Oral Versus Intravenous Dexamethasone in Community-acquired pneumonia study

Published: 30-06-2011
Last updated: 29-04-2024

To assess the bioequivalence of 6 mg dexamethasone tablet administered PO as an alternative to 5,26 mg dexamethasone-disodiumphosphate (= 4 mg dexamethasone) solution administered IV

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

Summary

ID

NL-OMON36192

Source
ToetsingOnline

Brief title
OVID study

Condition

- Respiratory tract infections

Synonym
lower respiratory tract infection, Pneumonia

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Dexamethasone, Pharmacodynamics, Pharmacokinetics, Pneumonia

Outcome measures

Primary outcome

Extent of exposure reflected by the area under concentration time curve

(AUC0-24)

Secondary outcome

Cmax, Tmax and Ctrough

Study description

Background summary

Community-acquired pneumonia (CAP) is a significant cause of infection-related morbidity and mortality in the developed world. The mainstays of CAP treatment are early diagnosis and appropriate antimicrobial treatment. Adjunctive therapy for CAP may help to reduce disease severity. During pneumonia, locally produced cytokines are required to control and eliminate the primary infection. A balanced cytokine response should be sufficient to control the local infection and should not be excessive to prevent systemic effects. An ideal intervention reduces the systemic complications of the inflammatory response without affecting the resolution of local inflammation. Corticosteroids have often been suggested as adjunctive therapy for pneumonia. Recently, Meijvis and co-workers reported a significant reduction in length of hospital stay for patients with pneumonia who received dexamethasone-disodiumphosphate 5 mg intravenously daily for four days [Meijvis 2011].
The present study is designed to evaluate oral administration of dexamethasone as an alternative to the intravenous route because this would be less uncomfortable for the patient (no risk of phlebitis) and be easier to administer (possibly even on an outpatient basis and no hamper of an early intravenous-to-oral switch of antibiotics). As the water solubility of dexamethasone is very low, dexamethasone is administered intravenously in the form of a water-soluble phosphate ester. This prodrug hydrolyses rapidly in the body to form the dexamethasone-free alcohol [Hare 1975; Rohdewald 1987]. Five milligrams of dexamethasonedisodiumphosphate ester equal 3,8 mg dexamethasone-free alcohol [Hare 1975]. Oral preparations of dexamethasone are based on dexamethasone-free alcohol.

The bioavailability of oral dexamethasone has been reported to be between 70-80% of the equivalent intravenous dose in healthy volunteers [Duggan 1975; Loew 1986]. Concerns about delayed gastric emptying and subsequent impaired absorption might prevent extrapolation of these findings to patients with pneumonia. To our knowledge, there are no reported studies in patients with pneumonia evaluating oral administration of dexamethasone with regard to bioavailability. In pregnant women, known to have delayed gastric emptying, the bioavailability of the oral route has been calculated as 72% of the intramuscular route [Elliott 1996]. Based on these findings, we hypothesize that for patients with pneumonia oral dosing of dexamethasone should be approximately 1,5 times the equivalent intravenous dose.

In summary, intravenous dexamethasone treatment for four days in uncomplicated community-acquired pneumonia has clinical benefit but could hamper an early iv-to-oral switch of antimicrobial treatment. A bioequivalent oral dosing regimen could overcome this limitation and is less uncomfortable for the patient.

Study objective

To assess the bioequivalence of 6 mg dexamethasone tablet administered PO as an alternative to 5,26 mg dexamethasone-disodiumphosphate (= 4 mg dexamethasone) solution administered IV

Study design

This is an open-label randomized study to compare the pharmacokinetics en pharmacodynamics of dexamethasone tablet administered PO, and dexamethasone solution administered IV in patients with pneumonia.

Intervention

Subjects will be assigned to 6 mg dexamethasone starting dose administered PO, followed by 3 times 6 mg dexamethasone PO once daily or
5,26 mg dexamethasonedisodiumphosphate (= 4 mg dexamethasone) starting dose administered IV, followed by 3 times 5,26 mg dexamethasonedisodiumphosphate (= 4 mg dexamethasone) IV once daily

Study burden and risks

Intravenous dexamethasone treatment for four days in uncomplicated community-acquired pneumonia has proven clinical benefit but could hamper an early iv-to-oral switch of antimicrobial treatment. A bioequivalent oral dosing regimen could overcome this limitation and is less uncomfortable for the patient. Conducting this study with thirty patients and requiring 13 blood samples from each patient, will provide relevant information on the

bioequivalence of oral versus intravenous dexamethasone. Future patients with pneumonia will benefit from the possibility to administer dexamethasone orally.

Contacts

Public
Sint Antonius Ziekenhuis

Koekoekslaan 1
3435 CM Nieuwegein
NL
Scientific
Sint Antonius Ziekenhuis

Koekoekslaan 1
3435 CM Nieuwegein
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Aged 18 years and older
- Presenting to the emergency room with suspected pneumonia (to be confirmed within 24 hours from admission)
- Pneumonia is defined as a new or progressive infiltrate on a chest X-ray plus at least two of the following criteria: cough, sputum production, temperature >38°C or <35°C, ausculatory findings consistent with pneumonia, leucocytosis or leucopenia (>10 g/l, <4 g/l or >10% rods in leucocyte differentiation), C-reactive protein >3 times the upper normal limit
- Corticosteroid naive at time of presentation

Exclusion criteria

- Patients needing corticosteroid treatment above study medication
- Failure to obtain written consent to participate
- Patients using fenytoine, barbiturates, rifampicine, erythromycin, clarithromycine, aprepitant, colchicine, everolimus, itraconazol, ketoconazole, pazopamib, tipranavir, vinorelbin
- Moribund patients (defined as expected to die within 24 hours)
- Patients with proven or suspected allergy to dexamethasone
- Patient not capable of taking tablets orally

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-09-2011
Enrollment:	30
Type:	Actual

Medical products/devices used

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

Product type:	Medicine
Brand name:	nvt
Generic name:	Dexamethason tablet 1,5 mg PCH
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	30-06-2011
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-12-2011
Application type:	First submission
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	EUCTR2011-002346-12-NL
CCMO	NL36999.100.11
Other	volgt na goedkeuring