Original Article

Period-Prevalence and Risk Factors for Delirium in a Tertiary Referral ICU: A prospective cohort study

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Abstract

Background: Delirium is common in intensive care and leads to increases in morbidity, mortality, Intensive Care Unit (ICU) length of stay, and hospital length of stay. Certain risk factors predict the appearance of delirium.
Study Objectives: To determine the rates of delirium, the rate of risk factors, and their relationship to the occurrence of delirium in an adult ICU.
Methods: Single-centre, prospective, observational study. Demographic and treatment data were collected. The Confusion Assessment Method for ICU (CAM-ICU) was performed twice daily to assess for delirium continuously during a 3-week period. Statistical analysis was used to determine the relationship between risk factors and the occurrence of delirium.
Results: 86 patients were screened, 44 patients were included, and 260 patient-days were analyzed. The incidence of delirium was 42.9%, the prevalence of delirium in ICU was 50%. Urinary catheters and use of opioids were the most common factors with a positive association for occurrence of delirium. Exposure to daylight and sleeping for more than 4 hours at night were the factors most commonly associated with a lack of delirium.
Conclusion: The rates of delirium in ICU were high and risk factors occurred frequently. Addressing modifiable risk factors, including the promotion of adequate sleep, could improve outcomes.

Keywords

Delirium, Incidence, Prevalence, Sleep, Intensive Care Unit

Key Points

1. Delirium occurs frequently in ICU, with an incidence of 42.9% and a prevalence of 50%.
2. Risk factors for delirium occur frequently, with many of these being modifiable.
3. Poor sleep is now recognized as a risk factor for delirium, and ICU patients experience poor sleep frequently.

Introduction

Delirium is an acute disturbance of mental function, which is associated with worse patient outcomes. It manifests as fluctuating confusion and inattention.[1] It presents as either a hyperactive, hypoactive, or mixed picture. Delirium is considered to be a type of end-organ failure and is commonly secondary to a cerebral or systemic disease.[1,2] The pathophysiology of delirium remains somewhat unclear, but is postulated to consist of a disturbance in neurotransmitters including acetylcholine, dopamine, and serotonin, as well as having a neuro-inflammatory element.[3]

Many risk factors have been associated with delirium.[4] Some of the risk factors most commonly recognized in the Intensive Care Unit (ICU) include patient factors like pre-existing cognitive impairment, hypertension, and alcohol use; acute illness factors like illness severity and APACHE-II score, the need for certain sedatives and opioids, endotracheal intubation, and the use of psychoactive medications; and environmental factors like the lack of sunlight, loud noise levels, and bright lights during night time.[5,6,7] Sleep disturbances are considered a risk factors and are thought to also play a role in the occurrence of delirium in ICU. Sleep deprivation and poor quality sleep seem to be associated with a higher incidence of delirium in hospital and the ICU.[8,9]

It is important to be able to recognize and manage delirium since it is associated with worse outcomes like an increased ICU length of stay (LOS) and increases in short and long-term mortality.[3, 10-12]

The Confusion Assessment Method for ICU (CAM-ICU) is a well validated tool for the assessment of delirium in the ICU, with a sensitivity ranging between 95-100%, and a specificity between 93-98%.[13] The CAM-ICU utilizes the Richmond Agitation and Sedation Score (RASS) to first determine whether patients will be able to be assessed using the tool.[14] Using the CAM-ICU,

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the prevalence of delirium in ICU has been estimated to be between 30% and 60%.[10]

Rapid Eye Movement (REM) sleep starts to occur more frequently during the night after 4 hours of sleep.[15] This is the type of sleep that is most restorative and provides the body with better healing, therefore being more likely to prevent delirium.[15] It is known that risk factors for delirium occur frequently, but it is not known how often patients at risk for delirium fail to get 4 or more hours of sleep at night while in ICU.

The main objective of this study was to determine the rates of delirium and its association with risk factors, including lack of sleep, in a tertiary-referral ICU.

Methods

This was a single-centre, prospective, observational study over three consecutive weeks from February to March 2015. It was undertaken at the Intensive Care Unit at John Hunter Hospital, which is a tertiary-referral, mixed medical and surgical, university-affiliated unit. A discrete, manageable time period was chosen, which then dictated the number of patients and therefore the size of the study. Approval was granted by the local Human Research Ethics Committee. This study was deemed as "Low or Negligible Risk" and therefore the approval process was abridged and the need for informed consent was waived.

All adult patients admitted to ICU during the study period were screened. Inclusion criteria was admission to the participating hospital's ICU. Exclusion criteria was age under 18 years, non-English speaking, or discharged within 48 hours of being admitted. The following data was collected from all patients that met inclusion criteria and had none of the exclusion criteria within 24 hours of ICU admission: age, admission category and source, diagnostic group, APACHE-II score, urea, presence of coma, infection, metabolic acidosis, sedative administration, past history of cognitive impairment, tobacco and alcohol use, antipsychotic or sedative medication use, contraindication to oral or enteral feeds. Descriptions of opioid, sedative or antipsychotics administered, presence of invasive catheters, respiratory support, physical restraints, and contact with sunlight.

Each patient-day episode was made up of twice-daily assessments using CAM-ICU to identify delirium. CAM-ICU was performed only by the study team. This was made up of ICU medical staff that had undergone specific training and validation on performing CAM-ICU tests, in an effort to decrease bias. The staff undertaking the assessments had read educational material, watched an educational video, and were seen performing the CAM-ICU by an experienced clinician who would then accredit them as capable of performing the test reliably. Study staff would first determine the RASS, and if this was above a score of -4, they would proceed to the series of questions that make up the second part of the CAM-ICU assessment. If the RASS was -4 or -5 due to sedation, the assessment would cease there, and the patient would be marked as "unable to assess".[14] Estimation of sleep quantity was recorded as a qualitative variable (greater than or less than 4 hours in any 12 hour period) according to the observations made by the bedside nurses.

Data was de-identified and stored electronically in a password-protected file, which was kept in a computer in the ICU offices under lock and key.

There was no follow up after patients left the ward or after the study dates.

Descriptive statistics are presented as percentages with numerator and denominator. Medians and interquartile ranges are given. Categorical data was analysed using Fisher's exact test and chi-square test. Odds ratios and 95% confidence intervals (95% CI) are provided when appropriate. P-values of less than 0.05 are considered significant. Statistical analysis was performed using GraphPad Prism 8.0 for MAC OS.

Results

Patients were screened between 20/2/2015 until 15/3/2015. A total of 86 patients were screened for eligibility and 44 were included in the study. The demographic characteristics, reasons for admission to ICU, and presence of risk factors for delirium on admission of these patients can be seen in Table 1.

The 44 patients who were included in the analysis had a total of 260 ICU patient-days throughout the study period. With each patient-day having a daytime and a nighttime assessment, there was a total 520 possible assessments.

The RASS was too low (-4 or -5) to make it possible for patients to be assessed with the CAM-ICU a total of 85 ICU patient-days. This led to 67.3% (175/260) of patient-day episodes being able to be analyzed for delirium.

Of the times patients could be assessed with the CAM-ICU, patients were delirious 42.9% (75/175) of patient-days, 37.6% (62/165) of the time during the day and 32.7% (50/153) during the night.

Of the cohort, 50% (22/44) of patients were delirious at least once throughout their stay in ICU.

The frequency with which risk factors for delirium associated with acute illness were present during each patient-day and their statistical effect on the occurrence of delirium can be seen in Table 2.

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Table 1. Demographic characteristics, admission type, severity scores, and risk factors for delirium on admission of to ICU.

Variable	Cohort
Male gender	59.1% (26/44)
Age [med (IQR)]	61 (48-71)
Source of admission	
Emergency dept.	31.8% (14/44)
Operating Theatre	31.8% (14/44)
Ward	18.2% (8/44)
Other	18.2% (8/44)
APACHE II score [med (IQR)]	19 (13-24)
Previous Dementia	11.4% (5/44)
Heavy alcohol use	18.2% (8/44)
Active smoker	15.9% (7/44)
Antipsychotics before ICU admission	47.7% (21/44)
Metabolic acidosis	47.7% (21/44)
Presence of infection	43.2% (19/44)
Urea on admission(mmol/L) [med (IQR)]	6.9 (4.3-10)
Coma at any time during ICU stay	64.6% (168/260)

The bedside nurse on each 12-hour shift observed ICU patients and recorded when they slept for more than 4 hours during the day and night. Duration of sleep can be seen in Table 3.

Discussion

This study provides an informative glance of delirium and its risk factors in ICU. The characteristics of the cohort were similar to previous reports in that most of the patients were male, with similar median age, and similar APACHE-II score on admission to ICU.[10-16,17]

The rate at which risk factors for delirium were present on admission was somewhat different to previous reports, possibly due to the hospital's characteristics in terms of its geographical location, the population that presents to it, and the services it provides.[5-18]

Obtaining a reliable figure for the rates at which delirium presents itself is difficult.[19] By definition, delirium is fluctuant, which means that delirium needs to be constantly assessed to be able to be adequately identified.[20] The 260 ICU patient-days with a total of 520 assessments during the study period makes it possible to have enough assessments to obtain a representative picture.

The rate at which oversedation (RASS -4 and -5) occurred in this study was significant (32%), but still within the lower range of the 30% to 60% reported in the critical care literature.[21,22] This study showed an incidence of 42.9%, higher than in other similar reports, while the prevalence of 50% was closer to what has previously been reported.[18-23,24] The incidence might have been slightly higher because of the strict adherence to the assessment schedule by the study team. This might have allowed for identification of more episodes of delirium than if assessments were carried out less frequently. The prevalence might have been similar to previous reports because of it being a period prevalence, rather than a point prevalence. Reporting both is important because it allows for ease of comparison with other reports.[25]

Of the risk factors evaluated there was a wide variability in the frequency at which they appeared. Some, like indwelling urinary catheters, being present in 91% of patient-days and others, like the use of physical restraints, only being found in 11% of patient-days. When looking at the relation between these risk factors and the occurrence of delirium, we can see that there were risk factors which had no association with delirium, a positive association with delirium, and a negative association with delirium. The risk factors with no statistical association with delirium in this study were the presence of coma, invasive mechanical ventilation, and non-invasive mechanical ventilation. This is different to other previously published data.[26] To find a reason why this is the case here is difficult and not within the scope of this study.

The risk factors associated with a higher chance of delirium were the use of sedatives, opioids,

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Table 2. Frequency of delirium risk factors associated with acute illness per patient-day.

Variable	Cohort		CAM-ICU +	CAM-ICU -	P-value	OR (95% CI)
Presence of drains	25.4% (66/260)	Drain yes	24	14	0.0054	2.891 (1.349 to 5.826)
		Drain no	51	86		
Indwelling urinary catheter (IDC)	91.2% (237/260)	IDC yes	72	83	0.0078	4.916 (1.461 to 16.26)
		IDC no	3	17		
Use of restraints	11.9% (31/260)	Restraints yes	25	4	<0.0001	12.00 (4.053 to 33.02)
		Restraints no	50	96		
Use of antipsychotic medication (ASM)	12.3% (32/260)	ASM yes	43	22	<0.0001	4.764 (2.493 to 9.167)
		ASM no	32	78		
Use of sedatives	54.2% (141/260)	Sedatives yes	53	30	<0.0001	5.621 (2.968 to 10.80)
		Sedatives no	22	70		
Use of opioids	64.6% (168/260)	Opioids yes	47	27	<0.0001	4.538 (2.323 to 8.421)
		Opioids no	28	73		
Preceding period of coma	64.6% (168/260)	Preceding coma yes	2	6	0.4689	0.4292 (0.08639 to 1.788)
		Preceding coma no	73	94		
Invasive mechanical ventilation (IMV)	55.4% (144/260)	IMV yes	38	39	0.1280	1.606 (0.8676 to 2.867)
		IMV no	37	61		
Non-invasive mechanical ventilation (NIV)	13.5% (35/260)	NIV yes	11	18	0.6821	0.7830 (0.3634 to 1.813)
		NIV no	64	82		
Tracheostomy	11.4% (30/260)	Trachie yes	6	22	0.0129	0.3083 (0.1225 to 0.7663)
		Trachie no	69	78		
Sleeping >4hs/night	55% (143/260)	>4hs/night	34	66	0.0086	0.4272 (0.2333 to 0.7999)
		<4hs/night	41	34		
Exposure to daylight	55.4% (144/260)	daylight yes	38	69	0.0186	0.4614 (0.2496 to 0.8763)
		Daylight no	37	31		

antipsychotics, drains, indwelling urinary catheters, and physical restraints. These are mostly the same to what has been previously identified in other studies.[24]

The factors that were associated with a lower occurrence of delirium were tracheostomies, exposure to daylight, and observed night-time sleep of more than 4 hours. Patients who received and were ventilated through tracheostomies likely required less sedation, which could then have led to a lower incidence of delirium.[27] Exposure to daylight and sleeping for more than 4 hours at night were associated with a lower chance of delirium. This is likely due to daylight helping to regulate the sleep-wake cycle of critically ill patients, possibly through the mechanism of melatonin secretion which then helps patient have a better night sleep.[28,29]

Table 3. Frequency of sleep for more than 4 hours of ICU patients during a 12-hour period.

	Day	Night
More than 4 hours	85 (45%)	143 (88.3%)
Less than 4 hours	104 (55%)	19 (11.7%)
Total episodes recorded	189	162

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Sleep is difficult to measure in the ICU. The definitive way to quantify and assess the quality of sleep involves use of polysomnography.[30] Observed sleep is unreliable, but provides a crude measure of the duration of sleep. In this study, a 4-hour period was used as a measure of sleep, as duration of REM sleep is known to increase with each sleep cycle after 4 hours. REM sleep is important for memory, learning, healing and most importantly here, associated with reduced delirium.[15] By looking at the observed sleep during the day and the night, we can see evidence that sleep-wake cycles are quite disrupted. Of the episodes observed, 45% of the time patients sleep for more than 4 hours during the day and more than 10% of the time patients had less than 4 hours of sleep at night. Even when patients had more than 4 hours of sleep at night, it is possible that they were still not getting the 7 to 9 hours required to have adequate, restorative sleep.[31] It is well described that the quality and quantity of sleep in intensive care is poorer than that obtained at home.[31] This disruption is then likely translated to delirium, as seen in how those patients that were observed to sleep for more than 4 hours at night had a lower association with delirium.[32]

When devising strategies to prevent and treat delirium, it is first important to have a clear picture of what are the risk factors involved that lead to delirium, how often these occur, and which are the ones that can be modified. From this data we can see that quantity of sleep is related to delirium. Good quality and quantity of sleep, along with protection of the sleep-wake cycle, is something that can be promoted in ICU. A combination of non-pharmacological and pharmacological strategies could potentially be implemented in ICU to help improve sleep and therefore decrease the occurrence of delirium.[33-35] By decreasing delirium we might be able to obtain better patient-centered outcomes.[36]

Our study has limitations. Firstly, this was a single-center study and results cannot be extrapolated to units with different profiles and patient acuity. Secondly, the measure of sleep is possibly subjected to observer and recall bias. This study had a small sample size and a relatively short study period, which are also important limitations of the study.

Conclusion

In this study, the incidence of delirium was 42.9% and the prevalence was 50%, close to the numbers reported in other similar, high acuity, tertiary-referral units. Patients admitted to ICU have many demographic and acute illness risk factors that put them at high risk for delirium. Delirium is a manifestation of organ failure and may be inevitable in those with severe illness and multiorgan involvement. However, the promotion of practices that lead to preservation of the sleep-wake cycle may translate to improvements in the rates of delirium. There is a need for more research into how sleep is affected during critical illness and periods of sedation. This would be useful in adding another dimension to the way that delirium is addressed, translating into better patient outcomes.

Conflicts of Interest

The authors have no conflicts of interest to disclose.

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