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

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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...

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON29148

Bron
NTR

Verkorte titel
VASOCONTROL-I

Aandoening

Anesthesia

Ondersteuning

Primaire sponsor: University Medical Center Groningen, dept of Anaesthesiology
Overige ondersteuning: funding=sponsor

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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.

Onderzoeksproduct en/of interventie

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.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

 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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	N.v.t. / één studie arm

Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-04-2021
Aantal proefpersonen:	36
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL9312
Ander register	METc Brabant : to be anounced after submission

Resultaten