



# **Guidelines for the Management of Agitation & Delirium**

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## CONTENTS

| <b>SECTION</b> | <b>TITLE</b>   | <b>PAGE</b> |
|----------------|--|-------------|
| 1.             | INTRODUCTION   | 1           |
| 2.             | COMMON POTENTIALLY REVERSIBLE CAUSES OF DELIRIUM                             | 1           |
| 3.             | DIAGNOSING DELIRIUM  | 1           |
| 4.             | NON-PHARMACOLOGICAL MEASURES FOR THE MANAGEMENT OF BOTH AGITATION & DELIRIUM | 2           |
| 5.             | PHARMACOLOGICAL MANAGEMENT OF DELIRIUM                                       | 3           |
|                | 5.1 Drug Options in Order of Use   | 3           |
|                | 5.2 Haloperidol  | 3           |
|                | 5.3 Olanzapine   | 4           |
|                | 5.4 Lorazepam & Midazolam  | 4           |
|                | 5.5 Levomepromazine  | 5           |
| 6.             | PHARMACOLOGICAL MANAGEMENT OF AGITATION                                      | 5           |
|                | 6.1 Lorazepam  | 5           |
|                | 6.2 Midazolam  | 6           |
|                | 6.3 Levomepromazine  | 6           |
|                | 6.4 Phenobarbital  | 6           |
| 7.             | COMMUNICATION & DECISION MAKING  | 6           |
| 8.             | REFERENCES   | 7           |
|                | <b>APPENDICES:</b>   |             |
|                | Appendix 1: The Confusion Assessment Method (CAM)                            |             |
|                | Appendix 2: Diagnostic Algorithm for the Detection of Agitation & Delirium   |             |

## 1. INTRODUCTION

This policy is dealing with those patients who are dying, and have delirium and/or agitation at the end-of-life. Both are common in palliative care patients at the end-of-life, with incidence as high as 85%. Many causes are reversible and must be excluded e.g. infection / steroids / nicotine withdrawal. The assumption for this guidance is that the patient is dying with advanced and irreversible disease but may not be in the last days of life.

Delirium and agitation at the end of life can be difficult to manage in some patients. It is essential the correct management comprises non-pharmacological as well as pharmacological approaches. Both have a number of possible underlying causes and these overlap.

Agitation without delirium can occur as a result of anxiety or psychological/spiritual distress and commonly due to unrelieved constipation or urinary retention.

This policy advocates a '**THINK DELIRIUM**' and **STEPWISE** approach. All patients who exhibit signs of agitation should be assessed for delirium and a management plan agreed and documented based on this assessment. Misdiagnosis of delirium as agitation can result in unnecessary distress for the patient as symptoms may be treated incorrectly.

**DELIRIUM** is reversible in up to 50% of cases, therefore potentially reversible causes must have been excluded.

## 2. COMMON POTENTIALLY REVERSIBLE CAUSES OF DELIRIUM

- Alcohol
- Biochemical abnormalities e.g. hypercalcaemia, uraemia
- Cardiovascular causes
- Cerebral pathology
- Constipation
- Dehydration
- Haematological causes
- Infections
- Medications e.g. opioids & steroids
- Nutritional deficiencies
- Withdrawal from alcohol / nicotine
- Withdrawal from drugs e.g. antipsychotics, benzodiazepines, opioids

Managing delirium needs a multidisciplinary and multimodal approach including both pharmacological and non-pharmacological approaches. The main barrier to optimal management of delirium is poor detection and misdiagnosis.

## 3. DIAGNOSING DELIRIUM

There are different sub-types of delirium below which can present with different clinical features:

- Hyperactive delirium: Characterised by heightened arousal. Patients can be restless, agitated or aggressive

- Hypoactive delirium: Characterised by withdrawal. Patients can be quiet or sleepy
- Mixed delirium

All forms of delirium can be diagnosed on the basis of clinical features. The clinical diagnostic criteria for the diagnosis of delirium are shown in the table 1 below:

| <b>Table 1: DSM – V Criteria for the Diagnosis of Delirium</b> |  |
|--|--|
| <b>A</b>   | Disturbance in attention e.g. reduced ability to direct, focus, sustain and shift attention and awareness (reduced orientation to the environment).  |
| <b>B</b>   | The disturbance develops over a short period (usually hours to days), represents an acute change from baseline attention and awareness and tends to fluctuate during the course of the day.  |
| <b>C</b>   | Change in cognition e.g. memory deficit, disorientation, language disturbance, perceptual disturbance.   |
| <b>D</b>   | The disturbances in Criteria A and C are not better explained by a pre-existing, established or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal such as coma.  |
| <b>E</b>   | There is evidence from the history, physical examination or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal e.g. due to drug abuse or medication or exposure to a toxin or multiple aetiologies. |

To aid in correct diagnosis of delirium by health professionals, these criteria have been developed in to a screening tool named the Confusion Assessment Method (CAM). This should be used to determine if a patient has delirium, when this diagnosis is suspected on the basis of the above clinical features. The CAM can be found in Appendix 1.

If delirium is diagnosed using this tool, management should comprise both non-pharmacological and pharmacological approaches outlined below. Agitated patients who do not meet the diagnostic criteria for delirium should be treated appropriately for agitation

#### **4. NON-PHARMACOLOGICAL MEASURES FOR THE MANAGEMENT OF BOTH AGITATION & DELIRIUM**

- Familiar environment
- Familiar healthcare team
- Adequate lighting
- Visible clock and calendar
- Sensory impairment aids
- Mobility aids
- Maintain good sleep hygiene
- Cognitively stimulating activities
- Effective communication
- Re-orientation

- Reassurance
- Consider involving family / those important to the patient / carers to help with this
- Verbal / non-verbal techniques to manage distress

It should be recognized that the types of non-pharmacological measures used should be tailored to the patient in the context of their clinical situation. For example, it may not be in the patient's best interests to keep them in a bay to help orientate them, if they are also felt to be in the last hours of life.

## 5. PHARMACOLOGICAL MANAGEMENT OF DELIRIUM

Ensure all reversible causes are being addressed.

The use of medication to relieve delirium can be challenging and needs an MDT approach.

Combinations of antipsychotic medications should be avoided where possible to avoid side effects. If found to be ineffective, an antipsychotic medication should be titrated up to its full dose before being abandoned in favor of the next line alternative.

**Benzodiazepines should not be used in isolation to treat delirium as they can worsen the condition**, they can be added to antipsychotic therapy for patients with hyperactive delirium to enhance the treatment efficacy.

Antipsychotic medications should be used at the lowest possible dose for the lowest possible time to avoid unnecessary side effects.

### 5.1 Drug Options in Order of Use

|        |   |
|--------|---|
| Step 1 | Haloperidol OR Olanzapine   |
| Step 2 | Benzodiazepine <b><u>in addition to</u></b> Haloperidol or Olanzapine |
| Step 3 | Levomepromazine (+phenobarbital if severe and uncontrolled symptoms)  |

### 5.2 Haloperidol

- Haloperidol is an antipsychotic medication
- The Haloperidol dose should be halved when converting from oral to subcutaneous administration unless the overall dose is small and this would not be practical.
- Haloperidol when given once daily due to the sedative side effects of Haloperidol, it should be given in the evening time
- Haloperidol can be delivered via syringe driver
- Haloperidol should be used with caution in patients with cardiac abnormalities and / or seizures and should be avoided in patients with Parkinson's Disease
- The maximum dose of Haloperidol is 8mg in 24 hours orally or SC.

#### **Doses:**

1<sup>st</sup> line doses 0.5mg-1.5mg PO stat followed by prn 2-hourly.

2<sup>nd</sup> line doses 0.5mg-1.5mg SC stats or 1.5mg-3mg stats if symptoms severe.

Syringe pump driver dose 1.5mg-8mg/24 hours via continuous subcutaneous infusion (CSCI).

If breakthrough dose is unsuccessful in relieving the symptoms of delirium, then a dose of Benzodiazepines should be co-administered.

If a patient's symptoms are not well controlled on regular dosing, titrate the dose up by 1.5mg every 24 hours. If the medication is causing drowsiness, this dose can be split across morning and night.

### **5.3 Olanzapine**

- Olanzapine is an antipsychotic medication
- There is no evidence to suggest dose alteration when switching from oral to subcutaneous administration
- When given once daily, due to the sedative side effects of Olanzapine, it should be given in the evening time
- Olanzapine can be delivered via syringe driver and should be diluted in water for injection
- Olanzapine should be used with caution in patients with cardiac abnormalities and / or seizures and, when given subcutaneously **is the preferred medication for patients with Parkinson's Disease in the last hours to days of life**
- The maximum dose of Olanzapine is 10mg in 24 hours
- Olanzapine is not licensed for treatment of delirium and the injectable formulation needs to be ordered on a named patient basis

#### **Doses:**

1<sup>st</sup> line doses    2.5mg PO or SC stat followed by prn 2-hourly.

Syringe pump driver dose 2.5mg-10mg/24 hours via continuous subcutaneous infusion (CSCI).

If breakthrough dose is unsuccessful in relieving the symptoms of delirium, then a dose of Benzodiazepine should be co-administered, Lorazepam or Midazolam as appropriate.

If a patient's symptoms are not well controlled on regular dosing, titrate the dose up by 2.5mg po every 24 hours. If the medication is causing drowsiness, this dose can be split across morning and night.

### **5.4 Lorazepam and Midazolam**

- Lorazepam and Midazolam are Benzodiazepine medications
- Neither should be used for the treatment of delirium without co-prescription of an antipsychotic medication
- Lorazepam and Midazolam can be used prn to potentiate the effects of antipsychotics in the treatment of symptoms of delirium

For further guidance on Lorazepam and Midazolam and appropriate dosing please see the agitation section of this document.

### **5.5 Levomepromazine**

- Levomepromazine is used for delirium if Haloperidol or Olanzapine plus augmentation with Midazolam is unable to manage the symptoms adequately
- It is an antipsychotic from the Phenothiazine class
- Commonly used in Palliative Care as an anti-emetic and at higher doses for terminal agitation not settling with Midazolam
- Usually used in conjunction with Midazolam
- 0.9% sodium chloride to be used as the diluent
- Onset of action 30 minutes duration of action up to 24 hours
- Side effects include hypotension and lowering the seizure threshold thereby increasing the likelihood to have a seizure. It is contraindicated in patients with Parkinson's Disease
- Patients at high risk of seizures should have Midazolam co-administered to lessen the risk of seizures

#### **Doses:**

|                       |   |
|-----------------------|---|
| Breakthrough SC doses | 12.5mg-25mg PRN (up to 50mg if symptoms severe) |
| CSCI doses            | 50mg-200mg/24 hours                             |

If a patient's symptoms are not well controlled, titrate the dose up by 25mg-50mg SC every 24 hours.

## **6. PHARMACOLOGICAL MANAGEMENT OF AGITATION**

Sections 2 and 4 of this policy outline the potentially reversible causes and non-pharmacological management for both agitation and delirium. In addition agitation can be caused by:

- Pain
- Urinary retention
- Anxiety
- Depression/psychiatric illness
- Existential distress

#### **Drugs in order of use**

Step 1 Lorazepam or Midazolam

Step 2 Benzodiazepine + Levomepromazine

Step 3 Midazolam + Levomepromazine + Phenobarbital

### **6.1 Lorazepam**

- Lorazepam can be given SL, PO, PR, SC, IM or IV

- This policy advocates the use of Lorazepam via the oral route
- Side effects include drowsiness, impaired psychomotor skills, cognitive impairment and hypotonia (which may result in falls)
- Paradoxical agitation and hyper-arousal can occur

**Doses:**

0.5-1mg PO PRN 4 hourly MAX 4mg in 24 hours

**6.2 Midazolam**

- Midazolam can be given via the SC, IV or buccal route
- This policy advocates use of the SC route
- Side effects are those of the benzodiazepine class as above

**Doses:**

2.5 – 10mg SC prn  
CSCI – 10 – 60mg over 24 hours

**6.3 Levomepromazine**

- Refer to section 5.5

**6.4 Phenobarbital**

- Phenobarbital is a long acting barbiturate
- It may be used for agitation and delirium in the imminently dying where a combination of Midazolam and Levomepromazine are ineffective
- Stat doses are given IM as the formulation can be an irritant given SC. When given via a syringe driver it should be diluted with WFI to 10 times its volume and not mixed with any other drug

**Doses:**

- 100-200mg IM PRN
- 600-2400mg via CSCI/24 hours (exceptionally 3800mg)

**In exceptional cases where agitation persists despite maximal therapy Propofol can be considered. This decision should always be made by the senior doctor responsible for the Inpatient Unit and in consultation with anaesthetist colleagues.**

**7. COMMUNICATION & DECISION MAKING**

Discussion with the patient (where possible) and those important to the patient should be undertaken when a diagnosis of delirium or agitation is reached and should include an explanation of the diagnosis and the potential for reversibility.

Providing written information on the causes and management for those close to the patient may help improve their understanding and confidence in making decisions.

If the patient recovers from an episode of delirium or agitation it is important to offer information to the patient about what happened and the treatment decisions which were made, acknowledging that patients may not recollect fully the details.

Patients suffering from delirium and/or agitation may lack mental capacity to make decisions regarding their care. In these circumstances a full mental capacity assessment should be undertaken and documented, and if the patient is found to lack capacity, decisions should be made in their best interest in accordance with the Mental Capacity Act 2005. Communication with patients and those important to them is essential through this process.

## **8. REFERENCES**

Merseyside and Cheshire Palliative Care Network Audit Group Standards and Guidelines 2010

Palliative Care Formulary 5<sup>th</sup> Edition 2015

Crawford GB, Agar M, Quinn SJ, Phillips J, Litster C, Michael N, Doogue M, Rowett D, & Currow DC. Pharmacovigilance in Hospice/Palliative Care: Net Effect of Haloperidol for Delirium. *Journal of Palliative Medicine*. 2013; **16(11)**: 1335-1341.

Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegel AP, Horwitz RI. Clarifying Confusion: the confusion assessment method. A new method for detecting delirium. *Ann Internal Med*. 1990; 113:941-948

**Confusion Assessment Method (CAM) Diagnostic Algorithm**

|                            |  |                            |  |
|----------------------------|--|----------------------------|--|
| <b>Date of Assessment:</b> |  | <b>Time of Assessment:</b> |  |
|----------------------------|--|----------------------------|--|

|          |  | Yes | No |
|----------|--|-----|----|
| <b>1</b> | Acute onset and fluctuating course? (Acute change in mental status from baseline, fluctuating behavior through the day).                   |     |    |
| <b>2</b> | Inattention? (Difficulty focusing attention, easily distracted, difficulty keeping track of what is being said).                           |     |    |
| <b>3</b> | Disorganised thinking? (Disorganised or incoherent thinking, rambling or irrelevant conversation, unclear or illogical flow of ideas).     |     |    |
| <b>4</b> | Altered level of consciousness? (This feature is shown by any answer other than 'alert', including hyperalert, lethargic, stupor or coma). |     |    |

**The diagnosis of delirium by CAM requires the presence of features 1 and 2 and either 3 or 4.**

|                    | Yes | No |
|--------------------|-----|----|
| Delirium detected? |     |    |

**Diagnostic Algorithm for the Detection of Agitation and Delirium**