
Case Report,

Monitoring Analgesia in COVID 19 Ventilated Patients in an Intensive Care Unit – Case Series

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Abstract:

Critically ill COVID 19 patients requiring prolonged mechanical ventilation, receive analgesics and sedatives to prevent agitation which may cause patient ventilator asynchrony. Anticipating the physiological response to painful stimuli, such as endotracheal tube suctioning or repositioning, is difficult and titrating analgesics and sedatives may be improved by continuous non-invasive monitoring of levels of analgesia. We describe our initial experience using the PMD-200 monitor with the NOL™ index algorithm (Medasense Biometrics, Ramat Gan Israel) to provide continuous, non-invasive monitoring of analgesia in COVID 19 ventilated patients. Publication of deidentified patient data was determined EC exempt.

Key words: COVID-19, analgesia monitoring, NOL, pain management, mechanical ventilation

Introduction:

Managing pain in ventilated patients who cannot self-report their pain is a challenging task of high importance. Patient analgesia requirements vary significantly during the period of mechanical ventilation, which is typically prolonged in Covid-19 patients compared to other ICU patients. In addition, these patients present with unique characteristics that may be related to virus shedding. Covid-19 patients may develop tolerance to the opioid effects since they are administered as a continuous infusion, which makes evaluating the adequacy of analgesia prior to painful stimuli even more difficult. Pain can present acutely as agitation, delirium and ventilator dyssynchrony, and when chronically inadequate, may cause post-traumatic stress disorder, depression, anxiety, and chronic pain syndrome. All these detrimental effects can lead to an increased length of intensive care and hospital stay, and mortality [1]. Vital signs are not sensitive nor specific enough to indicate measure pain levels and taking pain scores based on behavioral features in the non-communicating patient is challenging and requires training and experience. Practice

guidelines emphasize that adequate analgesia be established before adjusting sedation and interruptions in sedation (“sedation vacation”) be scheduled to assess cognitive function and readiness for weaning from mechanical ventilation [2]. In addition, excessive opioid analgesia has been shown to delay readiness for weaning and lead to well documented side effects and complications. The challenges and special considerations associated with management of sedation in COVID 19 patients have recently been outlined by D. Hanidziar and E. Bittner in a recent publication and the authors summarize that sedation management in patients with COVID-19 needs to reflect individual properties and side effect profiles of agents, unique patient characteristics (prolonged intubation and virus shedding), and health care system limitations (large numbers of patients, ICU patients in emergency rooms and operating rooms, and drug shortages). [9]

The Nociception Level (NOL) PMD-200 monitor (Medasense Biometrics Ltd., Ramat Gan, Israel), is able to reliably quantify mild to intense noxious stimulation during anesthesia and surgery and

outperforms hemodynamic indices (blood pressure, heart rate) in its ability to distinguish between noxious and non-noxious stimuli [5]. The monitor's algorithm is based on advanced statistical and machine learning technologies; it combines multiple autonomic signals (finger photoplethysmogram amplitude, skin conductance, heart rate, heart rate variability and their time derivatives) into a single index, the NOL index [3]. The index ranges from 0 (absence of nociception) to 100 (extreme nociception), and is calibrated at the beginning of the monitoring period to the autonomic 'signature' present at the finger probe, giving an index value that is tailored to each individual patient. Maintaining a NOL range between 10 and 25 is recommended as an adequate level of analgesia, a range derived and validated in multiple studies [4,5, 6]. In this report we describe our observations using NOL in two deeply COVID 19 patients in the ICU. The introduction of the system was led by three anesthesiologists including the head of the acute pain service at our hospital. This is the first time the system has been used for the monitoring of analgesia in COVID 19 mechanically ventilated patients.

Methods:

Four COVID 19 patients were monitored with the NOL bedside monitor for durations of up to 10 days. BIS™ Bispectral Index (Medtronic, CO, US) monitoring was used in addition to continuous MAP, HR and SpO2 monitoring to assess adequacy of sedation. Clinical data including vital signs, drugs and diagnostic information was accessed through the hospital Metavision ICU information system (IMDsoft Israel) and NOL recordings were downloaded on a USB stick and manually matched to the Metavision reports. NOL trends over 4 hours were continually displayed on the monitors, although access to the patient and monitor was restricted by safety protocol, and the NOL index was not used to guide therapy as part of a structured protocol. Midazolam and fentanyl infusions were used for analgesia and sedation. Midazolam dosages were 6-7 mg per hour with fentanyl dosages of 100-200 mcg per hour, both within clinically accepted ranges [10]. Patients received rocuronium during the initial days of mechanical ventilation. Clinicians could adjust fentanyl dosage after reviewing trends under the guidance of the head of the pain service.

Results:

Patient #18:

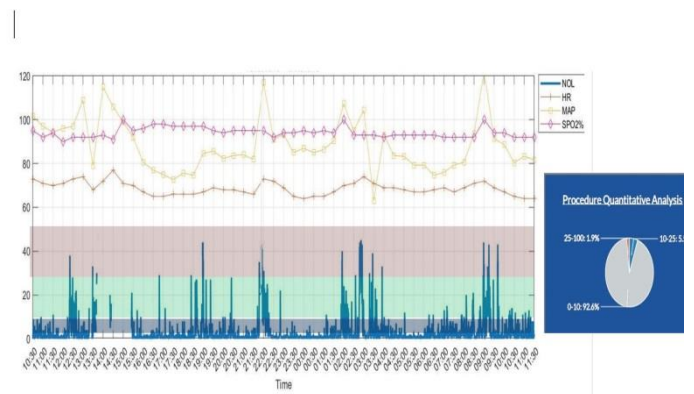


Figure 1- Patient 18 Day 9 – Fentanyl 100 mcg/hr, Midazolam 6-7 mg/hr

Figure 1- Patient 18 Day 9 – Fentanyl 100 mcg/hr Midazolam 6-7 mg/hr

Patient #18 fentanyl dosages had been reduced from 200 mcg/hr to 100 mcg/hr on day 9 in the ICU. The average and cumulative NOL values after the halving of fentanyl dose remained steady for 24 hrs suggesting the dosage decrease was safe and warranted, possibly preventing delayed extubation from an fentanyl overdose. CPOT and RASS scores of zero and -4 matched on day 9 were consistent with the NOL trends.

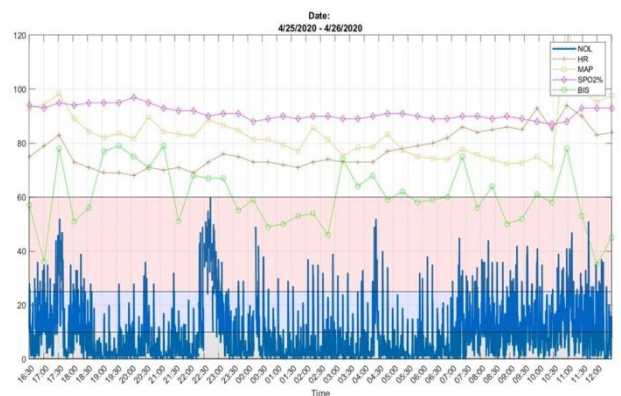


Figure 2 - Patient 18 Day 13- Fentanyl 100 mcg/hr, Midazolam 8 mg/hr

Figure 2 - Patient 18 Day 13- Fentanyl 100 mcg/hr Midazolam 8 mg/hr

Four days later, Patient #18's NOL values were typically higher and more reactive on the same dose of fentanyl, possibly indicating tolerance to fentanyl. BIS values too were unstable. The patient's SpO2 values were also lower, possibly due to ventilator dyssynchrony from agitation. An increase in fentanyl infusion would be warranted in a non-observational trial.

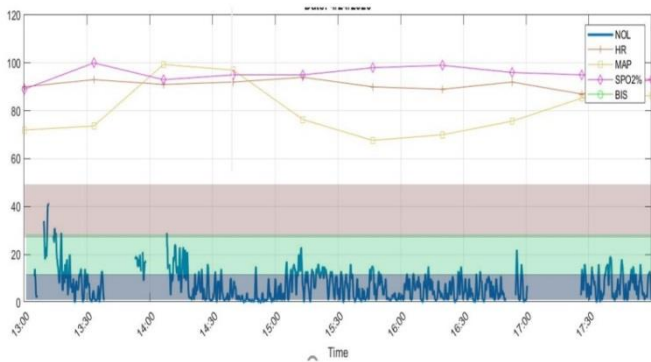


Figure 3 – Patient 6 – Fentanyl 200 mcg/hr, Midazolam 5 mg/hr, Rocoronium.

Figure 3 – Patient 6 – Fentanyl 200 mcg/hr Midazolam 5 mg/hr Rocoronium

Patient 6 had a fixed rate pacemaker that appeared to be set to 90 BPM therefore it was of interest to assess NOL performance in this patient as HR values were generally constant. NOL tracings were below 10 92% of the time. At 16:15 fentanyl dosage was reduced to 150 mcg/hr with no appreciable change in NOL values. No adverse events were reported during this evaluation.

Discussion:

NOL appeared to reflect the level of patient analgesia and these two examples suggest NOL may be valuable in titrating opioid infusion rates to prevent overdosing or underdosing. The NOL index range between 10 and 25 appears a suitable target for adequate analgesia in heavily sedated patients in the ICU, as it is in the operating room for patients under general anesthesia. A prospective trial in which the NOL index guides therapy for COVID-19 patients will confirm these findings. For such a trial to be viable, central station (remote) NOL monitoring and ability to change fentanyl infusion rates based on NOL trend reviews will be helpful. As patients typically receive large amounts of fentanyl (100-200 mcg/hour), given the current shortages in opioid supply, safely reducing opioid dosages would be of benefit to the patient and to the hospital system as a whole. Although fentanyl and midazolam dosages were within clinically accepted ranges at all time, NOL values were low most of the time and suggested an opportunity to manage analgo-sedation using lower drug dosages.

NOL index monitoring has been recommended for difficult to sedate patients and for COVID 19 patients in the recent critical care sedation and analgesia Spanish guidelines (7, 8).

The NOL index may be of assistance to clinicians

managing the analgesia of critically ill COVID 19 patients. Further work needs to be done to develop the clinical protocol and to study the impact of NOL monitoring on patient outcomes specific to the ICU.

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