Safety, tolerability and sedative properties of intranasal dexmedetomidine premedication in elderly people

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27385

Source
NTR

Brief title
KUKIDEX-1

Health condition

pharmacodynamics
pharmacokinetics
hemodynamic changes

Sponsors and support

Primary sponsor: University Medical Center Groningen
Source(s) of monetary or material Support: fund=initiator=sponsor

Intervention

Outcome measures

Primary outcome

• Number of patients per dose cohort experiencing hypotension (signs of hypoperfusion, systolic, diastolic or mean arterial bloodpressure >30% below baseline) 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

Secondary outcome

• 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

Study description

Background summary

The hemodynamic changes and sedative effects after intranasal administration of a single dose of dexmedetomidine to elderly subject are studied and the pharmacokinetic profile is studied

Study objective

Single dose intranasal dexmedetomidine can be administered safely to elderly people as premedication with respects to hemodynamic changes, irrespective of the concurrent use of betablocking medication

Study design

Baseline measurement take place at T=0 (approximately 2 hours before planned surgery). There after hemodyamic, respiratory and sedative measurement take place every 2.5 minutes in the first 45 minutes and every 5 minutes in the next 45 minutes. After 90 minutes the trial is ended.

Intervention

• Patients planned for maxillofacial surgical procedures under general anesthestia fulfilling the age criterium will be given the patient information brochure by the administration clerks in the maxillofacial outpatient department. Patients will be asked to read the information carefully within the next 2 days. After this period the patient will be asked telephonically whether or not they are interested in participation and are willing to give consent. When patients give verbal consent they will be asked to fill in the consent form and return it in the envelope included in the PIF.

The surgical procedure will be planned by the maxillofacial department in conjunction with the investigational team and the patient. The patient will be informed of the time and day of the planned surgery and study by the outpatient department. On the day of the planned surgery the patient will have been admitted to the maxillofacial ward as is usual. Patients will not receive premedication with sedative properties. Patients will have been asked to refrain from eating solids or liquids that are not clear as of 6 hours preceding the planned time of the start of the study and to abstain from any oral intake 2 hours previous to this moment. This period of fasting is normal for patients undergoing a procedure under anesthesia but will now start 90 minutes earlier because of the study period. Normal medication can be taken with a small amount of water.

The patients will be transferred to the Holding area two hours in advance of the start of the planned general anesthetic. Here the patient is met by the investigational team. The patient will be asked to sign the consent form. Patients will be in their hospital bed in a semi-supine position with a upper-body elevation to make them comfortable but no more than 30 degrees. Standard monitoring equipment will be attached to the patient, consisting of a three lead ECG, non-invasive bloodpressure monitoring, pulse-oximetry and nasal-prongs for measurement of end-tidal carbondioxide. An intravenous cannula will be placed in the patients non-dominant hand, the antecubital fossa on the non-dominant side or, in case this fails any of the two sites on the dominant side.

Base-line measurement of bloodpressure, ECG, pulserate, end-tidal carbondioxide and oxygen saturation are taken and recorded. After recording these parameters the study medication will be administered. Study medication can be either dexmedetomidine in a dosage corresponding to the planned dose for the cohort the patients will be participating in or placebo. Patient and investigator will be blinded to the study medication.

This study will use the hospitals clinical stock of dexmedetomidine and NaCl 0,9%. The hospital pharmacy will provide coded, blinded packages with either dexmedetomidine or

placebo. The concentration of the preparations of study medication will remain constant at 100microgram per milliliter throughout the study. Investigators will adjust the volume of drug (or placebo) to administer according to the patients bodyweight and the planned dosage.

Dosing: the cohorts of patients will be sequentially enrolled into the study. Each cohort will only start in the study after a safety check of the data of the previous cohort will be done by the PI and the Sponsor

The first cohort will receive 0.5 microgram per kilogram dexmedetomidine or placebo (normal saline) from a blinded container prepared by the pharmacy. The second cohort will receive 1.0 microgram per kilogram dexmedetomidine or placebo (normal saline), the third cohort will receive 1.5 microgram per kilogram dexmedetomidine or placebo (normal saline) and the fourth cohort will receive 2.0 microgram per kilogram dexmedetomidine or placebo (normal saline).

Drug administration will be intranasally by use of a atomizer device (MAD1, Wolfe Troy Medical Inc., Utah, USA). After administration the patient will be asked to stay in the supine position. During 90 minutes after drug adminstration serial measurements will be made and recorded of blood pressure, pulse rate, oxygen saturation, end-tidal carbon dioxide and sedation depth as measured by the modified Observers Assessment of Alertness/Sedation: MOAA/S grading will be done every 5 minutes from the time of dosing until complete recovery or for a minimum of 90 minutes. Each sedation level will be scored on a 5-point scale ranging from 0 (does not respond to painful trapezius squeeze) to 5 (responds readily to name spoken in normal tone) as per the table below:
Modified Observer’s Assessment of Alertness/Sedation

Responsiveness Score

Responds readily to name spoken in normal tone 5 (alert)

Lethargic response to name spoken in normal tone 4

Responds only after name is called loudly and/or repeatedly 3

Responds only after mild prodding or shaking 2

Responds only after painful trapezius squeeze 1

Does not respond to painful trapezius squeeze 0

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During the first 45 minutes after drug administration bloodpressure will be measured and recorded at 2,5 minute time intervals, pulse rate, oxygen saturation, end-tidal carbondioxide will be continuously measured and will be recorded at 2,5 minute time intervals. After 45 minutes the time intervals will be changed to 5 minutes. Six blood samples will be taken from the venous cannula or by venepuncture if sampling from the cannula fails: at 10, 15, 20 , 30,45 and 90 minutes after drug administration respectively. For each of the samples taken the allowed time of deviation from the planned sampling time will be 60 seconds. We expect to take no more than 36 ml of blood per patient per session (3 ml for flushing out the saline in the system, 3 ml for the actual blood sample, 6 sampling times per session).

Planned surgery can start 90 minutes after drug administration or later, depending on the proceedings in the operating theatre. If planned surgery starts later than 90 minutes after drug administration, measurements will continue as before to ensure safety. When surgery is to commence the patient will be brought in their bed to the operating theatre.. Here the investigational team will hand over the patient into the care of the anesthesia team planned to administer the general anesthetic for the maxillofacial procedure. The anesthesia team is informed by the investigational team of the patients participation and a full handover of the proceedings and events during the study period is given. The study period ends here for this patient and responsibility of direct patient management as defined by UMCG protocol is handed over to the attending anesthesia team.

After the handover the anesthesia team can proceed with the normal tasks and proceedings for the planned general anesthesia and surgery.
Should the patient experience any of the stopping-criteria specified above the anesthesiologist attending to the general anesthetic will be immediately informed of this event. This anesthesiologist will then evaluate the event together with the investigational team to conclude whether it is considered safe to continue with the general anesthetic. If proceeding is not considered safe, the patient will be informed of the decision and will be transferred to the post-anesthetic care unit. The investigational team will ensure proper treatment of the patient by the relevant consulting specialist, depending on the nature of the event. When no treatment by another consulting specialist is needed, the patient is observed in the post-anesthetic care unit until all standard criteria for discharge to the ward are met, after which the patient can be transferred back to the ward with a complete handover of the events.

Should the patients planned surgery be postponed on the basis of meeting stopping criteria the patient will be given a new appointment and will not be enrolled into the study again.

Patients can leave the hospital no less than 1 hour after the last administration of a sedative or hypnotic and no less than 2 hours after administration of an antagonist . This is standard procedure after any type of procedural sedation.

Contacts

Public
UMCG, EB32, Hanzeplein 1

C.R.M. Barends
Postbus 30.001

Groningen 9700 RB
The Netherlands
050-3616161
Scientific
UMCG, EB32, Hanzeplein 1

C.R.M. Barends
Postbus 30.001

Groningen 9700 RB
The Netherlands
050-3616161

Eligibility criteria

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) ¡Ý 17.5 and ¡Ü 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.

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 type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2016
Enrollment:	48
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL4992
NTR-old	NTR5513
Other	METC : 2015/536

Study results