Development of a pharmacokinetic/pharmacodynamic model of dexmedetomidine, and the effect of repeated auditory stimulation on pharmacodynamics of dexmedetomidine.*

Published: 13-12-2012
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To develop a PKPD dexmedetomidine model, and to assess the effect of continuous auditory stimulation on dexmedetomidine pharmacodynamics.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON39625

Source
ToetsingOnline

Brief title
Dexmedetomidine PKPD and effect of stimulation

Condition

- Other condition

Synonym
pharmacodynamic, Pharmacokinetic

Health condition

gezonde vrijwilligers, dus geen aandoeningen

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Dexmedetomidine, pharmacodynamic, pharmacokinetic

Outcome measures

Primary outcome

To develop a pharmacokinetic/pharmacodynamic (PKPD) model for dexmedetomidine,

for use in plasma concentration targeted and effect site targeted TC

Secondary outcome

To assess the effect of stimulation on dexmedetomidine pharmacodynamics and

EEG-monitoring.

To develop a PKPD model based on haemodynamic side effects (changes in cardiac

output).

Study description

Background summary

Dexmedetomidine is an α2-adrenoceptor agonist that has only recently been registered for human use in Europe. It has sedative, analgesic and anxiolytic properties, but patients remain arousable. This makes it an ideal drug for procedures such as conscious sedation, awake craniotomies, and sedation in Intensive Care Units (ICU). Pharmacokinetic models of (anaesthetic) drugs can be used in target controlled infusions (TCI), to deliver stable plasma concentrations of drug. There are several models available for dexmedetomidine at this time, but the most often used models (Dyck and Talke) underpredict the plasma concentration at higher concentrations. Also, plasma concentrations aren*t what the clinician is interested in, but in the effect. Therefore,

pharmacokinetic/pharmacodynamic (PKPD) models can be developed to model the concentration of the effect site (or a mathematical representation of the effect site). This has been done for many anaesthetic drugs, but not for dexmedetomidine. Additionally, we want to investigate the effect of stimulation on the pharmacodynamics of dexmedetomidine. The reason for this is that patients under dexmedetomidine sedation are arousable by noises or touch. An operating room or ICU is never quiet, and there are always sounds of monitors, alarms, and talking between team members or activity around another patient in the same room, therefore the stimulation of the patient in such an environment may have a profound effect on the sedative effect of dexmedetomidine.

Study objective

To develop a PKPD dexmedetomidine model, and to assess the effect of continuous auditory stimulation on dexmedetomidine pharmacodynamics.

Study design

Pharmacokinetic/pharmacodynamic modelling study.

Intervention

Dexmedetomidine will be infused by target controlled infusion using the Dyck model. The targets are, in order, 1, 2, 3, 4, 6 and 8 ng/ml. Each target step will be maintained for 30 minutes. After 35 minutes at a target of 8 ng/ml, or earlier if one of the dexmedetomidine cessation criteria is met, dexmedetomidine infusion will cease.

Study burden and risks

Dexmedetomidine has been registered outside of the EU for over a decade, and is safe to use in controlled settings, such as an operating room or intensive care unit. The targets used in this study will be higher than the package insert indicates, but our dexmedetomidine cessation criteria will prevent individuals from reaching dangerously high concentrations. Other studies using similar criteria have had individuals safely reaching measured concentrations of up to 14-16 ng/ml. Our maximum target concentration will be 8 ng/ml. An intravenous line (drug and fluid infusion) and an arterial line (for blood sampling and blood pressure/cardiac output monitoring) will be inserted before starting the study. These lines will be inserted by a certified anaesthesiologist. Possible risks include hematoma, infiltration, embolism and phlebitis, but these risks are considered rare, especially in volunteers. All other monitoring will be non-invasive, as in routine clinical care.

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

American Society of Anesthesiologists (ASA) Physical Status 1
No medical history of significance
No chronic use of medication, alcohol, drugs or tobacco (oral contraceptives excluded).

Exclusion criteria

Contraindications for use of dexmedetomidine
Known intolerance to dexmedetomidine
Body mass index (BMI) <18 or >35 kg/m2
Volunteer refusal
Pregnancy, or currently nursing

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-06-2013
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	dexmedetomidine
Generic name:	precedex
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	13-12-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-03-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-04-2013
Application type:	Amendment

Review commission: METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2012-005443-24-NL
CCMO	NL42818.042.12