The influence of age on EEG signals and consciousness during anesthesia (TIARA)

Published: 28-06-2021
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To evaluate the relationships between BIS* parameters, age, and depth of anesthesia in patients undergoing surgery under general anesthesia.

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

Summary

ID

NL-OMON54342

Source
ToetsingOnline

Brief title
TIARA study

Condition

- Other condition

Synonym
consciousness during anesthesia, EEG signals

Health condition

De invloed van leeftijd op EEG signalen en bewustzijn tijdens anesthesie

Research involving
Human

Sponsors and support

Primary sponsor: Medtronic Trading NL BV
Source(s) of monetary or material Support: Medtronic

Intervention

Keyword: Age, Bispectral (BIS□) system, depth of anesthesia, EEG signals

Outcome measures

Primary outcome

Primary Objective(s)

To evaluate the relationships between BIS parameters, age, and depth of anesthesia in patients undergoing surgery under general anesthesia.

Primary Endpoint

All data gathered by the BIS* system during general anesthesia, including:

* EEG waveforms

* EMG

* BIS Number

* Total Power

* Anesthesia records

Secondary outcome

Secondary Objective(s)

To investigate BIS parameters, depth of anesthesia and physical and cognitive states in the study subject population.

Secondary Endpoint

Assessments of the subject*s demographics, age and blood panel as well as the

physical and cognitive state using:

* Mini Mental State Examination (MMSE)

* Mini Nutritional Assessment (MNA®-SF)

* Edmonton Frail Scale (EFS)

Study description

Background summary

Brain function monitoring with Bispectral Index* (BIS*) technology during surgical procedures gives anesthesia providers the ability to directly monitor the anesthetic effect on the patient*s brain and optimize the anesthetic dosing for the individual.
The BIS technology converts raw EEG data acquired from the frontal cortex into a single number between 0 (isoelectric EEG) and 100 (fully awake). Given the numerous changes that occur in brain anatomy and physiology with typical aging, it is reasonable to assume that the EEG patterns of elderly patients and young patients under general anesthesia differ.
In general, elderly patients are more sensitive to anesthetic agents. Less medication is usually required to achieve a desired clinical effect, and drug effect is often prolonged[1]. We might thus hypothesize that the BIS* technology should be age adjusted under the assumption that the anesthetic state is also dependent on the patient's physical, mental, and cognitive state.

Study objective

To evaluate the relationships between BIS* parameters, age, and depth of anesthesia in patients undergoing surgery under general anesthesia.

Study design

this is a multicenter, non-invasive, interventional data collection study to improve the current BIS* algorithm. Subjects undergoing a standard of care, elective non-ambulatory surgery under general anesthesia will be recruited. Eligible patients 18 years and older, will be informed of the study and invited to participate. Each eligible and consented subject will undergo the study assessments and procedures. The BIS* sensors will be applied to the patient*s

forehead before anesthesia is administered. The BIS* data will be collected throughout the surgery. The data recorded during the surgery will be provided to Medtronic.
It is planned to enroll up to 100 subjects from 2 centers. It is anticipated that approximately 35% of enrolled patients will be between ages 18-64 years old, and approximately 65% of patients will be above the age of 65 years. In addition to basic demographic data collection, three assessments, the Mini Mental State Examination (MMSE), the Mini Nutritional Assessment (MNA®-SF), and the Edmonton Frail Scale (EFS) will be administered to each subject prior to surgery.

Intervention

Subjects will be considered enrolled at the time they sign the informed consent. Basic demographic and Medical History data will be collected at the baseline visit, and subjects will be given three assessments:
* Mini Mental State Examination (MMSE)
* Mini Nutritional Assessment (MNA®-SF)
* The Edmonton Frail Scale (EFS)
During the surgical procedure, the BIS* sensors will be placed on the subject*s forehead before any anesthetics are given, and data will be collected throughout the duration of the surgery. The subject will also be fitted with Nellcor* pulse oximetry sensors.
Prior to induction subjects will be assessed using the Modified Observer*s Assessment of Alertness/Sedation Scale (MOAA/S).
A slower induction of anesthesia will be achieved by setting a lower initial target propofol dose and making an incremental increase in the targeted dose. This is a conservative approach which maintains consistency across all study subjects, and will ensure safety of the elderly patients included in the study, which should also closely align with standard institutional practices. The propofol will be administered using target-controlled infusion (TCI) pump, and the initial targeted effective site concentration (Ce) will be half of the effective site propofol concentration based on drug Instructions for Use (IFU) and on the subject*s body mass used for induction. The TCI will calculate the initial bolus and infusion rate required to rapidly achieve and maintain this drug level based on propofol's population pharmacokinetics using the Schnider Model. At this step, the depth of anesthesia will be assessed using MOAA/S after an equilibrium time of approximately 5 minutes (from the start of propofol infusion.) After this initial step, the target effect site concentration is subsequently adjusted in an attempt to maintain the desired level of sedation and three-quarters of the Ce will be administered. This second step will also require depth of anesthesia assessment using MOAA/S after an equilibrium time of approximately 5 minutes. Lastly, the final/full Ce of the propofol will be administered, and the MOAA/S will be assessed after another equilibrium time of 5 minutes is reached. The specified induction period will last approximately 15 minutes in order to record and monitor the BIS values, EEG readings, and MOAA/S scores across the anesthetic agent

introduction into the subject. After these steps, anesthesia will be delivered and maintained per institutional guidance.
During the anesthesia maintenance phase, anesthesia medications will continue according to standard practice without any other intervention.

At the beginning of induction, the depth of anesthesia will be assessed to ensure a MOAA/S of 0 has been obtained.

The administration of anesthetic drugs, neuro-muscular blocking agents (NMBA), NMBA reversal drugs, anti-nausea drugs, and drugs that reduce pain will be recorded on the eCRF (administration time and dosage).
BIS values and EEG data will be recorded with a USB storage device connected to the BIS complete monitor. Blood pressure, EtCO2, SpO2, pulse rate, respiration rate, end-tidal anesthetic gas, FiO2%, EtO2%, and temperature will be gathered from the hospital computerized database and the Nellcor system, digital records, labeled with patient ID, will be provided to Medtronic. The BIS data file labeled with patient ID will be provided to Medtronic.
Only adverse events related to the BIS* and Nellcor* systems will be reported.

Study burden and risks

Medtronic has determined that this is a study of a *non-significant risk device* due to the nature of the devices being tested. Utilizing the FDA criteria1,2 listed below to distinguish between significant and non-significant risk devices, Medtronic has determined that:

* The investigational device is not intended as an implant and does not present a potential for serious risk to the health, safety, or welfare of a subject;
* The investigational device is not purported or represented to be for use supporting or sustaining human life and does not present a potential for serious risk to the health, safety, or welfare of a subject;
* The investigational device is not for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health, and does not present a potential for serious risk to the health, safety, or welfare of a subject; and
* The investigational device does not otherwise present a potential for serious risk to the health, safety, or welfare of a subject.

The potential risks of these devices have been assessed and are not greater than those of currently approved and marketed devices of the same type (e.g., pulse and tissue oximeters, EtCO2 monitors, non-invasive blood pressure monitors, ECG or respiration monitors). Society may benefit from more accurate anesthesia monitors.

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. >=18 years of age
2. ASA physical status I-III
3. Able and willing to participate in the study and sign the informed consent form
4. Will undergo non-ambulatory elective surgery under general anesthesia
5. Has an expected surgery time >1 hour

Exclusion criteria

1. Pregnant
2. Unwilling to undergo EEG measurement

3. Undergone brain surgery procedure or had a cerebrovascular accident or severe head trauma in the last 10 years
4. Alcohol or illicit drug use, which prevents normal functioning in society or has led to organ toxicity. Chronic use of opioids, narcotics, or analgesics, which may limit a subject's responsiveness to analgesic dosages.
5. Known or suspected electroencephalograph abnormality (e.g., epilepsy or scarring)
6. Presence of a major psychiatric condition such as Bipolar disorder/ schizophrenia/ Alzheimer's disease/ dementia/ Parkinson's disease /major depression
7. Severe visual or auditory disorder
8. Cannot understand or is unwilling to perform the study assessments, according to the investigator's judgment

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):	10-11-2021
Enrollment:	50
Type:	Actual

Medical products/devices used

Generic name:	Bispectral (BIS□) index complete monitoring system
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	28-06-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	25-08-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	18-07-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	16-03-2023
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	NL74977.058.20