CLINICAL IMPACT OF SLEEP DEPRIVATION ON DELIRIUM IN CRITICAL CARE

AN EVIDENCE BASED PROSPECTIVE OBSERVATIONAL STUDY

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Abstract: Sleep deprivation associated with delirium are conditions commonly reported in intensive care unit patients, characterized by sleep disruption, an increase in light sleep, decrease of slow wave sleep and rapid eye movement sleep. The most common types of delirium in this cohort patients are hypoactive and mixed-type of delirium which develops in 2-24 hours from admission. As per a study, delirium is known to develop due to an imbalance in the synthesis, release, and inactivation of some neurotransmitters, specifically by acetylcholine deficiency and dopamine activation. Delirium usually presents as a group of symptoms with an acute onset and a fluctuating course which have been categorized into cognitive and behavioral groups. This is a prospective observational cohort study conducted at Glenegales Aware Global Hospitals, L.B Nagar, and Hyderabad. For a study period of six months, 200 patients admitted with the hospitalization history of more than 24 hours in critical care units were enrolled as study population. Patient data collection form, contains the socio-demographic details of the patients and Observational study Informed Consent form was prepared for patients understanding for agreeing to participate in the study. The sleep deprivation and delirium assessment were done using CAM-ICU Worksheet and NEECHAM Confusion Scale. In this study, sleep being the major factor to affect the delirium development (at least once during their course of hospitalization) is clinically significant with P-value 0.031 when correlated. It is concluded that inadequate sleep (70.8%) patients are at higher risk of developing delirium in the ICUs, indicating ICU patients are at risk of developing delirium which is temporary within the ICU during the course of hospitalization (resolves with relevant patient orientated management).

Index Terms: Delirium, ICU, sleep deprivation, prospective, observational, evidence-based study, CAM-ICU, NEECHAM, intensive care unit, critical care, terminal care, REM, NREM, circadian rhythm.

I. INTRODUCTION

The intensive care unit (ICU) syndrome is a range of psychological reactions leading to organic brain dysfunction, including fear, anxiety, depression, hallucinations, fluctuating levels of consciousness and delirium. ICU syndrome could be a temporary disorder in which the patient experiences a cluster of significant psychological symptoms, which can be within the sort of reversible mental illness, delirium or acute brain failure [1]. Sleep deprivation associated with delirium are conditions commonly reported in intensive care unit patients, characterized by sleep fragmentation, an increase in light sleep, decrease of slow wave sleep and rapid eye movement sleep. The most common types of delirium in this cohort patients are hypoactive and mixed-type of delirium which develops in 2-24 hours from admission. Though the pathways of sleep associated delirium to understand the mechanism have advanced, the actual phenomena are not yet well explored. However, there is a theory that different areas in the brainstem transmit informational stimuli to the thalamus and cortex required for circadian rhythm regulation. As per another theory, delirium is known to develop due to an imbalance in the synthesis, release, and inactivation of some neurotransmitters, specifically by acetylcholine deficiency and dopamine activation. The relationship between sleep deprivation and delirium has been demonstrated to be reciprocal in the critically ill patients. The correlation between the delirium onset and sleep deprivation is hypothesized due to an imbalance in neurotransmitters and altered melatonin metabolism. A better exploration is required in the aspects of mechanism & factors that affect the sleep deprivation and delirium, which can be implemented in the development of new methods for preventing and control of aggravating outcomes in the critically ill patients [4].

The most widely used scale for assessing delirium in critically ill patients is Confusion Assessment Method for Intensive Care Unit (CAM-ICU) which can be used at beside in nonverbal mechanically ventilated patients. Four main features that are important for assessing delirium in CAM-ICU are: Acute Onset or Fluctuating Course, Inattention, altered level of Consciousness, Disorganized Thinking. Few studies indicate different sensitivities for the CAM-ICU. This difference in sensitivities can be illustrated by a wide range of heterogeneity seen in the patients included in the study but mainly by a different level of training and experience among the assessors involved in the reviews. Thus, it is difficult to demonstrate with what efficacy these instruments work without adequate preparation, but it is sensible to state that a considerable proportion of critically ill patients with delirium remain undiagnosed if these instruments are applied without proper training to the health care providers. In recent times, two systematic reviews evaluated the accuracy of CAM-ICU [11,12] and concluded that it is an accurate instrument for the diagnosis of delirium in critically ill patients. However, in the only study which was conducted in a non-research setting, most of the delirious patients were not detected by CAM-ICU [11,13].

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The NEECHAM (Neelon and Champagne) Confusion Scale contains nine scaled parameters divided into three levels. Each level provides three characteristic parameters. Level-I deals with information processing and orientation (score ranging from 0 – 14 points). It evaluates components of cognitive status: attention and alertness, verbal and motor response, and memory and orientation. Level-II deals with behavior (score ranging from 0 – 10 points). It evaluates behavior and performance ability: general appearance and posture, sensory-motor performance, and verbal responses. Level-III deals with physiological control (score ranging from 0 – 6 points). It evaluates vital function stability: vital signs, oxygen saturation stability and urinary continence control. The total NEECHAM scale score is the product sum of the scores on the three scales. The scale can be rated in 5-10 minutes from observations and measurements of vital signs. The ratings may range from 0-30 where zero indicates minimal function and 30 means normal function; the threshold point is 24. The score from 0–24 points indicates delirium as three types: mild, moderate and severe [14].

**Epidemiology:**

The medical practitioner ought to take into account delirium, or acute central nervous system pathology, as the brain’s type of “organ pathology.” Delirium is very common in ICU patients because of factors like comorbidity, critical ill health, and iatrogenesis. This complication of hospital stay is very risky in older persons and has associated with prolonged hospital stays, institutionalization, and death. Neurological pathology compromises the patient’s ability to be off from mechanical ventilation or attain full recovery and independence [5]. It postulated that aspects of the intensive care unit, such as sleep deprivation and sensory overload or monotony, are causes of the syndrome [1]. In summary, an intensive care unit psychopathy doesn’t develop in all patients. Instead, several patients are in danger of hypoactive, hyperactive, or mixed hypoactive and hyperactive delirium [3].

**Etiology:**

- Sensory deprivation – The sensory impairment will be observed when a patient is kept isolated in a closed room with no windows.
- Sleep deprivation – The continuous noises and disturbance with hospital staff round the clock to check vital signs, give medications may cause inadequate sleep to the patient.
- Stress – In most scenarios’ ICU patients will be in a condition of no hope on life.
- Continuous lights – Continuous disturbance of normal biorhythms with lights switched on round the clock in the ICU, i.e., no reference to day or night.
- Lack of orientation – Patient’s loss of knowledge about time and date [5].

**Pathophysiology:**

Circadian rhythm is distinguished by three states that is Non-Rapid Eye Movement (NREM) sleep, and Rapid Eye Movement (REM) and wakefulness. Each state is manifested by characteristic behavioral and physiologic pattern with specific neurophysiologic mechanism associated with its generation and regulation. The components of brainstem trigger various neurotransmitters to stimulate areas of brain in the midbrain and the cortex. The extra-thalamic control modulatory system also known as the ascending reticular activating system (ARAS), or the reticular activating system (RAS), is a group of connected nuclei in the brains of vertebrates that regulates the wakefulness and circadian transitions. The ARAS provides cholinergic, noradrenergic, and glutamatergic stimulation to the thalamus, hypothalamus, and basal forebrain resulting in cholinergic and glutamatergic excitation of the cortex. An active cortex that exhibits a characteristic pattern manifests wakefulness. Various factors affect the need and timing of sleep onset, also influence the noradrenergic projections to midbrain and forebrain structures to inhibit activity in the ARAS, resulting inactivation of inhibitory GABAnergic impulses to the cortex. During wakefulness, there is increased sympathetic tone and decreased parasympathetic tone that maintains most organ systems in a state of action or readiness. The progression of sleep stages occurs in cycles of 60 to 120 minutes throughout the sleep period. Various circadian environmental and ontological factors affect the pattern of sleep stage occurrence [3].

On the contrary, declining levels of tryptophan (Figure 1) which is an amino acid that crosses BBB and a precursor to neurotransmitters – serotonin and melatonin, are associated with delirium in postoperative patients older than 50 years [6]. In a study, it was found that the delirium in the ICU patients who are mechanically ventilated is somehow related to altered levels of tryptophan [7]. However, it is also possible that production of other metabolites of tryptophan – kynurenine, leads to a pathway that results in neurotoxins predisposing to delirium [8] In patients who are more prone to delirium, i.e., elderly and those with pre-existing neurological diseases, it was found that quicker central nervous system response to inflammatory mediators will be present [9].
Clinical manifestations:

Delirium usually presents as a group of symptoms with an acute onset and a fluctuating course. These symptoms have been categorized into cognitive and behavioral groups. Cognitive symptoms include disorientation, inability to assist attention, diminished visuospatial ability, altered level of consciousness and impaired short-time memory. Behavioral symptoms include disturbed sleep-wake cycle, hallucinations, irritability, and delusions [10].

Pharmacotherapy:

Melatonin: In a retrospective, observational cohort study, development of delirium was significantly lower in the melatonin group compared with that in the control group that is 9 (7.7%) versus 28 (24.3%) patients (p = 0.001). Melatonin is a hormone that regulates the homeostasis of sleep and wakefulness. As discussed earlier the artificial light settings during night-time hours in the ICU tends to affect the innate production of melatonin, which further affects the circadian cycle in critically ill patients. The study reported that the patients who developed delirium in the control group had 20.9 delirium-free days without coma in 28 days compared with 19.9 days in the melatonin group (p = 0.72). In the melatonin group, melatonin was administrated a median dose of 3.5 mg at night over a range of 1-10mg for a mean ± SD of 6.3 ± 7.9 days. The study concluded that the development of ICU delirium was significantly lower in the melatonin group compared to non-melatonin group [15].

Non-pharmacological Management:

Non-pharmacological approaches, such as physical and occupational therapy, decrease the duration of hospital and ICU stay and also provide better management of delirium and hence should be encouraged. The ultimate goal is to correct any imbalances, restore patient’s health, and bring them back to normal as quickly as possible. To prevent ICU syndrome, several critical care units are: Providing periods for sleep, Using more liberal visiting policies, Preventing the patient from unnecessary excitement, Orienting the patient to date, time and place, Asking the patient if there are any concerns, Communicating with the family to obtain information regarding cultural and religious beliefs, Coordinating ICU lights with the normal day-night cycle, Monitoring patient’s fluid and nutrition status, Reorientation methods, Avoiding physical restraints correction of sensory deficits, Behavior modification, Usage of ear plugs in prevention of agitation induced by instrumental beeping and sounds, Psychiatric consultation (if required).

II. OBJECTIVE

To assess and evaluate the sleep deprivation inducing delirium epidemics in a tertiary care hospital, specifically in the critically ill patients. To evaluate and provide management approaches to overcome this hurdle and to achieve better therapeutic outcomes.

III. METHODOLOGY

This is a prospective observational cohort study conducted at Gleneagles Aware Global Hospitals, L.B Nagar, Hyderabad, for a study period of six months. 200 patients admitted with the hospitalization in the Intensive Critical Care Unit, Medical Intensive Care Unit, Cardiac Intensive Care Unit, Respiratory Intensive Care Unit were enrolled as study population. Subjects with age limit greater than
or equal to 18 years with history of hospitalization into critical care for at least 24 hours were included in the study. Pregnant and lactating women, pediatric patients and patients with history of psychological illness & dysfunctions were excluded from the study. Patient data collection form, contains the socio-demographic details of the patients and Observational study Informed Consent form was prepared for patients understanding for agreeing to participate in the study. The sleep deprivation and delirium assessment were done using CAM-ICU Worksheet and NEECHAM Confusion Scale. Patient relevant data for the study was obtained from patient case records, ICU charts, medication charts, directly from patient/ attenders.

IV. RESULTS

Among 200 patients admitted into the ICU, 144 patients were found to have adequate sleep (72.00%), 2 patients were found to be drowsy (1.0%), 19 patients were found to be with good sleep (9.50%), 24 patients were found to have inadequate sleep (12.00%), 1 patient found to be irritable (0.50%), 1 patient found to be with normal sleep (0.50%), 9 patients are found to be sedated (4.50%) (Table 1, Figure 2).

<table>
<thead>
<tr>
<th>Sleep Pattern</th>
<th>No. of subjects</th>
<th>% of subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate</td>
<td>144</td>
<td>72.00</td>
</tr>
<tr>
<td>Drowsy</td>
<td>2</td>
<td>1.00</td>
</tr>
<tr>
<td>Good</td>
<td>19</td>
<td>9.50</td>
</tr>
<tr>
<td>Inadequate</td>
<td>24</td>
<td>12.00</td>
</tr>
<tr>
<td>Irritable</td>
<td>1</td>
<td>0.50</td>
</tr>
<tr>
<td>Normal</td>
<td>1</td>
<td>0.50</td>
</tr>
<tr>
<td>Sedated</td>
<td>9</td>
<td>4.50</td>
</tr>
<tr>
<td>Total</td>
<td>200</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Table 1: Distribution of patients based on sleep pattern

Figure 2: Distribution of patients based on sleep pattern

Among 200 patients admitted into to the ICU, 144 patients were found to have adequate sleep (72%) out of which 25 developed mild, 26 developed moderate, 37 developed severe type of delirium and 56 were non-delirious. Among 2 patients found to be drowsy (1.0%), 1 was severely delirious and 1 was non-delirious. Among 19 patients found to be with good sleep (9.5%), 2 developed mild, 2 developed moderate, 2 developed severe types of delirium and 13 were non-delirious. Out of 24 patients found to have inadequate sleep (12.0%), 5 developed mild, 5 developed moderate, 7 developed severe delirium and 7 were assessed to be non-delirious. The 1 patient found to be irritable (0.50%) developed severe delirium. 1 patient found to be with normal sleep (0.50%) developed mild delirium. Out of 9 patients found to be sedated (4.50%), 2 developed moderate and 5 developed severe delirium. From the P-value 0.031 the Correlation between sleep and delirium development was clinically significant. Deprivation of sleep tends to enhance the risk of developing delirium in critically ill patients (Table 2, Figure 3).
V. CONCLUSION

In this study, sleep being one of the major factors to affect the delirium development (at least once during their course of hospitalization) is clinically significant with P-value 0.031 when correlated. It is concluded that inadequate sleep (70.8%) patients are at higher risk of developing delirium in the ICUs (Table 1, Figure 2), indicating ICU patients are at risk of developing delirium which is temporary within the ICU during the course of hospitalization (resolves with relevant patient orientated management).

REFERENCES


