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CASE REPORTS

Guiding opioid-free intravenous antinociception with the Analgesia Nociception Index: a case report

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Abstract
Background: Opioid-free anesthesia decreases the incidence of opioid adverse events, but its optimal antinociceptive depth has not been clearly defined. Personalizing intraoperative opioid-free infusions with a nociception monitor may be the solution.
Case report: We describe the feasibility and potential limitations of titrating opioid-free antinociception during major abdominal surgery using the Analgesia Nociception Index (Mdoloris, Lille, France) in an obese patient. After stabilizing the patient's nociception-antinociception balance intraoperatively we quickly reversed anesthesia and the patient did not require postoperative opioids.
Conclusion: Personalizing opioid-free antinociception with a nociception monitor is feasible. It may optimize intraoperative antinociception and improve postoperative comfort.

PALAVRAS-CHAVE
Nocicepção;
Dor;
Medicina perioperatória;
Monitorização

Antinocicepção intravenosa sem opioides orientada pelo Índice de Analgesia/Nocicepção: relato de caso

Resumo
Introdução: A anestesia sem opioides diminui a incidência de eventos adversos associados aos opioides, mas a profundidade antinociceptiva ideal dessa abordagem não está claramente definida. Personalizar a infusão intraoperatória sem opioides com o uso de monitor de nocicepção pode ser a solução.
Relato de caso: Descrevemos a viabilidade e as eventuais limitações da titulação da antinocicepção sem opioides através do uso do Índice de Analgesia/Nocicepção (Mdoloris, Lille, França) durante cirurgia abdominal de grande porte em paciente com obesidade. Depois de estabilizar o equilíbrio nocicepção-antinocicepção da paciente no intraoperatório, revertemos rapidamente a anestesia e a paciente não precisou de opioides no pós-operatório.

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Conclusão: A personalização da antinocicepção sem opioides por meio do emprego de monitor de nocicepção é factível. A abordagem pode otimizar a antinocicepção intraoperatória e melhorar o conforto pós-operatório.

Introduction

Opioid-free anesthesia (OFA) has been shown to decrease postoperative complications associated with opioids and may be a useful tool for enhanced recovery after surgery.[1]

However, to this day little is established on the use of nociceptive monitors and their capacity to guide the antinociceptive component of OFA. Analgesic management of the morbidly obese patient presents a unique challenge in perioperative medicine.[2] Opioids are the most potent available analgesics, but they are also responsible for considerable side effects. Most notably, obese patients may develop postoperative respiratory depression and obstructive apnea which can lead to hypercapnia, hypoxemia, and even death.[2] In addition, obesity continues to increase in incidence and anesthesiologists, now more than ever, need to find alternatives in perioperative monitoring and therapy that will improve patient outcome. OFA is a potential solution to this problem as administering non-opioid analgesics that have limited effect on respiratory drive and that decrease the need for postoperative opioids could allow such patients to awaken more comfortably, quickly, and safely.[3] However, this approach can be limited by unclear analgesic goals and non-opioid analgesics can themselves be responsible for adverse events.

A goal-directed approach, which targets adequate antinociception (e.g., by measuring nociceptive-antinociceptive balance) and narcosis (e.g., with a frontal electroencephalogram) could reduce the negative effects of excessive drug infusion. The Analgesia Nociception Index (MDoloris, Lille, France) has been shown to guide intraoperative opioid based antinociception and to predict postoperative pain.[4,5] By analyzing the high frequency domain (i.e., 0.15 to 0.5 Hz) of heart rate variability and correcting for respiratory rate variability, the ANI attempts to measure the autonomic nervous system's balance as a surrogate to nociception. Since heart rate variability is predominantly mediated by the parasympathetic system, the ANI displays a unitless number that increases with parasympathetic activity (i.e., 0 – no parasympathetic tonus, 100 – no sympathetic tonus).[5] Nociception stimulates a sympathetic response and consequently the more noxious a stimulus the lower the value. An important observation is that heart rate variability is not merely an indicator of nociception, but also of the patient's stress response and inflammation.[6]

Although ANI has been substantially investigated during opioid based anesthesia, its utility in OFA remains to be determined.

Written informed consent was obtained and this manuscript adheres to the CARE guidelines.

Case report

We report the case of a 56-year-old American Society of Anesthesiology (ASA) 3 woman who suffered from urinary incontinence due to a vesicovaginal fistula of the trigone that required combined laparoscopic and open cystectomy with ileal conduit urostomy. The patient was treated at the CHU Rennes and gave consent for this publication. She weighed 140 kg for a height of 162 cm (Body Mass Index – BMI of 53 $kg.m^{-2}$). In addition to her morbid obesity she also suffered from type 2 diabetes and hypertension. We decided to avoid intraoperative opioid use and opted for combined intravenous and inhaled opioid-free anesthesia.

The patient fasted preoperatively for at least 6 hours for solids and 2 hours for clear liquids. She was monitored with standard ASA monitors, Bispectral Index (Covidien, Dublin, Ireland), ANI, and TOF-Watch (Alsevia Pharma, Paris, France). An 18-gauge peripheral intravenous catheter was placed, and crystalloid infusion was set at 3 $mL.kg^{-1}.h^{-1}$. Mean blood pressure, Bispectral Index, and ANI goals were set to be greater than 70 mmHg, between 40 and 60, and between 50 and 70, respectively. After 3 minutes of preoxygenation, dexmedetomidine, ketamine, and lidocaine infusions were started at infusion speeds of 2.3 $\mu g.kg^{-1}.h^{-1}$, 0.12 $mg.kg^{-1}.min^{-1}$, and 0.85 $mg.kg^{-1}.h^{-1}$, respectively. A bolus of 150 mg of propofol led to loss of consciousness and, upon adequate ventilation, 10 mg of cisatracurium and 12 mg of dexamethasone were administered. Sevoflurane was titrated to maintain Bispectral Index between 40 and 60. Ketamine and dexmedetomidine infusion were modified to maintain ANI between 50 and 70. Infusion rates of ketamine and dexmedetomidine were modified by 10% to 50% at the anesthesiologist's discretion. If ANI increased and Bispectral Index decreased despite steady sevoflurane end-tidal values, dexmedetomidine was lowered first. Cisatracurium was infused to have a train-of-four count of 0 during the laparoscopic portion of the operation. A central venous catheter and urinary catheter were placed and 1 g of paracetamol as well as 100 mg of ketoprofene were administered prior to incision. Anesthesia lasted 516 minutes, surgery 441 minutes (185 minutes of laparoscopy), and extubation occurred 10 minutes after the end of surgery. An episode of hypotension (70/40 mmHg) associated with bradycardia (40 bpm) occurred at induction and resolved with tracheal intubation. Heart rate and mean blood pressure remained over 50 bpm and 70 mmHg throughout the rest of the anesthetic. No vasopressors or inotropic agents were required.

Table 1 Analgesia Nociception Index, Bispectral Index, heart rate, mean blood pressure and anesthetic administration.

Monitoring	Induction	Intubation	Incision	Insufflation	Exsufflation	Laparotomy	Surgery end
ANI	61	64	76	97	79	40	54
BIS	42	40	43	48	37	48	46
HR (bpm)	40	70	53	52	61	62	60
MBP (mmHg)	50	75	72	75	77	78	73
Anesthetic administration							
Ketamine (mg. $kg^{-1}.h^{-1}$)	0.12	0.12	0.10	0.10	0.10	0.09	0
Dexmedetomidine (μg. $kg^{-1}.h^{-1}$)	2.3	2.3	1.4	1.4	0.9	0.85	0
Sevoflurane MAC	*	*	0.7	0.2	0.2	0.3	0.4
Propofol (mg)	150	*	*	*	*	*	*

ANI, Analgesia Nociception Index; BIS, Bispectral Index; HR, heart rate; MBP, mean blood pressure.

Bispectral index and ANI remained in target range for 84% and 60% of case time, respectfully. Neuromuscular blockade was fully reversed at the end of surgery. Key intraoperative events are further detailed in Table 1.

The patient was extubated in the operating room and arrived at the post-anesthesia care unit with a blood pressure of 115/70 mmHg, heart rate of 67 bpm and pulse oximetry of 92% with mask oxygen at 6 $L.min^{-1}$. Pulse oximetry quickly rose to 98% with mask oxygen at 8 $L.min^{-1}$. Oxygen was progressively decreased, and pulse oximetry remained above 94% for the rest of the post-anesthetic care. Besides a two-hour infusion of lidocaine 0.4 $mg.kg^{-1}.h^{-1}$, no other analgesic was administered. The patient had no complaints and was discharged 159 minutes after admission to the post-anesthesia care unit. Paracetamol adequately controlled pain on the ward. Renal function remained normal during her hospitalization, but her postoperative stay was complicated by a surgical site infection at day 8 which required care. She returned home 23 days after surgery.

Discussion

This case report demonstrates the feasibility of goal-directed opioid-free intravenous and inhaled anesthesia for an obese patient undergoing major abdominal surgery. The patient did not receive any opioids during the entire perioperative period. Furthermore, we show both the possibility and the challenges of applying a goal-directed antinociception protocol during OFA. Although our strategy allowed for an early recovery from anesthesia in the immediate postoperative period, our compliance to protocol could be improved regarding ANI (i.e., 60% of case time with ANI between 50 and 70). Compliance to the goal-directed anesthesia protocol, however, was considerably better concerning BIS (i.e., 84% of case time with Bispectral index in range established by the protocol). One of the main limitations of using non-opioid analgesics is their relatively long action. Our patient, for example, remained with an ANI over 70 for more than an hour despite decreasing the dexmedetomidine infusion by 40%. Additionally, the multiple perioperative tasks undertaken by anesthesiologists often hinder protocol compliance. Using a decision support or even a fully automated system that couples a nociceptive monitor with analgesic infusion pumps may help clinicians improve their protocol compliance.[7] Despite these difficulties, however, we were still able to stabilize the patient's nociception-antinociception balance and maintained the ANI between 50 and 70 until the end of surgery without any intraoperative hemodynamic instability. We were then able to quickly reverse anesthesia and the patient did not develop postoperative nausea, respiratory insufficiency, or obstructive apnea. The complete omission of opioids in the perioperative analgesic management of our patient may have been a determinant factor in the patient's rapid recovery in the postoperative care unit.

It is important to note that although many studies have investigated the effects of OFA on postoperative opioid requirement, to our knowledge little is published on nociceptive monitoring and OFA. By optimizing the patient's nociception-antinociception balance intraoperatively, it may be possible to completely remove, in some patients, the need for postoperative opioids. Our team is currently investigating the effects of opioid sparing techniques during goal-directed antinociception and future studies, including case series, retrospective analyses, and randomized controlled trials, will determine if intraoperative optimization of antinociception improves postoperative comfort and outcome. Some populations, such as the morbidly obese, may very well benefit from this personalized opioid-free analgesic strategy. Goal-directed opioid-free antinociception is feasible and may optimize perioperative analgesia, which could lead to improved postoperative comfort.

Glossary

ANI, Analgesia Nociception Index; BPM, Beats Per Minute; BMI, Body Mass Index; CARE, Case Report.

Conflicts of interest

The authors declare no conflicts of interest.

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References

1. Wu CL, King AB, Geiger TM, et al. American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus

Statement on Perioperative Opioid Minimization in Opioid-Naive Patients. Anesth Analg. 2019;129:567–77.
2. Nightingale CE, Margarson MP, Shearer E, et al. Peri-operative management of the obese surgical patient 2015: Association of Anaesthetists of Great Britain and Ireland Society for Obesity and Bariatric Anaesthesia. Anaesthesia. 2015;7: 859–76.
3. Bakan M, Umutoglu T, Topuz U, et al. Opioid-free total intravenous anesthesia with propofol, dexmedetomidine and lidocaine infusions for laparoscopic cholecystectomy: a prospective, randomized, double-blinded study. Brazilian J Anesthesiol (English Ed). 2015;65:191–9.
4. Turan G, Ar AY, Kuplay YY, et al. Analgesia Nociception Index for perioperative analgesia monitoring in spinal surgery. Brazilian J Anesthesiol (English Ed). 2017;67:370–5.
5. Abdullayev R, Uludag O, Celik B. Analgesia Nociception Index: assessment of acute postoperative pain. Brazilian J Anesthesiol. 2019;69:396–402.
6. Williams DWP, Koenig J, Carnevali L, et al. Heart rate variability and inflammation: A meta-analysis of human studies. Brain Behav Immun. 2019;80:219–26.
7. Coeckelenbergh S, Zaouter C, Alexander B, et al. Automated systems for perioperative goal-directed hemodynamic therapy. J Anesth. 2020;34:104–14.