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Case Report

Case of a Hypertensive Crisis in Diffuse Axonal Injury

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A B S T R A C T

This case considers underdosing of analgesics as a prime contributor to hypertension in diffuse axonal injury (DAI) patients who are being mechanically ventilated. In the air medical environment, obtunded patients' hemodynamic parameters are the primary tools available in diagnosing complex disorders such as an acute rise in intracranial pressure (ICP) when invasive ICP monitoring is not available. Therefore, differential diagnoses must follow a continuum, from most severe to least, in order to deal with sudden-onset hypertension rapidly. Not until all critical differentials have been eliminated is analgesia considered. Mimicking the signs of ICP, a compensatory rise in the mean arterial pressure (MAP) is displayed in an acute pain response for mechanically ventilated patients. Therefore, poor analgesic coverage should be considered early in DAI patients who are being ventilated, especially when an increased metabolic drive may be occurring, forcing the therapeutic dosing intervals to be increased. This patient was transferred from Europe back to North America via a fixed wing aircraft, a 16-hour transport time.

Case Report

A 36-year-old woman with a history of a head-on collision and subsequent ejection landed in a frontally placed cephalic position at approximately 80 km/h. The patient was medically stabilized at the scene, and on arrival at the hospital, intubated via rapid sequence intubation with succinylcholine to stabilize a crashing airway. A continuous propofol infusion was maintained at 2 mg/kg/hr for sedation and preventative seizure control. Morphine was administered intermittently every 4 hours by hospital staff. Long-term paralysis was not initiated because there would be an inability to complete periodic neurologic assessments while on neuromuscular blockers. A computed tomographic (CT) scan of the head showed widespread intracerebral hemorrhages representative of DAI, and invasive ICP monitoring revealed an elevated ICP at 19 mm Hg. The patient's vital signs were stable at this point, requiring only sedation. The head of the hospital stretcher was set at an elevation of 30 degrees on evaluation in an attempt to maintain ICP in the physiological zone. A trauma set revealed hemoglobin of 9.8 g/dL, hematocrit of 45%, normal coagulation studies, platelet count of 175 K/mm^3, and an unremarkable chemistry panel. She was not on anticoagulants according to her next of kin. A consult with the receiving physician at a higher-level trauma center was conducted, and organization of a flight crew to transfer the patient back to North America was completed by the sending facility. ICP monitoring was discontinued before transport because the observation of such was not available or part of the protocols instituted. Instead, the device was clamped, and a sterile cap was placed on the external ventricular drain to ensure infection or a possible pneumocephalic injury would not occur. The head of the transport stretcher was maintained at an elevation of 30 degrees. Transport staff were instructed to continue the intermittent doses of morphine every 4 hours by the sending physician. Initiation of transport on the critical, but stable, patient was conducted 3 days after the accident occurred via a fixed wing medevac. Approximately 2 hours into transport, the patient's blood pressure (BP) rose to 182/106 mm Hg with an MAP of 131 mm Hg, signifying a hypertensive state. Analysis of the ventilator revealed no high-pressure alarms for the possibility of an airway obstruction; however, a reduction in cerebral perfusion pressure (CPP) from hypoxia could have led to an exacerbation of the cephalic injury. This prompted a subsequent decrease in tidal volume to avoid any risk of potential asphyxia. The BP continued to elevate further despite the interventions. The positive end-expiratory pressure (PEEP) was lowered from 7 mm Hg to 5 mm Hg in another attempt to maintain CPP while simultaneously promoting a therapeutic end-tidal carbon dioxide ($ETCO_2$) of 35 to 45 mm Hg, the main determinant of a patent airway.

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Rebreathing spikes on the $ETCO_2$ waveform appeared, indicating a potential lack of sedation, and an increase in the rate of propofol was initiated to further sedate the patient. The rebreathing marks disappeared after further sedation; however, the hypertensive state mentioned remained.

The patient was displaying early signs of a further increase in ICP based on an abrupt rise in BP to 182/106 mm Hg and an MAP of 131 mm Hg, as previously mentioned, with persistent bradycardia at 51 beats/min. The respiratory pattern was unable to be assessed because the patient was being mechanically ventilated. With the MAP rising acutely during the interfacility transport, there was an inability to assess the invasive ICP monitoring to rule out a further increase in ICP. Therefore, this query was based solely on the signs that encompass it. The ventilator did not show any high-pressure alarms, and $ETCO_2$ was stable at 37 mm Hg.

Discussion

Multiple scenarios were considered for the reason behind this hypertensive crisis. The initial hypothesis of a compensatory rise in the MAP, combined with a pulse that did not fluctuate farther than 51 to 56 beats/min, promoted the query of hypertension resulting from an increasing ICP as the primary diagnosis. All efforts to reduce the hypertensive state, based on the elevated BP and MAP, focused on adjusting the tidal volume and PEEP. Increased pleural volumes from mechanical ventilation could increase the amount of blood shunted cephalically, and the addition of PEEP with most ventilators at an intrinsic setting of 5 mm Hg also contributed to this shunt. With the patient's PEEP setting at 7 mm Hg, decreasing both PEEP and the tidal volume were attempts to lower the acute rise in ICP. This was an intervention integrated to manipulate the MAP according to the following formula: CPP = MAP − ICP.

A contribution to the rise in the BP and MAP, which indicated a hypertensive crisis, could also have been the patient's heightened metabolism from the underlying cerebral damage. Resting energy expenditure is influenced by malnutrition.[1,2] The results of 1 study showed that malnutrition affected 40% to 50% of the patients in the intensive care unit; the length of stay in the hospital correlated with an increased malnourishment rate.[3] Because this patient was mechanically ventilated for multiple days, the normal weight-based therapeutic dose of propofol may not have been sufficient to overcome the patient's elevated metabolic rate. This leads to a greater breakdown of sedative by the body in an intrinsic effort to reduce stimulation to the brain. Thus, caloric requirements and specific metabolism are essential components of the care of these patients,[4] especially in considering dosing intervals and therapeutic indices.

Finally, involving analgesia in the treatment strategy was considered. A patient who is intubated and sedated therapeutically will not display any outward signs of pain; however, this does not conclude that the body is not compensating for the diseased state hemodynamically. This deviation from normotension could be the body's way of attempting to return to a homeostatic balance in which an increase in diastolic BP might be considered a reliable physiological indicator for pain intensity that health care professionals may rely on during caregiving.[5] Just as the heart rate and MAP rise when stubbing a toe, so too do the MAP and heart rate in someone who is unconscious and experiencing pain.

The contemplation of increased ICP was considered the primary differential because acute pain commonly presents with tachycardia, and the patient's pulse did not reflect this. With bradycardia and an MAP of 131 mm Hg present, the likelihood of increasing ICP occurring was high. However, it seemed necessary to rule out the less critical scenarios in a timely manner before invasive medical treatment for a condition that cannot be proven in this particular transport environment was acknowledged. This is an important consideration before deciding to use medications that reduce increased ICP, such as mannitol or hypertonic saline, which could potentially cause rebound hypovolemic states and further metabolic imbalance.

Differential Diagnoses

In the setting of increased ICP, an acute hypertensive crisis, reflected by a rise in MAP and BP, leads to a tentative diagnosis of an exacerbation of the cephalic injury until disproven otherwise. Once these time-critical differentials are dismissed, an inadequate amount of analgesia is considered as a prime contributor to the hypertensive state. Not only can an acute response to pain in sedated patients lead to tachycardia and increased myocardial oxygen consumption, the combined use of analgesics and sedatives may ameliorate the stress response in critically ill patients.[6] This complements early detection of changes in a patient's heart rate and BP, enabling practitioners to detect problems and intervene in a timely fashion, reducing the risk of complications.[7] In the transport of mechanically ventilated patients, these are without question the most reliable features of pain that may present.

Nevertheless, critically head-injured (comatose) patients whose initial CT scan is unremarkable or does not show a mass lesion, midline shift, or abnormal cisterns remain at substantial risk of developing significant secondary cerebral insults because of elevated ICP and reduced CPP.[8] With this statement in mind, the patient's previous CT scan revealed DAI; therefore, an even higher index of suspicion for an exacerbation of ICP was considered, especially when the patient's MAP became elevated to 131 mm Hg at altitude in the absence of invasive monitoring. In combination with a lack of change in the patient's heart rate, a primary diagnosis of rising ICP was likely. This is further solidified by confirming that, even with the possibility of ICP waveform analysis, ICP monitoring was associated with poor outcomes and was found to be an independent risk factor for mortality.[9] Consequently, even with the possibility of invasive monitoring, a reliance on the signs of rising ICP are still a primary factor in its diagnosis.

The relationship between PEEP and ICP exists in the following formula: CPP = MAP − ICP. PEEP improves hypoxemia but has been reported to impede cerebral venous return, potentially causing a further increase in ICP.[10] As a secondary diagnosis for the cause of hypertension, an acute decrease in cerebral venous return because of the present PEEP setting could have been the root of the problem. The original setting of 7 mm Hg was decreased to 5 mm Hg, and this had the possibility of improving the CPP, alleviating any further cephalic injury.

In the transport environment, the assessment of sedation and analgesia was further disrupted by the patient's mechanically ventilated state. Literature shows that, within the intensive care unit, a substantial proportion of patients experience inappropriate levels of sedation (ie, under- or oversedation).[11] An environment such as a fixed wing aircraft can place further strain on providers' ability to assess acute pain or lack of sedation in addition to those experienced in the hospital. These supplemental stressors include hypoxia, hypothermia, and vibration. This compounds not only the pathophysiology of the patient but also the practitioner's ability to mentally comprehend certain situations, considering their current hypoxic state at altitude as well. Adequate patient preparation requires the consideration of how best to mitigate these stressors and decrease their impact on the patient's already impaired physiological status as a consequence of the effects of major illness or trauma.[12]

With the final diagnosis of poor analgesic coverage in a post–axonal injury patient suffering from hypertension, reflected by a BP of 182/106 mm Hg and an MAP of 131 mm Hg, it seems that starting with the more benign diagnosis of pain should have been a priority as a differential for this patient. Once analgesia is ensured, acute exacerbation of ICP becomes a plausible diagnosis. In the future, assuring analgesia is a priority before transport will create an additional pillar for treatment protocols in mechanically ventilated patients. This is not only to prevent further elevation in the MAP of a patient with diffuse axonal injury but also to foster a comfortable state for any ventilated patient in the transport environment.

Treatment Strategies

An initial decrease in tidal volume during mechanical ventilation was introduced in an attempt to decrease the increased ICP. This was used to reduce any compensatory response to a decreased CPP from the increased tidal volume. With the tidal volume calculation of 6 to 10 mL/kg of ideal body weight, a decrease from 8 mL/kg to 7 mL/kg revealed no further change in BP; therefore, a decrease to 6 mL/kg was completed. No further changes were observed in the MAP, the airway remained stable, and $ETCO_2$ was consistent at 37 mm Hg. The frequency of mechanical ventilations was also increased from 16 breaths/min to 20 breaths/min, inducing hypocapnia and thus producing cerebral arterial vasoconstriction to lower cerebral blood flow. $ETCO_2$ was decreased from 37 mm Hg to 32 mm Hg.

Next was the consideration of the initial PEEP setting, and 7 mm Hg was the value used for this patient in order to facilitate the ventilator's ability to provide proper airway retention. Physiologically, there is an inverse relationship between PEEP and MAP (the higher the PEEP setting, the lower the MAP theoretically). This inverse relationship contributes to venous return to the heart and, subsequently, cephalically, with higher PEEP values. Based on this concept, PEEP was decreased to 5 mm Hg. No observational changes in the MAP resulted from the shift in PEEP.

With direct orders from the neurosurgeon on call, propofol was implemented before leaving the sending hospital at an infusion rate of 2 mg/kg/hr. Propofol is widely used as a sedative agent in neurosurgical critical care because it is generally assumed that it has properties that are advantageous to the injured brain.[13] This is a short-acting lipophilic general anesthetic, acting through central nervous system depression by means of gamma-aminobutyric acid receptor agonism.

Propofol has a quick onset of action and is easily titrated, which is convenient when attempting to avoid possible hypotension. Along with its quick onset of action and reduction pharmacologically, it was the ideal medication for this patient's increase in ICP. The infusion rate was initially set to 2 mg/kg/hr, which was then titrated to 2.2 mg/kg/hr for facilitation of further sedation. A query of the patient being undersedated, which could have led to a rise in the BP and MAP, was the primary reason for the increased dosage and continued sedation with propofol.

In correspondence to the analgesia statement made, this intervention was not an initial priority because 5 mg morphine was given 2 hours before transport. With the average dose of 5 mg morphine having a considerably longer duration of analgesia (4-6 hours),[14] an undermedicated patient analgesically was not considered in the treatment regimen. However, on elimination of the previous differentials, an acute pain response resulting in elevation of the BP and MAP was a possibility. A lack of analgesia became likely when sedation, although increased in dosage, seemed to be ineffective on the current hypertensive state, which revealed a BP of 182/106 mm Hg and an MAP of 131 mm Hg. An additional 5 mg morphine was administered intravenously, and, shortly after, the patient's MAP returned to a stable state (normovolemia) at 93 mm Hg.

Summary

The administration of morphine maintained the MAP within normovolemic parameters (93 mm Hg). A scheduled dosing interval of 5 mg morphine every 2 hours, instead of every 4 hours, was initiated on the assumption that an increased metabolism ensued from the diseased state. The patient remained quiescent, and on examination by the receiving physician, further exacerbation of the traumatic brain injury was not detected by an updated CT angiogram and invasive ICP monitoring. The patient remained in an irreversible coma state induced by the traumatic brain injury until her family decided on termination of mechanical ventilation, resulting in death of the patient. Ensuring that analgesic administration by the sending facility was completed, as well as considering an infusion of analgesia rather than intermittent doses, has been instilled into the pretransport protocol for all mechanically ventilated patients.

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