Brief Communication

Pain Measurement in Mechanically Ventilated Patients with Traumatic Brain Injury: Behavioral Pain Tools versus Analgesia Nociception Index

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Abstract

Introduction: Pain is highly prevalent in critically ill trauma patients, especially those with a traumatic brain injury (TBI). Behavioral pain tools such as the behavioral pain scale (BPS) and critical-care pain observation tool are recommended for sedated noncommunicative patients. Analysis of heart rate variability (HRV) is a noninvasive method to evaluate autonomic nervous system activity. The analgesia nociception index (ANI) device (Physiodoloris®, MDoloris Medical Systems, Loos, France) allows noninvasive HRV analysis. The ANI assesses the relative parasympathetic tone as a surrogate for antinociception/nociception balance in sedated patients. The primary aim of our study was to evaluate the effectiveness of ANI in detecting pain in TBI patients. The secondary aim was to evaluate the impact of norepinephrine use on ANI effectiveness and to determine the correlation between ANI and BPS. **Methods:** We performed a prospective observational study in 21 deeply sedated TBI patients. Exclusion criteria were nonsinus cardiac rhythm; presence of pacemaker; atropine or isoprenaline treatment; neuromuscular blocking agents; and major cognitive impairment. Heart rate, blood pressure, and ANI were continuously recorded using the Physiodoloris® device at rest (T1), during (T2), and after the end (T3) of the painful stimulus (tracheal suctioning). **Results:** In total, 100 observations were scored. ANI was significantly lower at T2 (Median [min – max] 54.5 [22–100]) compared with T1 (90.5 [50–100], $P < 0.0001$) and T3 (82 [36–100], $P < 0.0001$). Similar results were found in the subgroups of patients with (65 measurements) or without (35) norepinephrine. During procedure, a negative linear relationship was observed between ANI and BPS ($r^2 = -0.469$, $P < 0.001$). At the threshold of 50, the sensitivity and specificity of ANI to detect patients with BPS ≥ 5 were 73% and 62%, respectively, with a negative predictive value of 86%. **Discussion:** Our results suggest that ANI is effective in detecting pain in ventilated sedated TBI patients, including those patients treated with norepinephrine.

Keywords: Behavioral pain scale, Intensive Care Unit, pain assessment, traumatic brain injury

Introduction

Pain is highly prevalent in critically ill trauma patients, especially those with a traumatic brain injury (TBI).[1] Behavioral pain tools such as the behavioral pain scale (BPS) and critical-care pain observation tool (CPOT) are recommended for sedated noncommunicative patients.[2,3] Analysis of heart rate variability (HRV) is a noninvasive method to evaluate autonomic nervous system activity. The analgesia nociception index (ANI) device (Physiodoloris®, MDoloris Medical Systems, Loos, France) [Figure 1a] allows noninvasive HRV analysis. The ANI assesses the relative parasympathetic tone as a surrogate for antinociception/nociception balance in sedated patients.[4] The primary aim of our study was to evaluate the effectiveness of ANI in detecting pain in TBI patients. The secondary aim was to evaluate the impact of norepinephrine use on ANI effectiveness and to determine the correlation between ANI and BPS.

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Methods

We performed a prospective observational study in 21 deeply sedated TBI patients. Exclusion criteria were nonsinus cardiac

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rhythm; presence of pacemaker; atropine or isoprenaline treatment; neuromuscular blocking agents; and major cognitive impairment. Heart rate, blood pressure, and ANI were continuously recorded using the Physiodoloris® device at rest (T1), during (T2), and after the end (T3) of the painful stimulus (tracheal suctioning) [Figure 1b].

Results

In total, 100 observations were scored. Patients' characteristics were resumed in Table 1.

The mean values of the changes in BPS, CPOT, ANI, MAP, and HR at the 3 times (baseline, during painful stimulation, and at recovery time) are shown in Table 1. The mean BPS, CPOT, MAP, and HR values were significantly changed overtime, increasing during suctioning, and decreasing at recovery time (5 min after the procedure) ($P < 0.05$) [Table 2].

ANI was significantly lower at T2 (Median [min – max] 54.5 [22–100]) compared with T1 (90.5 [50–100], $P < 0.0001$) and T3 (82 [36–100], $P < 0.0001$) [Table 2]. Similar results were found in the subgroups of patients with (65 measurements) or without (35) norepinephrine [Table 3]. During procedure, a negative linear relationship was observed between ANI and BPS ($r^2 = -0.469$, $P < 0.001$). At the threshold of 50, the sensitivity and specificity of ANI to detect patients with BPS ≥5 were 73% and 62%, respectively, with a negative predictive value of 86%.

Discussion

Our results suggest that ANI is effective in detecting pain in ventilated sedated TBI patients, including those patients treated with norepinephrine.

To the best of our knowledge, our study is the first to evaluate the ANI device for pain assessment in deeply sedated mechanically ventilated patients with TBI.

Pain assessment is an immense challenge for clinicians, especially in the context of the Intensive Care Unit (ICU), where the patient is often unable to communicate verbally; current guidelines recommend that intensivists should use some valid observable behavioral scales and physiological indicators, such as the BPS and COPT in patients with intact motor function.[5]

However, these scores have some limitations, including the inter-rater variability and the lack of determination of the level of anxiety and discomfort.[6]

There have been no formal validation studies of the reliability of theses scores to evaluate the behavior of pain in the TBI population. The literature review found that TBI patients were underrepresented (<17%) in studies validating the use of behavioral pain tools in critically ill adults.[1,7]

Another criterion used to assess pain in ICU patients is vital signs. Although hemodynamic changes are easily accessible in the ICU, their validity for pain assessment is not strongly confirmed.[8]

The performance of ANI was evaluated in the prediction of immediate postoperative pain after adult general anesthesia.[9,10]

Few studies have shown the value of this device in the monitoring of pain in sedated critically ill patients.[11]

Table 1: Baseline demographic and clinical characteristics

Variables	Values
Age median (minimum-maximum)	34 (19-90)
Sex (male) (%)	17/21 (81)
Weight (kg), mean±SD	75.67±9.26
Body surface (m^2), mean±SD	1.91±0.14
IGS II, median (IQR)	32 (28.5-8.5)
SOFA, median (IQR)	9 (7-10)
Brain lesions, *n* (%)	
EDH	4/21 (19.05)
SDH	3/21 (14.28)
SAH	2/21 (9.52)
Contusion	8/21 (38.10)
No lesions	4/21 (19.05)
TBI localization area, *n* (%)	
Frontal	5/17 (29.42)
Temporal	2/17 (11.76)
Parietal	1/17 (5.88)
Frontotemporal	7/17 (41.18)
Parietotemporal	1/17 (5.88)
Occipital	1/17 (5.88)
TBI severity, *n* (%)	
Mild (GCS ≤8)	8/21 (38.09)
Moderate (GCS 9-12)	6/21 (28.58)
Severe (GCS ≥13)	7/21 (33.33)
ISS score, median (minimum-maximum)	25 (17-41)
RASS score, median (minimum-maximum)	−5 (−5-0)
Sedatives midazolam (IV infusion)	
Administration (%)	14/21 (67)
Median dose (mg/kg/h) (minimum-maximum)	0.23 (0.13-0.34)
Analgesics	
Fentanyl (IV infusion)	
Administration (%)	13/21
Median dose (mg/kg/h) (minimum-maximum)	2.3 (1.25-3.4)
Remifentanil (IV infusion)	
Administration (%)	8/21
Median dose (µg/kg/h) (minimum-maximum)	4.65 (2.5-8.57)
Morphine SC bolus (mg)	
Administration (%)	1/21
Median dose (mg)	20
Norepinephrine (µg/kg/min)	
Administration (%)	14/21
Median (IQR)	0.26 (0.26-0.57)

Values are expressed as mean±SD; *n* (%) or median (IQR).
EDH: Extradural hemorrhage; SDH: Subdural hemorrhage; SAH: Subarachnoid hemorrhage; SD: Standard deviation; IQR: Interquartile range; IGS: Index Gravity Score; SOFA: Sequential Organ Failure Assessment; TBI: Traumatic brain injury; GCS: Glasgow Coma Scale; ISS: Injury Severity Score; RASS: Richmond Agitation-Sedation Scale; IV: Intravenous

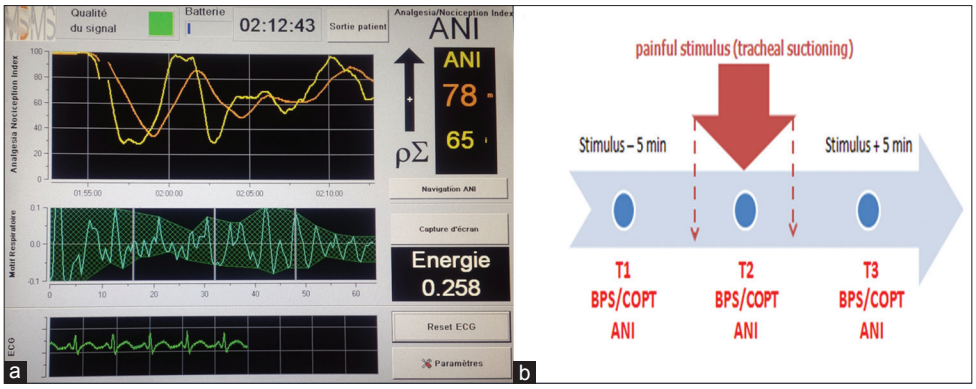

Figure 1: (a) PhysioDoloris™ analgesia monitor (In this screenshot: instantaneous analgesia nociception index value = 65; mean analgesia nociception index value = 78). (b) Time points for analgesia nociception index measurements

Table 2: Variables at different time points

Parameters	T1	T2	T3	*P*†	*P*‡
ANIi	90.5 (50-100)	54.5 (22-100)	82 (36-100)	<0.001	<0.001
ANIm	85 (42-100)	68.5 (32-100)	73.5 (37-100)	<0.001	<0.001
RASS score	−5 (−5-1)	−5 (−5-1)	−5 (−5-1)		
HR (bpm)	84.36±16.31	96.64±17.58	85.91±17.83	<0.001	<0.001
SBP (mmHg)	131.47±15.19	144.51±18.07	138.89±61.55	<0.001	0.277
DBP (mmHg)	68.63±8.23	75.88±9.67	70.20±9.89	<0.001	<0.001
MAP (mmHg)	89.73±7.25	97.95±9.33	90.96±7.96	<0.001	<0.001
RR (/min)	21 (12-34)	24 (14-34)	22 (10-35)	<0.001	<0.001
BPS	3 (3-4)	4 (3-9)	3 (3-4)	<0.001	<0.001
CPOT	0 (0-1)	1 (0-7)	0 (0-1)	<0.001	<0.001

†*P* (T1 vs. T2); ‡*P* (T2 vs. T3). Values are expressed as mean±SD; median (minimum-maximum); T1, T2, T3: Before, during, and 5 min after the painful stimulus; respectively. ANIi: Instantaneous ANI value, between 0 and 100; ANIm: Mean ANI value, between 0 and 100; RASS: Richmond Agitation-Sedation Scale; HR: Heart rate; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MAP: Mean arterial pressure; RR: Respiratory rate; BPS: Behavioral pain scale; CPOT: Critical-care pain observation tool; ANI: Analgesia nociception index; SD: Standard deviation

Table 3: Variables at different time points: Impact of norepinephrine

Parameters	T1	T2	T3	*P*†	*P*‡
Norepinephrine: No (*n*=35 measurements)					
ANIi	88 (50-100)	56 (30-96)	80 (47-100)	<0.001	<0.001
ANIm	85 (42-100)	66 (32-98)	72 (37-100)	<0.001	0.023
HR (bpm)	96.43±14.52	108.60±13.25	97.14±17.54	<0.001	<0.001
SBP (mmHg)	127.48±14.19	144.43±21.34	128.08±13.21	<0.001	<0.001
DBP (mmHg)	70.71±7.25	78.97±8.17	72.94±10.96	<0.001	<0.001
MAP (mmHg)	89.6±7.47	99.34±8.92	90.97±7.25	<0.001	<0.001
Norepinephrine: Yes (*n*=65 measurements)					
ANIi	92 (63-100)	50 (22-100)	82 (36-100)	<0.001	<0.001
ANIm	84 (54-100)	69 (46-100)	75 (44-100)	<0.001	0.028
HR (bpm)	77.86±13.29	90.20±16.27	79.86±14.91	<0.001	<0.001
SBP (mmHg)	133.62±15.38	144.55±16.23	144.71±75.29	<0.001	0.987
DBP (mmHg)	67.51±8.55	72.21±10.66	68.72±9.02	<0.001	0.024
MAP (mmHg)	89.80±7.19	97.20±9.53	90.95±8.37	<0.001	<0.001

†*P* (T1 vs. T2); ‡*P* (T2 vs. T3). Values are expressed as mean±SD; median (minimum-maximum); T1, T2, T3: Before, during, and 5 min after the painful stimulus, respectively. ANIi: Instantaneous ANI value, between 0 and 100; ANIm: Mean ANI value, between 0 and 100; heart rate (beat/min); SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MAP: Mean arterial pressure; SD: Standard deviation; ANI: Analgesia nociception index; HR: Heart rate

Scientific evidence is not yet sufficient to conclude on the validity of the ANI in assessing pain in the context of the ICU, especially in TBI patients.

In the current study, the ANI scores, when compared to baseline values, decreased approximately 40% during endotracheal suctioning and increased >50% by the recovery time.

In the study by Broucqsault-Dédrie *et al*.,[11] ANI decreased approximately 19% during painful situations compared to baseline. The chosen painful stimulus was patient turning for washstand. It should be noted that in that study, the majority of patients included were admitted for respiratory or hemodynamic failure and they were under deep sedation.

Our findings are in line with those of Broucqsault-Dédrie *et al*.[11] who found that ANI is effective in detecting pain in deeply sedated critically ill patients, including those patients treated with norepinephrine.

In this preliminary study, no sample size calculation was performed, which may limit the precision of our estimates. Further large interventional studies are required to confirm our results and to determine the value of this device in titrating the analgesic requirements of this vulnerable group of critically ill patients.

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Conflicts of interest

There are no conflicts of interest.

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