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Heart rate variability and cardiac baroreflex inhibition-derived index predicts pain perception in burn patients

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ARTICLE INFO

Article history:
Accepted 22 April 2016

Keywords:
Burns
Heart rate variability
Nociception
Procedural pain
Physiologic monitoring
Signal processing

ABSTRACT

Background: Dressing changes induce acute pain in burn patients. This pain is difficult to predict and may be therefore undertreated. Two different non-invasive electrophysiological indices from heart rate variability and baroreflex inhibition-derived indices, analgesia/nociception index (ANI) and cardiovascular depth of analgesia (CARDEAN), have been proposed to predict and better assess adequacy of anti-nociception. The aim of this study was to evaluate these techniques as early pain alert tools in conscious burnt patients during dressing changes' procedures.

Methods: Twenty adult burnt patients undergoing scheduled wound treatment procedures were included in this prospective observational study. Pain intensity was assessed using a 0–10 numerical rating scale (NRS) and was compared with both ANI and CARDEAN, during the procedures. Non parametric rank sum test and linear discriminant analysis were used for evaluating potential differences of measured variables between periods with different pain intensities. Receiver-operating characteristic (ROC) curves were built to assess their performance to detect pain within following 15 s.

Results: The sensitivity and specificity of ANI to detect pain were 67% and 70% and those of CARDEAN were 77% and 80%, with area under the curve (AUC) values of 0.75 and 0.83, respectively. Their combination increased AUC to 0.87.

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http://dx.doi.org/10.1016/j.burns.2016.04.017

Conclusions: Both ANI and CARDEAN indices during wound treatment procedures seem to discriminate periods with and without pain within 15 s, serving as a potential complementary tool for early optimized pain control.

1. Introduction

According to the American Burn Association, approximately 486,000 burnt patients receive medical treatment each year [1]. Although advances in medical management have decreased mortality rate, pain control remains a challenge and may be involved in post-traumatic stress disorders (PTSD) and depression [2–4]. According to the International Association for the Study of Pain, burn pain management faces great challenges due to lack of research and complexity of its unique nature [5]. Furthermore, different studies have found that the management of burn pain can be inadequate, particularly upon dressing removal that has been considered the time of greatest perceived pain [5,6].

Different techniques assessing adequacy of anti-nociception during surgery have been tested [7–9]. The analgesia/nociception index (ANI) is a 0–100 non invasive index of analgesia/nociception balance calculated from heart rate variability (HRV) [10], based on respiratory influences on the RR time series, allowing a continuous quantitative measurement of HRV. Similarly, cardiac baroreflex inhibition has been studied for assessing adequacy of anti-nociception in unconscious surgical patients [11]. CARDEAN (Cardiovascular Depth of Analgesia) is a 0–100 non-invasive index that detects beat-by-beat occurrence of minor, short lasting, rises in systolic blood pressure, followed by minor increase in heart rate, reflecting inhibition of the cardiac baroreflex upon a nociceptive stimulus [11].

Whereas ANI has already been tested for immediate postoperative pain intensity assessment in conscious patients [12,13] neither ANI nor CARDEAN have been investigated for the evaluation of procedural pain in conscious burnt patients. Thus, the aim of this study was to assess predictive value of real time changes of both ANI and CARDEAN for pain in a specialized burn ICU setting.

2. Methods

2.1. IRB/consent

This prospective observational study was approved by the Institutional Review Board (Comité d' Evaluation de l' Ethique des projets de Recherche Biomédicale-CEERB-Paris Nord, study identifier IRB00006477, University Paris 7, AP-HP) and performed between January and June 2014 at the burn ICU at St Louis Hospital, Paris, France. Following, written informed consent was given from each patient.

2.2. Patients

Twenty burnt subjects were enrolled in the study. Exclusion criteria were age <17 or >75 years, presence of non-sinus rhythm, current use of β-blockers, alpha-2 agonists, anticholinergic drugs, autonomic nervous system disorders, stroke or any other neurologic deficits, hypotension associated with administration of vasopressors, history of psychiatric disease and inability to understand verbal orders.

2.3. Study protocol and measurements

Pain intensity was assessed by using a 0–10 numerical rating scale (NRS) that allows patients to rate the perceived pain from 0 (no pain) to 10, as the worse possible pain [14]. NRS values between 1 and 3 were considered as low pain, between 4 and 6 as moderate pain and NRS ≥7 as severe pain. All patients were educated about NRS before the procedures. NRS was evaluated before starting the procedure and each time the patient perceived pain. The investigator was therefore able to ''mark'' on the monitor perception of pain and thenafter its intensity. The analgesia strategy was left to the discretion of anesthesiologist in charge, blinded to the ANI and CARDEAN monitoring, and included i.v. boluses of morphine and additional i.v bolus of sufentanyl 0.1–0.2 μg/kg, during severe pain. Every patient received an i.v. bolus of 2–3 mg of morphine 10–15 min before the procedure along with 0.3 mg/kg of ketamine.

2.3.1. ANI measurement

All patients were monitored with an electrocardiogram (ECG), oscillometric blood pressure with a measuring interval of 5 min and pulse oximetry, using a Phillips Intellivue MP50 monitor. ANI was recorded using the PhysioDoloris monitor (MetroDoloris, Lille, France). It is a non-invasive device that takes an ECG analog output from the patient monitor and displays an average measurement of ANI made over the previous 120 s, based on respiratory influence on the RR interval. It permits a quantitative measurement of HRV, that is the variability of RR in the ECG time series, primarily mediated by parasympathetic and sympathetic outflow from the central nervous system to the sinoatrial node [15]. For this reason and according to published recommendations, a 250 Hz digitized ECG signal is used for R wave detection, automatic filtering and RR interval computation [15]. HRV is measured using a fast Fourier transformation of the ECG signal that gives rise to two main spectral peaks: high frequency fluctuations corresponding to 0.15–0.5 Hz and mediated predominately by parasympathetic outflow and low frequency fluctuations (0.04–0.15 Hz) that reflect both sympathetic and parasympathetic influences on RR time series [9,15]. When parasympathetic tone is present, each inspiration induces slight tachycardia, corresponding to the respiratory sinus arrhythmia,

Please cite this article in press as: Vasilios P, et al. Heart rate variability and cardiac baroreflex inhibition-derived index predicts pain perception in burn patients. Burns (2016), http://dx.doi.org/10.1016/j.burns.2016.04.017