Safety, tolerability and sedative properties of single dose intranasal dexmedetomidine premedication in elderly subjects.

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This study aims to evaluate the safety, tolerability and sedative proporties of a single dose of intransally administered dexmedetomidine in person odler than 65 years, differentiating between person using beta-blocking medication and those not...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac arrhythmias
Study type	Observational invasive

Summary

ID

NL-OMON42654

Source
ToetsingOnline

Brief title
KUKIDEX-1

Condition

- Cardiac arrhythmias
- Anxiety disorders and symptoms
- Vascular hypertensive disorders

Synonym
cardiovascular instability, changes in bloodpressure and heartrythm

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: Pharmacodynamics, Pharmacokinetics, Sedation

Outcome measures

Primary outcome

* Number of patients per dose cohort experiencing hypotension (defined as: a decrease in systolic, diastolic or Mean Arterial bloodpressure of >30% from baseline bloodpressure) for more than 5 minutes

* Number of patients per dose cohort experiencing bradycardia (defined as: a heart rate below 40 beats per minute) for more than 1 minute with evidence of inadequate tissue perfusion (hypotension, dizziness, syncope)

* Maximum change from baseline in heart rate

6.1.2

Secondary outcome

Secondary study parameters/endpoints (if applicable)

* Maximum change from baseline in systolic, diastolic or mean arterial bloodpressure in 2,5 to minute intervals

* Time of peak plasma level of dexmedetomidine

* Peak plasmalevel dexmedetomidine

* Per cohort and compared to placebo and other dosage cohort:

* Mean change in mOAA/S over time at 2,5-5 min intervals

Use of concomitant antihypertensive medication

Study description

Background summary

Dexmedetomidine is a sedative with anxiolytic and sedative properties. It has been used succefull as a preoperative anxiolytic in children. In adults evidence suggests it has better properties than benzodiazepines. The intranasal adminstration of dexmedetomidine has been proven to be simple, reliable and comfortable.The hemodynamic side effect profile of this route in persons older than 65 years and persons using beta-blocking medication and the pharmacokinetic profile in this group have not been described.

Study objective

This study aims to evaluate the safety, tolerability and sedative proporties of a single dose of intransally administered dexmedetomidine in person odler than 65 years, differentiating between person using beta-blocking medication and those not using betablocking medication.

Study design

Persons older than 65 years are assigned two either of two study arms. One arm holds subject using beta-blocking medication and one arm holds those that do not. Patients are not given any sedative premedication Two hours prior to the start of surgeyr they are transproted to the Holding area. Here, baseline measurement of ECG, blodo pressure and oxygensaturation are taken. This is normal prior to any type of surgery under general anesthesia. After baselin measurement a single dose dexmedetomidine is spray into the nose. Dosage is dependant onthe cohort the subject is participating in. There are four dose cohorts in each arm: 0,5microgram/kg, 1,0 microgram/kg, 1,5 microgram/kg en 2,0 microgram/kg. In each cohort 6 subject are included. Five subject will receive dexmedetomidine, one will receive normal saline as placebo. The hospital pharmacy will prepare a randomisation list and doubleblind ampoules.

Over the next 90 minutes ECG, bloodpressure, oxygensaturation and sedationlevel are measured per 2.5 minute interval during the first 45 minutes and at 5 minute intervals during the last 45 minutes. Ananesthesiologist or sedationpractitioner will be in attendance at all times. After 90 minutes the subject can wait in the Holding area for transport to the opertating theatre. surgery to commence. After the oepration the dexmedetomidine has stopped working.

After every subject the safety of progression with the study is evaluated and after completion of each dose cohort the safety of dose-escalation is evaluated. Criteria to halt progression/ dose escalation are:
* Bradycardia (heart rate <40 bpm for more than 1 minute; with signs of inadequate tissue perfusion *(hypotension, dizziness, syncope)
* Hypotension (Systolic, diastolic or mean arterial bloodpressure >30% below baseline) for more than 5 minutes
* QTcF change from baseline >100 msec or total QTcF of >500 msec;
* Oxygen saturation [SpO2] <90% not resolved by simple verbal or light tactile stimulation
* Any serious adverse events (SAEs) which are considered by the PI as related to study drug;
* Any clinically significant AEs that the Sponsor and PI consider a safety concern;
* Sustained MOAA/S score of *1 for *5 consecutive minutes.

* If any of the above events are experienced in *2 beta blocked patient receiving dexmedetomidine treated patients, then no further cohorts of beta blocked patients will be enrolled. If only 1 patient in a beta blocked cohort experiences one of the above adverse events, then the decision to escalate will be made of the basis of an evaluation of the seriousness, requirement for intervention and probable cause of the event.
The same rule is applicable to the non-beta blocking medication arm.
* Any of the above events experienced by *3 of 5 dexmedetomidine treated patients will define the Maximum Tolerated Dose and no further patients will be enrolled at the equivalent or higher dose level

Study burden and risks

Subject participate only once in this study. The study takes place in the same location as the surgery. No further visits are required. subject wil not be given any sedative premedication. They are transported two hours prior to surgery to the Holding area. Here the normal baseline measurements are taken. They will be given a single dose of dexmedetomidine intranasally (or placebo). Intranasal dexmedetomidine has been prove to be a comfortable way of administration. After administration subject are asked to rest in their hospital beds, not to start a conversation on their own initiatief or keep themselves awake actively, and to respond to the investigators questions. During the study period 6 venous blood samples of 6 mls are taken from teh preoperative intravenous canula. The time between dxmedetomidine administration and the induction of general anesthesia is 2 hours which allows for the effects of dexmedetomidine to have minimized or be gone.
The anesthetist giving the general anesthetic can easily accomodate for any residual effects by using dose reduction. The attendance of an anesthetist or sedation practitioner is above and beyond the standard for monitoring patients under light procedural sedation
The planned maxillofacial surgery kan always proceed. Subjects do not have to

return to the hospital for followup visits. Subject do not have to stay in the hospital longer.

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

1. Planned for a maxillofacial procedure under general anesthetic in the UMCG planned on one of the planned study days
2. Completed and cleared through the pre-anesthetic screening as per the standard protocol
3. Adult, men and women, over 65 years of age, inclusive.
4. Body Mass Index (BMI) * 17.5 and * 30.5 kg/m2, inclusive, and a total body weight >50 kg, at screening and check-in.
5. American Society of Anesthesiologists (ASA) Physical Status 1 or 2 as determined in the preprocedural anaesthesiological screening

6. Obtain a score of I or II using the Modified Mallampati Scoring.
7. Understand the study procedures in the informed consent form(s) (ICF(s)), and be willing and able to comply with the protocol.
8. For inclusion in the beta blocked arm subjects only: taking beta blocking medication at home in any dose or prescription.

Exclusion criteria

1. For inclusion into the non-beta blocked arm: taking any type of beta-receptor blocking medication
2. Contraindications for the use of dexmedetomidine
3. Known intolerance to dexmedetomidine
4. History or presence of significant cardiovascular disease (ASA >2), or significant cardiovascular disease risk factors, significant coronary artery disease, or any known genetic pre disposition to cardiac arrhythmia (including long QT syndrome.)
5. History or presence of significant (ASA >2) pulmonary, hepatic, renal, hematological, gastrointestinal, endocrine, immunologic, dermatologic, neurological (inclusive of any seizure disorder), or psychiatric disease.
6. History of any illness or medication use that, in the opinion of the PI, might confound the results of the study or pose an additional risk to the patient by their participation in the study.
7. Surgery within the past 90 days prior to dosing judged by the PI to be clinically relevant.
8. History of febrile illness within 5 days prior to dosing.
9. History or presence of alcoholism or drug abuse within the past 2 years.
10. Hypersensitivity or idiosyncratic reaction to components of dexmedetomidine, placebo components, or to compounds related to the study medications.
11. Single 12-lead ECG demonstrating QTcF interval >450 msec at screening ;12. Patient refusal

Study design

Design

Study phase:	2
Study type:	Observational invasive
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):	31-03-2016
Enrollment:	48
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Dexdor
Generic name:	Dexmedetomidine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	17-12-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-01-2016
Application type:	First submission
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	EUCTR2015-004587-11-NL
CCMO	NL55716.042.15