Dexamethasone in community-acquired pneumonia.

Published: 05-12-2011
Last updated: 01-05-2024

Primary Objective: - To confirm the effect of dexamethasone on clinical outcome in patients admitted with CAP.Secondary Objectives: - To study what patients admitted with CAP benefit most from dexamethasone therapy. Predefined subgroup analysis...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory tract infections
Study type	Interventional

Summary

ID

NL-OMON43565

Source
ToetsingOnline

Brief title
Santeon-CAP study

Condition

- Respiratory tract infections

Synonym
Pneumonia, respiratory tract infection

Research involving
Human

Sponsors and support

Primary sponsor: Sint Antonius Ziekenhuis
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Community-acquired pneumonia, Dexamethasone, Pneumonia

Outcome measures

Primary outcome

Length of hospital stay.

Secondary outcome

- 30-day mortality;

- Admission to ICU after initial admission on the ward.

Study description

Background summary

Community-acquired pneumonia (CAP) is a common infection. Approximately 20 percent of all episodes of pneumonia result in hospitalization. It is the leading cause of community-acquired infection requiring intensive care unit (ICU) admission. Especially elderly patients may have a severe illness with a high morbidity and mortality rate. In pulmonary infections, the release of cytokines and other inflammatory mediators from alveolar macrophages serves as a mechanism by which invading pathogens are eliminated. However, this reaction of the innate immune system can be potentially harmful when excessive release of circulating inflammatory cytokines causes damage to the patient, particularly the lung. Interest in the role of corticosteroids in the pathophysiology of critical illness has existed since the early part of the 20th century. On ICU, early treatment with corticosteroids to attenuate systemic inflammation is widespread. At the same time, outside the ICU little evidence is available on the effect of treatment with corticosteroids in patients diagnosed with CAP. Theoretically, early initiated administration of corticosteroids in the course of a CAP can lower systemic and pulmonary inflammation. This may lead to earlier resolution of pneumonia and a reduction of complications (sepsis, mortality).

The present study is designed to confirm the beneficial effects of adjunctive dexamethasone therapy in a larger sample of patients with pneumonia, additionally aiming at assessing what patients benefit from dexamethasone treatment mostly. To do so, a large multicenter study will be conducted comparing a 4 days dexamethasone 6 mg per os course with placebo in 600

patients and with predefined subgroup analyses planned.

Study objective

Primary Objective:
- To confirm the effect of dexamethasone on clinical outcome in patients admitted with CAP.

Secondary Objectives:
- To study what patients admitted with CAP benefit most from dexamethasone therapy. Predefined subgroup analysis based on:
o disease severity score (PSI 1-3 vs. PSI 4-5);
o CRP level at admission;
o causative microorganism (Pneumococcus antigentest positive vs. negative);
o cytokine response (IL-6 and IL-10) over time;
o cortisol level over time;
o procalcitonin over time.

Study design

Prospective, randomized, double-blinded, placebo controlled, multiple centre, intervention study.

Intervention

Patients presenting with a community-acquired pneumonia, eligible for inclusion in the study, are treated with one bolus of dexamethasone 6 mg (1 tablet of 6 mg) on the emergency department and dexamethasone 6 mg once daily for the following 3 days.

Study burden and risks

Burden: In this study participants are required to take one tablet (either dexamethasone or placebo) daily during the first four days of admission. Data collected for this study are in part data collected in routine clinical care. Blood samples are taken daily as part of routine care. Additional blood samples are collected for the study at timepoints that venapuncture is performed as part of routine clinical care. Participants are requested to fill a quality of life questionnaire twice. We refer to Appendix 6 for an overview of blood sampling and other tests. In this appendix a distinction is made between routine clinical care and study related procedures.

Risks: Participants taking placebo are not expected to run a study related risk. Some adverse side effects have been attributed to corticosteroids, like hyperglycaemia or opportunistic infections. In the recent Ovidius study the most frequently observed side effects of dexamethasone was hyperglycaemia.

There was no increased need of glucose lowering therapy in the treatment group.
. For a detailed description we refer to section 7.1
Potential Benefits: The aim of the study is to confirm the faster recovery of patients treated with dexamethasone, leading to a reduced length of stay. Additionally we hope to demonstrate a reduced mortality in patients admitted with more severe pneumonia (PSI 4-5).

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 aged 18 to 100 years with a community-acquired pneumonia which requires admission.
Criteria to determine a community-acquired pneumonia:
- Chest radiograph showing new opacities.

In combination with two of the following findings:
0 Cough
0 Production of sputum
0 Temp >38,0 °C or <36,0 °C
0 Audible abnormalities by chest examination compatible with pneumonia
0 Leukocytosis (>10.000 cells/mm3), leftward shift (>10%) or leucopenia (<4000 cells/mm3)
0 CRP >15 mg/l (three fold higher than the upper limit of normal)

Exclusion criteria

- Immunocompromised patients:
0 Patients with a known congenital or acquired immunodeficiency.
0 Patients who received chemotherapy less than 6 weeks ago.
0 Patients who received corticosteroids in the last 6 weeks.
0 Patients who received immunosuppressive medication in the last 6 weeks (e.g. cyclosporin, cyclophosphamide, azathioprine).
0 Patients with COPD who are on systemic corticosteroids for COPD.
- Patients who require ICU treatment.
- Patients with tropical worm infection.
- Patients with dexamethasone intolerance.
- Pregnant and breastfeeding women.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-12-2012

Enrollment:	600
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Dexamethasone
Generic name:	Dexamethason
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	05-12-2011
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-01-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-06-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-11-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-12-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	28-01-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-12-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-01-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-04-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-01-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-02-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
EudraCT	EUCTR2011-004566-14-NL
CCMO	NL38162.100.11