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Point/Counterpoint

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Determining the Need for Pain Medications for a Patient With a Disorder of Consciousness

CASE SCENARIO

A 23-year-old man was admitted to your inpatient traumatic brain injury service 5 days ago. He was a restrained driver of a car involved in a high-speed head-on motor vehicle collision 4 weeks prior to the rehabilitation admission. His Glasgow Coma Scale score at the scene was 6. He was subsequently intubated. Imaging in the acute care hospital revealed bifrontal contusions and scattered foci of hemorrhage consistent with diffuse axonal injury. Other injuries sustained included 2 left rib fractures and left radial and ulnar fractures (treated with open reduction and internal fixation). A tracheostomy tube and a percutaneous gastrostomy tube were placed on day 6 after injury. He had no posttraumatic seizures and was weaned off medications for seizure prophylaxis after 7 days.

Since admission to rehabilitation, he has been afebrile. His electrolyte levels have been unremarkable, and he has a normal white blood cell count. He has periods of tachycardia (maximal heart rate 120) that may occur more often when he is in a wheelchair or receiving therapy, although tachycardia also can occur while he is in bed. Follow-up chest and upper extremity radiographs upon rehabilitation admission reveal some evidence of callus formation. Heterotopic ossification in the left elbow is not appreciated. He does not demonstrate diaphoresis. Other than at surgical sites, his skin is intact. He is moving his bowels almost daily and is voiding spontaneously with no evidence of urinary retention. He opens his eyes spontaneously, and his pupils are reactive bilaterally. He has roving eye movements, but it is not clear whether he is tracking. He extends his extremities in response to nail bed pressure. He displays no evidence of following commands or any other reproducible demonstration of awareness of self or environment, although at times it appears that he may grimace. There has been no clear pattern with regard to when he grimaces. His mouth is predominantly closed; for this reason, at times it is difficult to perform oral care. Spasticity (as measured by the modified Ashworth Scale) is 3/4 for bilateral shoulder abduction and elbow flexion and extension and 3/4 for bilateral hip abduction, hip and knee extension, and ankle plantar flexion.

Current medications include albuterol (by nebulizer) every 6 hours; amantadine, 200 mg at 8 AM and 1 PM; pantoprazole, 20 mg daily; enoxaparin, 40 mg subcutaneously daily; and docusate (Colace), 100 mg twice a day. Acetaminophen, 650 mg every 6 hours, has been prescribed, but acetaminophen has only been administered approximately daily because of uncertainty in determining pain. Some members of the treatment team are concerned that the grimacing and intermittent tachycardia are indeed related to pain and suggest that the patient be given opioid medications, either as scheduled doses or as needed for pain. How do you respond?

Dr Caroline Schnakers will present arguments in favor of more aggressive use of opioid pain medications and suggestions regarding how to prescribe them, and Dr Michael Marino will present arguments supporting a more conservative use of these medications, regardless of prescribing strategy.

Caroline Schnakers, PhD, Responds

I would be in favor of initiating more aggressive pain treatment in this patient, who seems to be in a vegetative state (VS; ie, presence of eye opening in the absence of any oriented/willful behaviors) [1]. Several arguments justify such a decision. This patient is still in a subacute stage and could recover consciousness at any

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time. Indeed, several variables must be considered when formulating a prognosis. Among the most important variables are the cause of the injury and the time since the injury [1]. Patients in a VS as a result of trauma have a better outcome 1 year after injury than do patients in a VS for nontraumatic reasons (10%-30% versus 0-3% in attaining a level of moderate disability). Furthermore, a recovery of target conscious behaviors (such as visual pursuit and response to command) within 8 weeks after injury has been linked to good functional outcome. Patients are usually considered to be in a permanent VS when they are in such a state for more than a year (in cases of trauma), because they have almost no chance of recovery (less than a 5% chance).

The patient in this case has a traumatic brain injury that was sustained only 4 weeks ago. Even though his VS is persistent, it is far from being permanent and could still evolve. He could evolve to a minimally conscious state (MCS; ie, the presence of fluctuating but reproducible conscious behaviors) [2], and previous studies have reported that brain activation in persons in an MCS is similar to that of control subjects in response to noxious stimuli. Specifically, this response involves the primary and secondary somatosensory cortices and the posterior insula, which are important components in the sensory-discriminative aspects of pain processing, as well as the anterior cingulate cortex (ACC), anterior insula, and prefrontal cortices, which participate in the motivational-affective and cognitive-evaluative aspects of pain processing. The activation of these areas (particularly the ACC and the insula) suggests that patients in an MCS may perceive the unpleasant aspect of painful stimuli. Intact connectivity between primary and associative cortices has also been observed in these patients, suggesting the existence of an integrated and distributed neural processing that makes plausible the existence of conscious pain perception in this population [3]. Undertreating a patient who may recover and perceive pain consciously constitutes an obvious clinical and ethical issue.

This concern is particularly relevant in this case, because we know that differentiating the VS from the MCS in patients can be challenging. Voluntary and reflexive behaviors can be difficult to distinguish, and subtle signs of consciousness can be missed because of fluctuations in vigilance or motor/verbal impairments (approximately 40% of patients diagnosed as being in a VS are misdiagnosed and are in fact conscious) [4]. Because clinical management, from rehabilitation strategies to end-of-life decision making, often depends on behavioral observations, potential sources of misdiagnosis should be diminished as much as possible. The presence of pain in patients with a severe brain injury may constitute a bias to the behavioral assessment and therefore decrease the probability of observing signs of consciousness. Indeed, a recent study reported a modulation of the level of consciousness according to the presence/absence of analgesics in a patient diagnosed as being in a VS. The patient showed signs of consciousness (ie, feeding per os and verbalizations) in the presence of the pain treatment, whereas he did not display these signs when the treatment was stopped [5]. Such a result is not that surprising. Patients in an MCS usually present with limited attentional resources. The presence of pain could reduce these resources even more and prevent the patient from interacting with his or her surroundings and showing any sign of consciousness. Finally, and most importantly, authors of several neuroimaging studies reported an activation of the affective pain network (ie, the ACC and insula) in 30% of patients in a VS [3]. Even though previous neuroimaging studies also suggest an altered perception in patients in a VS [3], the activation of the affective pain network might denote the presence of residual pain perception in some of those patients. In addition, because a minority of patients behaviorally diagnosed as being in a VS have previously shown brain activation in response to active cognitive tasks [6], it is also plausible to assume that a percentage of patients who do not show behavioral signs of consciousness may be able to perceive external stimuli, such as pain. Therefore, with regard to the current uncertainty, we should take the safer course by treating all patients with disorders of consciousness as if they had the potential to perceive pain and suffer.

In the subacute stage, patients with traumatic brain injury may present with several sources of pain such as unresolved fractures or spasticity. Severe spasticity has been reported in 60% of patients with severe brain injury and has been related to time after the injury and to pain [7]. The report of callus formation at fractures sites, as well as the presence of moderate to severe spasticity, should be sufficient to initiate an analgesic treatment in our patient. The use of acetaminophen may not be sufficient to treat pain in this case. The medical team observed potential indicators of pain such as grimaces. Facial expressions linked to pain are known to provide the most specific and sensitive nonverbal cues for pain, and facial expression is the most common component assessed by behavioral pain assessment tools for noncommunicative patients [8]. Previous scientific investigations have shown that facial expression is a consistent marker of pain across life span, cultures, and species [9]. Previous studies have also shown that such a marker may activate a brain network associated with the affective processing of pain in healthy volunteers [10].

In our patient, "There has been no clear pattern as to when he grimaces." This behavior could therefore be unrelated to pain (eg, pathological activation of subcortical pathways in the thalamus and limbic system) [1]. I would therefore recommend attempting to reproduce this observation in a pain-related condition, for example, when the patient's painful areas are mobilized (eg, bilateral hip abduction and/or