14.1 GENERAL PRINCIPLES

- Delirium can be defined as: “A transient organic brain syndrome characterised by the acute onset of disordered arousal and cognition, accompanied by disturbances of perception and psycho-motor behaviour.” ¹

- The prevalence of delirium in advanced cancer is between 25-80%. It often has multiple aetiologies. ², ³

- Delirium is often unrecognised in patients with advanced cancer but early detection may lead to improved patient outcomes. ³, ⁴

14.2 GUIDELINES

14.2.1 Assessment of Delirium

- Delirium is a clinical diagnosis. Table 14.1 outlines the DSM IV criteria necessary for diagnosis and some of the commonly listed clinical features. ¹ [Level 4]

<table>
<thead>
<tr>
<th>Table 14.1</th>
<th>Diagnosing delirium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Diagnosis</td>
<td>Associated Clinical Features</td>
</tr>
<tr>
<td>All of the following should be present:</td>
<td>Some of the following may be present:</td>
</tr>
<tr>
<td>- Disordered consciousness</td>
<td>- Poor concentration</td>
</tr>
<tr>
<td>- Change in cognition</td>
<td>- Disorientation</td>
</tr>
<tr>
<td>- Fluctuation</td>
<td>- Loss of short term memory</td>
</tr>
<tr>
<td>- Developing over a short period</td>
<td>- Hallucinations</td>
</tr>
<tr>
<td>- Aetiologically related to a medical condition</td>
<td>- Paranoid ideas</td>
</tr>
<tr>
<td></td>
<td>- Restlessness or aggression</td>
</tr>
</tbody>
</table>

- Delirium may be hyperactive or hypoactive. Hypoactive delirium is more common than hyperactive delirium in palliative care patients, although is often not diagnosed. ⁵ [Level 4]

- Features of hypoactive delirium include slowed motor function, lethargy, confusion and decreased awareness and interaction with their surroundings. These features may mimic depression. ⁵ [Level 2-]

- The role of neuroleptic medication in hypoactive delirium is uncertain at present. ⁵ [Level 4]
14.2.2 Reversible causes of delirium

- Delirium is often reversible although this may not apply in the last 24-48 hours of life. 4 [Level 2-]
- Some of the potentially reversible causes of delirium are listed in Table 14.2. 2, 6 [Level 4]

<table>
<thead>
<tr>
<th>Table 14.2 Reversible causes of delirium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
</tr>
<tr>
<td>Biochemical abnormalities e.g.</td>
</tr>
<tr>
<td>hypercalcaemia, uraemia</td>
</tr>
<tr>
<td>Cardiovascular causes</td>
</tr>
<tr>
<td>Cerebral pathology</td>
</tr>
<tr>
<td>Constipation</td>
</tr>
<tr>
<td>Drugs</td>
</tr>
</tbody>
</table>

14.2.3 Management of delirium

- It is important to use both pharmacological and non-pharmacological measures in the management of a patient with delirium. 2 [Level 4]
- Non-pharmacological measures may include: a well-lit and quiet room, familiar faces, explanation, reassurance and the avoidance of isolation and loneliness. 2 [Level 4]
- Drugs, in particular opioids, are a common cause of delirium. A review of medication, including drugs recently discontinued, should be performed. 4 [Level 2-]
- If the patient is distressed, delirium may require specific drug management. Table 14.3 lists the pharmacological options. 7, 8, 9, 10 [Level 2+]
- Neuroleptics such as haloperidol and atypical antipsychotics remain the drugs of choice. 6 [Level 2++]
- Benzodiazepines may exacerbate delirium and should be used with caution. 6, 7, 8 [Level 2++]
- The aim of treatment should be to control the delirium. The treatment may at times cause a reduction in the level of consciousness. 9 [Level 4]
- The aim of treatment and any expected change in level of consciousness should be discussed with the patient, relatives and multi-disciplinary team where possible and documented in the case notes. 11 [Level 4]
- Figure 14.1 outlines a pharmacological approach to the management of delirium. Drugs should only be used when the delirium is causing distress to the patient and should be titrated according to clinical need. The manifestation of distress may influence the treatment used e.g. overlying anxiety may be better treated with benzodiazepines; paranoia may be better managed with neuroleptics. 7, 8, 12 [Level 4]
14.2.4 **Committee on Safety of Medicines (CSM) warning for olanzapine and risperidone**\(^{13,15}\) [Level 2]

- Olanzapine and risperidone are associated with an increased risk of stroke in elderly patients with dementia. The CSM has advised the following:
  - Risperidone or Olanzapine should not be used for treating behavioural symptoms of dementia.
  - In acute psychotic conditions in elderly patients with dementia, risperidone should be limited to short term use under specialist advice. Olanzapine is not licensed for the management of acute psychoses.
  - The possibility of cerebrovascular events should be considered carefully before treating any patients with a history of stroke or transient ischaemic attacks. Risk factors for cerebrovascular disease should also be considered e.g. hypertension, diabetes, smoking, atrial fibrillation.

- Observational studies suggest that similar to the atypical antipsychotics, treatment with conventional antipsychotic drugs may increase mortality.\(^ {16}\) [Level 3]

14.2.5 **Mental Capacity**

- Where the patient is shown to lack the capacity to consent to treatment, the Mental Capacity Act 2005 must be followed. Lasting Power of Attorney, Advanced Decisions and Independent Mental Capacity Advocates should be utilised where appropriate.\(^ {11,14}\) [Level 4]
Figure 14.1 Pharmacological management of delirium in advanced cancer [Level 4]

Diagnosis of delirium using DSMIV criteria.

Reversible causes investigated and treated where appropriate.

Is patient able to swallow?

YES

Start haloperidol 0.5mg-5mg orally at night.

Are there any side effects?

NO

Continue regimen.

YES

Consider atypical anti-psychotic e.g. Olanzapine.

Dose: 2.5mg orally at night and as required.

Prescribe haloperidol 0.5mg-3mg subcutaneously prn.
Consider haloperidol 3mg-10mg as a subcutaneous infusion via a syringe driver over 24 hours.

NB. Drug treatment only indicated where the patient is distressed.

NB. Subcutaneous: oral potency of haloperidol is 2:1.
<table>
<thead>
<tr>
<th>Name of drug</th>
<th>Class of drug</th>
<th>Dosage</th>
<th>Side effects</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol</td>
<td>Long acting dopamine antagonist.</td>
<td>Oral 0.5mg-5mg tds orally. Maximum dose 30mg/24 hours Subcutaneous 1.5mg-5mg as subcutaneous bolus dose every 8 hours 5mg-10mg subcutaneously via syringe driver over 24 hours. Maximum parenteral dose is 18mg in 24 hours.</td>
<td>Extra-pyramidal reactions.</td>
<td>First line treatment for delirium. Note. The parenteral dose should be lower than the corresponding oral dose because of the absence of first pass metabolism. The same dose should not be prescribed for both routes.</td>
</tr>
<tr>
<td>Levomepromazine</td>
<td>Long acting phenothiazine.</td>
<td>Oral 12.5mg-50mg orally daily. Subcutaneous 6.25mg-25mg as subcutaneous bolus dose every 6-8 hours 12.5mg-200mg subcutaneously via syringe driver over 24 hours.</td>
<td>High risk of sedation High doses may precipitate seizures.</td>
<td>In a patient with a history of seizures consider the addition of midazolam. Note. The parenteral dose should be lower than the corresponding oral dose because of the absence of first pass metabolism. The same dose should not be prescribed for both routes.</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>Atypical antipsychotic.</td>
<td>Usually given orally 2.5mg-10mg daily Can be given by CSCI but specialist advice should be sought</td>
<td>Weight gain, drowsiness, dry mouth. See guidelines for CSM warning.</td>
<td></td>
</tr>
<tr>
<td>Risperidone</td>
<td>Atypical antipsychotic.</td>
<td>500micrograms orally initially. Increase by 500micrograms bd alternate days. Maintenance dose usually 1-3mg / day. Maximum dose is 4mg daily.</td>
<td>Weight gain, drowsiness, dry mouth. See guidelines for CSM warning.</td>
<td>May need lower starting dose and slower titration in elderly patients and patients with renal impairment. Interacts with CYP2D6 inhibitors e.g. fluoxetine so some drug interactions may be significant.</td>
</tr>
<tr>
<td>Midazolam</td>
<td>Short acting benzo-diazepine.</td>
<td>2.5mg-10mg as subcutaneous bolus doses. 10mg-100mg subcutaneously via syringe driver over 24 hours.</td>
<td>Possible paradoxical agitation.</td>
<td>Will not improve cognition in delirium.</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Short acting benzodiazepine.</td>
<td>2mg-15mg orally daily in divided doses. 10mg via rectal route prn. 5mg-10mg intravenously prn.</td>
<td>Possible paradoxical agitation.</td>
<td>Will not improve cognition in delirium.</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>Long acting barbiturate.</td>
<td>100mg-200mg as bolus intramuscular injections. 600mg-2400mg subcutaneously via syringe driver over 24 hours.</td>
<td>Used in the dying phase to as third line agent to control agitation/delirium. Can use sodium chloride 0.9% or water as diluent but anecdotal evidence suggests may get fewer side reactions with sodium chloride 0.9%.</td>
<td></td>
</tr>
</tbody>
</table>
14.3 STANDARDS

1. The DSM IV criteria should be used in the diagnosis of delirium. [Grade D]
2. Reversible causes of delirium should be treated where appropriate. [Grade D]
3. All patients should have a clinical examination at initial assessment of delirium. [Grade D]
4. All patients should have a review of medication at initial assessment of delirium. [Grade D]
5. The reason for the use of psychotropic medication should be documented in the case notes. [Grade D]
6. Haloperidol is the drug of choice for the management of delirium where the cause is unknown. [Grade C]
7. Inpatients with delirium should be reviewed every four hours to ensure adequate symptom control. [Grade D]

14.4 REFERENCES


14.5 CONTRIBUTORS

<table>
<thead>
<tr>
<th>Lead Contributors</th>
<th>External Reviewer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr C Finnegan</td>
<td>Dr A Thorns</td>
</tr>
<tr>
<td>Specialist Registrar in Palliative Medicine</td>
<td>Consultant in Palliative Medicine</td>
</tr>
<tr>
<td>St Johns Hospice</td>
<td>St Pilgrims Hospice in Thanet</td>
</tr>
<tr>
<td>Wirral</td>
<td>Margate</td>
</tr>
</tbody>
</table>

Dr F Ahmad
Specialty Registrar in Palliative Medicine
Loros Hospice
Leicester

Dr K Marley
Specialty Registrar in Palliative Medicine
Marie Curie Hospice
Liverpool

Dr C Lewis-Jones
Consultant in Palliative Medicine/Medical Director
St Johns Hospice
Wirral
and
Wirral University Teaching Hospital NHS Foundation Trust

Dr A Fountain
Consultant in Palliative Medicine
Halton and St Helens Primary Care Trust
Halton

Dr L Beddows
Consultant in Old Age Psychiatry
St Catherine’s Hospital
Wirral