# Post-operative delirium after hip fracture treatment: a review of the current literature

## Postoperatives Delir nach Hüftfraktur-Behandlung: eine Übersicht der aktuellen Literatur

## Abstract

Delirium is a common accompaniment of physical illness in old age, affecting approximately one out of five of those admitted to medical wards, the number being higher for elderly with fractured femurs. Although its existence has long been recognized its exact pathophysiology has not yet been fully elucidated. The present article presents up-to-date information concerning the etiology, pathophysiology, prevention and treatment of the post-operative delirium after hip-fracture treatment. The fact that its diagnosis remains mainly clinical requiring a high index of suspicion, both from nursing and medical staff, results in important under-recognition of the syndrome. Delirium is a medical emergency and if not promptly and urgently treated, or even better prevented, may have serious consequences for the patient and the family members. Proper measures for its prevention and treatment result in shorter hospital stay of the patients, less financial cost and better surgical outcome and rehabilitation of the elderly patient.

**Keywords:** delirium, post-operative, hip fracture, femoral neck fracture

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## Zusammenfassung

Das Delirium ist eine allgemeine Begleiterscheinung von Krankheitszuständen bei älteren Patienten. Etwa jeder fünfte stationär aufgenommene Patient ist nach Schätzungen betroffen, vor allem ältere Patienten mit Femurfraktur. Trotz unbestrittenen Auftretens solcher Delire bleibt die zugrundeliegende Pathophysiologie ungewiss. Der vorliegende Beitrag beschreibt den aktuellen Wissensstand zur Ätiologie, Pathophysiologie, Prävention und Behandlung des postoperativen Delirs nach Hüftfraktur-Behandlung. Die Diagnose ist nach wie vor klinisch und verlangt Erfahrung von Ärzten und Pflegepersonal. Daher wird dieses Syndrom oft nicht erkannt. Das Delirium ist ein medizinischer Notfall. Wird es nicht unverzüglich behandelt oder noch besser verhindert, können ernste Folgen für Patienten und Angehörige eintreten. Rechzeitig ergriffene Maßnahmen haben kürzere Krankenhausaufenthalte, verminderte Kosten und bessere Heilungs-, und Rehabilitationsaussichten älterer Patienten zur Folge.

## Introduction

Hip fracture in older people results in increased mortality [36], impaired quality of life and persistent physical morbidity [51]. The increasing age in an ageing population has as consequence the increase of hip fractures and the movement of nursing and medical care towards a group of people with many co-morbid situations [102], [103]. The number of elderly persons with hip fractures will double to 2.6 million by the year 2025. The lifetime risk of hip fracture is 11.1% for men and 22.7% for women. Almost half of all hip fractures occur in patients aged 80 or over. An estimated 18% to 28% of older hip fracture patients die within one year of their fracture [117]. In common with other general hospital populations, the elderly hip fracture population has high reported rates of psychiatric illness, which suggest an adverse effect in several important outcomes [37].

Delirium, depression and dementia are reported to be the three commonest psychiatric disturbances in elderly

with hip fracture [37]. Delirium, as a concept, stretches back to the age of Hippocrates and has survived repeated attempts of definition and redefinition over the past 2000 years. The word is derived from the latin term meaning "off the track". It was not until 1 AD that Celsus coined the term delirium for acute mental disturbance [55]. Many accounts from literature refer to delirium and those include Shakespeare's death of Falstaff, Lady Mac Beth's sleepwalking, the post-partum delirium of Tolstoy's Anna Karenina, Dickens' account of Fagin's, and last but not least the famous King Lear.

It is a relatively common disorder, especially among elderly people with physical illness. It has a high morbidity and mortality, is often under-recognised and under-treated, and provides a unique opportunity to delve into acute and florid psychiatric symptomatology, which may aid our understanding of phenomenology [28]. Although it is increasingly recognized that delirium is a serious complication of physical illness [8], there has been relatively little research in this area. Perhaps this is due to the fact that in clinical practice, delirium is seen primarily by consultation-liaison psychiatrists and consultation geriatricians, who may find it difficult to set up a study outside their own ward. Furthermore, research with delirious patients poses special ethical problems, including informed consent [52]. Another important problem is that there is no commonly accepted terminology for the illness and the diagnostic criteria may differ slightly depending on the diagnostic system that is applied in every case.

# Epidemiology of delirium and post-operative delirium after hip-fracture treatment

Delirium is a complex neuropsychiatric syndrome with an acute onset and fluctuating course. It is common in all medical settings, occurs in about 15%-20% of all general admissions to hospital [112], with higher frequency in elderly people and in those with pre-existing cognitive impairment [2]. Delirium is underidentified in clinical practice as non detection rates of 33%-66% are reported [42]. Nurses and physicians have been shown to consistently underdiagnose delirium [77]. Incidence rates of delirium in medical inpatients range between 5% and 10% with one study reporting a rate of over 50% in a mixed group of medical and surgical patients over the age of 60. Both the prevalence and the incidence of delirium are particularly high in surgical inpatients, especially in people undergoing cardiothoracic and emergency orthopaedic procedures, cataract removal, or those in intensive care units. Rates in cancer units have also been described, with prevalence and incidence rates of 42% and 45%, respectively [54], [13], [60], [78], [50].

The fact that, especially in elderly patients, delirium has a negative impact on the prognosis has been confirmed in several recently published prospective studies that were mainly focused on length of hospital stay, functional ability, cognitive function and mortality. Length of hospital stay is usually reported to be extended [24], [69]. The functional outcome is negatively affected by the presence of delirium [24], [93], [119], [68], [21], [64]. It has also a serious impact on the rehabilitation outcome [89]. Delirium in nondemented femoral neck fracture patients is associated with the development of dementia and a higher mortality rate. Patients with preoperative or postoperative delirium should therefore be assessed not only for the etiology of the delirium but also for any underlying organic brain disorder. Questions that remain unanswered are whether postoperative delirium is a marker of undetected dementia and whether postoperative delirium contributes to the development of dementia [57]. Surgery may have a stronger impact on cognitive function than environmental change shortly after admission in elderly patients with femoral neck fractures [100]. In hospital populations most studies report prevalences of between 10% and 20% for medical in-patients [45].

Postoperative delirium is a frequent complication in elderly patients following operation for hip fracture [87], [22], [37], the incidence varying between 16% and 62%. Current research literature notes that 10% to 50% of elderly postoperative patients experience delirium. Patients who have had femoral neck fractures can experience delirium three times more than patients undergoing non-orthopaedic surgery [43]. Postoperative delirium is associated with increased morbidity and mortality [81], [83] as well as increased length of hospitalization, resulting in increased suffering and cost. The differential diagnosis for postoperative delirium is extensive and ranges from an awareness under anesthesia to an imbalance of cerebral oxygen supply and demand. Some forms of postoperative delirium are treatable and others are not. It is important to recognize treatable forms of delirium. Patients with pre-existing psychiatric disorders and organic brain disorders have a higher incidence of postoperative delirium, as do very old and very young patients.

# Pathophysiology of post-operative delirium after hip fracture treatment

Several theories concerning the pathophysiology of delirium include metabolic encephalopathy, intoxication by drugs [especially anticholinergic ones] and polypharmacy, hypoglycemia, surgical stress responses, peri-operative hypoxemia, and hypotension. It has been suggested that the type of anesthesia, administration of opioids, sleep deprivation and non relieved pain may play a role in the development of postoperative delirium [27], [113]. Despite these, the pathophysiology of delirium has not been studied much and is not well understood.

There are landmark studies dating back to the 1940s, but pathogenesis of delirium remains poorly understood [1]. The most comprehensive update on all literature and research on the pathophysiology of delirium was written

by Trepacz and Van der Mast. They pose that certain neuroanatomical and neurotransmitter systems may represent a 'final common neural pathway' for the diverse etiologies of delirium. Particular brain regions, especially right-sided, are implicated in delirium. Reduced cholinergic function, excess release of dopamine and both decreased and increased serotonergic activity may underlie the different symptoms of delirium. Disease and trauma that are main risk factors for delirium lead to a physical stress response and may alter cerebral neurotransmission. Age-related changes in central neurotransmission, stress management and hormonal regulation, as well as immune response may underlie the vulnerability of elderly people to delirium [111].

However no studies have examined the interface between the neuroendocrine and the immune systems in delirium [11]. Raised levels of cytokines occur in the common causes of delirium, such as infection. Their infusion promotes delirium in 30%-50% of patients receiving the cytokine interleukin-2 as treatment for cancer [96]. Insulin-like growth factor I (IGF-I) and somatostatin are peptides that have important neurotrophic properties. In particular, somatostatin inhibits the release of cytokines [109]. Somatostatin and IGF-I would appear to be important peptides in relation to cognitive function. Infusion of a somatostatin analogue has been found to improve memory in patients with Alzheimer's disease [18] and IGF-I administration attenuates the cognitive deficit in brain-injured rats [98]. Elevated levels of IGF-I and somatostatin may represent a general neuroprotective response to brain injury. If this is the case, then they have a potential role in the treatment or prevention of delirium [98], [18]. They may have a role also in the treatment of related conditions such as Alzheimer's disease [20], stroke disease [29] and head injury [35].

# Clinical features of post-operative delirium after hip fracture treatment

Clinical features of delirium can be summarized as impairment of consciousness, thinking, memory, psychomotor behaviour, perception, and emotion [108]. Impairment of consciousness characteristically fluctuates often, with a deterioration in the evening when environmental stimulation is least. Awareness is impaired and alertness to the environment can either be falsely increased or lowered. Very minor degrees of impaired consciousness can occur, such as difficulty in estimating the passage of time (tested by asking the patient to estimate how long the interview has lasted).

Disordered attention is another key clinical feature of delirium. At interview, the patient appears to have impaired concentration and distractibility. Simple tests of concentration include: serial 7s where the patient counts backwards in sevens from 100; spelling the word "world" backwards; saying the months of the year backwards, or

counting down from 20 to 1. The interpretation of these assessments should take into account the patient's age and educational attainment.

The sleep/wake cycle is almost always disturbed, with marked periods of drowsiness, sleeping during the day, and insomnia at night. Excessive dreaming with persistence of the experience into wakefulness is common - experiences which have also been described in Lewy body dementia where there is a profound cholinergic deficit, and the associated dopaminergic deficit may underlie the delirium-like states that are a characteristic feature of that condition [70].

Thinking is progressively disturbed. Initially, speech is slowed or speeded up, with the capacity to make judgements and to grasp abstract concept becoming more obviously impaired as the delirium proceeds. Incoherent and disorganised thoughts supervene with the progression of the illness. The patient may seem to be cut off from the external world, and increasingly occupied with inner thoughts and experiences, which are often abnormal in nature.

Disturbance of memory is another cardinal feature of delirium - short term, immediate, or working memory is demonstrated by tests of attention such as digit span, which examines immediate memory over a period of seconds; long term anterograde memory relates to a period of minutes (for example, the ability to remember a fictitious name and address after two or five minutes); and long term memory relates to recalling days, weeks, and months [5].

There may be disturbances of psychomotor behaviour, with little spontaneous activity when the disturbance is mild, although inner experiences such as hallucinations or delusions may result in quick reactions. Purposeless behaviour, such as groping or picking, can occur, with complex stereotyped movements and rarely, the mimicking of a work pattern - occupational delirium [12]. Lipowski described the hypoactive and hyperactive syndromes, while recognising that a mixed form could occur. Abnormalities of perception are usual and may favour the diagnosis of the hyperactive form of delirium. Initial changes may include disturbances of the perception of shape (micropsia or macropsia) with depersonalisation, derealisation, illusions, and hallucinations - commonest in the visual mode, consisting of flashes of light - but may be fully formed to encompass fantastic scenes of people and animals. Lilliputian hallucinations (where people and objects appear small) are characteristic [56].

# Diagnosis and differential diagnosis of postoperative delirium after hip fracture treatment

Diagnosis of post-operative delirium remains mainly clinical. The clinical features already described will give the necessary clues for an almost certain diagnosis of delirium (see Tables 1 and 2 for the diagnostic criteria

**Table 1: DSM-IV-(Text Revision) criteria for delirium**

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a. Disturbance of consciousness (that is, reduced clarity of awareness of the environment, with reduced ability to focus, sustain, or shift attention)

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b. A change in cognition (such as memory deficit, disorientation, language disturbance) or the development of a perceptual disturbance that is not better accounted for by a pre-existing established or evolving dementia

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c. The disturbance developed over a short period of time (usually hours to days) and tends to fluctuate during the course of the day

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d. Where the delirium is due to <u>general medical condition</u> – there is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition
Where the delirium is due to <u>substance intoxication</u> – there is evidence from the history, physical examination, or laboratory findings of either 1 or 2:

    1. The symptoms in criteria (a) and (b) developed during substance intoxication

    2. Medication use – etiologically related to the disturbance

Where the delirium is due to <u>substance withdrawal</u> – there is evidence from the history, physical examination, or laboratory findings that the symptoms in criteria (a) and (b) developed during or shortly after the withdrawal syndrome
Where delirium is due to <u>multiple etiologies</u> – there is evidence from the history, physical examination, or laboratory findings that the delirium has more than one etiology (for example, more than one etiological general medical condition, a general medical condition plus substance intoxication, or medication side effects)

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e. Delirium not otherwise specified – this category should be used to diagnose a delirium that does not meet criteria for any of the specific types of delirium described. Examples include a clinical presentation of delirium that is suspected to be due to a general medical condition or substance use but for which there is insufficient evidence to establish a specific etiology, or where delirium is due to causes not listed (for example, sensory deprivation)

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according to DSM-IV-R and ICD-10 respectively, and Table 3 for differential diagnosis of delirium).

Standardized mental tests are a very useful diagnostic modality which is of great help for the diagnosis of delirium. The most widely diagnostic tests used for this purpose are the confusion assessment method (CAM) [41], the mini-mental state examination (MMSE) and the organic brain syndrome scale (OBS scale) [6]. The confusion assessment method is a structured interview focusing on the most prominent clinical symptoms of delirium. The mini-mental state examination is a tool used to evaluate cognitive impairment. It is designed to test abilities in orientation, memory, attention, naming objects, following verbal and written commands, writing a sentence spontaneously, and in copying a complex polygon. The organic brain syndrome scale is composed of a disorientation subscale and a confusion subscale. The first is based on the interview with the patient, the second is based on the observations of the interviewer or the nursing staff [9].

There are no specific laboratory or imaging studies that certify the diagnosis of post-operative delirium but they may be extremely helpful as far as it concerns the underlying cause or the subsequent pathophysiologic mechanisms of the syndrome. Laboratory studies include complete blood cell count with differential in order to diagnose possible infection or anemia, electrolytes and glucose, renal and liver function tests, urine analysis, thyroid function tests, drug screening, thiamine and vitamin-B12 levels and erythrocyte sedimentation rate. Neuroimaging studies include CT scan and MRI of the head, as well as electroencephalogram. Electrocardiogram, pulse oxymetry and chest x-ray may be helpful.

Differential diagnosis of postoperative delirium includes depression and dementia mostly taking into consideration that they share many common clinical characteristics.

**Table 2: ICD 10 diagnostic criteria for delirium**

For a definite diagnosis, symptoms, mild or severe, should be present in each of the following areas:

a.   Impairment of consciousness and attention (ranging from clouding to coma; reduced ability to direct, focus, sustain and shift attention)

b.   Global disturbance of cognition (perceptual distortions, illusions and hallucinations – most often visual; impairment of abstract thinking and comprehension, with or without transient delusions, but typically with some degree of incoherence; impairment of immediate recall and of recent memory, but with relatively intact remote memory; disorientation for time as well as in more severe cases for place and person)

c.   Psychomotor disturbances (hypo- or hyperactivity and unpredictable shifts from one to the other; increased reaction time; increased or decreased flow of speech; enhanced startle reaction)

d.   Disturbance of the sleep/wake cycle (insomnia or, in more severe cases, total sleep loss or reversal of the sleep/wake cycle; daytime drowsiness; nocturnal worsening of symptoms; disturbing dreams or nightmares, which may continue as hallucinations after awakening)

e.   Emotional disturbances, for example, depression, anxiety or fear, irritability, euphoria, apathy or wandering, perplexity

**Table 3: Differential diagnosis of delirium**

|  | Diagnosis | | | |
|---|---|---|---|---|
|  | **Delirium** | **Dementia** | **Depression** | **Schizophrenia** |
| Onset | Acute | Insidious | Variable | Variable |
| Course | Fluctuating | Steadily progressive | Diurnal variation | Variable |
| Consciousness and orientation | Clouded; disoriented | Clear until late stages | Generally unimpaired | Unimpaired but patient may be perplexed in acute stage |
| Attention and memory | Poor short term memory; inattention | Poor short term memory without marked inattention | Poor attention but memory intact | Poor attention but memory intact |
| Psychosis present? | Common (psychotic ideas are fleeting and simple in content) | Less common | Occurs in small number (psychotic symptoms are complex and in keeping with prevailing mood) | Frequent (psychotic symptoms are complex and often paranoid) |
| Electroencephalogram | Abnormal in 80%-90%; generalised diffuse slowing in 80% | Abnormal in 80%-90%; generalised diffuse slowing in 80% | Generally normal | Generally normal |

# Risk factors for post-operative delirium after hip fracture treatment

There is a great variety of factors that have been correlated with the development of postoperative delirium [9]. Preoperative, intraoperative, and postoperative risk factors may give rise to the manifestation of delirium state in patients after hip fracture treatment.

Advanced age [60], [26], [4], [31], [32], [33], [80] and pre-existing dementia [80], [25], [31], [60], [26], [4], [45] are preoperative risk factors that are highly possible to cause postoperative delirium. There is some evidence that postoperative delirium may be the result of preoperative factors that include male sex [80], [25], [32], [33], history of cardiovascular disease [31], [80], history of congestive heart failure [120], [80], depression [26], [31], [6], reduced level of activities of daily life [80], [60], anticholinergic drugs [31], [26], [6], neuroleptic drugs [6], [31], antidepressants [31], [6]. On the other hand there is no convincing evidence that the following preoperative risk factors are associated with postoperative delirium; impaired sight and hearing, history of cerebrovascular disease, history of stroke [120], abnormal fluid and electrolyte parameters [80], [31], endocrine diseases [120], alcohol abuse [120], medicine abuse, prolonged waiting time for operation [80], [31], [32], [33], use of benzodiazepines and type of fracture [80], [60]. The only intraoperative risk factor that may be responsible for postoperative delirium has proven to be hypotension [31], [32], [33], [25]. There is no convincing evidence that postoperative delirium may be a direct or an indirect result of intraoperative risk factors such as morphine or benzodiazepines given as premedications, general or spinal and epidural anesthesia [6], anticholinergic drugs and hypoxia.

There is also no convincing evidence that a series of postoperative risk factors may cause postoperative delirium. These factors include pneumonia, urinary tract infection [25], elevated temperature, hypoxia, treatment with large doses of opioids, inadequate analgesia, inadequate nourishment, and postoperative fluid therapy.

# Prevention of post-operative delirium after hip fracture treatment

Prevention of delirium, particularly in older people, is of great importance. Education of medical and nursing staff can increase the recognition of the syndrome and knowledge of risk factors is probably the most important information to have. The fact that delirium is often multifactorial in origin necessitates a broad intervention strategy. Many studies have attempted to prove the effectiveness of interventions in various different settings but have suffered from being underpowered, non-blinded, or without identified and valid outcome measures [94]. Any consideration of the prevention of delirium should be influenced by an appreciation that there are predisposing and precipitating factors for the illness, and that the traditional view that any acute illness can be the cause of the syndrome ignores the fact that delirium not infrequently arises when a person is already in hospital. If there is too fulsome a concentration on the acute problem, the opportunity to intervene to ameliorate other risk factors may be missed [86].

A study was undertaken to determine the effect of music on elders undergoing elective hip and knee surgery who experience acute confusion and delirium postoperatively. Music listening was introduced as an intervention to an experimental group. Nurses documented episodes of acute confusion and delirium experienced by elders post-surgically. Scores from a readiness-to-ambulate profile to determine if patients were cognitively ready for postoperative therapy were evaluated. There was a significant decrease in the number of episodes of postoperative confusion among those in the experimental group compared with those in the non-listening control group. In addition, the experimental group had significantly higher scores on the readiness-to-ambulate profile than the control group. These findings indicate that music listening is an effective nursing intervention that can be used to decrease acute postoperative confusion and delirium in elders undergoing elective hip and knee surgery [97]. Another intervention programme consisted of staff education, co-operation between orthopaedic surgeons and geriatricians, individual care and planning of rehabilitation, improved ward environment, active nutrition, improved continuity of care and prevention and treatment of complications associated with delirium. The main result of the study was that the incidence of delirium was significantly lower than in all previously published studies. The incidence of other postoperative complications was also lower, and a larger proportion of the patients regained independent walking ability and could return to their previous living conditions on discharge. The intervention programme reduced the incidence and duration of delirium and improved functional outcome for elderly patients treated for femoral neck fractures [58].

Supplemental oxygen, when indicated and monitored by pulse oximetry, was the cause for the reduction in delirium in another study [15]. Regional analgesia using single-injection regional blocks and continuous neuraxial and peripheral catheters can play a valuable role in a multimodal approach to pain management in the critically ill patient to achieve optimum patient comfort and to reduce physiologic and psychological stress. By avoiding high systemic doses of opioids, several complications like withdrawal syndrome, delirium, mental status changes, and gastrointestinal dysfunction can be reduced or minimized [101].

Postoperative cognitive dysfunction (POCD) is quite frequent. If late POCD seemed not related to the type of anaesthesia and analgesia provided, early POCD (interval delirium) was found to be related to perioperative haematocrit and transfusion requirement and to postoper-

ative pain. Epidural analgesia using local anaesthetics and/or opioids was found to be probably better than parenteral opioids for the control of postoperative pain and the prevention of postoperative morbidity and mortality. However, well implemented protocols of parenteral analgesics could be nearly as efficient [16].

# Treatment of post-operative delirium after hip fracture treatment

Delirium is a medical emergency, and prompt attention to obvious precipitating factors should be the first aim of management. Four key steps in management have been described - addressing the underlying causes, maintaining behavioural control, preventing complications, and supporting functional needs. In practice, the commonest causes are drugs, infections, fluid balance and metabolic disorders, cerebral hypoxia, pain, sensory deprivation, urinary retention, and faecal impaction (especially in people with pre-existing dementia). Preoperative assessment of the patients physical and mental status and medications is very important. Pre-existing sensory or perceptual deficits compound a patients chances of developing confusional states. The mainstay of intra-operative preventive measures is maintaining good oxygenation, normal blood pressure, correct drug dosage and normal electrolyte levels. Drug cocktails should be avoided. Atropine, scopolamine and flurazepam should be used only if necessary, and the dose should be as low as possible. Glycopyrrolate may be a better choice than atropine as the former is a quaternary amine and should penetrate the blood-brain barrier less effectively than will atropine. Ambulatory surgery should be encouraged because elderly patients are maintained in the familiar home environment. Adequate postoperative analgesia, especially in patients who cannot communicate easily because of endotracheal tubes or tracheostomy, is crucial. Nurses should be well versed in detecting the earliest signs of delirium, which in the elderly may be withdrawal rather than agitation. The central nervous depressants, H2-antagonists, anticholinergics, digitalis, phenytoin, lidocaine and aminophylline should be used with discretion. In general, drugs with short elimination half-lives are preferable to long-acting drugs [14].

During the postoperative period patients are at high risk for delirium, but delirium occurring at this time is particularly amenable to therapeutic efforts. Systematic strategies to detect and manage the condition, which involve providing preoperative psychological support (education and reduction of anxiety), the use of patient controlled analgesia, and careful postoperative management, have significant benefits over traditional reactive care and can reduce the incidence of delirium [17], [79].

Many drugs may cause delirium, but particularly psychotropic agents. Anticholinergic drugs (or drugs with anticholinergic side effects like tricyclic antidepressants) are particularly potent sustances, and a careful drug history is essential. A raised white blood cell count or specific symptoms (such as a fever) may direct attention towards an infection, one cave at being that asymptomatic bacteriuria is common in older people, and the finding of a urinary tract infection does not necessarily mean that it is the cause of the symptoms. Dehydration can easily be treated with intravenous fluids. Congestive cardiac failure is another common cause of delirium, particularly in older people, its deleterious effect being mediated through cerebral hypoxia. Severe pain is a relatively unrecognised and readily treatable cause of delirium and is particularly associated with elective surgery [63], [38], [59].

While there are no randomised controlled trials of interventions such as noise control, light intensity, reassurance, and stimulus modification, these environmental manipulations are still recommended as an integral part of the management of delirium [2] (see Table 4).

Drug treatment of delirium requires careful consideration of the balance between the effective management of symptoms and potential adverse effects. Prescribing is often influenced by pressure from relatives, time constraints, or difficulties in communication between medical and nursing staff. The use of psychotropic drugs complicates the ongoing assessment of mental status, can impair the patient's ability to understand or cooperate with treatment, and is associated with a greater incidence of falls. It is therefore important to clarify the reasons for using drugs to treat delirium: is the primary aim to alleviate delirium or to contain problem behaviour?

Sedative compounds can improve agitation but may worsen cognitive impairment. A minority of patients require sedation to protect themselves. Less medication is required in cases in which delirium is identified early by screening, but there is a lack of studies of the effectiveness of pharmacological prophylaxis in high risk populations [10]. A careful analysis of the risks and benefits of drug treatment should be carried out before embarking on treatment. In some patients, the cessation of "deliriogenic" drugs may be effective. Early identification of the symptoms of delirium results in a reduced use of medicines [10].

Antipsychotic drugs are the mainstay of treatment and are effective in all types of delirium. Except in cases of delirium caused by alcohol or sedative hypnotic withdrawal, neuroleptics are the treatment of choice, resulting in improvement before elucidation of the underlying cause [82]. Neuroleptics ameliorate a range of symptoms, are effective both in patients with a hyperactive or hypoactive clinical profile, and generally improve cognition [2], [10], [92]. Chlorpromazine, droperidol, and haloperidol have similar effects, but haloperidol is preferred because it has fewer active metabolites, limited anticholinergic effects, less sedative and hypotensive effects, and can be administered by different routes [34], [2]. It has been shown that prophylactic haloperidol significantly reduces post-operative delirium compared with placebo in elderly patients undergoing hip surgery [46]. Although the use of high potency antipsychotic drugs like haloperidol brings

Table 4: Environmental factors in treating delirium

**Providing support and orientation**

- Communicate clearly and concisely; give repeated verbal reminders of the day, time, location, and identity of key individuals, such as members of the treatment team and relatives

- Provide clear signposts to patient's location including a clock, calendar, chart with the day's schedule

- Have familiar objects from the patient's home in the room

- Ensure consistency in staff (for example, a key nurse)

- Use television or radio for relaxation and to help the patient maintain contact with the outside world

- Involve family and caregivers to encourage feelings of security and orientation

**Providing an unambiguous environment**

- Simplify care area by removing unnecessary objects; allow adequate space between beds

- Consider using single rooms to aid rest and avoid extremes of sensory experience

- Avoid using medical jargon in patient's presence because it may encourage paranoia

- Ensure that lighting is adequate; provide a 40-60 W night light to reduce misperceptions

- Control sources of excess noise (such as staff, equipment, visitors); aim for <45 decibels in the day and <20 decibels at night

- Keep room temperature between 21.1°C to 23.8°C

**Maintaining competence**

- Identify and correct sensory impairments; ensure patients have their glasses, hearing aid, dentures. Consider whether interpreter is needed

- Encourage self care and participation in treatment (for example, have patient give feedback on pain)

- Arrange treatments to allow maximum periods of uninterrupted sleep

- Maintain activity levels: ambulatory patients should walk three times each day; non-ambulatory patients should undergo a full range of movements for 15 minutes three times each day

an increased risk of extrapyramidal side effects, the actual reported incidence is low [10], [48]. Intravenous administration of haloperidol seems to be less likely to cause extrapyramidal side effects in patients with delirium [74]. Droperidol is more suitable when a faster onset of action or greater sedation is required. Pimozide is a potent calcium antagonist and may be more appropriate for treating delirium that is accompanied by hypercalcaemia [66]. The dose of an antipsychotic drug is determined by the route of administration, the patient's age, the amount of agitation, the patient's risk of developing side effects, and the therapeutic setting. Low dose oral haloperidol (1 mg to 10 mg/day) improves symptoms in most patients. Olanzapine (5-10 mg) and risperidone (1.5-4 mg) have been used successfully in uncontrolled case series [104], [105], [106]. These atypical compounds cause less sedation and fewer extrapyramidal effects, and studies of neuropsychological effects in normal elderly volunteers suggest that they have other advantages [7]. However, they are only available in oral forms, and the advantage of using them for short term treatment, which is typical in delirium, is unclear. The adage in psychopharmacology in older people is "start low, go slow" and, if the patient's clinical condition allows, starting doses of 0.5 mg a day of haloperidol and risperidone and 2.5 mg a day of olanzapine are appropriate.

Other treatments such as anticholinesterase drugs have been used with some success, and serotonin antagonists such as trazodone may be helpful [118], [99]. Benzodiazepines are first line treatment for delirium that is associated with seizures or withdrawal from alcohol or

sedatives [67]. They are also a useful adjunctive treatment for patients who cannot tolerate antipsychotic drugs because lower doses can be used [73] and their effects can be rapidly reversed with flumazenil. The therapeutic aims of drug treatment should be explicit since anxiolytic, sedative, and hypnotic effects occur as doses are increased. Benzodiazepines can both protect against delirium and be a risk factor for it; this highlights the need for judicious use in patients dependent on alcohol or benzodiazepines. Lorazepam has several advantages such as its sedative properties, rapid onset, and short duration of action; it also has a low risk of accumulation; there are no major active metabolites; and its bioavailability is more predictable when it is given intramuscularly. Lower doses are necessary in elderly patients, those with hepatic disease, or those receiving compounds that undergo extensive hepatic oxidative metabolism (for example, cimetidine and isoniazid). The recommended upper limits for intravenous lorazepam are 2 mg every four hours [99]. Giving adequate initial doses reduces the risk of paradoxical excitement (that is, disinhibition with worsening of behavioural disturbance).

Disturbances of cholinergic metabolism are implicated in cases in which delirium is caused by hypoxia, traumatic brain injury, or hypoglycaemia, or is drug related. Anticholinergic delirium is generally treated conservatively by withdrawing the offending agent and occasionally by administering physostigmine [2]. Other procholinergic agents used to counter cholinergic deficits in dementia have theoretical potential but are not recommended owing to the risk of causing adverse effects.

Current smoking has been identified as a possible protective factor against delirium [19], but the usefulness of nicotine replacement treatment in protecting against delirium has not been tested. Trazodone and mianserin are antidepressant compounds that share antagonistic actions at 5-HT2 (serotonin) receptors. Open studies of low dose treatment of delirium with these compounds have found a rapid reduction of non-cognitive symptoms in particular. This effect was independent of the mood altering actions of the drugs [82], [85]. Other reports have advocated the use of light therapy [47], but the usefulness of this treatment needs to be more fully evaluated before it is used routinely.

Many patients with delirium are discharged before their symptoms are fully resolved; this factor must be accounted for in planning their care after discharge. The continuing need for rehabilitation must be explicitly documented. Problems with attention and orientation are especially persistent [53]. Further episodes may be prevented by addressing risk factors such as medication and sensory impairment. The psychological sequelae of delirium have not been studied enough, but depression and post traumatic stress disorder have been described. Most patients dismiss the episode of delirium once it has passed, but a significant minority have lingering concerns that an episode of delirium may represent the first step towards loss of mental faculties and independence. Other patients experience "silent delirium" and are ashamed or afraid to admit to symptoms. A post-hospital visit to the treatment environment can facilitate adjustment and clarify the transient nature of delirium symptoms [23].

## Conclusions

Hip fractures are a very common problem in elderly, especially in ages over 75 years old [49]. Due to the increased age of hip fractured patients many co-morbid situations are almost always present. Among these, psychiatric disturbances account for an important number of major post-operative complications, including post-operative delirium. Prefracture cognitive impairment and incident cognitive impairment during hospitalization are risk factors for poor functional outcomes [30]. In spite of the fact that post-operative delirium is a well recognised syndrome its pathophysiology remains poorly understood. Apart from that, very high numbers of under-recognition from both nursing and medical staff have been reported. These data lead to the disappointing fact that a large number of post-operative deliria are not prevented, although they could have been so, nor are they recognized and treated early. Proper education concerning the risk factors and the major clinical manifestations is cornerstone of post-operative delirium prevention and principles and practice of its treatment. A systematical approach to elderly hip-fracture patients could lead to proper identification of risk factors for development of post-operative delirium and early recognition of the first clinical signs that would be helpful both for the prevention and the immediate treatment of the disease resulting in better outcomes.

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