

Review Article

Delirium in Palliative Medicine: A Review

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Abstract

Delirium is a devastating complication of general medical and surgical populations but of particular importance in palliative medicine. It is a clinical syndrome that is often not recognized and, therefore, not treated appropriately. The presence of delirium is a predictor of increased morbidity and mortality, longer hospitalization, and more likely discharge to a nursing facility. This article reviews the pathophysiology, etiology, diagnosis, and treatment of delirium in the palliative medicine population. J Pain Symptom Manage 2012;44:583–594. © 2012 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.

Key Words

Delirium, palliative medicine, antipsychotic

Introduction

Delirium is a neuropsychiatric diagnosis that is very common in general medical and surgical populations. It is of particular importance in palliative medicine as the incidence ranges from 28% to 88% depending on the stage of illness, with the higher number occurring at end of life.^{1–4} Delirium is a clinical syndrome with myriad presentations often divided into motoric subtypes—hypoactive, hyperactive, and mixed.^{5–7} It is underdiagnosed, particularly

the hypoactive subgroup, which may be more common in the palliative medicine population.^{8,9} The *Diagnostic and Statistical Manual of Mental Disorders* defines delirium related to a medical condition as “1) a disturbance in consciousness with reduced ability to focus, sustain, or shift attention, 2) a change in cognition that is not better accounted for by a preexisting, established, or evolving dementia, 3) the disturbance that develops over a short period (hours to days) and tends to fluctuate during the course of the day, 4) the evidence that the disturbance is caused by the direct physiological consequences of a general medical condition.”¹⁰ Additional symptoms include alteration in sleep-wake cycle, short- and long-term memory deficits, delusions, hallucinations, and emotional lability.¹¹ The presence of delirium is a predictor of increased morbidity and mortality, longer hospitalization, and more likely discharge to a nursing facility.^{11–14} This article reviews the pathophysiology, etiology, diagnosis, and treatment of delirium in the palliative medicine population.

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Pathophysiology

There has been research trying to find the one common pathway that would explain all deliriums. There are numerous theories, all with some evidence to support them. It is likely that the symptoms of delirium are the expression of many different abnormalities that impact neurotransmitters and neurons in different areas of the brain. Theories include 1) decreased oxidative metabolism with an impact on neurotransmitter systems leading to cerebral dysfunction; 2) direct effects on neurotransmitters such as decreased acetylcholine and increased dopamine; changes also have been documented to norepinephrine, gamma-aminobutyric acid, glutamate, and serotonin; 3) neurotransmitter changes in normal aging making the elderly more at risk; 4) increased inflammatory cytokines that impact neurotransmitter systems; 5) stress reactions leading to blood-brain barrier changes, and hypothalamic-pituitary-adrenal axis increases leading to neurotransmitter synthesis changes; and 6) changes in intraneuronal signal transduction affecting neurotransmitter synthesis and release.¹⁵

The leading theory is decreased cholinergic activity accompanied by dopaminergic increase.^{16–18} Anticholinergic medications have been shown to cause inattention, which is one of the cardinal symptoms in delirium. This neurotransmitter also is involved in arousal, learning and memory, rapid eye movement sleep, behavior, mood, thought, perception, and orientation.¹⁶ Anticholinergic medications can cause slowing of the electroencephalogram, a common finding in delirium. Serum anticholinergic levels correlate with severity of delirium and decrease as symptoms improve.¹⁸ Dopaminergic excess causes a decrease in cholinergic activity.¹⁷ Dopaminergic agonist medications such as L-dopa, bupropion, and cocaine can cause delirium. Dopamine antagonists are used therapeutically.

Etiology

There are several studies defining risk factors for the development of delirium in a general medical population, with varying results.^{19,21,22} An early study in the elderly identified urinary tract infection, low serum albumin, elevated white count, and proteinuria

as risk factors.²⁰ In a later study, factors were age, visual impairment, severe illness, cognitive impairment, and dehydration (increased BUN/creatinine ratio).²² Groups were categorized as low (zero risk factors), intermediate (one to two risks), or high risk (three to four risks) and developed delirium 3%, 16%, and 23%, respectively. Additional studies have identified advanced age, cognitive impairment, preexisting severe chronic illness, and functional impairment.²¹ Five precipitating factors were identified in a general medical geriatric population: 1) the use of physical restraints, 2) malnutrition (serum albumin <3.0 mg/dL), 3) the addition of more than three medications, 4) the use of bladder catheterization, and 5) iatrogenic events.²²

Multiple precipitating factors have been identified in cancer and palliative medicine patients (Table 1). In a study of delirium in this population, a median of three precipitating factors was identified, with a range of one to six.^{2,4} Psychoactive medications, metabolic disturbances,

Table 1
Etiologies of Delirium

Metabolic disturbance
Hypercalcemia
Hyponatremia
Hypernatremia
Dehydration
Glycemic derangements
Organ failure
Renal failure
Liver failure
Respiratory failure
Medications
Opioids
Benzodiazepines
Anticholinergic agents
Steroids
Sepsis
Pneumonia
Urinary tract infection
Brain pathology
Primary brain tumor
Brain metastases
Leptomeningeal disease
Nonconvulsive status epilepticus
Hypoxia
Withdrawal
Alcohol
Benzodiazepines
Hematologic
Disseminated intravascular coagulation
Anemia

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