study group before;
-Aspiration pneumonia;
-Hospitalisation for two or more days in the last 14 days;
-History of cystic fibrosis.For all control groups:
-Fits inclusion criteria for patient group;
-Present or recent hospitalisation (14 days);
-Use of antibiotics in the last 14 days, including maintenance antibiotic

therapy.Control group 1 and 2 - Related healthy controls and unrelated healthy individuals
-Active infectious respiratory complaints defined as defined as two or more respiratory symptoms (cough, nasal congestion, runny nose, sore throat or sneezes);
-Temperature >38.0 *C
-Chronic pulmonary disease: COPD, asthma, cystic fibrosis, bronchiectasis;
Control group 3 - Patients with stable COPD
-Temperature >38.0 *C;
-Stable disease;
-Recent exacerbation (<1 month) defined as increased respiratory symptoms with need of antibiotic and/or corticosteroid therapy.Control group 4 - Patients with exacerbation of COPD
-Current pneumonia;
-Recent exacerbation (<1 month) defined as increased respiratory symptoms with need of antibiotic and/or corticosteroid therapy.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-03-2020
Enrollment:	980
Type:	Actual

Ethics review

Approved WMO

Date:	21-12-2017

Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-02-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
ClinicalTrials.gov	NCT03315403
CCMO	NL63200.094.17