Application of the ELFI-TECH monitor for measurement of nociception

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

Summary

ID

NL-OMON42818

Source
ToetsingOnline

Brief title
ELFITOR 2

Condition

- Other condition

Synonym
hemodynamics, pain measurements

Health condition

monitoring

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Elfi-Tech Ltd.

Intervention

Keyword: healthy volunteers, hemodynamics, nociception

Outcome measures

Primary outcome

Elfitor

Secondary outcome

Cardiac output

Blood pressure

Pulse oximetry

ECG monitoring

NoL

Study description

Background summary

Accurate measurement of nociception during anesthesia remains a challenging task. Nociception, which is defined as the neural process of encoding and processing noxious stimuli (noxious stimuli are actually or potentially tissue damaging events), will elicit behavioral, autonomic and hormonal responses in conscious and unconscious individuals. Detection of behavioral responses during anesthesia is often difficult due to the use of sedatives and muscle relaxants. Hence, anesthesiologists rely on autonomic nervous system responses to assess the nociceptive level of the patient. Most anesthesia health care providers, if not all, use changes in heart rate and blood pressure as markers of the occurrence of acute nociceptive events. While these variables may suffice when intense nociceptive stimuli occur, mild and moderate stimuli are often not detected or detected too late.

In recent years various indices of nociception have been developed with varying success in actually detecting nociceptive events. These indices derive a numerical value from single variables (such as heart rate variability, skin conductance, skin vasomotor reflex, the electroencephalogram, pupil diameter) or a combination of signals. There are various new developments, one of which is the Nociception Level or NoL has recently been studied by us at LUMC (P13.069). We successfully studied the relationship between nociceptive stimuli and NoL during anesthesia and surgery. A completely new technology is the Elfitor device (Elfi-Tech, Rehovot, Israel), which is based on dynamic light scattering (DLS) and which continuously and non-invasively measures skin blood flow, skin blood flow variability, heart rate, heart rate variability, respiration, oxygen saturation, hemoglobin concentration, blood pressure and cardiac output. Additionally the system allows rheologic measurements from endothelial red blood cell interaction.

Study objective

In the current study we will apply the Elfitor and collect its derived parameters during nociceptive stimulation in healthy volunteers without and with the administration of a low-dose opioid analgesic. Our study aim is to assess whether the various parameters derived from the device correlate with nociceptive stimulation and standard hemodynamic parameters.

Study design

The subjects will arrive at 8 AM in the laboratory K5-120 and will receive an intravenous access line. Next they will be familiarized with the setup, pain tests, pain scoring and monitoring devices.

After a 30 min rest period the pain tests will be applied. Heat and electrical pain tests are performed in random order. The duration of the test sequence is about 2 hours.
Then after another 3 min rest, the opioid remifentanil will be infused using a target controlled infusion system (Remifusor, Glasgow University). The target blood concentration is 2 ng/mL. The complete sequence of testing will be repeated, again with the electrical and heat pain tests randomized in sequence.

Total duration of the study is 5 hours. Subjects will remain in the laboratory until the effects of remifentanil are completely worn off (this usually takes about 20 min). Only fit subjects are allowed to leave the laboratory.

The following measurements will be obtained during pain stimulation:

1. Elfitor (positioned on the inside of second digit and outside of the wrist) ipsilateral from where pain is applied, preferably the non-dominant hand (this leaves the dominant had for pain scoring). The data will be logged on a laptop

PC and will be analyzed off-line. Most important parameters will be: heart rate, heart rate variability, blood flow, blood flow variability, plethysmogram, blood pressure, stroke volume, stroke volume variability, Mayer waves, and endothelial-red blood cell interaction.

2. Continuous non-invasive cardiac output and blood pressure using the Nexfin/finger cuff device, positioned on the fourth digit (ring finger) of the hand at which the Elfitor is placed. The Nexfin estimates finger systolic and diastolic blood pressure and cardiac output.

3. Pulse oximetry and ECG monitoring will be performed as safety measures.

4. NoL fingerprobe, positioned on the third digit of the non-dominant hand. The NoL combines information from several physiological parameters which represent different autonomic pathways. This information includes the photoplethysmogram, skin conductance level, fluctuations in skin conductance, and their time derivatives.

Electrical pain stimulation
All participants will be familiarized with the study design, pain tests and scoring system. Pain intensity is scored using an 11-point numerical rating score (NRS) ranging from 0 (no pain) to 10 (maximum tolerated pain).

Test 1. Electrical pain is induced by placing electrodes on the tibial surface of the right leg. Electrical currents are applied using a locally designed and constructed computer interfaced current stimulator (CICS, Leiden University Medical Center, Leiden, The Netherlands). A preset increasing current at 0.5 mA/s is delivered and subjects are instructed to score the first time they feel pain (pain threshold, PTh) and the highest pain sensation they feel during the stimulation (pain tolerance, PTol) by pushing a button.
This test is performed three times, 5-10 min apart.

Test 2. The values of PTh and PTol are used to construct a linear distribution of 8 interpolated currents. For example if PTh is 11 mA and PTol 20 mA, the interpolated temperatures are 12, 13, 14, 15, 16, 17, 18 and 19 mA. These 8 currents are subsequently presented in random order to the participants at 3-5 min intervals. All subjects are blinded to the sequence and intensity of the stimuli. They will be asked to rate the different stimuli on the 11-point NRS.

Heat pain stimulation.
An electronic Visual Analogue Scale (eVAS) will be used to quantify pain intensity in response to a noxious thermal stimulus. The thermal stimulus will be applied on the volar side of the forearm using a thermal probe (a 3 * 3 cm thermode) of the TSA-II NeuroSensory Analyzer (Medoc Ltd, Ramat Yishai, Israel). This is a computer-controlled device capable of generating highly reproducible thermal stimuli. The eVAS will be measured electronically using a

slide potentiometer (length = 10 cm) that can be moved from the left (0 or no pain) to the right (10 or most intense pain imaginable). Using a hand the subject can move the slide during the heat stimulator test. The eVAS is recorded and collected on disk for further analyses. In this study a constant increase in temperature will be applied, from 32 to 51 oC in 3 min after which the stimulus will be terminated, or at any time earlier when the eVAS score equals 10 cm. The test will be performed three times, 5-10 min apart; each time the thermode will be repositioned to prevent sensitization or adaptation.

Intervention

Remifentanil infusion (blood target concentration 2 ng/ml)
Pain testing

Study burden and risks

The burden of the study is mild. Heat and electrical pain testing may give temporary red coloration of the skin. We have ample experience with both electrical and heat pain testing, and no other side effects are known to occur with these experimental pain models.

Remifentanil infusion may give hypotension, nausea and vomiting. However, at the indicated concentration we expect these side effects to be absent or, if they occur, of a mild nature. They are relatively easy to treat since remifentanil has a short plasma half-life of 2-3 minutes. Overall the burden to the subjects is mild.

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

Subjects of either sex, aged 18-34 years with a body mass index < 30 kg/m2.

Exclusion criteria

Severe medical disease including hypertension, liver/renal disease, neurological disorders, diaphragmatic hernia/pyrosis; (history of) psychiatric or neurological disease; pregnancy/lactation; allergy to study medication; (history of) illicit drug abuse/alcoholism.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-11-2015

Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	14-07-2015
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	24-11-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
CCMO	NL53666.058.15