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The Syndrome of Neurocognitive Impairment and Pain Management in Neurointensive Care Patients

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Abstract. Sedatives and analgesics are commonly used and warranted in the majority of ICU patients. Neurocritical patients present a particular challenge in these dimensions of critical care since their assessments are marred by confounders, staff goals of maintaining comfort, and the need for cooperative awake patient for neurological assessments. In the literature, there is a dearth of information on the topic of analgesia, sedation and delirium among the neurocritically ill patients. No objective instrument has been validated in this population. Outcomes and responses to pharmacologic treatment are not reported, and recommendations as to management can only be considered based on expert opinion. Much needs to be done in this vulnerable patient population to a better guide care. This review elaborates on the current knowledge on the issues of delirium as well as the current practice in managing pain, and sedation in neurocritically ill patients.

Keywords: Delirium, Sedation, Analgesia, Neurocritical Care.

Delirium in Neurocritical Care

Delirium is a syndrome of cognitive disturbance characterized by inattention and general reduction in the level of consciousness that is not explained by an underlying dementia. It fluctuates over the course of the

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day and is usually a manifestation of an underlying disease process (*i.e.* general medical condition, metabolic, toxic, *etc*)[1].

It has the same cerebral, systemic physiologic and metabolic insults associated with coma[2,3], and it is regarded as one of the transitory stages coma patients may experience.

Based on anatomical/physiological mapping of the brain, it also occurs with focal brain lesions involving the frontal, right parietal or basal ganglia structures[4,5].

Incidence and Significance of Delirium

The frequency of delirium varies from 15-60% in the general medical and surgical wards, and is the most common complication affecting the elderly population during their hospitalization[6-9].

Its incidence in the intensive care unit (ICU) admitted patients varies between 11% and 87%[10]. This variability could be explained by the fluctuating nature of delirium, the lack of unified protocols among studies to screen for it, and the infrequent application of delirium screening tools. In 2001, a survey in the practice of health care providers in ICU found that only 16% of the group used a validated instrument to screen for delirium[10].

In a recent survey of 1,384 healthcare professionals, including 970 physicians, 322 nurses, 23 respiratory care practitioners, 26 pharmacists, 18 nurse practitioners, and physician assistants, found that the rate improved. 59% of the respondents do screen for delirium and 33% of them use a specific screening tool[11].

The exact incidence of delirium in Neurosciences Critical Care Unit (NCCU) has not been studied before, and it is unknown even if the same figures can be used from medical and surgical ICUs and applied them to NCCU patients. An estimate can be based from epidemiological studies that were conducted on various neurological and neurosurgical diseases. Caeiro *et al.* assessed 68 consecutive patients with acute subarachnoid hemorrhage (SAH) and reported an incidence of 16% in this population[12]. In fact, delirium could be the presenting symptom in 1.4% of patients with SAH[13].

In a prospective study in the ICU, 139 Guillain-Barré Syndrome (GBS) patients were compared to 55 patients without GBS found that

31% of the GBS patients had mental status changes in the form of vivid dreams, illusions, hallucinations, and delusions compared to 16% in non GBS patients. These mental status changes had a median of 9 days after the onset of the disease to manifest and persisted for a median of 8 days[14].

The incidence of delirium after ischemic or hemorrhagic strokes is reported to be ranging between 13-48%[15,16].

In a cross sectional study, 202 patients who presented with neurological illness to the emergency department found that delirium occurred in 14.9% of the study group, 22.7% were in coma at time of presentation, and the rest had no arousal disturbances.

No firm conclusion can be extrapolated about the incidence of delirium in the NCCU based on these studies because of the difference in study design, heterogeneity of the patient population, difference in screening tools used, and difference in disease entities studied. It is fair to say that the incidence is variable but needs further epidemiological data to document the exact occurrence of delirium in this population.

Significance of Delirium

The occurrence of delirium in patients admitted to the hospital particularly to the ICU has different implications on the clinical outcome. The prolonged need for mechanical ventilation, total hospital stay, long-term cognitive deficit, morbidity, and mortality are negatively affected by delirium[14].

Two hundred twenty-four (224) patients were prospectively evaluated and found that 81.7% of the cohort had delirium during their hospital stay. They had higher 6-month mortality rate compared to those who did not develop delirium (34% *vs*. 15%, p = 0.03) with a hazard ratio of 3.2. They had longer hospital stay, fewer median days alive without mechanical ventilation, and had higher incidence of cognitive impairment at hospital discharge[17].

Pisani *et al*. stated that the longer duration of ICU delirium is associated with higher mortality within one year post ICU admission (hazard ratio (HR) 1.10; 95% CI 1.02-1.18). Hazard ratio of 1.10 means that the risk of death increases by 10% for each day of delirium in the ICU[18].

In another study, patients with altered mental status had higher incidence of tracheal extubation failure. Seventy-nine percent (79%) of the patients failed extubation when their Glasgow Coma Scale (GCS) was less than 8% *vs*. 33% and failure rates when the GCS was more than 8%[19].

In addition to the higher mortality and prolonged ICU stay, patients who develop delirium during their hospital stay had a higher chance of developing dementia in the long run. Girard *et al*. studied 126 mechanically ventilated patients and followed them for 12 months. It was found that 71% of their patients had cognitive impairment and 36% of them were graded as severe cognitive deficit. The duration of delirium was an independent predictor of worse cognitive performance after adjustment of other contributing co-factors[20].

In the United States, delirium affects 2-3 million elderly patients during their hospital admission, accounting for over 4 billion U.S. dollars in Medicare expenditures and median cost of about US$25,000-30,000 per patient. It is unknown what percentage of these expenses is the direct result of cognitive impairment/delirium. In addition, these figures might be higher in the future as it is estimated that in the next 3 decades the cost of care for patients > 65 will increase 10-fold[21].

Risk Factors and Pathophysiology

There are many factors that make patients more vulnerable to develop delirium during their hospital stay. Some of these factors are inherited predisposing conditions such as age, while others are precipitating factors that occur during the illness. The interplay between these two major categories makes patients more or less prone to develop delirium. It was shown before that risk stratification of these patients into high or low risk is possible, and is dependent upon the number of risk factors present[9,22,23]. The presence of three or more factors in any given patient increases the likelihood to develop delirium by 60% or higher.

Neurocritical care patients are particularly prone to delirium based on this risk stratification. No study evaluated this subset of patient population, but it is known from indirect clinical studies that they are at a high risk to develop delirium. Focal lesion in a strategic location, high ICP, stroke, subarachnoid hemorrhage, GBS, and many other diseases may significantly increase the incidence of delirium[4,14-16].

Additionally, and based on our knowledge of the pathophysiology of delirium, it is not surprising for any neurological illness to have higher incidence of delirium. There is a strong belief supporting the role of central neurotransmitters as the major player in delirium incidence. Excessive dopaminergic activity, depletion in cholinergic stores, serotonin, and gamma-aminobutyric acid are implicated in the occurrence of delirium which are also major players in many neurological conditions that are dealt in the NCCU[24-26]. Refer to Table 1 for risk factors.

Table 1. Risk factors for delirium[7,9,23,27-31].

Factors present prior to admission	Factors that may occur during illness
Age >70	Hypo or Hyper (Na, Glucose, Thyroid)
History of dementia	Fever or hypothermia
History of depression	Renal failure
History of stroke, epilepsy	BUN/Creatinine ratio >= 18
History of heart failure	Liver disease
Visual or hearing impairment	Cardiogenic or septic shock
Transfer from nursing home	Use of physical restraints
Illicit drug use	Central venous catheters
Alcohol abuse	Rectal or bladder catheters
Malnutrition	Medications
HIV	

Instruments for the Assessment of Delirium

For many years, delirium diagnosis was based on the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) guideline, which implicates a formal assessment of patients by psychiatrists to diagnose and manage delirious patients in the ICU. Over the last few years, many diagnostic tools have been evaluated and validated, so that non-psychiatrists, such as nurses and other physicians could screen for and diagnose delirium at the bedside.

Confusion Assessment Method (CAM) was developed and was found to be easy to use and apply at the bedside, with quick data acquisition that is both reliable and valid. It has a sensitivity of 94-100%, specificity of 90-95% and excellent interobserver reliability (kappa of 0.81-1.0)[32]. It lacks the applicability in patients that are not able to verbalize their responses and has limited value in the ICU population.

The Confusion Assessment Method for the ICU (CAM-ICU) was then developed to monitor delirium in patients who are unable to speak, such as those on mechanical ventilation. Four features are evaluated in

this tool: 1) Acute onset of changes or fluctuations in the course of mental status, 2) Inattention, 3) Disorganized thinking, and 4) Altered level of consciousness. The patient is determined to be delirious if he/she manifests both features 1 and 2 plus either feature 3 or 4. It takes 2-3 minutes to complete and can be repeated frequently. It has a sensitivity and specificity of 85-100% with excellent interrater reliability (kappa of 0.92-0.96)[33].

Intensive Care Delirium Screening Checklist (ICDSC) on the other hand, depended on points system to assess the presence of delirium over a period of 24 h shift. It has eight components that are marked either present or absent. These points are: 1) Altered level of consciousness, 2) Inattention, 3) Disorientation, 4) Hallucination, delusion or psychosis, 5) Psychomotor agitation or retardation, 6) Inappropriate speech or mood, 7) Sleep/wake cycle disturbance, and 8) Symptom fluctuations. It has 99% sensitivity, 64% specificity, and 94% inter-observer reliability[34].

Both CAM-ICU and ICDSC were compared and found to have a good agreement as tools to screen for delirium in the ICU setting with kappa coefficient of 0.80[35].

The applicability of these two tools in the NCCU population had never been studied or validated. It is unknown if they carry the same sensitivity or specificity given the different disease processes, and the variability in terms of predisposition and occurrence of delirium. When CAM-ICU instrument was validated, the authors excluded any neurological diagnosis that could confound the diagnosis of delirium. Their study was based on mechanically ventilated patients admitted to the medical or coronary ICU units. Unaltered or inferred in any conclusions about reliability of the CAM-ICU in our NCCU population until a proper validation in this subset of patients was done.

On the other hand, authors of the ICDSC conducted their validation of the tool on both medical and surgical ICU's, yet they did not clarify if patients with neurological diagnoses were excluded or not.

From epidemiological studies on patients with neurological or neurosurgical diseases, it is known that delirium occurs with variable rates. This variability could be explained by the lack of unified assessment among the NCCU units, which makes the screening/diagnosis of delirium less standardized.

Medications to Treat Delirium

Before instituting any drug therapy, one should attempt the nonpharmacological approaches that help reorienting patients to the surrounding. One should always think of delirium as a syndrome that could represent an underlying physiological derangement, such as hypoxia, hypoglycemia, and electrolyte abnormalities. All efforts should be made to effectively treat these disturbances before institution of pharmacotherapy.

Neuroleptics (Chlorpromazine and haloperidol) are the most common medications used to treat delirium. They act by antagonizing the dopamine-mediated neurotransmission at the cerebral synapses and basal ganglia[36].

Chlorpromazine is not preferred in the ICU because of its strong anticholinergic, sedative, and alpha-adrenergic antagonism. Haloperidol has lesser sedative effect and a lower risk of inducing hypotension than chlorpromazine[36,37].

Neuroleptics can cause dose dependant QT-interval prolongation leading to increased risk of ventricular arrhythmias[36]. Special care should be directed toward patients with prior cardiac history and they should be monitored closely.

Extrapyramidal symptoms are not unusual side effects of the neuroleptics[36,37]. One should always keep in mind the life threatening neuroleptic malignant syndrome that may develop with these medications.

Despite its popularity of being the drugs most commonly used to treat delirium, haloperidol was never studied in a randomized fashion. One study that used IV haloperidol in an unblinded, non-randomized trial showed fewer occurrences of extrapyramidal side effects compared to enteral form[37]. Sedation and Analgesia Task Force stated that Haloperidol is the preferred agent for the treatment of delirium in critically ill patients (Grade of recommendation = C)[38].

The newer antipsychotics/neuroleptic drugs are currently being studied more systematically to evaluate their efficacy and applicability in patients with delirium. Skrobik *et al*. evaluated patients with delirium in the ICU where 45 patients received Haloperidol versus 28 patients that

received olanzapine. It was concluded that the severity of delirium was decreased as well as the dose of benzodiazepines in both arms. More extrapyramidal side effects occurred with haloperidol use[39].

Quetiapine was assessed in a prospective, multicenter, randomized double-blinded pilot study, where delirious ICU patients received either quetiapine 50 mg every 12 h (n = 18) or placebo (n = 18). Quetiapine was associated with shorter time to first resolution of delirium, had reduced duration of delirium, and less agitation. Both groups had similar rates of mortality and length of ICU stay.

A safety trial conducted by Girard *et al*. and randomly assigned patients to receive haloperidol (n = 35), ziprasidone (n = 30), or placebo (n = 36) every 6 h for up to 14 days. Twice each day, the frequency of study drug administration was adjusted according to delirium status, level of sedation, and side effects. During the 21-day study period, patients in the haloperidol group spent a similar number days alive without delirium or coma (median 14 days) as did patients in the ziprasidone and placebo groups (mean 12.5 days). No difference was found in hospital length of stay, ventilator-free days, and mortality. The rates of extrapyramidal side effects in the two treatment groups were similar. Because of the small number they had in the study, the authors proposed for a larger trial to evaluate if the use of antipsychotics in ICU delirium is appropriate[20].

Analgesia

There are many factors that contribute to the occurrence of pain in NCCU. These include: Trauma, major surgical procedure, pre-existing disease, invasive monitoring devices (such as catheters, central lines, and endotracheal tubes), nursing care (airway suctioning, dressing changes, and mobilization), and prolonged immobility[40,41].

In addition to the stress response (tachycardia, persistent catabolism, hypercoagulability, increased myocardial oxygen consumption, and immunosuppression) that may occur, unrelieved pain may lead to agitation and disturbed sleep-wake cycle which are factors predisposing patients to develop or exacerbate pre-existing delirium[43,44]. In critically ill patients, systematic and consistent pain assessment is of paramount importance. Multiple tools have been validated in many clinical scenarios to assess for pain in order to manage it in a timely fashion. These tools include: Verbal Rating Scale (VRS), Visual Analogue Scale

(VAS), and Numeric Rating Scale. Visual Analogue Scale (VAS) is reliable and valid for many patient populations. It is used frequently in ICU, although it was not specifically tested in the ICU setting[44-47].

Visual analogue scale (VAS) comprises a 10-cm horizontal line with descriptive phrases at the end of the scale ranging from "no pain" to "severe pain" and it is scored based on patients' report of their experience of pain. Any of these tools could be used to assess pain and analgesia in the NCCU, hence, proper validation still needed in order for the authors to generalize their use as dependable clinical instrument.

Analgesic Medications and their Implications in NCCU

Three classes can be used as analgesics: acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), and opioids. The first two can be used as adjunctive or as add on treatment in critically ill patients. Opioids are attractive because of their rapid onset of action, their easy titration, and multiple routes of administration, the lack of accumulation, and relatively low cost. They act by binding to specific opioid receptors in the central and peripheral nervous systems as agonists, partial-agonists, or agonist-antagonists[48].

Many side effects should be anticipated when these medications are given such as nausea, vomiting, constipation, hypotension, respiratory depression, and allergic reactions. In general, Opioids have no effect on the Intracranial Pressure (ICP) or cerebral blood flow (CBF), but caution has been issued with the use of morphine in traumatic brain injury (TBI) patients due to reports of elevated ICP[43,44].

Opioids may affect patients with an existing high ICP when it causes hypotension. This hypotension may impair cerebral perfusion and decrease blood flow exacerbating cerebral ischemia (as referred in this paragraph and the following paragraph)[48]. In addition, if respiratory depression occurs, this may lead to hypercarbia leading to cerebral vasodilation that increases cerebral blood volume and ICP will increase as a result[48].

Very high doses of morphine and fentanyl have been shown to induce seizure-like activity in patients undergoing general anesthesia[49-51].

None of these reports documented electrographic seizures, suggesting that the abnormal movements may represent narcotic-induced rigidity or

myoclonus rather than true seizure activity. Moreover, opioids may lead to depression of the level of consciousness that make the assessment of patients limited. Sometimes, opioids may exacerbate delirium and agitation.

Sedation

Despite the frequent use of sedatives in the ICU, the indications of when to use and what to administer is not entirely clear. Sedatives are used to treat anxiety and agitation that frequently affect the ICU admitted patients. Anxiety and agitation are not synonymous. Not all patients with anxiety have agitation as some anxious patients are withdrawn and hypoactive. Causes for anxiety in the ICU are multi-factorial and include: inability to communicate, continuous noise, continuous dim light, excessive stimulation, frequent assessment by physicians and nurses, lack of mobility, and sleep deprivation[52,53]. Agitation is common in the ICU affecting about 71% of patients in the medical-surgical ICU's. It could result from an underlying anxiety, delirium, pain, or adverse drug effect[52].

It could lead to ventilator desynchrony, increase in oxygen consumption, and inadvertent removal of catheters and essential devices endangering patients and their safety. Before instituting any sedatives, physicians should evaluate and treat for the presence of hypoxia, hypoglycemia, hypotension, pain, and withdrawal from alcohol or other drugs[54-57].

Sedatives reduce the stress response and improve the tolerance of routine ICU procedures. It is unknown if they have an effect on the long-term outcome of patients admitted to the ICU or NCCU.

It is also unknown what the best protocol for sedation; however, continuous infusions of medications may provide more constant level of pain control and sedation, but it may increase the duration of mechanical ventilation and the length of intensive care stay[58,59].

Kollef *et al*. showed when continuous sedation was used instead of intermittent options; there was increase of 5 days in the duration of mechanical ventilation and 8 days in the length of hospital stay[59].

Another group of investigators led by Kress, demonstrated that intermittent sedation with daily interruption of opioids and sedatives decreased the duration of mechanical ventilation and length ICU stay[60].

Strom *et al*. challenged the need for sedation in patients admitted to the ICU. Patients were randomly assigned to receive either no sedation (n = 70) or sedation with 20 mg/ml propofol for 48 h, 1 mg/ml midazolam thereafter with daily interruption until awake (n = 70, control group). They treated both groups with boluses of morphine (2.5-5 mg) as needed. The investigators concluded that patients who received no sedation had significantly more days without ventilation (n = 55; mean 13.8 days, 95% CI 0.3-8.1, p = 0.0191), had shorter stay in the ICU (HR 1.86, 95% CI 1.05-3.23; p = 0.0316), with no difference in the rate of accidental extubations, need for CT or MRI, or ventilator associated pneumonia[61].

With respect to bedside evaluation and titration of sedation, the neurologically injured patients may be the most difficult patients to manage. To date, there is no data on the proper sedation that should be implemented in the NCCU. The authors believe that intermittent sedation makes more sense because of the need for repeated neurological examination to properly manage these patients. This is not permitted when continuous infusions are being instituted. Yet, there are no randomized trials to address this issue.

Sedation Assessment Tools

Ideally, any assessment tool should carry the ability to describe the degree of sedation or agitation within well-defined categories, present simple data to compute and record, guide the titration of therapy, and have validity and reliability. Several sedation scales have been validated and studied in different ICU populations. Some of these scales are: Riker Sedation-Agitation Scale (SAS), Motor Activity Assessment Scale (MAAS), The Ramsay Scale, The Vancouver Interaction and Calmness Scale (VICS), and the Richmond Sedation-Agitation Scale (RASS). What is common among all of these scales is that they have a point system with overly aggressive combative patients on the one end of the scale to the much sedated unarousable individuals on the other end.

Up to date, none of these scales had been validated or applied in NCCU setting.

Sedative Medications and their Implications in NCCU

Three classes of medications are used to sedate patients in the ICU: 1) Benzodiazepines (diazepam, lorazepam, midazolam); 2) Propofol, and 3) Central alpha agonists (dexmedetomidine, clonidine).

Sedation and Analgesia Task Force published clinical guideline for the use of sedation in critically ill adult patients. They reviewed all the published literature and comparative studies of the types of sedation that should be used in any ICU. Their recommendations are: 1) Diazepam or midazolam should be used for rapid sedation of acutely agitated patients (level C), 2) Propofol is the preferred sedative when rapid awakening (*e.g.* for neurologic assessment or extubation) is important (level B), 3) Midazolam is recommended for short term use only, as it produces unpredictable awakening and the extubation time when infusions continue is longer than 48-72 h (level A), 4) Lorazepam is recommended for the sedation of most patients via intermittent intravenous administration or continuous infusion (level B), 5) the titration of the sedative dose to a defined endpoint is recommended with systematic tapering of the dose or daily interruption with retitration to minimize prolonged sedative effects (level A), 6) triglyceride concentrations should be monitored after two days of propofol infusion, and the total caloric intake from lipids should be included in the nutrition support prescription (level B), and 7) the use of sedation guidelines, an algorithm or a protocol is recommended (level B)[38].

Before the conclusion on this subject, special considerations and side effect profiles of drugs when they are used in patients with neurological diseases should be taken into account before implementing the guideline.

Beznodiazepine have amnestic, sedative, and anticonvulsant properties, which are favorable in patients with neurological diseases. Care should be undertaken when benzodiazepines are used to prevent over sedation. Respiratory depression should be monitored for especially when narcotics are given as analgesics as they may have additive effect. In many studies, it was proven that benzodiazepines have no effect on the intracranial pressure or cerebral blood flow[62,63].

Other side effects to watch for include: nausea, vomiting, vertigo, confusion, excessive somnolence, hypotension, hypotonia, and muscular weakness.

Propofol is ultra short acting drug that has favorable effect on the ICP and it decreases it by reducing the cerebral blood flow (CBF) and cerebral oxygen metabolism[64].

It suppresses seizure activity when given at high doses. There are some animal and clinical studies suggesting a proconvulsant property of propofol at induction of anesthesia or during infusion at low doses[65]. Propofol may cause hypotension due to vasodilation and causes a negative inotropic effect which may cause does dependent respiratory depression. It has the ability to potentiate the sedative effects of other medications such as opioids and benzodiazepines.

Special attention should be given to the rare occurrence of propofol infusion syndrome of metabolic acidosis, hyperkalemia, rhabdomyolysis, and hypoxia with prolonged infusion of the drug.

Clonidine and Dexmedetomidine have the advantage of being effective sedative agents without posing patients to significant reduction in the level of arousal, attention or cognition. This property makes it an attractive option in our NCCU patients where neurological assessment is preserved while achieving the goal of a non-agitated or anxious patient.

The most undesirable effects include dry mouth, bradycardia, hypotension, lightheadedness, and the rebound hypertension that may occur after rapid withdrawal of the medication.

There is no data on the effect on these medications on seizure threshold.

Conclusions

Recently, the topic of delirium in the ICU became an expanding area of active research. Still there are many areas yet to be explored in the field of Neurocritical care on the background of sparse epidemiological studies. Part of the reason could be related to the relatively new and evolving concept of NCCU units. In the past, most of the neurocritical patients were admitted and actively managed within the general ICU. Lately, it became obvious that neurologically impaired patients represent a different and unique subset of patients that need to be managed and cared for in sub-specialized units.

The combination of delirium and neurocritical care is an example for the need of active research in order to better understand the disease and its implications.

Upon review of the subject of delirium, sedation, and analgesia, it became clear that there are not enough data about epidemiology, risk factors, assessment tools, and protocols to guide the recognition and treatment of patients in NCCU.

Sedation, analgesia, and delirium should be evaluated collectively in one screening protocol rather than tackling each one separately.

It is known in the literature that there is confusion among studies on the definition, recognition, and evaluation of anxiety, agitation, and delirium. One of the downsides of implementing protocols to treat each manifestation separately is that each one of the three could be a manifestation of the other. For example, anxiety could indicate agitation and agitation could indicate an underlying delirium, but each syndrome could occur on its own. If there are protocols managing single entity at a time, physicians might be under-treating the other symptom. In addition, some of the drugs that are given to treat agitation as an example could exacerbate and worsen delirium. If this is not considered in a clear protocol that combines the treatment of both, the end result will be treating one and worsening another. This may have a huge impact on the outcome measures. There is a movement towards implementing this combined protocol in the ICU and we believe that NCCU should adopt that idea.

In critically ill trauma patients, a multidisciplinary team designed a protocol to assess pain by using Visual/Objective Pain Assessment Scale (VAS/OPAS), agitation by Richmond Agitation Sedation Scale (RASS), and delirium by Confusion Assessment Method for the intensive care unit (CAM-ICU). Haloperidol was used to treat delirium and agitation as follows: If the duration of mechanical ventilation was predicted to be less than 48 h or if there was a contraindication to benzodiazepines, Propofol is the drug of choice. Intermitted sedation with benzodiazepines was given if the expectation of mechanical ventilation duration was > 48 h. Patients with the potential for elevated intracranial pressures, continuous infusion of propofol were initiated. 58 patients in the protocol group were compared to 61 historical controls from the same institute when the protocol was not implemented yet. It was found that

the median duration of mechanical ventilation in the protocol group was 1.2 days (0.5-3.0) compared to 3.2 days (1.0-12.9) in the control group ($p = 0.027$). At 28 days follow up, the protocol group had 26.4 ventilator free days (13.9-27.4) compared to 22.8 days (10.5-26.9) in the control group ($p = 0.007$). Hospital length of stay was 12 days (7-17) in the protocol group in contrast to 18 days (10-27) in the control ($p = 0.036$). Opiate equivalents and propofol use per patient was significantly reduced in the protocol group in contrast to control from 2,465 mg (± 1,242 mg) to 1,641 mg (± 1,250 mg) and from 19,232 mg (± 22,477 mg) to 10,057 mg (± 14,616 mg), respectively ($p < 0.001$, $p = 0,01$).

Such a protocol could be adapted or modified to be used in the NCCU, yet further clinical trials should be undertaken to answer these questions.

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متلازمة ضعف الإدراك والتحكم في الألم بمرضى العناية المركزة للمخ والأعصاب

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المستخلص. يشيع استخدام المهدئات والمسكنات في غالبية مرضى وحدة العناية المركزة. مرضى العناية المركزة للمخ والأعصاب يشكلون تحديًا خاصًا في هذه الأبعاد من الرعاية الحرجة لأن تقييمهم يربكه الكثير من العوامل الأخرى والتي منها حاجة العاملين في الوحدة على تقديم الراحة التامة للمريض وفي نفس الوقت إبقاء المريض متعاونًا لتقييم عمل الجهاز العصبي.

في الأبحاث السابقة، هنالك شح في المعلومات عن موضوع المهدئات والمسكنات وحالات الهذيان الحاصلة في مرضى العناية الحرجة للمخ والأعصاب.

لم يتم تقييم أداة أو وسيلة مناسبة لمعرفة شيوع هذه المواضيع المهمة. كذلك لا توجد معلومات عن التفاعل والاستجابة للأدوية في هذه الوحدة، وكل التوصيات للعلاج مستندة بشكل كلي على رأي الخبراء في هذا المجال. هنالك الكثير مما يجب القيام به لمساعدة هؤلاء المرضى في وحدة العناية للمخ والأعصاب، لغرض الوصول لخدمة أفضل.

في هذا البحث، سيتم عرض معرفتنا بموضوع حالات الهذيان فضلاً عن الممارسة الحالية في استخدام المهدئات والمسكنات في مرضى العناية المركزة للمخ والأعصاب.