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Comparison of the Surgical Pleth Index™ with haemodynamic variables to assess nociception–anti-nociception balance during general anaesthesia

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Key points

- The Surgical Pleth Index offers a measure of the balance between noxious stimulation and anti-nociception during surgery.
- The SPI value could be affected by intravascular filling status of the patient and by conditions such as chronic hypertension.
- The current study compared heart rate (HR), mean arterial pressure (MAP), and the SPI for the measurement of the balance between nociception produced by a neurosurgical head holder and anti-nociception from a remifentanil infusion.
- The performance of the SPI response to head holder at indicating the anti-nociception level was comparable with that of MAP and HR.
- Low intravascular volume status and chronic treatment for high arterial pressure lowered the responses of those indexes to the stimulation.

Background. The Surgical Pleth Index (SPI) is proposed as a means to assess the balance between noxious stimulation and the anti-nociceptive effects of anaesthesia. In this study, we compared SPI, mean arterial pressure (MAP), and heart rate (HR) as a means of assessing this balance.

Methods. We studied a standard stimulus [head-holder insertion (HHI)] and varying remifentanil concentrations (CeREMI) in a group of patients undergoing neurosurgery. Patients receiving target-controlled infusions were randomly assigned to one of the three CeREMI (2, 4, or 6 ng ml^{-1}), whereas propofol target was fixed at 3 $\mu g\ ml^{-1}$. Steady state for both targets was achieved before HHI. Intravascular volume status (IVS) was evaluated using respiratory variations in arterial pressure. Prediction probability (Pk) and ordinal regression were used to assess SPI, MAP, and HR performance at indicating CeREMI, and the influence of IVS and chronic treatment for high arterial pressure, as possible confounding factors.

Results. The maximum SPI, MAP, or HR observed after HHI correctly indicated CeREMI in one of the two patients [accurate prediction rate (APR)=0.5]. When IVS and chronic treatment for high arterial pressure were taken into account, the APR was 0.6 for each individual variable and 0.8 when all of them predicted the same CeREMI. That increase in APR paralleled an increase in Pk from 0.63 to 0.89.

Conclusions. SPI, HR, and MAP are of comparable value at gauging noxious stimulation–CeREMI balance. Their interpretation is improved by taking account of IVS, treatment for chronic high arterial pressure, and concordance between their predictions.

Keywords: anaesthetic techniques, i.v.; monitoring, depth of anaesthesia; pain, acute

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During the past few years, several tools have been developed to monitor the balance between the intensity of noxious stimulation and anti-nociception during surgery under general anaesthesia.[1] These tools aim at providing each patient with an appropriate, individually tailored anti-nociception regimen. Complex neural and neuroendocrine pathways are activated by noxious stimulation. This makes the identification of an ideal monitorable pharmacodynamic target difficult. In contrast to the monitoring of the hypnotic component of anaesthesia by the measurement of electroencephalogram-derived variables, assessment of the nociception–anti-nociception balance is indirect in nature, apart from evoked potentials.[2 3] Variables studied include the spinal withdrawal and H reflex,[4] the RIII reflex threshold,[5] the response spectral entropy of the electroencephalogram,[6 7] the skin vasomotor reflex,[8] the skin conductance,[9 10] and the pupil diameter.[11]

The recently renamed Surgical Pleth Index™ (SPI), previously known as the Surgical Stress Index™, has been demonstrated to be a function of the intensity of surgical

stimulation and the depth of the anti-noxious component of anaesthesia provided by an opiate infusion,[12] or regional anaesthesia.[13] In addition to its strong correlation to opiate concentration,[14] the increase in SPI in response to noxious stimulation has been demonstrated to be a predictor of the occurrence of patient movement.[15]

The calculation of SPI relies on a balanced sum of normalized heart beat intervals (HBIs) and plethysmographic pulse wave amplitudes,[12] both of which are controlled by the balance between sympathetic and parasympathetic tone. SPI has been shown to change with noxious stimulation even in patients receiving β-blocking agents, when compared with those receiving an appropriate dose of fentanyl.[16] However, other factors known to influence autonomic reactions independently of a noxious stimulus might interfere with the accuracy of this variable in evaluating the nociception–anti-nociception balance. Factors that may be relevant include intravascular volume status (IVS), diabetes, or chronic high arterial pressure and anti-hypertensive drugs.

This study was designed to compare the performance of SPI and haemodynamic variables, at gauging the nociception–anti-nociception balance of patients submitted to an intense and standardized noxious stimulation under general anaesthesia, and at identifying confounding factors that potentially impede their interpretation.[17] The standardized stimulus was the insertion of a pin head holder just before intracranial neurosurgery, in patients submitted to variable anti-nociception levels. Variation in anti-nociception was achieved by comparing patients receiving one of three different remifentanil concentrations as estimated by a pharmacokinetic model. IVS and treated chronic high arterial pressure were tested as potential confounding factors.

Methods

Patient recruitment, sample size, and randomization

After approval by our Institutional Review Board and informed consent, 33 patients undergoing intracranial neurosurgery were recruited for this prospective double-blind randomized study. Exclusion criteria included age below 18 and above 80, impaired cardiac function, and a past medical history of diabetes.

Sample size calculation was performed using G*Power© software (version 3.0.3, Franz Faul, Universitat Kiel, Germany)[18] and based on the intention to perform multiple regression analyses. Considering a squared multiple correlation coefficient (R^2) of 0.3 as being relevant, a set of three predictors (anti-nociception level indication, IVS, and history of chronic high arterial pressure), and an α-value of 0.05, a total sample size of 30 was required to achieve a power of 0.8.

Patients were randomly assigned to one of the three groups, according to the effect-site concentration of remifentanil (CeREMI) to be achieved during the study period, namely 2, 4, or 6 ng ml^{-1}. The randomization was obtained using an Excel™ (Microsoft™ Office Excel 2003, Microsoft Corporation, Luxembourg, Zaventem, Belgium) random number function-generated list that was available to the nurse in charge of preparing anaesthetic medications, but blinded to the anaesthesiologist in charge of the procedure. Blinded syringes were prepared with 25, 50, or 75 μg ml^{-1} remifentanil in normal saline. The patients were assigned a number in the randomization list according to the sequential order of their recruitment.

Anaesthesia protocol

All patients were planned for an early morning surgery and fasted for 6 h before induction of anaesthesia. Patients with a past medical history of chronic high arterial pressure received their usual anti-hypertensive medications on the morning of surgery at the time of premedication, except that angiotensin-convertase inhibitors and angiotensin II antagonists were withheld on that morning, but still given the day before. Premedication consisted of alprazolam 0.5 mg and atropine 0.5 mg given orally 1 h before surgery. Upon arrival in the operating theatre, two 18 G i.v. cannulae were sited and standard monitoring was applied including an Sp_{o_2} sensor. Careful attention was paid to the position of the Sp_{o_2} sensor on a thumb, and this was not changed throughout the study period. A crystalloid solution (Plasmalyte A®, Baxter International Inc., IL, USA) was infused through one venous cannula and a colloid solution (Voluven®, Fresenius Kabi, Bad Homburg, Germany) through the second one. The total infusion rate for both infusions combined was kept constant at 2 ml kg^{-1} h^{-1} throughout the study.

A target-controlled infusion (TCI) of remifentanil was started using an ASENA PK TCI® pump (Cardinal Health Alaris Products, Basingstoke, UK), and the pharmacokinetic model of Minto and colleagues.[19] The effect-site concentration target was set on the pump at 4 μg ml^{-1} in all patients, hence leading to a CeREMI of 2, 4, or 6 ng ml^{-1} once steady state had been obtained according to the remifentanil concentration in the blinded syringe (25, 50, or 75 μg ml^{-1}). Once CeREMI was achieved, a propofol TCI was started (Master TCI®, Fresenius Kabi) to obtain an effect-site concentration of 3 μg ml^{-1} (model of Marsh and colleagues).[20] The effect-site concentrations of propofol and remifentanil were kept constant throughout the study. Immediately after loss of consciousness, patients received a 0.2 mg kg^{-1} dose of cisatracurium to facilitate tracheal intubation. No further dose of neuromuscular blocking agent was administered thereafter. Once the airway was secured and mechanically ventilated with a 50% oxygen–air mixture (end-tidal carbon dioxide partial pressure maintained between 4.0 and 4.7 kPa), an arterial line was inserted into the radial artery at the wrist (20 G catheter), on the same side as the one for the Sp_{o_2} sensor, and contralateral to the non-invasive arterial pressure cuff. Normothermia was maintained throughout the study using a forced-air warming device.

Standard noxious stimulation

The standard noxious stimulation consisted of a Mayfield head-holder insertion (HHI) (Mayfield® Modified Skull Clamp, Integra™, Plainsboro, NJ, USA). This device allows