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Peer Reviewer of *World Journal of Psychiatry*, Qing-Zhong Wang, PhD, Associate Professor, Institute of Chinese Materia Medica, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China.
wangqingzhong3@gmail.com

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Risk factors, preventive interventions, overlapping symptoms, and clinical measures of delirium in elderly patients

Xi Mei, Yue-Hong Liu, Ya-Qing Han, Cheng-Ying Zheng

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Xi Mei, Yue-Hong Liu, Ya-Qing Han, Cheng-Ying Zheng, Department of Psychiatry, Ningbo Kangning Hospital, Ningbo 315201, Zhejiang Province, China

Corresponding author: Cheng-Ying Zheng, BSc, Professor, Department of Psychiatry, Ningbo Kangning Hospital, No. 1 Zhuangyu South Road, Zhenhai District, Ningbo 315201, Zhejiang Province, China. zhengchengying@126.com

Abstract

Delirium is an acute reversible neuropsychiatric syndrome caused by multiple factors. It is associated with many adverse clinical outcomes including cognitive impairment, functional decline, prolonged hospitalization, and increased nursing service. The prevalence of delirium was high in department of cardiology, geriatric, and intensive care unit of hospital. With the increase in the aged population, further increases in delirium seem likely. However, it remains poorly recognized in the clinical practice. This article comprehensively discusses the latest research perspectives on the epidemiological data, risk factors, preventive interventions, overlapping symptoms, and clinical measures of delirium, including specific measures to manage delirium in clinical real-world situations. This article helps readers improve their knowledge and understanding of delirium and helps clinicians quickly identify and implement timely therapeutic measures to address various delirium subtypes that occur in the clinical settings to ensure patients are treated as aggressively as possible.

Key Words: Delirium; Risk factors; Preventive interventions; Research progress; Review; Clinical practice

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Core Tip: This paper reviews the whole delirium process and its latest research progress in risk factors, preventive interventions, identification of superimposed symptoms, and clinical measures to provide a comprehensive and systematic account of delirium and present the latest medical information. This article helps readers improve understanding of delirium and helps clinicians quickly identify and take timely therapeutic measures to address the various delirium subtypes that occur in the clinic setting. This is to ensure that patients can be treated as aggressively as possible.

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INTRODUCTION

Delirium is a group of syndromes characterized by acute changes in attention, consciousness, and cognitive function that cannot usually be attributed to pre-existing neurocognitive disorders. According to ICD-11, delirium is an acute or subacute onset of attention deficit (*i.e.*, diminished ability to direct, focus and maintain attention) and impaired consciousness (*i.e.*, diminished orientation to the environment), with symptoms often fluctuating throughout the day with other cognitive deficits (*e.g.*, memory, language, visuospatial function, or perceptual deficits) that can interfere with the sleep-wake cycle; the etiology is often nonpsychiatric behavioral disorders, substance or drug intoxication or withdrawal.

Regarding delirium incidence, epidemiological data vary across countries or regions, medical scenarios, and assessment methods[1]. In **Table 1**, the highest delirium incidence was found in post-surgical patients, intensive care unit (ICU) patients, and patients with dementia, with extremely high incidence in the elderly population with dementia (up to 56%), postcardiac surgery patients (range: 11%-46%), and patients in the ICU ward (range: 19%-82%).

Delirium leads to increased treatment needs, longer hospital stays, and increased burden of care for patients, with extremely high medical costs. However, 30%-40% of delirium cases can be prevented[1-3]. Therefore, a comprehensive and systematic understanding of the entire delirium process is important for preventing and responding to its occurrence. This study reviews the whole delirium process and its latest research progress in risk factors, preventive interventions, identification of superimposed symptoms, and clinical measures to provide a comprehensive and systematic account of delirium and to present the latest medical information.

LITERATURE REVIEW METHODOLOGY

A search of PubMed and EMBASE databases was performed in July 2022. The search strategy focused on terms for "delirium AND risk factors AND epidemiology," "delirium AND preventive interventions," "delirium AND overlapping symptoms," "delirium AND clinical measures," and "delirium AND prevention and therapy" in 10 years. Although 8290 papers were initially evaluated, only those that fulfilled the following criteria were included in the study: (1) The article was published in English; (2) The trials included original data, as full articles in peer-reviewed journals were included; (3) The studies were representative of the general population or of specific patient populations; and (4) When two or more articles reported data from the same study sample, only the most relevant article was considered. Ultimately, 128 articles were retrieved, which were manually examined for relevance, and 89 articles were identified for further assessment.

RISK FACTORS

Delirium is usually not triggered by a single factor. Patients are often exposed to multiple risk factors, broadly classified into inherent (or predisposing) and controllable risk factors (or precipitating)[4]. Identifying various factors, such as brain tissue hypoxia, inflammation, and drowsiness triggered by sedation, and controlling them can help prevent or improve delirium[5]. Patients with more inherent risk factors can trigger delirium with the action of a few controllable factors[6,7].

Predisposing factors

Advanced age: Delirium is very common among hospitalized older adults; however, its etiology remains unclear[6]. With increase in age, organs deteriorate, and brain and cerebrovascular functions decline even in a non-diseased individual[8]. Neurons use glucose provided by the cerebral microvascular system to produce ATP *via* glycolysis as an energy uptake pathway[9]. The accumulation of neuronal and cerebral microvascular damage throughout life disrupts the energy uptake pathway, leading to inadequate energy uptake and decreased energy metabolism in the brain or specific areas of the brain. This can result in dysfunction in various ways and lead to delirium development in older individuals[10].

Cognitive decline or impairment: Dementia and neurodevelopmental delay are risk factors for delirium. Patients with Alzheimer's disease have a relatively high risk of delirium. Delirium occurred at a significantly higher rate in patients with faster cognitive decline than in those with slower cognitive decline[11]. The same higher prevalence of delirium exists for neurodevelopmental delays in childhood[12]. This evidence confirms that a low cognitive level is a risk factor for delirium.

History of delirium: The duration of delusions varies greatly among individuals, with most cases lasting a few days and some lasting several months. Persistent delirium is not uncommon, with 20% of patients still having some symptoms 6 mo after delirium onset[13]. In such cases, the likelihood of delirium recurrence is extremely high. Patients who have experienced delirium once are more likely to experience delirium again. Moreover, delirium may be a predictor of

Table 1 Incidence and prevalence of delirium

| Country or region/manuscript type | Medical scenario | Assessment method | Incidence (%) | Prevalence (%) |
|-----------------------------------|-------------------------------|---------------------|---------------|----------------|
| United States[1] | Community | NR | NR | 1-2 |
| Italy[79] | Community | DSM-5 | NR | 3.6 |
| Spain[80] | Community | DSM-4 | NR | 0.96 |
| Jordan[81] | Postcardiac surgery | CAM-ICU | 9 | NR |
| Poland[82] | Postcardiac surgery | DSM-5 (age ≥ 65 yr) | 21.4 | NR |
| | | DSM-5 (age ≥ 80 yr) | 33.5 | NR |
| Czech[83] | ICU | CAM-ICU | 26.1 | NR |
| Systematic review[84] | ICU | Hyperactive | 4 | 4 |
| | | Hypoactive | 11 | 17 |
| | | Mixed | 7 | 10 |
| Canada[85] | Dementia Ward | CAM (MMSE ≥ 10) | 1.6 | 3.4 |
| | | CAM (MMSE < 10) | 6.9 | 33.3 |
| Italy[86] | Dementia Clinic | CAM | NR | 13.3 |
| Australia[87] | Hospice care | DSM-5 | 40.2-45 | 42-88 |
| Systematic review[88] | Hospice care | NA | 29 | 35 |
| Australia[89] | Post-stroke (3 d) | DSM-4 | 25 | NR |
| Portugal[90] | Post-stroke (1 d) | DRS | 2 | NR |
| Systematic review[25] | Post-stroke | NA | NR | 13-48 |
| Holland[91] | Psychiatric Outpatient Clinic | DRS-R98 (probable) | NR | 19 |
| | | DRS-R98 | NR | 2 |

NR: Not reported; NA: Not available; ICU: Intensive care unit; DSM: Diagnostic and Statistical Manual of Mental Disorders; DRS: Delirium Rating Scale; CAM: Confusion Assessment Method.

cognitive decline and dementia[14]. History of delirium is common in patients with Alzheimer's disease dementia and dementia with Lewy bodies[15].

History of emotional disturbance: Severe depressive symptoms in preoperative patients were significantly associated with higher delirium incidence[16]. A cohort study showed that depression and post-traumatic stress disorder severity were positively associated with delirium duration during a 3-mo follow-up[17].

History of alcohol abuse: During alcohol withdrawal, norepinephrine hyperexcitability causes symptoms such as increased blood pressure, tremors, and anxiety, which can be controlled with adrenergic agonist drugs[18]. Such drugs are also used to prevent delirium in elderly patients undergoing cardiac surgery or other procedures, including clonidine or dexmedetomidine treatment[19]. Opioids increase norepinephrine release, thereby increasing the risk of delirium development[20,21]. The use of benzodiazepines in the clinical management of alcohol withdrawal syndrome has been associated with disrupted sleep patterns and delirium[22].

Malnutrition: Nutritional deficiency is a risk factor for delirium development[23]. Preoperative malnutrition is correlated with postoperative delirium. Moreover, elevated nutrition levels may reduce the risk of postoperative delirium[24].

Visual and auditory impairment: Visual and hearing impairment increases risk of delirium; in general medical patients, the risk of delirium is 2.1-3.5 times higher in patients with visual impairment than in those without. In contrast, in surgical patients, the risk of delirium is 1.1 and 1.3 times higher in patients with visual and hearing impairment, respectively[1].

Other factors: Other factors include frailty, cardiovascular disease, cerebral atrophy, white matter disease, low education level, male sex, and comorbidities[10].

Precipitating factors

Brain function impairment: Delirium is affected by various factors of brain function, including cerebrovascular injury [25], altered metabolic levels in the brain[26], neurotransmitter imbalance[27], and damage to brain network connections

[28,29]. Excessive microglial activation, impaired endothelial barrier function, and blood-brain barrier dysfunction may be associated with delirium and severe cognitive impairment[30].

Acute somatic diseases: Acute somatic illnesses such as sepsis, hypoglycemia, and liver failure can increase the risk of delirium[31]. Septicaemia-related encephalopathy is a common neurological complication of sepsis that is poorly understood and is associated with increased morbidity and mortality. The clinical manifestations of the disease ranges from mild confusion and delusion to severe cognitive impairment and deep coma[30]. Recent popular theories such as the brain-gut axis, brain-kidney axis, and brain-spleen axis suggest that physical health can affect brain function to a certain extent[32,33].

Infection: Patients who develop delirium after infection show a significant increase in the presence of synaptic damage markers[34]. Patients with neocoronary pneumonia may also develop cerebral hypoxia and delirium[35].

Drug use: Drug use and withdrawal, including changes in medication use, are associated with delirium. Benzodiazepines, dihydropyridines, L-type calcium channel blockers commonly used to treat hypertension, antihistamines, and opioids may pose a high risk of delirium[36].

Sleep rhythm disorders: Sleep rhythm disturbance and sleep deprivation are important factors in delirium development in ICU patients[37]. Sleep disorders and delirium share many symptoms, and their similarity has led to the belief that they are highly correlated[38].

Electrolyte imbalance: Electrolyte imbalance is a risk factor for delirium. Studies have reported that in 53 patients with delirium with serum electrolyte imbalance, correction led to a significantly shorter delirium duration in 18 patients than in 35 patients without electrolyte correction[39].

Environment: The probability of delirium increases by being in a 24-h light environment in the ICU ward or by changes in the senses, including vision and hearing, due to environmental changes[40].

Pain and surgical anesthesia: Both pain and anesthetic drug use for pain relief may trigger delirium; however, the interaction between the two and the extent of their contribution to delirium remains unclear[36]. A multicenter randomized clinical trial, among patients over 65 years old with fragile hip fractures, reported no significant difference in the incidence of delirium between general anesthesia and regional anesthesia within 7 d after surgery[41].

Other factors: Other factors include poor feeding, drug combinations, lack of communication, and physical restraint (physical activity restriction).

PREVENTIVE INTERVENTIONS

Prevention, targeting controllable factors, can effectively control delirium, including reducing its incidence by avoiding functional brain damage or preoperative precautions. Yale University School of Medicine conducted a randomized controlled trial for delirium prevention that demonstrated the feasibility of a multimodal non-pharmacologic protocol to reduce the delirium incidence from 15% to 9%[4]. In this study, the delirium prevention protocol focused on managing the following six risk factors: disorientation, inactivity, sleep deprivation, visual impairment, hearing impairment, and dehydration. This prevention program also applies to healthcare settings such as nursing homes[42]. The long-term care plan adaptation for elderly patients with high delirium risk factors in the geriatric ward care can effectively prevent delirium[43].

Non-pharmacological approaches to effective delirium prevention include occupational therapy. Tobar provides a detailed review of the role of occupational therapy in delirium prevention in critically ill patients and provides a vision for future research in this area[44]. Environmental improvements, including minimizing noise and light at night and promoting sleep consolidation, can also help prevent delirium onset[45]. Reducing physical activity limitations is also important to allow patients to move early; physical activity restriction triples the odds of delirium[46].

Pharmacological approaches to delirium prevention include the use of melatonin to preventing delirium. Melatonin improves sleep quality and increases sedation levels, preventing and reducing delirium incidence. However, melatonin does not reduce delirium duration in patients who already have delirium[47]. In response to sleep problems, it is also necessary to determine in the clinic whether the problem is organic or functional; organic diseases, such as heart and respiratory disease, can also include sleep problems. In functional sleep problems, adjusting the sleep rhythm can help prevent delirium occurrence. In addition, patients with sleep problems caused by fear of surgery and changes in the sleep environment are considered functional. The use of melatonin in such cases improves sleep rhythm and prevents delirium[48]. The use of other sleep-improving drugs, such as ramelteon, for delirium prevention has also been studied[49].

Antipsychotic use for delirium prevention remains highly controversial. A randomized placebo-controlled study showed that haloperidol had a preventive effect in elderly hip surgery patients at risk of delirium[50]. Numerous studies have been conducted on haloperidol for delirium prevention[51,52]. A risperidone trial for delirium prevention in postoperative cardiac patients found that postoperative delirium incidence was significantly lower in the 1 mg risperidone group than in the placebo group (11.1% *vs* 31.7%, $P = 0.009$)[53]. A review of studies concluded that antipsychotic medication use was not related to delirium duration, severity, or place of care and that there was high heterogeneity among studies[54]. Second-generation antipsychotics are more effective than placebo in preventing delirium onset; however, delirium severity was not reduced in patients receiving prophylactic antipsychotics[55].

IDENTIFICATION OF OVERLAPPING SYMPTOMS

Clinical manifestations

The clinical manifestations of delirium are complex and vary, and they are described by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, as altered attention, significantly different from the basal level and accompanied by changes in consciousness, cognitive decline, and sleep rhythm disturbances[56]. Delirium has a rapid onset and appearance of symptoms, duration of several hours or days, and a fluctuating nature. For ease of memory, the diagnostic criteria for delirium have been described more simply as A (attention and awareness), disturbances in attention and awareness; B (short period, hours or days), developing over a short period, usually hours or days; C (cognitive deficit), cognitive decline; D (disturbances in A and C), other cognitive deficits that interfere with A and C judgment, such as a complete coma state, are excluded; and E (exposure to medical conditions or drugs), exposure factors, such as surgery and medications.

The diagnostic process consisted of two basic steps. First, a bedside patient assessment was performed to determine the level of attention and arousal and the presence of other cognitive deficits, psychotic features, or mental status abnormalities. Second, the patient's baseline attention and consciousness status were determined by accompanying relatives or caregivers to obtain evidence of acute change.

Assessment methods

After the initial diagnosis, the patient must be further evaluated to obtain more details, including features such as delusions, hallucinations, and mood changes. These details are very important and affect the patient's subsequent treatment or management plan.

Neuropsychological scales: More than 50 assessment tool scales have been developed, with varying conditions of use, mainly including use when delirium first appears or is suspected, when monitoring delirium in hospitalized patients on a regular daily basis, during brief screening, during detailed symptom documentation and neuropsychological assessment, and when assessing delirium severity[57]. Table 2 shows the commonly used neuropsychological scale of delirium assessment.

Ancillary investigations: Delirium assessment should also consider its precipitating factors; therefore, detailed ancillary examinations such as blood, computed tomography (CT), magnetic resonance imaging (MRI), and electroencephalography (EEG) should be performed. In routine blood parameters, the mean red blood cell volume and aspartate aminotransferase can be delirium predictors in trauma patients[58]. Routine blood tests should corroborate the patient's medical history and clinical features. In addition, some cases of delirium are caused by primary central nervous system disease. Specific brain tests, such as CT or MRI, EEG, lumbar puncture, and antibody testing for autoimmune encephalitis, are selectively performed in such cases. However, it is not reasonable to perform CT in all patients with delirium. A study that included 1653 patients showed that only 11% of patients had positive CT findings, with cerebral hemorrhage being the most common cause of delirium[59]. MRI showed that reduced cerebral blood flow, oxygenation, and abnormal glucose uptake might be associated with delirium, including a high white matter signal in the brain[60].

Differential diagnosis and superimposed symptoms

Although there are similarities in clinical manifestations between the delirium and dementia subtype, including fluctuating cognitive decline exhibited by dementia with Lewy body (DLB), visual hallucinations or delusions exhibited by DLB and Parkinson's disease dementia, and attention deficit in severe Alzheimer's disease (AD), all are similar to delirium presentation. However, there are also significant differences: in terms of the mode of onset, delirium is acute and dementia is slowly progressive; concerning duration, delirium usually lasts for a few hours or days, while dementia lasts for a long time; and there is decreased arousal in delirium and that in dementia remains relatively intact.

Previous studies have shown that symptoms such as dementia and depression sometimes appear in parallel with delirium, leading to poor prognosis and high in-hospital mortality and readmission rates. Identifying delirium superimposed dementia (DSD) is important for timely treatment. Patients with dementia who suddenly present with symptoms such as irritability, unexplained falls, resistance or reluctance to communicate with caregivers, drowsiness, and hallucinations need to be closely monitored for DSD and promptly treated symptomatically[61]. Delirium and depression are very common neuropsychiatric syndromes in the elderly, and accurate condition determination is necessary for providing the best treatment plan. However, the considerable clinical overlap of symptoms makes proper identification difficult, leading to adverse medical outcomes, such as clarifying whether the patient's mood disorder is a manifestation of delirium or depression or the comorbidity or primary stage before implementing therapeutic measures [62].

CLINICAL MEASURES AFTER DELIRIUM ONSET

The best management strategy is a multifaceted intervention focused on treating precipitating illnesses, reviewing medication regimens, managing distress, mitigating comorbidities, and maintaining environmental comfort. Clinical measures are divided into non-pharmacologic, non-antipsychotic, and antipsychotic measures.

Table 2 Common delirium assessment scales

| Name | Time (min) | Application | Sensitivity (%) | Specificity (%) | Rigorous training | Suitable for examining DSD |
|--|------------|--|-----------------|-----------------|-------------------|----------------------------|
| Confusion Assessment Method (CAM) [92,93] | 3-10 | No ICU | 46-94 | 63-100 | Yes | Yes |
| The 4A's test (4AT)[94] | < 2 | No ICU | 86-100 | 65-82 | No | Yes |
| The 12-item Stanford Proxy Test for Delirium (S-PTD)[95] | 5 | No ICU | 80 | 90 | No | No |
| Richmond Agitation Screening Scale (RASS)[96,97] | 1 | Delirium has just started | 65-75 | 82-90 | No | Yes |
| The Recognizing Acute Delirium As part of your Routine (RADAR)[98] | < 1 | Delirium has just started | 73 | 67 | No | Yes |
| Confusion Assessment Method for ICU (CAM-ICU)[99] | < 5 | ICU | 28-100 | 53-99 | Yes | Yes |
| Intensive Care Delirium Screening Checklist (ICDSC)[100] | 7-10 | ICU | 73-97 | 69-97 | Yes | No |
| Delirium Triage Screen (DTS)[101] | < 1 | Screening | 82 | 96.1 | No | No |
| Ultra Brief 2 Item Screener (UB-2)[102, 103] | < 1 | Screening | 93 | 64 | No | No |
| Simple Question for Easy Evaluation of Consciousness (SQEEC)[104] | < 1 | Screening | 93 | 81 | No | No |
| Delirium Rating Scale revised-98 (DRS-R98)[105] | 20 | Detailed neuropsychological assessment | 57-93 | 82-98 | Yes | Yes |
| Memorial Delirium Assessment Scale (MDAS)[106] | 7-10 | Detailed neuropsychological assessment | 64-82 | 75-100 | Yes | No |
| CAM Severity (CAM-S)[107] | 5 | Detailed neuropsychological assessment | NR | NR | No | No |

NR: Not reported; ICU: Intensive care unit; DSD: Delirium superimposed dementia.

Non-pharmacologic measures

Non-pharmacological measures are recognized to be effective in dealing with delirium. The intervention protocols vary among studies and mainly include orientation, cognitive stimulation, early activity, non-pharmacological sleep improvement, sensory impairment correction, identification and intervention of potential controllable risk factors or postoperative complications, pain management, gastrointestinal function improvement, supplemental nutrition, and enhancing oxygen delivery.

The Hospital Elder Life Program (HELP) is a systematic non-pharmacological intervention program[63]. According to the British Institute for Health Care Excellence guidelines for preventing, diagnosing, and managing delirium, HELP added entries for coping with hypoxia, infection, pain, and constipation[64].

After delirium onset, non-pharmacological approaches are an indispensable way. Summarily, the main points are ABCDEF: A (assessing, preventing, and managing pain); B (both spontaneous awakening and spontaneous breathing trials), promoting spontaneous awakening and breathing; C (choice of analgesia and sedation), selection of a reasonable analgesic regimen; D (delirium assessment, management, and prevention), delirium pre-assessment, management, and prevention; E (early mobility), early activity; and F (family engagement), family involvement[65].

The primary treatment of delirium is still focused on identifying and managing potential triggers. In practice, the choice of clinical measures will vary according to patient-specific situations. It is crucial to summarize treatment strategies that minimize delirium severity and duration.

Non-antipsychotic measures

Antiepileptic drugs: Valproic acid is effective in both case reports and retrospective cohort studies for delirium treatment [66,67]. Valproic acid can be administered orally or intravenously and is effective in patients with delirium associated with alcohol withdrawal, a history of traumatic brain injury, or mood disorders. Valproic acid should be avoided in pregnant women and patients with significant hepatic or pancreatic dysfunction, active bleeding, or low platelet counts. Before starting valproic acid treatment, patients should have their blood counts and liver enzyme levels checked and monitored.

Alpha-2 agonists: Dexmedetomidine, an alpha-2 agonist, effectively reduces agitation associated with delirium, decreases CNS sympathetic activity, and indirectly reduces the risk of drug combinations by reducing the use of other delirium medications. A national study showed that dexmedetomidine effectively controlled delirium in postoperative patients

other than those undergoing cardiac surgery[68].

Melatonin: The effects of melatonin on delirium have been described previously. Case and retrospective studies have shown that ramelteon helps treat delirium, especially active delirium[69,70]. Melatonin is well-tolerated and safe in the population. The role of melatonin and its receptor agonists in delirium treatment deserves to be studied in-depth. It can enhance sleep consolidation and maintain a good sleep-wake cycle in delirious patients.

Vitamin B1: Nutritional deficiencies, especially vitamin B deficiencies, are associated with delirium[71]. Vitamin B1 deficiency can lead to a range of changes in mental status, including Wernicke's encephalopathy (a triad of nystagmus, oculomotor paralysis, and altered mental status), Korsakoff's syndrome (irreversible memory impairment, usually the result of untreated Wernicke's encephalopathy), and delirium.

Antipsychotic measures

Although no medications have been approved by the United States Food and Drug Administration (FDA) specifically for treating delirium, antipsychotic medications are often used as first-line medications to respond to and manage patients when non-pharmacologic measures are insufficient to control or improve symptoms. However, antipsychotic use for delirium treatment remains controversial. Several studies have shown that the benefits of using antipsychotic medications outweigh the risks for patients, particularly in improving agitation and psychotic symptoms[72,73]. For the control of delirium incidence, duration, severity, length of hospital stay, and mortality, antipsychotic use does not achieve satisfactory results[54].

Obvious psychotic symptoms, such as hallucinations and delusions, can be controlled using antipsychotic drugs. Antipsychotic medications' sedative effect can effectively resolve agitation in patients with delirium. For the core delirium symptoms, including decreased attention and cognition, there is no evidence that antipsychotic medications are effective. More importantly, patients should be carefully monitored for adverse reactions and side effects after antipsychotic medication use.

The choice of medication should be based on the actual clinical situation of the patient to choose the option that maximizes the benefit[74]. For patients with severe circadian rhythm and perceptual disturbances, sedative antipsychotics, such as quetiapine, can be selected for nighttime use; for patients with overexcited delirium, haloperidol can be selected and administered intravenously or intramuscularly for those who cannot tolerate oral administration; for delirium in patients with PD or DLB, quetiapine is preferable because first-generation antipsychotics can aggravate motor symptoms in patients with PD; if these two groups of patients need parenteral medication, olanzapine or ziprasidone can be selected to be administered intramuscularly at minimal doses; olanzapine and risperidone can be selected for patients who cannot swallow; and olanzapine can be used to exert its antiemetic effect when delirium occurs in cancer patients.

Drug dosage was initially administered at the lowest dose and frequency, as assessed by symptom severity[74]. In addition, three major critical values need to be monitored: QTc prolongation (increased risk of sudden death from ventricular tachycardia), extrapyramidal symptoms, and all-cause death in patients with dementia. QTc prolongation is usually associated with antipsychotic use. An investigational study conducted by Pfizer for FDA comparing the QTc interval before and after the use of the maximum daily dose found QTc prolongation ranging from 4.7 ms (haloperidol) to 20.3 ms (ziprasidone)[75]. Patients with delirium should have an electrocardiogram before receiving antipsychotic medication and ensure no significant QTc prolongation interval during treatment. Patients with delirium receiving antipsychotics must also be monitored for extrapyramidal symptoms, such as inability to sit still, rigidity, and dystonia, which can exacerbate emotional disturbances and cause them to change their treatment plans.

DISCUSSION

The complexity and variability delirium symptoms make determining treatment plans more difficult. Patients with delirium are usually admitted to the hospital from the emergency room. The key to treatment is to quickly identify the cause and promptly remove susceptibility factors and triggers, while supporting with symptomatic treatment, maintaining electrolyte balance, and supplementing nutrition. It is also important to prevent complications such as falls, aspiration (aspiration pneumonia), decubitus ulcers, and deep vein thrombosis. A thorough physical examination, detailed history taking, and necessary ancillary laboratory tests are important for detecting the primary cause. Common factors that cause delirium, including infection, cerebrovascular factors, pharmacological factors, surgical anesthesia, and major physical diseases of the heart, lungs, liver, and kidneys, were excluded. Symptomatic treatment of delirium caused by such factors effectively improves symptoms.

In addition, numerous somatic diseases can cause mild edema in the brain cells, leading to transient consciousness impairment. From this perspective, non-pharmacological measures, although not directly therapeutic, can facilitate and accelerate recovery. These include psychotherapy (suggestion), environmental measures (placement of familiar objects in the room), soft lighting (light therapy), and restraint (use during the attack period to avoid accidents). Subsequently, after correcting the primary physical illness, the brain function was restored and delirium symptoms disappeared.

A primary method to prevent delirium is to simply shorten hospitalization, as much as possible[76,77]. Unfamiliar environment, and lack of separation between day and night and disorientation are frequent during admission are also major causes for delirium. Notably, early discharge is beneficial to patient recovery when their health condition is accurately assessed[78].

The following aspects should be noted for the more controversial use of psychiatric drugs. First, psychiatric medications (first or second generation) usually inhibit a person's cognitive-behavioral activity. The principle is to use them as little as possible and for as short a time as possible. Second, psychiatric drugs were selected in the following cases: (1) The patient was agitated; (2) There were many hallucinatory delusions; (3) Behavioral disturbances; (4) Sleeplessness at night; and (5) Non-cooperation and poor compliance with general supportive therapy. Third, ECG should be checked regularly during treatment with psychiatric drugs, and QT interval changes should be closely monitored. When the following two factors are encountered: (1) Prolonged QT interval suggested by ECG on admission; and (2) electrolyte disturbance, psychiatric drugs should be used with caution. The safety of valium drugs is higher than that of psychiatric medications. When the two factors mentioned above improve after clinical treatment, psychiatric drugs or tranquilizer administration should be considered. When using valium, attention should be paid to whether the patient has obstructive respiratory diseases, myasthenia gravis, and other valium contraindications. Protective restraint is more appropriate when both psychotropic drugs and tranquilizers are at greater risk of use. Fourth, clinical readiness to assess the benefit of patients with psychotropic medications: (1) From the patient's perspective, the improvement of psychiatric-behavioral symptoms; and (2) from the caregiver's perspective, there is usually a significant psychosomatic burden of care for patients with delirium, and the severity of the caregiving burden directly affects the quality of patient care.

Patients usually recover within 7-10 d, with a few recovering in 2-4 wk, rarely developing into chronic delirium. Delirium has also been reported to have long-term effects on cognition[24]. The cognitive impairment that occurs after delirium onset in ICU patients is similar to that caused by moderate traumatic brain injury. Moreover, delirium can lead to more severe dementia in AD patients in addition to original dementia, and the risk of dementia development after delirium onset in older adults is eight times higher than that in normal older adults.

CONCLUSION

Summary and outlook

This study comprehensively discussed the latest national and international research perspectives on delirium in terms of risk factors, preventive interventions, overlapping symptoms, and clinical and specific measures to clinically deal with delirium in real-world situations.

Key points

This paper reviews the whole delirium process and its latest research progress in risk factors, preventive interventions, identification of superimposed symptoms, and clinical measures to provide a comprehensive and systematic account of delirium and present the latest medical information. This article helps readers improve understanding of delirium and helps clinicians quickly identify and take timely therapeutic measures to address the various delirium subtypes that occur in the clinic setting. This is to ensure that patients can be treated as aggressively as possible.

FOOTNOTES

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Country/Territory of origin: China

ORCID number: Xi Mei 0000-0002-5091-8747; Cheng-Ying Zheng 0009-0003-5778-6550.

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