Evaluation of pharmacokinetic and –dynamic characteristics of norepinephrine for the augmentation of arterial blood pressure in healthy volunteers prior to and during general anesthesia

No registrations found.

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

Summary

ID

NL-OMON29148

Source
NTR

Brief title
VASOCONTROL-I

Health condition

Anesthesia

Sponsors and support

Primary sponsor: University Medical Center Groningen, dept of Anaesthesiology
Source(s) of monetary or material Support: funding=sponsor

Intervention

Outcome measures

Primary outcome

The primary endpoint of this study will be the association between ABP and plasma concentrations of norepinephrine (awake state), and the association of ABP and plasma concentrations of norepinephrine during steady-state general anesthesia with propofol and remifentanil.

Secondary outcome

- Evaluation of the effect of the interaction between propofol, remifentanil and norepinephrine on hemodynamics during general anesthesia.
- Evaluation of the effect(s) of endogenous norepinephrine plasma concentration on the relationship between administered dose (and plasma concentration) of norepinephrine and induced hemodynamic alteration(s).
- Evaluation of the Beloeil norepinephrine PKPKD model.
- Assessment of changes in mean systemic filling pressure prior to and after induction of general anesthesia, as assessed by arm stop-flow measurements by application of a rapidly inflated tourniquet.
- Evaluation of the dose-dependent effect of administered norepinephrine on plasma melatonin concentrations prior to and after induction of general anaesthesia.

Study description

Background summary

Intraoperative hypotension is an important risk-factor for the development of renal, myocardial and cerebral complications following surgery. Therefore, vasopressors such as norepinephrine, are commonly used for maintaining or restoring arterial blood pressure (ABP) during general anesthesia. There is however surprisingly little information on the dose-response of norepinephrine, both in awake patients, and in patients under general anesthesia. Also, the administration of norepinephrine is reactive, i.e. follows when hypotension has already occurred, and should ideally be proactive, i.e. to prevent hypotension from developing, ultimately minimizing the risk of postoperative organ injury. In this study, the pharmacokinetic (PK) characteristics, as well as the pharmacodynamic (PD) characteristics of norepinephrine will be assessed in healthy volunteers during awake conditions and during a steady-state standardized general anesthesia using target-controlled infusions of propofol and remifentanil.

Study objective

To assess the effect of the administration of norepinephrine on ABP while subjects are awake

and subsequently, to study the effects of the interactions of norepinephrine and anesthetics (propofol and remifentanil) on ABP under steady-state conditions during general anesthesia.

Study design

Phase 1:
- norepinephrin: Baseline; before and after Ringerlactate bolus (at 5 min); at the end of infusion of epinephrin bolus (at 15 minutes) and 2 and 5 minutes thereafter; just before start of continuous infusion of norepinephrin (at 30 minutes); just before every incremental step of continuous norepinephrin infusion (at 45, 60, 75, 90 and 105 minutes); 2, 5 and 30 minutes after continuous infusion of epinephrin stopped.
- melatonin: just before start of continuous infusion of norepinephrin (at 30 minutes), just before some incremental steps of continuous norepinephrin infusion (at 60, 90 and 105 minutes); 30 minutes after continuous infusion of epinephrin stopped.

Phase 2:
- norepinephrin: 15 minutes after start of propfol/remifentanil infusion; at the end of infusion of epinephrin bolus (at 15 minutes) and 2 and 5 minutes thereafter; just before start of continuous infusion of norepinephrin (at 30 minutes); just before every incremental step of continuous norepinephrin infusion (at 30, 60, 90, 120, 150 and 180 minutes) and after the noxious stimuli half way during each step (45, 75, 105, 135 and 165 minutes); when continuous infusion of epinephrin and propofol and remifentanil stopped and 2, 5, 10, 20 and 30 minutes thereafter.
- propofol/remifentanil: 15 minutes after start of propfol/remifentanil infusion; just before start of continuous infusion of norepinephrin (at 30 minutes); just before every incremental step of continuous norepinephrin infusion (at 30, 60, 90, 120, 150 and 180 minutes); when continuous infusion of epinephrin and propofol and remifentanil stopped and 2, 5, 10, 20 and 30 minutes thereafter.
- melatonin: just before start of continuous infusion of norepinephrin (at 30 minutes), just before every incremental step of continuous norepinephrin infusion (at 30, 60, 90, 120, 150 and 180 minutes); 30 minutes after continuous infusion of epinephrin stopped.

Intervention

Phase 1: While the subject is awake, norepinephrine will be administered in a standardized step-up dosing scheme.
Phase 2: After a wash-out phase, general anesthesia will be induced using a standardized propofol – remifentanil dosage administration. Once steady-state has been achieved, norepinephrine will be administered, again in a standardized step-up dosing scheme and surgical incision will be mimicked using noxious electrical tetanic stimulation.
During interventions, arterial blood samples will be drawn for the determination of drug concentrations. Hemodynamic effects (including ABP) will be continuously monitored.

Contacts

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Eligibility criteria

Inclusion criteria

 American Society of Anesthesiologists (ASA) Physical Status I or II
 No exclusion criterion is present
 Informed, and willing to give written informed consent.

Exclusion criteria

 Refusal of the volunteer to participate
 Pregnancy
 Diseases involving the cardiovascular system (hypertension, coronary artery disease, prior acute myocardial infarction, any valvular and/or myocardial disease involving decrease in ejection fraction, arrhythmias, which are either symptomatic or require continuous medication/pacemaker/automatic internal cardioverter defibrillator)
 A difference > 15 mmHg in measured systolic or diastolic blood pressure value (SBP, DBP) between the left and right upper arm, as determined by non-invasive cuff oscillometry during the screening visit.
 An increased risk of difficult mask ventilation or tracheal intubation, as judged by the anesthesiologist-researcher.
 Pulmonary disease
 Gastric or endocrinologic diseases
 End-stage liver or kidney failure
 Use of tricyclic antidepressive medication or MAO inhibitors.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2021
Enrollment:	36
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

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	NL9312
Other	METc Brabant : to be anounced after submission

Study results