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Prevention of Postoperative Delirium in the Elderly

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Abstract

Postoperative delirium is especially common among the elderly. With advancements in health care, patients are undergoing surgery at an older age putting them at risk for delirium. Postoperative delirium results in more severe complications, higher costs, longer length of stay, and can be detrimental for friends and family. Health care professionals and family often wonder if postoperative delirium can be prevented. An extensive literature review was conducted to identify risk factors for postoperative delirium. For pharmacological agents studied, dexmedetomidine had a lower rate of delirium compared to propofol, midazolam, lorazepam, and morphine. Sevoflurane, COX-2 inhibitors, antipsychotics, and clonidine have resulted in lower rates of delirium in a limited number of studies. Therefore, further research is indicated. The following risk factors for postoperative delirium were identified: postoperative hypoalbuminemia, postoperative hematocrit less than 30%, postoperative cardiogenic shock, postoperative acute infection, residing in an institution rather than independently before surgery, cardiac valve surgery, cognitive function impairment, hypertension, alcoholism, severity of atherosclerosis, older age, use of opioids, and use of benzodiazepines. The following literature review provides insight into the pharmacologic and non-pharmacologic risk factors for developing postoperative delirium, and measures for providers to reduce these risk factors in their surgical practice.

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Definition/Description

Definitions of delirium vary in their descriptions. Maldonado et al (2009) describe delirium as a neurobehavioral syndrome caused by the transient disruption of normal neuronal activity secondary to systemic disturbances. Katznelson et al (2009) simplifies a definition as an acute deterioration of brain function characterized by fluctuating consciousness and an inability to maintain attention. Delirium has also been hypothesized to be a central nervous system response to systemic inflammation during a state of blood brain barrier compromise (Rudolph et al, 2008). This definition indicates a cause for delirium while many other sources state that no single cause of delirium has been identified. While no single cause has been identified and definitions vary, commonalities can be derived from various sources. One common feature is that delirium is an acute disorder. Chang, Tsai, Lin, Chen, and Liu, (2008) point out that delirium is different than dementia since dementia is prolonged and progressively worsens. Delirium often has a rapid onset, brief duration, and fluctuation of symptoms throughout the day (Angelino and Schmidt, 2007). Common features include cognitive impairment, clouding of consciousness, and difficulty sustaining and shifting attention (Angelino and Schmidt, 2007). Memory impairment, irrelevant speech, hallucinations, and delusions are also common among delirious patients (Chang et al, 2008). Delirium often occurs after episodes of stress such as acute illness, trauma and surgery. While definitions of delirium are inconsistent, there is clearly a devastating impact on patients, families, and society.

Impact on Patients, Families, and Society

The elderly are the fastest growing part of the United States (U.S.) population (Rosborough, 2006). The Centers for Disease Control and Prevention (CDC) population projector (2005) estimates that the U.S. population of residents 65 years and older will reach 46,790,727 by 2015. People are also living longer lives. The life expectancy of men and women at 65 years is 17.2 years and 19.9 years, respectively (CDC, 2007). Functional reserve diminishes and the prevalence of chronic conditions increases with age (Rosborough, 2006). Patients aged 75-84 years followed by patients aged 65-74 years undergo the greatest number of procedures compared to other age groups (CDC, 2006). These figures are significant since age is a strong risk factor for delirium (Angelino and Schmidt, 2007). As the aging population increases and surgical procedures are performed on older patients, postoperative delirium will be an immense challenge for providers.

Postoperative delirium is a highly prevalent condition with unfortunate consequences. Crosby and Marcantonio (2010) claim that incidence can be as high as 60% after some types of surgery and as high as 80% in critical care units. According to a literature review by Maldonado et al (2009), delirium is associated with increased morbidity/mortality, increased cost of care, hospital-acquired complications, poor functional and cognitive recovery, decreased quality of life, prolonged hospital stays, and increased placement in specialized intermediate and long-term care facilities. In one study, patients with postoperative delirium had an average intensive care unit (ICU) stay of 4.1 days versus 1.9 days for non-delirious patients. The length of total hospitalization was 10 days for delirious patients and 7.1 days for non-delirious patients. All of these figures were statistically significant (Maldonado et al, 2009). Pratico et al (2005) found that hospitalization mortality reached 10-26% among patients who developed postoperative delirium and mortality reached 22-76% during following months. The negative effects of delirium may persist long after surgery. Katznelson et al (2009) found that only 4% of patients experience full resolution of symptoms and functional decline still persists six months after hospital discharge. One study among cognitively intact elderly patients found that postoperative delirium led to a worse cognitive outcome and an increased risk of dementia (Wacker, Nunes, Cabrita, and Forlenza, 2006). After adjusting for age, comorbidity, severity of illness, degree of organ dysfunction, nosocomial infection, hospital mortality, and other potential confounders, one study found that delirium was associated with 39% higher ICU costs and 31% higher hospital costs (Milbrandt et al, 2004). Milbrandt (2004) also found that higher severity and duration of delirium were significantly associated with incrementally greater costs. It is estimated that $6.9 billion of Medicare hospital expenditures are attributed to delirium (Katznelson et al, 2009).

Not only does postoperative delirium increase economic costs, but it also causes non-economic suffering. Patients, family members, and health care professionals are all affected by this poorly understood disease.

Pathophysiology

The pathophysiology of postoperative delirium is poorly understood (Katznelson et al, 2009). The most discussed theory involves alterations of neurotransmitters such as gamma-aminobutyric acid, glutamate, acetylcholine, dopamine, serotonin, and norepinephrine. While all of these neurotransmitters have been found to be altered in delirious patients, a decrease in acetylcholine and an increase in dopamine appear to play an important role in delirium (Robertson and Robertson, 2006). Many factors thought to cause delirium such as hypoxia, anemia, hypotension, older age, dementia, infection, surgery, and certain drugs have been shown to increase dopamine and/or decrease acetylcholine. Anything that causes an inflammatory response releases cytokines, which also increases dopamine and decreases acetylcholine. Robertson and Robertson (2006) describe how aging can potentiate delirium since there are morphologic changes in the brain. There is a decrease in overall size, a decrease in the number of neurons, a loss of dendrites and synapses, increased levels of cortisol, decreased levels of acetylcholine, and an increased release of dopamine. A recent article classifies etiologies of delirium as either direct brain insults or aberrant stress responses (Maclullich., Ferguson, Miller, de Rooij, and Cunningham, 2008). Direct brain insults may include hypoxia, hypotension, hypoglycemia, infarcts, brain hemorrhage, trauma, and the effects of certain drugs. The aberrant stress response has the potential to become harmful when exaggerated or when it affects a brain already compromised. The central nervous system's response from certain stressors, such as infection and anxiety can then cause delirium. While MacLullich et al (2008) sought to classify delirium, they also state their theory of neurotransmitter involvement. Like other literature sources, they also suggest that the overactivity of the dopaminergic system and the underactivity of the cholinergic system play a role in delirium. More research is needed to better understand the pathophysiology of postoperative delirium.

Literature Review

Even though the pathophysiology of postoperative delirium is poorly understood, many risk factors have been identified. Dasgupta and Dumbrell (2006) suggest that cognitive impairment, older age, functional impairment, sensory impairment, depression, preoperative psychotropic drug use, psychopathological symptoms, institutional residence, and greater comorbidity are associated with postoperative delirium. Bekker and Weeks (2003) add that nutritional deficiency, alcohol and benzodiazepine withdrawal, traumatic injury, and drugs with anticholinergic properties are also predisposing factors for delirium. There are numerous propositions, but what do the research studies suggest? The following is a research review of studies focusing on postoperative delirium. The goal of this review is to help providers identify strong risk factors and ways to prevent or minimize postoperative delirium.

Non-Pharmacological Risk Factors

A retrospective chart review was conducted on 288 patients who had open heart surgery (Chang et al, 2008). All patients were assessed by a psychiatrist and criteria for diagnosing delirium came from the Diagnostic and Statistical Manual of Mental Disorders, 4th edition. Data was collected on preoperative, intraoperative, and postoperative risk factors for delirium. Preoperative risk factors identified included older age, lower educational level, single marital status, history of psychological disorder, diabetes, history of stroke, history of renal disease, left ventricular ejection fraction (LVEF) of 30% or less, atrial fibrillation, emergency cardiac surgery, and cardiogenic shock. Intraoperative factors found were complex surgical procedures, circulatory arrest that lasted 30 minutes or longer, blood transfusion volume greater than one liter during surgery, and body temperature less than 25 degrees Celsius. Postoperative factors found included LVEF of 30% or less, atrial fibrillation, blood transfusion volume greater than one liter, blood loss volume greater than one liter, cardiogenic shock, unanticipated reoperation, hypoalbuminemia, acute infection, dehydration, hematocrit less than 30%, renal insufficiency, hepatic dysfunction, hypercarbia, and treatment with anticholinergic agents. Although there were many risk factors found, significant variables included postoperative hypoalbuminemia, postoperative hematocrit less than 30%, postoperative cardiogenic shock, and postoperative acute infection (Chang et al, 2008).

One study explored the relationship of preoperative anxiety and depression compared to postoperative delirium (Detroyer et al, 2008). The study of 104 patients having elective cardiac surgery found no association between anxiety, depression, and delirium occurrence. However, two significant preoperative risk factors were identified. Patients who resided in an institution and had valve surgery were more likely to develop postoperative delirium compared to those who lived independently and underwent coronary artery bypass graft (CABG).

Other studies have also recognized type of surgery as a risk factor for postoperative delirium. Herrmann, Ebert, Tober, Hann, and Huth (1999) analyzed neurochemical markers of brain damage and neurobehavioral outcomes in patients either undergoing valve replacement or CABG. Preoperative and postoperative levels of neurone-specific enolase (NSE) and protein S-100B were measured on 36 patients, 18 having valve surgery and 18 having CABG. Cognitive performance was measured using the Mini Mental State Examination (MMSE) and delirium was diagnosed according to DMS-IIIR criteria, Brief Psychiatric Rating Scale (BPRS) and the Delirium Rating Scale (DRS). Both groups showed an increase in NSE and S-100B postoperatively. However, patients undergoing valve replacement had higher levels of NSE than CABG patients. Only valve replacement patients developed delirium in the first three days after surgery and this group showed a greater decline in cognitive performance, which was detectable up to six months after surgery (Hermann et al, 1999). Veliz-Reissmüller, Agüero Torres, Lindblom, and Eriksdotter Jönhagen (2007) also found that patients undergoing valve replacement or valve and CABG surgery had a higher incidence of postoperative delirium than CABG patients alone.

Inflammatory markers in relation to postoperative delirium have been examined in other studies as well. One study drew levels of chemokines preoperatively, six hours postoperatively and postoperative day four (Rudolph et al, 2008). Subjects were matched by surgical duration, age, and baseline cognition. At six hours postoperatively, those who later developed delirium had higher levels of chemokines than matched controls. Lemstra, Kalisvaart, Vreeswijk, van Gool, and Eikelenboom (2008) measured levels of C-reactive protein (CRP), interleukin 6 (Il-6) and insulin growth factor 1 (IGF-1) preoperatively in elderly patients admitted for hip surgery. Patients were matched for age and disease severity. Researchers found that preoperative levels of CRP, Il-6, and IGF-1 did not differ between delirious and non-delirious patients.

Studies have also examined the relationship between cognitive function and postoperative delirium. Rudolph et al (2006) sought to determine the extent to which preoperative performance on tests of executive function and memory was associated with delirium after CABG. Eighty patients without preexisting delirium were included in the study. Executive functioning measures of verbal fluency, category fluency, Hopkins Verbal Learning Test learning, and backward recounting of days and months were significantly correlated with delirium. Patients were controlled for age, sex, education, medical comorbidity, mental status, and other cognitive domains. The study found that risk for delirium is specific to executive functioning impairment, not memory impairment (Rudolph et al, 2006). As mentioned previously, Veliz-Reissmuller et al (2007) found that type of surgery was a risk factor for delirium. The same study also measured cognitive function and memory. One-hundred seven patients over 60 years old without dementia underwent elective cardiac surgery. Age, gender, comorbidities, medications, and perioperative parameters were similar in all patients. Patients with preoperative subjective memory complaints and lower MMSE scores had a higher incidence of postoperative delirium. Lowery et al (2007) evaluated preoperative and postoperative neuropsychological performance in 100 patients without dementia undergoing elective orthopedic surgery. Patients who developed postoperative delirium had significantly slower simple reaction time and digit vigilance reaction time and greater fluctuation of choice reaction time at the preoperative assessment than those who did not develop postoperative delirium.

Other non-pharmacological risk factors have also been studied. A study at a medical/surgical ICU included 820 patients (Ouimet, Kavanagh, Gottfried, and Skrobik, 2007). Risk of delirium was independently associated with a history of hypertension, alcoholism, and severity of illness. One illness studied by Rudolph et al (2005) was atherosclerosis. Researchers investigated whether atherosclerosis of the ascending aorta, internal carotid arteries, and coronary arteries is predictive of postoperative delirium in subjects undergoing CABG. Thirty six male veterans were controlled for age, baseline cognition, and medical comorbidity. Carotid stenosis of 50% or more, and moderate to severe ascending aortic plaque were significantly associated with the development of delirium. As for coronary atherosclerosis, there was a trend toward a significant association for three or more vessels bypassed.

Pharmacological Risk Factors

Sedation/anesthesia.

Dexmedetomidine, an alpha 2 receptor agonist and close relative of clonidine, has been included in many studies (Wunsch and Kress, 2009). Maldonado et al (2009) investigated the effects of postoperative sedation on the development of delirium in cardiac valve procedures. Ninety patients were randomized to receive dexmedetomidine, propofol, or midazolam. The incidence of postoperative delirium was 3% for the dexmedetomidine group, 50% for the propofol group, and 50% for the midazolam group. The average cost of postoperative care was $7,025 for the dexmedetomidine group, $9,875 for the propofol group, and $9, 570 for the midazolam group. Researchers concluded that dexmedetomidine was associated with significantly lower rates of postoperative delirium and lower care costs. Older age was also a significant predictor of delirium (Maldonado et al, 2009). Dexmedetomidine and midazolam were also compared by Riker et al (2009). The double blind randomized trial included 375 medical/surgical ICU patients expecting to be mechanically ventilated for over 24 hours. There was no difference in the time spent in the target RASS range between dexmedetomidine and midazolam. The presence of postoperative delirium was 54% for the dexmedetomidine group and 76% for the midazolam group. Use of dexmedetomidine was also associated with a shorter time to extubation and lower rates of tachycardia and hypertension. Dexmedetomidine was associated with more bradycardia, but there was not a significant increase requiring treatment. Shehabi et al (2009) compared dexmedetomidine to morphine. This double-blind randomized controlled trial included 306 patients at least 60 years old. All patients were sedated with propofol and either dexmedetomidine or morphine. Both groups experienced similar rates of target sedation. The incidence of postoperative delirium was similar for dexmedetomidne and morphine, 8.6% and 15%, respectively. However, the dexmedetomidine patients spent three fewer days in delirium, were extubated earlier, had less systolic hypotension, required less norepinephrine, but experience more bradycardia. In another double-blind randomized controlled trial, Pandharipande et al (2007) compared dexmedetomidine to lorazepam for sedation of 106 adults receiving mechanical ventilation in a medical/surgical ICU. Sedation with dexmedetomidine resulted in significantly more days alive without delirium or coma and a significantly lower prevalence of coma than sedation with lorazepam. The dexmedetomidine group also spent more time within one RASS point than the lorazepam group. The 28-day mortality rates were 17% and 27% for the dexmedetomidine and lorazepam groups, respectively.

Other sedatives and anesthetics have also been studied. Nishikawa, Nakayama, Omote, and Namiki (2004) compared the effects of propofol and sevoflurane for long-duration laparoscopic surgery on elderly patients. Fifty patients were randomized to receive either propofol or sevoflurane for both induction and maintenance of general anesthesia. No significant difference in rates of postoperative delirium was found between the two groups during the first three days after surgery. However, delirium scores on days two and three were significantly higher in the propofol group than the sevoflurane group. Although the incidence of postoperative delirium was similar in groups, this study suggests mental function may be altered more when using propofol rather than sevoflurance for sedation. Sieber et al (2010) studied the effects of light sedation versus deep sedation in elderly patients undergoing hip fracture repair. All 114 patients received spinal anesthesia, but were randomized to also receive either light sedation or deep sedation with propofol. The light sedation group had a 50% lower incidence of postoperative delirium than the deep sedation group. However, a major limitation to this study is that the two groups were different at baseline. More patients in the light sedation group lived independently and had higher MMSE scores before surgery.

Pisani et al (2009) examined 304 consecutively admitted ICU patients 60 years and older. Results indicated that the use of opioids or benzodiazepines in the ICU is associated with longer duration of delirium. Other variables associated with delirium were preexisting dementia, use of haloperidol, and severity of illness. Although this study was conducted in a medical ICU, one could theorize that these medications could cause delirium in surgical patients as well.

Other medications.

Literature has been published regarding statins and their effect on postoperative delirium. Katznelson et al (2009) sought to determine the association between preoperative administration of statins and postoperative delirium in a large prospective cohort of cardiac surgery patients with cardiopulmonary bypass (CPB). All 1,059 patients received the same anesthesia medications. Results were adjusted for independent predictors of postoperative delirium including older age, preoperative depression, preoperative renal dysfunction, complex cardiac surgery, perioperative intraaortic balloon pump support, and massive blood transfusion. Results showed that statins had a statistically significant protective effect by reducing the rate of delirium by 46%. Limitations to the study include the use of different statin medications, and not screening for delirium preoperatively or after the ICU stay. Another study focusing on the same topic found opposite results. Redelmeier, Thiruchelvam, and Daneman (2008) studied 284, 158 patients 65 and older having elective surgery. The rate of postoperative delirium was significantly higher among patients taking statins compared to patients not taking statins. The risk of postoperative delirium persisted after adjusting for multiple demographic, medical and surgical factors.

Impaired cholinergic transmission is believed to play a role in the development of delirium. Gamberini et al (2009) tested this hypothesis in a randomized controlled trial by giving rivastigmine, a cholinesterase inhibitor. One-hundred twenty-seven patients 65 and older having elective cardiac surgery received a placebo or 3 doses of 1.5 mg oral rivastigmine per day starting the evening before surgery until the evening of the 6th postoperative day. The results did not support the use of rivastigmine to prevent postoperative delirium, since 30% of patients in the placebo group and 32% of patients in the treatment group developed delirium. Donepezil is another cholinesterase inhibitor. Sampson et al (2007) studied its efficacy in preventing postoperative delirium. The double blind randomized controlled trial included 33 older patients without pre-existing dementia having elective total hip replacement. The results showed that donepezil did not significantly reduce the incidence of postoperative delirium.

Another theory is that the systemic inflammatory response syndrome (SIRS) contributes to the development of postoperative delirium. A variety of insults can cause SIRS such as infection, ischemia, infarct or injury. This results in a generalized inflammation of organs remote from the insult, which could lead to dysfunction of multiple organs (Phillips, 2004). Hala, Pavlik, and Wagner (2006) tested the relationship of SIRS and delirium by giving patients cyclooxegenase-2 (COX-2) inhibitors, since one of the terminal tissue effectors of SIRS in COX-2. The study included 86 patients 65 and older who underwent open-heart surgery. Patients were randomized into a control group and a treatment group, which received parecoxib 40 mg IV on arrival to the ICU plus 1 mg/kg/day on the day of surgery and the first postoperative day, then valdecoxib 2 x 20 mg by mouth on postoperative days 2 and 3. The incidence of postoperative delirium was the same for both groups, but the duration of postoperative delirium was significantly shorter in the treatment group than in the control group. Valdecoxib was withdrawn from the U.S. market in 2005 for serious cardiovascular events and skin reactions (Solomon, 2010). More research may be needed to evaluate some COX-2 inhibitors used today, such as celecoxib.

Antipsychotics and their relation to delirium have also been researched. Prakanrattana and Prapaitrakool (2007) implemented a randomized double-blind controlled trial involving 125 patients undergoing elective cardiac surgery with cardiopulmonary bypass. Patients received either a placebo or 1 mg of risperidone sublingually when they regained consciousness. Postoperative delirium occurred in 11.1% of the treatment group and 31.7% of the placebo group, showing that a single dose of risperidone decreased the incidence of postoperative delirium. Kalisvaart et al (2005) studied the use of haloperidol on elderly patients having hip surgery. The randomized double-blind placebo-controlled trial included 430 patients at least 70 years old. Either a placebo or 1.5 mg of haloperidol was given preoperatively and continued for up to 3 days postoperatively. Although the incidence of delirium did not differ significantly between groups, the haloperidol group had significantly less severe delirium and a shorter duration of delirium. The mean duration of delirium was 6.4 days shorter and the mean hospital stay was 5.5 days shorter in the haloperidol group than in the placebo group. Girard et al (2010) administered haloperidol, ziprasidone, or placebo every 6 hours for up to 14 days to 101 mechanically ventilated patients in a medical/surgical ICU. All three groups spent similar days alive without delirium or coma. Secondary outcomes such as ventilator-free days, hospital length of stay, and mortality did not differ between groups.

Clonidine is an alpha-2 adrenergic agonist, which is in the same drug class as the previously mentioned dexmedetomidine. Rubino et al (2010) evaluated clonidine's effect on neurological outcomes and respiratory function in 30 consecutive patients undergoing surgery for type-A aortic dissection. Patients were randomized to either a placebo or an IV clonidine bolus followed by continuous infusion starting and throughout the weaning period from mechanical ventilation. Results showed that IV clonidine reduced the severity of delirium, improved respiratory function, shortened ventilator weaning duration, and shortened ICU length of stay.

Recommendations

Based on the literature review, specific sedatives can be recommended to reduce the incidence of postoperative delirium. Dexmedetomidine has proven to be cost-effective and reduce rates of delirium compared to propofol, midazolam, and lorazepam. Dexmedetomidine also has a low rate of mortality, hypotension, hypertension, and tachycardia and has a shorter time to extubation. Bradycardia may be more prevalent with the use of dexmedetomidine, so it should be prescribed with caution to patients with existing bradycardia or at risk for bradycardia. Overall, dexmedetomidine seems to be a great choice for patients at risk for postoperative delirium.

Sevoflurane may be another option for sedation, but research is limited. It has shown to reduce the severity, but not incidence of delirium compared to propofol. However, this was only in one study, so more research needs to be done to validate this benefit. More research is also needed regarding light sedation versus deep sedation. Light sedation has been shown to reduce the incidence of delirium compared to deep sedation, but only in one study which had major limitations.

Opioids and benzodiazepines should also be prescribed with caution in the postoperative setting. Opioids are extremely effective for treating pain, but they can extend the duration of delirium. The same can be said for benzodiazepines. Prescribing becomes a fine line between providing effective symptom management and reducing delirium. Providers should minimize the use of opioids and benzodiazepines as much as possible without causing the patient to suffer.

Recommendations can also be made for other medications included in the literature review. Studies regarding statins had conflicting results. Therefore, the effectiveness of statins to prevent postoperative delirium is inconclusive and more research is warranted. Future studies should control for the degree of atherosclerosis. Studies may obtain different results because some patients taking statins may have less atherosclerosis because of the effectiveness of statins. However, patients taking statins may also have more atherosclerosis because their degree of atherosclerois may be the reason they started taking statins in the first place. Cholinesterase inhibitors such as rivastigmine and donepezil have not proven to be effective for preventing postoperative delirium. Cyclooxegenase-2 (COX-2) inhibitors may shorten the duration of delirium. However, providers should be aware that this finding was limited to one study involving the drugs parecoxib and valdecoxib. More research is needed to provide more evidence. Antipsychotics may be used to protect against delirium. Risperidone has been shown to decrease the incidence of postoperative delirium and haloperidol has been shown to decrease the severity and duration of postoperative delirium. Even though one study in the literature review was inconclusive, antipsychotics show an overall positive effect on postoperative delirium. Antipsychotics are commonly used in practice. However, they may cause serious side effects such as sedation, extrapyramidal reactions, seizures, neuroleptic malignant syndrome, QT prolongation, and the development of type 2 diabetes (Gutierrez, 2008). More research should be conducted, but overall it is recommended that antipsychotics be used with caution and only when the benefits outweigh the risks. Clonidine, an alpha-2 adrenergic agonist, has also been shown to reduce the severity of delirium, improve respiratory function, shorten ventilator weaning time, and shorten ICU length of stay. This is not surprising considering that it is in the same drug class as dexmedetomidine. More research should be conducted, but clonidine seems to have great potential to reduce postoperative delirium.

Non-pharmacological risk factors for developing postoperative delirium can also be concluded from this literature review. The strongest risk factors for postoperative delirium found in this review included postoperative hypoalbuminemia, postoperative hematocrit less than 30%, postoperative cardiogenic shock, postoperative acute infection, residing in an institution rather than independently, type of surgery especially cardiac valve surgery, cognitive function impairment, hypertension, alcoholism, and severity of illness. No risk was found for preoperative anxiety or depression. Risk associated with inflammatory markers, memory impairment, and atherosclerosis is inconclusive due to limited research or conflicting results. It should be noted that these risk factors are limited to the studies in this review. Many of the studies include other proposed risk factors in their introductions, even if they were not discovered in that particular study. One risk factor often proposed is older age. Older age has been accepted by the healthcare community as a strong risk factor for postoperative delirium, even though it was only studied in one piece of literature in this review. In fact, most of the studies controlled for age since it is well known to be a risk factor. Providers should know that age is a risk factor even though it was not well studied in the research of this literature review.

Providers should consider the pharmacological and non-pharmacological risk factors in this review. With knowledge of high risk patients, care can be optimized to prevent or minimize the harmful effects of postoperative delirium. If delirium does occur, the underlying cause should be identified and treated or removed. Providers should always include family to play a key role, since family members may know the patient's baseline cognitive status and can recognize early signs of delirium. They can also provide familiar faces, which may help reorient a delirious patient. Overall, some studies have provided ways to prevent and treat postoperative delirium, but much more research is needed.

Table 1. Summary of Pharmacological Recommendations

Medication	**Level of Evidence**
Dexmedetomidine	Strong
Sevoflurane	Moderate (more research needed)
COX-2 Inhibitors	Moderate (more research needed)
Antipsychotics (atypical and low-dose conventional)	Moderate (more research needed)
Clonidine	Moderate (more research needed)

Table 2. Summary of Risk Factors for Postoperative Delirium

Postoperative hypoalbuminemia
Postoperative hematocrit less than 30%
Postoperative cardiogenic shock
Postoperative acute infection
Residing in an institution rather than independently before surgery
Type of surgery especially cardiac valve surgery
Cognitive function impairment
Hypertension
Alcoholism
Severity of atherosclerosis

Older age
Use of opioids
Use of benzodiazepines

Diagnostic Tests, Treatment, and Follow-Up

Various tools can be utilized to diagnose delirium. The Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) states four main points of criteria to diagnose delirium:

Table 3. DSM-IV Diagnostic Criteria for Delirium (American Psychiatric Association, 2000)

Disturbance of consciousness (i.e., reduced clarity of awareness of the environment) with reduced ability to focus, sustain or shift attention.
A change in cognition or the development of a perceptual disturbance that is not better accounted for by a preexisting, established or evolving dementia
The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day.
There is evidence for the history, physical examination or laboratory results that the disturbance is caused by the direct physiological consequences of a general medical condition.

Different screening tools have been used to evaluate whether or not these criteria are met. The literature review found that many studies used the Mini Mental State Examination (MMSE) to evaluate cognitive function and the Confusion Assessment Method (CAM) to recognize delirium. The delirium observation screening (DOS) scale has also been used to recognize delirium. It was developed to facilitate early recognition of delirium by nurses during routine care. It includes 13 statements related to typical behavior of delirious patients:

Table 4. DOS Scale Statements (Koster., Hensens, Oosterveld, and Wijma, 2009)

The Patient: 1. Dozes off during conversation or activities.
2. Is easily distracted by stimuli from the environment.
3. Maintains attention to conversation or action.
4. Does not finish question or answer.
5. Gives answers that do not fit the question.

6. Reacts slowly to instructions.
7. Thinks to be somewhere else.
8. Knows which part of the day it is.
9. Remembers recent events.
10. Is picking, disorderly, restless.
11. Pulls IV tubes, feeding tubes, catheters, etc.
12. Is easily or suddenly emotional (frightened, angry, irritated).
13. Sees/hears things which are not there.
Never = 0 pts; Sometimes or always = 1 pt. A total score of 3 or more points indicates delirium.

One study found that the sensitivity and specificity of the DOS scale was 100% and 96.6% respectively, showing that the DOS scale is a good instrument for nurses to recognize delirium early (Koster et al, 2009). This indicates that providers may benefit by closely collaborating with nurses since they spend more time observing the patient. Communicating with family members may also be beneficial since they often recognize if the patient's behavior is an acute change from baseline. The electroencephalogram (EEG) may also be used as a diagnostic tool to accompany an assessment. The EEG in a delirious patient shows a generalized slowing, but the EEG is generally normal in a schizophrenic or depressed patient (Angelino and Schmidt, 2007). The EEG shows diffuse slowing in both delirium and dementia, but slowing is often marked in delirium and mild in dementia. Diagnosis of delirium may be difficult for a provider. However, by recognizing risk factors and symptoms, and utilizing resources such as nurses, family members, and diagnostic tools, an accurate diagnosis can be made to proceed to treatment.

There is scarce evidence to guide the treatment of delirium. Restraints may increase agitation and lead to loss of mobility, pressure ulcers, and aspiration. Therefore, they should be used only as a last resort to protect the safety of a patient or staff (Francis, 2010). Constant observation by someone familiar to the patient would be a better alternative to restraints. Reassurance, touch, and verbal orientation from a familiar person may also improve behavior. A meta-analysis revealed that non-pharmacological interventions reduce the risk of delirium by an average of only 13% (Kalisvaart et al, 2005). However, pharmacological treatment does not yield promising results either. Psychotropic medications are used in practice even though little data has been published to guide their use (Francis, 2010). Atypical antipsychotics such as quetiapine, risperidone, and olanzapine or a low-dose conventional antipsychotic such as haloperidol can be used with less side effects than a higher dose of haloperidol. Benzodiazepines act rapidly to control unsafe behavior, but can worsen confusion and sedation. Little evidence exists to support definitive treatment of postoperative delirium. Therefore, providers should focus on efforts to prevent delirium and identify the underlying cause as outlined in the recommendations of this literature review.

Follow-up for delirium has no clear timeline. Each patient may differ in severity and duration of delirium. Therefore, a plan for follow-up should be individualized according to the patient. The plan should also be discussed with family members or caretakers, since they spend more time with the patient and can better recognize the patient's progress or need for close follow-up. The first months following surgery are important since research has shown that functional decline still persists up to six months after discharge (Katznelson, 2009). Patients should also be followed by their primary care provider on a long-term basis since postoperative delirium has been associated with an increased risk of dementia (Wacker et al, 2006).

Patient and Family Counseling

Surgical candidates and their family members should be fully informed about the risk and consequences of delirium. They should be informed about the incidence of delirium, risk factors, and the potential to impact future quality of life. Postoperative delirium can devastate the physical and emotional wellbeing of patients and family members. With advancements in health care, an increasing number of surgeries are being done on elderly patients at high risk for delirium. Patients and family members have the right to be fully informed about postoperative delirium, so they can make an ethically responsible decision about proceeding with surgery. If surgery is performed, family should be instructed to report any unusual patient behavior so the underlying cause can be recognized and treated. Not only can family members recognize variations in cognitive function, but they can also reorient patients with their familiar faces.

Conclusion

Postoperative delirium is physically and emotionally devastating. Elderly patients, family members, and providers are searching for answers to this poorly understood condition. This literature review provides some insight into the pharmacological and non-pharmacological risk factors providers should consider when caring for elderly surgical patients. Dexmedetomidine has shown to be advantageous since it has much lower rates of postoperative delirium than other drugs used for sedation. Propofol, midazolam, lorazepam, and morphine had higher rates of postoperative delirium when compared to dexmedetomidine. Sevoflurane used for anesthesia has lower rates of delirium than propofol, but more studies are needed to support this claim. Studies have also shown that COX-2 inhibitors, antipsychotics (atypical and low-dose conventional), and clonidine may result in lower rates of delirium or a shorter duration of delirium. However, the relationship between these medications and postoperative delirium also need to be further studied. Although this literature review did not find concluding evidence for pharmacological intervention (other than dexmedetomidine), important risk factors for postoperative delirium have been identified. These risk factors include postoperative hypoalbuminemia, postoperative hematocrit less than 30%, postoperative cardiogenic shock, postoperative acute infection, residing in an institution rather than independently before surgery, cardiac valve surgery, cognitive function impairment, hypertension, alcoholism, severity of atherosclerosis, older age, use of opioids, and use of benzodiazepines. If providers can take anything from this review, it would be that prevention is crucial. Since most of the research on pharmacological intervention is limited, providers should focus on preventing the mentioned risk factors. Much more research is essential to influence the prevention and treatment of postoperative delirium. However, the information supplied in this literature review offers a step toward helping providers avoid such a costly condition.

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