BJA Advance Access published December 8, 2013

British Journal of Anaesthesia Page 1 of 7
doi:10.1093/bja/aet407

BJA

Prediction of immediate postoperative pain using the analgesia/nociception index: a prospective observational study

E. Boselli[1,2]*, L. Bouvet[1], G. Bégou[1], R. Dabouz[1], J. Davidson[1], J. -Y. Deloste[1], N. Rahali[1], A. Zadam[1] and B. Allaouchiche[1,2]

[1] Department of Anaesthesiology and Intensive Care, Édouard Herriot Hospital, HCL, Lyon, France
[2] Claude Bernard Lyon I University, University of Lyon, Lyon, France

* Corresponding author: Hôpital Édouard Herriot, Service d'anesthésie-réanimation, 5 place d'Arsonval, 69003 Lyon, France. E-mail: emmanuel.boselli@chu-lyon.fr

Editor's key points

- Poorly controlled pain on arrival in the recovery room disrupts the handover process and may worsen patient recovery.
- Nociception reduces parasympathetic tone and this affects heart rate variability, from which the analgesia/nociception index (ANI) can be derived.
- This study shows a strong relationship between the ANI and immediate postoperative pain on arrival in the recovery room.
- The ANI may assist in optimal titration of analgesia before emergence from anaesthesia.

Background. The analgesia/nociception index (ANI) is derived from heart rate variability, ranging from 0 (maximal nociception) to 100 (maximal analgesia), to reflect the analgesia/nociception balance during general anaesthesia. This should be correlated with immediate postoperative pain in the post-anaesthesia care unit (PACU). The aim of this study was to evaluate the performance of ANI measured at arousal from general anaesthesia to predict immediate postoperative pain on arrival in PACU.

Methods. Two hundred patients undergoing ear, nose, and throat or lower limb orthopaedic surgery with general anaesthesia using an inhalational agent and remifentanil were included in this prospective observational study. The ANI was measured immediately before tracheal extubation and pain intensity was assessed within 10 min of arrival in PACU using a 0–10 numerical rating scale (NRS). The relationship between ANI and NRS was assessed using linear regression. A receiver-operating characteristic (ROC) curve was used to evaluate the performance of ANI to predict NRS$>$3.

Results. A negative linear relationship was observed between ANI immediately before extubation and NRS on arrival in PACU. Using a threshold of $<$50, the sensitivity and specificity of ANI to discriminate between patients with NRS$\leq$3 and NRS$>$3 were both 86% with 92% negative predictive value, corresponding to an area under the ROC curve of 0.89.

Conclusions. The measurement of ANI immediately before extubation after inhalation-remifentanil anaesthesia was significantly associated with pain intensity on arrival in PACU. The performance of ANI for the prediction of immediate postoperative pain is good and may assist physicians in optimizing acute pain management.

Clinical trial registration. ClinicalTrials.gov NCT01796249.

Keywords: anaesthesia, general; analgesia; nociception; pain measurement

Accepted for publication: 18 August 2013

Severe immediate postoperative pain remains frequent after surgery, occurring in 20–40% of patients.[1] A recent study has shown that pain intensity may be high not only after major surgical procedures such as major orthopaedic surgery but also after several common minor-to-medium level surgical procedures, including haemorrhoidectomy, tonsillectomy or laparoscopic appendectomy, or cholecystectomy.[1] This study indicates that to reduce the incidence of severe postoperative pain, patients undergoing so-called minor surgery should be monitored more closely and that postoperative pain management should comply with existing recommendations.

Updated practice guidelines for acute pain management in the perioperative setting have been recently reported by the ASA Task Force on Acute Pain Management.[2] These guidelines state that anaesthesiologists should use standardized, validated instruments to facilitate the regular evaluation and documentation of pain intensity, the effects of pain therapy, and side-effects caused by the therapy. In a communicating patient who is awake in the post-anaesthesia care unit (PACU), pain intensity can be assessed using a 0–100 visual analogic scale, a 1–5 verbal rating scale, or a 0–10 numerical rating scale (NRS), although the standard method is still a topic of debate.[3]

The assessment of immediate postoperative pain may be obtained in PACU using different methods such as skin conductance or pupillary reflex measurement.[4–6] We have recently reported that it may also be obtained using the analgesia/nociception index (ANI), a 0–100 non-invasive index calculated from heart rate variability reflecting the parasympathetic tone.[7] To date, ANI has been used to assess the antinociception/nociception balance during general anaesthesia in adults and children or during labour pain, showing significant changes between painful and no-pain periods.[8–11] Similarly, the measurement of ANI during the immediate postoperative period was significantly correlated with pain intensity.[7] We hypothesized that ANI may be used not only for the assessment but also for the prediction of immediate postoperative pain. Our primary objective was to investigate the performance of ANI measured at arousal from general anaesthesia in the operating theatre for the prediction of immediate postoperative pain on arrival in PACU.

Methods

Study design

This prospective observational study was approved by the Institutional Review Board (Comité de Protection des Personnes Sud-Est III, study identifier CPP 2012-052 B, ClinicalTrials.gov identifier NCT01796249) and performed between October 2012 and April 2013 at Édouard Herriot Hospital, Lyon, France. The methodology followed the recommendations of STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) statement.[12] After written informed consent was obtained, ASA physical status I–III patients undergoing halogenated-based and remifentanil general anaesthesia in the room where the ANI monitor was placed were included. The procedures performed were ear, nose, and throat (ENT) surgery or orthopaedic lower limb surgery. The exclusion criteria were age <18 yr or >75 yr, arrhythmia, preoperative use of β-blockers, administration of anticholinergic drugs or neuromuscular block reversal in the previous 20 min, preoperative pain treated with opioids, psychiatric diseases, autonomic nervous system disorders, epilepsy, and inability to understand the verbal rating pain scale.

Anaesthetic technique

Alprazolam 0.1 mg kg^{-1}, hydroxyzine 1 mg kg^{-1}, or both were administered orally 1 h before induction of anaesthesia. After arrival in the operating theatre, patients were monitored with a three-lead electrocardiogram (ECG), non-invasive arterial pressure measurement and pulse oximetry. The anaesthetic induction was then performed using i.v. ketamine (0.1–0.5 mg kg^{-1}) to prevent postoperative hyperalgesia, propofol 2.5 mg kg^{-1} and remifentanil 1 μg kg^{-1} in 1 min if cisatracurium (0.15 mg kg^{-1}) was used or 2–4 μg kg^{-1} in 1 min to provide optimal intubation conditions in the absence of neuromuscular block.[13–15] The use of neuromuscular blocking agent was used at the discretion of the attending anaesthesiologist. After tracheal intubation, mechanical ventilation was initiated with a mixture of 60–70% O_2 and 30–40% air and adjusted to keep end-tidal CO_2 pressure between 30 and 35 mm Hg. Maintenance of anaesthesia was performed at the discretion of the anaesthesiologist with sevoflurane or desflurane adjusted to keep the minimal alveolar concentration between 0.8 and 1.2 and remifentanil 0.1–0.3 μg kg^{-1} min^{-1} in continuous infusion. In the case of use of cisatracurium, neuromuscular block was monitored by train-of-four (TOF) stimulation. Multimodal analgesia was provided at the discretion of the attending anaesthesiologist using i.v. paracetamol, ketoprofen, nefopam, tramadol, and morphine 0.1–0.2 mg kg^{-1} in combination according to respective contraindications.[2] In some cases, regional analgesia was used (peripheral nerve blocks or wound infiltration). At the end of the procedure, remifentanil and halogenated agents were discontinued, and 100% O_2 was given with a 10 litre min^{-1} fresh gas flow. To prevent residual paralysis if cisatracurium was used, spontaneous recovery from neuromuscular block at emergence from anaesthesia was assessed by a TOF ratio of $\geq$0.9.[16] In the case of a TOF ratio of $<$0.9, neostigmine 30–40 μg kg^{-1} and atropine 15–20 μg kg^{-1} were administered i.v. after four twitches were visible and patients were withdrawn from the study. Tracheal extubation was performed when the patient was alert, with a respiratory rate between 12 and 30 cycles min^{-1} and a temperature of $>$36.5°C, and then the patient was sent to PACU.

Study protocol and ANI measurement

At arousal from general anaesthesia, ANI was recorded immediately before tracheal extubation using the PhysioDoloris® monitor (MDoloris Medical Systems, Loos, France). It is a non-invasive device that takes an ECG analogue output from the patient monitor and displays an average measurement of ANI made over the previous 2 min. Details of ANI calculation have been previously described.[8 17] The ANI is a 0–100 index derived from the high-frequency component of heart rate variability reflecting the analgesia/nociception balance.[8] Briefly, local minima and maxima in the normalized high-frequency RR series of the QRS complex are automatically detected and the surface between the lower and upper envelopes is measured in four sub-windows, with area under the curve $(AUC)_{min}$ defined as the smallest sub-surface.[8] Then, ANI is computed in order to express a fraction of the total window surface (having a maximum possible value of 12.8 s), leading to a measure varying from 0 to 100 displayed continuously as a short-term average more than 2 min using the following formula: $ANI=100*[(5.1\times AUC_{min}+1.2)/12.8]$.[8] Higher ANI values indicate prominent parasympathetic tone, as observed during adequate analgesia.[18] In the case of nociception, the sympathetic tone increases and the parasympathetic tone decreases, leading to decreased ANI values.[18]

Immediate postoperative pain intensity was assessed within 10 min of arrival in PACU by using a 0–10 NRS (0=no pain and 10=worst pain imaginable), with NRS$\leq$3 corresponding to no or mild pain and NRS$>$3 corresponding to moderate-to-severe pain.[19] All patients were educated about NRS before surgery. Patients experiencing NRS$>$3 received i.v. morphine titration