CE Symptom Management Series
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Hyperactive Terminal Delirium in Hospice Patients

A Retrospective Cohort Study

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Terminal delirium is a common occurrence in patients at the end of life, and its presence is widely accepted as a poor prognostic indicator. The hyperactive subtype is characterized by psychomotor agitation that is distressing to patients, caregivers, and providers. The purpose of this study was to determine whether physical, psychosocial, or spiritual data collected at hospice admission are associated with development of hyperactive terminal delirium. In this retrospective cohort study, 154 patients were assigned to one of two cohorts depending on whether or not they had signs of hyperactive terminal delirium. Hospice admission data from the Hospice Item Set, psychosocial assessment, and spiritual assessment were analyzed using descriptive statistics, inferential statistics, and logistic regression. Although there were no statistically significant relationships among the physical, psychosocial, and spiritual variables and hyperactive terminal delirium, there were some findings that are clinically significant for nurses caring for patients at the end of life. Specifically, this study highlights the importance of ongoing physical, psychosocial, and spiritual assessment throughout the end-of-life trajectory, as well as prompt management of symptoms.

KEY WORDS
end of life, palliative care, terminal delirium

Delirium is a complex and distressing neurocognitive disorder that has many different etiologies. According to the American Psychiatric Association,[1] delirium manifests as disturbances in attention and cognition that develop for a short period, usually hours to days. At the end of life, delirium is referred to with a variety of terms including "terminal delirium," "terminal agitation," "terminal restlessness," and "terminal anguish."[2] Although there are numerous reversible and irreversible causes of delirium, the pathogenesis of terminal delirium is not well understood. Patients with terminal delirium may have no clear toxic or metabolic abnormality.[3]

Terminal delirium is a common occurrence in patients at the end of life, and its presence is widely accepted as a poor prognostic indicator.[2,4] A review of the palliative care literature found the prevalence of terminal delirium to be 44% to 88% in the weeks or hours preceding death.[5-8] There are hyperactive, hypoactive, and mixed subtypes of delirium (Table 1). Terms such as "terminal agitation" and "terminal restlessness" may suggest the hyperactive subtype of delirium; however, all of the delirium subtypes are represented in the literature, with hypoactive delirium being the most prevalent (68%-86%).[8]

Patients who have entered the "living-dying interval,"[9] the life period in which there is knowledge of life-threatening illness and death itself, progress along a trajectory of physical and emotional symptoms as well as a need to withdraw. Patients with cancer experience a variety of psychological and psychiatric problems that can affect their function, including depressive disorders, anxiety, and somatization.[10] Psychological or emotional distress in terminally ill patients can manifest as symptoms that are characteristic of terminal delirium, including agitation, sleep disturbance, decreased concentration, and social withdrawal.[11] Furthermore, distressed mood has been found to be predictive of terminal delirium in older adults.[12]

Processing impending death is essential to end-of-life closure and acceptance; however, this process also contributes to spiritual suffering in patients.[13] Spirituality is a unique experience that can mean different things to different people. In the literature, there have been characteristics of spirituality identified, including relationships with self, others, Higher Power/God, and nature; sense of meaning and purpose; love; transcendence; forgiveness; and hope.[14,15] Evidence suggests that spirituality is associated with better quality of life, greater coping with disease-related symptoms, better psychosocial well-being, and dignified dying.[16,17] Spirituality at the end of life is shaped by one's spiritual lens throughout his or her lifetime.[18]

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TABLE 1 Subtypes of Delirium[1]

Delirium Subtype	Characteristics
Hyperactive	• Increased psychomotor activity • Mood lability and agitation
Hypoactive	• Decreased psychomotor activity • Sluggishness and lethargy
Mixed	• Normal psychomotor activity • Disturbance of awareness and attention

Caregivers of end-of-life patients are often faced with the difficult role of watching loved ones experience the distressing symptoms of hyperactive terminal delirium, which, in turn, contributes to caregiver distress.[13,19,20] Caregivers of patients with terminal delirium experience significant distress that includes negative emotions (ie, anxiety, fear, anger, sadness, and guilt), difficult or deteriorating relationships, and feelings of helplessness or loss of control.[19] In addition, caregivers have reported personal suffering while caring for patients with terminal delirium.[13] The purpose of this study was to determine whether selected data collected at hospice admission were predictive of hyperactive terminal delirium. This study was conducted to answer the following question: is there physical, psychosocial, or spiritual data collected at hospice admission that are associated with development of hyperactive terminal delirium?

THEORETICAL FRAMEWORK

Szarpa et al[13] proposed a theoretical model that depicts the process of delirium at the end of life, which provides the guiding framework for this study. The theoretical model illustrates the temporal progression of physical and mental suffering and deteriorating sleep in the presence of overall physical decline, cognitive/psychological decline, end-of-life awareness, and withdrawal. The model posits that, although processing impending death is intrinsic to end-of-life closure and acceptance, the process also contributes to the spiritual and psychological suffering experienced by dying patients and their loved ones.

METHODS

Study Design

The purpose of this pilot research study was to explore whether physical, psychological, or spiritual data collected at admission to hospice were associated with hyperactive terminal delirium. The study used a retrospective cohort study design using chart review.

Sample and Procedures

After receiving institutional review board approval and hospice administrative approval, a randomly drawn, convenience sample of patients who died while receiving hospice care from one community-based hospice in the northeastern United States was obtained through the hospice's electronic medical record system. A total of 154 de-identified patient records were included in this sample. All deceased patients were 18 years or older and were receiving hospice services at the time of death. Electronic data were reviewed to determine whether the patients demonstrated symptoms of terminal delirium. Patients were assigned to one of two cohorts depending on whether or not they had symptoms of hyperactive terminal delirium. The sample included 82 patient records with symptoms of hyperactive terminal delirium and 72 patient records without symptoms of hyperactive terminal delirium.

Measurement Methods

Demographic data extracted from the medical records included age, sex, race, marital status, hospice admission diagnosis, place of hospice admission (ie, home, hospice inpatient unit, nursing facility), and place of death (ie, home, hospice inpatient unit, nursing facility). Data regarding physical symptoms were obtained from the Hospice Item Set (HIS).[21] The HIS is a seven-item data set that the Centers for Medicare & Medicaid Services require hospices to obtain and submit on each admitted patient. Required beginning in 2014, it is used to calculate quality measures. The specific items that were obtained from the HIS included (*a*) item J0900, pain screening; (*b*) item J2030, screening for shortness of breath; (*c*) item J2040, treatment for shortness of breath; (*d*) item N0500, scheduled opioid; (*e*) item N0510, as needed (PRN) opioid; and (*f*) item N0520, bowel regimen.

Centers for Medicare & Medicaid Services requires each hospice patient to have a psychosocial assessment within 5 days of admission.[22] There is no uniform psychosocial assessment instrument required, and it varies among hospices. In this study, one specific question in the psychosocial assessment was used to address the psychological variable: does the patient have any significant fears about their future? This question requires a dichotomous "yes" or "no" answer.

Hospices are also required to assess spirituality as part of their comprehensive admission assessment. Similar to psychosocial assessment, there is no uniform assessment instrument. In the spiritual assessment for this study site, there is a question that asks, "Are you spiritually active?" This results in a dichotomous "yes" or "no" answer.

In the electronic medical records of the study site, there was no standardized delirium assessment instrument used. To determine to which cohort the patient should be assigned, the investigator reviewed the electronic nursing

notes for each patient. Patients were assigned to the hyperactive terminal delirium cohort if there was documentation of symptoms, such as attention disturbance, disorientation, hallucinations, or delusions, which were consistent with the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*[1] diagnostic criteria for delirium.

Data Analysis

Data were analyzed using IBM SPSS (SPSS Inc, Chicago, Illinois) 25.0 computer software. Continuous and categorical variables (ie, the demographic characteristics of the study population) were analyzed using Wilcoxon rank sum and Fisher exact test, and the values obtained for the hyperactive terminal delirium and control groups were compared. Descriptive statistics, inferential statistics, and logistic regression were conducted to explore the study variables.

RESULTS

Table 2 presents the demographic characteristics of the study population. A total of 154 patient records were reviewed (82 with hyperactive terminal delirium and 72 in the comparison group). Overall, the sample was predominantly white, with a slight majority of female patients, and had an average age of 81 years. Most patients were admitted into residential hospice (home, 55.2%; nursing facility, 10.4%). Approximately 56% of patients died in their place of residence (home or nursing facility). The differences between the two groups were not statistically significant when stratified by age, sex, race, religion, marital status, and place of admission ($P > .05$). However, the difference was significant when stratified by place of death. Patients with hyperactive terminal delirium had a higher frequency of dying in the hospice inpatient unit, compared with those in the comparison group (55.6% vs 34.1%, $P < .05$).

With regard to the data collected from the HIS, most patients did not have shortness of breath (52.9%) or pain (53.9%) upon hospice admission (Table 3). Forty-five percent of those with shortness of breath had orders for treatment of it. The most common treatment for shortness of breath was oxygen (41.2%). For pain, a majority of patients had opioids ordered on a PRN basis (71.4%), and a majority did not have scheduled opioid orders (57.8%). A majority did not have a bowel regimen ordered (64.1%). The psychosocial assessment revealed that a slight majority of patients admitted to significant fears upon hospice admission (52%). Approximately 48% of the sample admitted to being spiritually active. There were no statistically significant differences between the two groups with regard to the physical, psychological, or spiritual data obtained in the chart review ($P > .05$).

Logistic regression analysis revealed place of death to be significantly associated with hyperactive terminal

TABLE 2 Characteristics of the Sample (N = 154)

	Comparison Group	Hyperactive Terminal Delirium Group	*P*
n	72	82	
Age, mean (SD), y	80.8 (13.8)	80.3 (13.6)	.803[a]
Range	41-103	45-99	
Sex, n (%)			
Female	54 (65.9)	38 (52.8)	
Male	28 (34.1)	34 (47.2)	.104[b]
Race, n (%)			
Asian	1 (1.2)	0 (0.0)	
African American or black	11 (13.4)	3 (4.2)	
Caucasian or white	68 (82.9)	66 (91.7)	
Hispanic	1 (1.2)	2 (2.8)	
Pacific Islander	0 (0.0)	1 (1.4)	.093[b]
Religion, n (%)			
Buddhist	1 (1.2)	0 (0.0)	
Catholic	31 (37.8)	37 (51.4)	
Christian	35 (42.7)	26 (36.1)	
Jewish	7 (8.5)	4 (5.6)	
Russian Orthodox	1 (1.2)	0 (0.0)	
None	7 (8.5)	4 (5.6)	
Unknown	0 (0.0)	1 (1.4)	.421[b]
Marital status, n (%)			
Married	23 (28.0)	21 (29.2)	
Divorced	8 (9.8)	8 (11.1)	
Separated	1 (1.2)	0 (0.0)	
Single	9 (11.0)	4 (5.6)	
Widowed	41 (51.0)	39 (54.2)	.714[b]
Hospice admission, n (%)			

(continues)

TABLE 2 Characteristics of the Sample (N = 154), Continued

	Comparison Group	Hyperactive Terminal Delirium Group	*P*
Home	47 (57.3)	38 (52.8)	
Nursing facility	11 (13.4)	5 (6.9)	
Hospice inpatient unit	24 (29.3)	29 (40.3)	.238[b]
Hospice death, n (%)			
Home	45 (54.9)	28 (38.9)	
Nursing facility	9 (11.0)	4 (5.6)	
Hospice inpatient unit	28 (34.1)	40 (55.6)	<.05[b]

[a]*Wilcoxon rank sum.*
[b]*Fisher exact test.*

delirium (Table 4). The risk of hyperactive terminal delirium was 2.3 times greater for those patients who died in the hospice inpatient unit versus those who died at home ($P < .05$). In addition, the risk of hyperactive terminal delirium was approximately 2.1 times greater for those who had PRN opioids prescribed ($P < .05$). There were no statistically significant findings with regard to the other variables under study.

DISCUSSION

The prevalence of hyperactive terminal delirium in this study was consistent with findings from other studies. In this study, almost 47% of the sample had documentation of symptoms of hyperactive terminal delirium. Although this is on the lower end of the range of previously reported overall terminal delirium prevalence,[5-8] it is important to note that this study only included hyperactive terminal delirium, whereas the literature shows that the hypoactive subtype of terminal delirium occurs more frequently.[8]

There were no statistically significant relationships among the physical, psychological, and spiritual data collected at hospice admission with hyperactive terminal delirium. However, there were some data that may be clinically significant for nurses caring for patients at the end of life. Of note, more than half of the sample reported significant fears upon hospice admission. This highlights the emotional needs of patients at hospice admission and the need for emotional support throughout the hospice journey. Although there was no relationship between fear and hyperactive terminal delirium in this study, there has been previous evidence of such a relationship in the literature.[12] The prevalence of fear emphasizes the need for a holistic approach to patients at the end of life and validates the hospice model of care. It also emphasizes the need for time to work through the fear and emotional issues. With more than half of patients enrolled nationally in hospice for 30 or fewer days,[23] this presents a challenge to the hospice team to mobilize resources and provide intense emotional support to patients and families before death.

Although slightly less than half of the sample admitted to being spiritually active, spirituality is still an important

TABLE 3 Study Variables

		Comparison Group	Hyperactive Terminal Delirium Group	*P*
	N = 154	72	82	
Hospice Item Set, n (%)				
J0900, pain screening	74 (48.7)	40 (49.4)	34 (47.9)	.872
J2030, shortness of breath screening	72 (47.1)	39 (48.1)	33 (45.8)	.871
J2040, treatment for shortness of breath	69 (45.1)	37 (45.7)	32 (44.4)	>.999
N0500, scheduled opioid	65 (42.2)	30 (36.6)	35 (48.6)	.144
N0510, PRN opioid	110 (71.4)	53 (64.6)	57 (79.2)	.051
N0520, bowel regimen	55 (35.9)	27 (33.3)	28 (38.9)	.503
Fears upon admission, n (%)	79 (52.0)	40 (49.4)	39 (54.9)	.519
Active spiritually, n (%)	74 (48.7)	40 (49.4)	34 (47.9)	.872

TABLE 4 Logistic Regressions

Variable	Odds Ratio	Significance	95% Confidence Interval
Relationship between hyperactive terminal delirium and place of death			
Hospice inpatient unit	2.3	$P < .05$	1.18-4.55
Relationship between hyperactive terminal delirium and opioid order			
Scheduled opioid	1.64	$P = .133$	0.863-3.14
PRN opioid	2.08	$P < .05$	1.02-4.39
Relationship between hyperactive terminal delirium and fear			
Fear on admission	1.04	$P = .810$	0.762-1.42
Relationship between hyperactive terminal delirium and spirituality			
Active spiritually	1.02	$P = .962$	0.535-1.93

component of end-of-life care. Spirituality broadly refers to the way individuals seek and express meaning and purpose as well as how they experience connectedness to the moment, self, others, nature, and the significant or sacred.[24] During the trajectory of critical illness and end of life, spirituality and expressions of spirituality can evolve. Thus, it is essential to foster spiritual care by continually assessing spiritual needs and inviting the expression of myriad forms of spirituality during the dying process.[25]

Overall, the sample demographics were consistent with those of the US population receiving hospice services.[23] In the United States, most hospice recipients are female, white, and 80 years or older. In addition, most hospice patients receive care in their residence, whether that is home or a nursing facility. This study sample did demonstrate a higher proportion of patients dying in the hospice inpatient unit than that of the national statistics. Although death in the hospice inpatient unit was a significant finding relative to hyperactive terminal delirium, the proportion was also greater in the comparison group. The reason for this is unclear.

The finding that the risk of hyperactive terminal delirium was 2.3 times greater for those patients who died in the hospice inpatient unit is not surprising, but it is concerning. Hospice patients who experience severe psychomotor agitation or other symptoms of hyperactive terminal delirium usually require palliative sedation.[26] Usually, this requires transfer to a higher level of care. This is concerning because death in the hospice inpatient unit may not have been concordant with the patients' and/or families' wishes and could have a negative impact on the families' grieving processes. There are options for managing these symptoms at home[27]; however, there needs to be a process in place to anticipate potential need through ongoing assessment.

Most of the patients in this study had PRN opioids ordered for pain, and this was associated with an increased risk of hyperactive terminal delirium. Although this finding was statistically significant, its clinical significance and relevance cannot be determined with the data collected in this study because the ongoing use of PRN opioids in this sample is not known. It is reasonable, though, for nurses to be aware of and assess for symptoms of delirium with opioid or any other psychoactive medication use. It was interesting that a majority of the sample did not have an ordered bowel regimen despite that patients were receiving scheduled and PRN opioids. Constipation is a well-established cause of delirium even in those who are not at the end of life and, thus, should be anticipated, and attempts should be made to prevent it.

IMPLICATIONS AND RECOMMENDATIONS FOR NURSING PRACTICE

Nurses caring for patients at the end of life must be vigilant about assessing for signs of hyperactive terminal delirium so that symptoms can be managed early. Fear is a common symptom at the end of life, and appropriate emotional and psychological support should be provided to mitigate the fears. All patients with scheduled or PRN opioids should have bowel regimens to minimize the risk of constipation.

STUDY LIMITATIONS

One limitation of this study is the possible misclassification of some hyperactive terminal delirium cases. Because this study was based on retrospective electronic medical record reviews, the accuracy of the data was dependent on the documentation recorded by the hospice clinical staff. In addition, because there was no validated screening tool used by this hospice, it is possible that symptoms may not have been consistently documented. Validated tools to screen for delirium should be implemented early, because it is often not practical to use them in advanced delirium.[28]

Although the demographics of this sample were consistent with the national demographics of hospice recipients,

it was still a homogeneous sample. This does not allow for generalizability to a wider population. Finally, because the data were collected at hospice admission, the temporal relationship between some of the variables could not be evaluated.

CONCLUSIONS

Despite study limitations, several things can be learned from this study. Hyperactive terminal delirium is a clinical problem that is prevalent at the end of life for which consistent assessment and treatment strategies are needed. The presence of hyperactive terminal delirium symptoms requires a higher level of care that may necessitate transfer out of the patient's home environment. Patients and families should be educated about this possibility so that they can be emotionally prepared.

Psychological distress, specifically fear, is prevalent at the end of life. Working with patients and families to cope with the emotional toll of terminal illness and impending death is essential. This may be particularly challenging in patients who are admitted to hospice late in their disease process.

Future studies should focus on a longitudinal, prospective approach using a validated delirium screening tool. This would allow for consistent classification of delirium and evaluation of the temporal relations of the variables.

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