

Managing terminal restlessness

Terminal restlessness presents many challenges, not least recognition of the problem and its causes.



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While we can do a lot to ease the discomfort and suffering of dying patients, dealing with terminal restlessness still presents us with a number of challenges. The first is to recognise the problem, the second is to discover its cause and the third is to deal with the situation effectively, compassionately and ethically. Helping the terminally ill to achieve a peaceful, dignified death is a very satisfying professional task. In contrast, allowing such a person to remain restless is not only distressing to the family, the staff and the other patients but the grief of the bereaved may also be compounded by the memory of unrelieved suffering.

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RECOGNISING THE PROBLEM

As the dying enter the final phase of life, most wish to slip into a coma and not wake up again. However, instead of a peaceful parting, we are sometimes confronted by a restless, noisy, aggressive patient. 'Dying crazy' is frightening to all and can even be dangerous to the staff and other patients. By recognising this as a situation that demands urgent attention and effective treatment, we can avoid an even greater disaster.

Look for the following features:¹

- **Sudden onset and fluctuating course.** It is often unexpected. While the patient may have seemed calm when you did your morning ward round, as darkness comes, the mild Dr Jekyll turns into the monstrous Mr Hyde.
- **Inattention.** Is the patient easily distracted? Is he following what you are saying?
- **Muddled thinking.** Check orientation and short-term memory. Is the speech incoherent or rambling? Are hallucinations or delusions present?
- **Altered level of consciousness.** Is the patient drowsy or over-vigilant and afraid? Fear is the most common emotional symptom of delirium.

The presence of these features should alert you to the possibility that the patient is delirious. Making a definite diagnosis of delirium is vital so that appropriate action can be taken. It is important to differentiate between delirium and dementia. Dementia has a more insidious onset with progressive impairment of memory, judgement and thinking. In dementia there is also a lack of fluctuation in symptoms and no alteration of the level of consciousness.

Delirium has been shown to be present in the last 2 weeks of life in more than 80% of patients with advanced cancer and 60% of terminal AIDS patients.² Some delirious patients are inactive with evidence of confusion, drowsiness and inattention. Others are overactive with agitation, aggression and hallucinations. However, more than 60% will have features of both

types and may fluctuate from one extreme to the other. Unfortunately delirium is frequently not properly recognised and as a result, it is often badly managed. In its early stages delirium may be mistaken for anxiety, anger, psychosis or even depression.

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DISCOVERING THE CAUSE

Having recognised its presence, is it really necessary to find the cause of the delirium? After all, the patient is dying, the causes are often multiple and irreversible, and let us not forget that our resources are limited. How will it benefit the dying person? Are we not just prolonging dying? These are important questions. The purpose of looking for the cause is not just academic curiosity, it is motivated by the knowledge that in about a third of delirious advanced cancer patients, the cause can be reversed. This is especially true if the delirium is drug induced, or the result of hypercalcaemia, infection or the all too easily overlooked impacted rectum and urine retention.³

There are several ways of remembering the myriad of possible causes of delirium. The acronym DIM-TOP is a handy one and has been slightly modified to suit this topic. This stands for drugs, infection, metabolic, trauma, oxygen lack and pressure.

Drugs

While many drugs may lead to delirium, only those that are commonly used in the care of dying patients will be considered here.

With the improved management of the severe pain of advanced cancer has come a rise in the incidence of opioid-induced neurotoxicity.⁴ Although the safety and efficacy of large doses of morphine has been adequately demonstrated, we need to be on the look-out for delirium associated with myoclonic jerking and an unexpected increase in pain. This situation is likely to arise in patients on high doses of parenteral morphine in the presence of impaired renal function or dehydration. It is due to the accumulation of the metabolites of morphine, especially morphine-3-glucuronide (M-3-G) which irritates the central nervous system and blocks the analgesic effect of morphine. Discontinue the morphine or change to another opioid such as transdermal fentanyl. If appropriate, carefully rehydrate the patient and prescribe a benzodiazepine such as midazolam for a short while to stop the jerking. These measures should rapidly correct the problem.

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High doses of steroids such as dexamethasone are commonly used in advanced cancer especially for the palliative treatment of cachexia, anorexia, cerebral tumours, spinal cord compression and neuropathic pain. In susceptible individuals high-dose steroids can lead to agitation, paranoia and insomnia.⁵

Various drugs such as metoclopramide, haloperidol, ondansetron

and cyclizine are very effective in treating nausea in terminal patients. Occasionally motor restlessness (akathisia) due to the blocking of dopamine or delirium due to anticholinergic side-effects may occur.⁶ Withdrawal of the offending drug is usually all that is needed. In fact it is good practice to withdraw all drugs that are not absolutely necessary for the dying patient's comfort. When a patient develops symptoms suggestive of delirium one of the first things to do is to carefully review the patient's prescription.

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Infection

While the management of infection in a 'normal' patient is usually straightforward, in the context of the terminally ill there are several other factors to consider. Hypostatic pneumonia has rightly been called 'the old man's friend'. We need to be certain that treatment of infection will help towards the goal of comfort care. While it is usually helpful to treat a bladder infection if it is causing distress, we need to consider whether the treatment of other infections is merely prolonging suffering. In such circumstances, it would be better to 'give death a chance'. Robert Twycross, one of the doyens of palliative medicine in Britain, has rightly stated: 'A doctor has neither the duty nor the right to prescribe a lingering death.'⁷

However, in the context of the current AIDS epidemic we need a slightly different approach. Tuberculosis, *Pneumocystis carinii* pneumonia and other pneumonias,

MAIN TOPIC

cryptococcal meningitis and severe candidiasis may all contribute to delirium and will usually respond to specific treatment. These infections should always be excluded before embarking on comfort care only in the dying AIDS patient.

METABOLIC

Hypercalcaemia is the most common metabolic abnormality in advanced cancer and often presents as delirium.⁸ It occurs especially in breast, squamous cell, lung and renal carcinomas as well as in multiple myeloma. Treatment with fluid replacement and bisphosphonates is worth considering in the context of a patient who still has a good performance status.

Most dying patients stop eating and even drinking at the end of life. Apart from the use of parenteral fluids in the specific situations outlined above, their routine use has no place in dying patients. Intravenous fluids and the resulting

hyponatraemia have even been implicated as a cause of delirium. Many researchers have shown that dehydration rather than causing distress, actually facilitates patient comfort through decreased consciousness.³

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The delirium of hepatic or renal failure in a terminal patient is also not reversible.

Trauma

A fall and a chronic subdural haematoma is a possibility in frail terminal patients.

Lack of oxygen

When delirium is due to hypoxia, oxygen seldom results in any improvement in patients with advanced cancer. Sedation is more appropriate.³

Pressure

Intracranial tumours and raised intracranial pressure may cause delirium and may initially respond to high doses of steroids. Following a good response, the steroids can be tapered down to a low maintenance dose or even withdrawn.

DEALING WITH THE SITUATION

Having recognised the problem and, where possible, established the cause, it remains to deal with the situation effectively, compassionately and ethically.

Table 1. Drugs for managing delirium in terminal patients^{2,9}

Indication	Drug	Dosage	Route*
Calming an agitated patient	Haloperidol	1.5 - 20 mg/24 h 2.5 mg bolus over 2-3 min Repeat after 30 min if needed Give a double dose after a further 30 min if necessary 20 - 30 mg/24 h	PO, PR, SC IV
Sedation of an aggressive patient	Midazolam	2.5 - 5 mg bolus over 2 - 3 min, repeat until effective sedation is achieved 10 - 20 mg	SC infusion IV
Deep sedation of a violent patient	Propofol	30 - 100 mg/24 h 20 - 50 mg bolus over 5 min 5 - 70 mg/h	SC SC infusion IV IV infusion
Deep sedation	Phenobarbital	200 mg 800 - 1 600 mg/24 h	SC/IM SC infusion

PO = per os; PR = per rectum; SC = subcutaneous; IV = intravenous; IM = intramuscular.
*In most cases the SC route is preferable. It is almost as rapidly effective as IV without the risks or the difficulty of finding a vein in an aggressive patient. An SC infusion is also easy to maintain and does not require splinting or restraining of the patient's arm.

- Respond to the situation calmly and ensure the safety of the patient and the staff.
- Carefully explain what is happening to the relatives and if possible, even to the patient. It is important that the family understand that the patient is not 'mad' and that the prognosis is very poor with no curative options. They should understand the need to maintain sedation until the end.
- Where there is aggression ensure that an adequate number of staff are constantly with the patient until the situation is under control.
- Use appropriate drugs in effective doses. This is not the time to be hesitant or tentative.² The choice of drugs is determined by the desired intent (Table I).
 - If the patient is agitated and needs to be calmed, the best drug is haloperidol. Used in correct doses it is effective, safe and versatile.
 - If aggressive, the patient needs to be sedated. A good choice is a benzodiazepine such as midazolam.
 - In an extreme situation with a

violent patient, it may be necessary to sedate the patient by means of an anaesthetic agent such as propofol or a barbiturate. Ongoing sedation by means of an infusion pump will be needed. While some reject the use of such measures as bordering on euthanasia, the clear intent is to make the patient manageable and not to cause death. Sedation will, however, have to be maintained at an appropriate level until death occurs.

- The question of artificial feeding and hydration needs to be carefully considered together with the family. There is no evidence that either contribute to the comfort of the dying patient, and thus in most cases both are unnecessary.¹⁰ In the few cases where there is a definite reason for giving fluids parenterally, 1.5 l/24 hours can be given by the SC route (hypodermoclysis). This, together with good mouth care, is adequate under these circumstances.

There is a wide range in the reported prevalence of the use of sedation for refractory delirium in

the medical literature. Sedation is required in about 25% of terminal patients in palliative care units and of these about 50% will be for delirium.¹¹

References available on request.

IN A NUTSHELL

Delirium is common in dying patients.

To recognise the problem look for features such as inattention, muddled thinking, altered level of consciousness of recent onset and with a fluctuating course.

Although in many cases delirium in dying patients is irreversible, infection, hypercalcaemia, faecal impaction, urinary retention and certain drug interactions may be reversible.

If aggressive and violent, use appropriate drugs in effective doses to adequately sedate the patient.

Carefully explain the cause of the strange behaviour to the patient's family and help them to understand the poor prognosis and the need for effective sedation.

SINGLE SUTURE

Prophylactic oophorectomy can help women at risk of cancer

Women who have the BRAC1 or BRAC2 germ-line mutations have an increased risk of breast and ovarian cancer. Research was conducted to determine whether oophorectomy would reduce the risk of coelomic epithelial cancer and breast cancer in women who carry these mutations. A total of 259 women who had undergone oophorectomy, and 292 matched controls who had not undergone the procedure, were enrolled in the study. The results showed that bilateral oophorectomy reduced the risk of coelomic epithelial cancer and breast cancer in women with BRCA1 and BRCA2 mutations (Rebbeck TR *et al.* *N Engl J Med* 2002; **346**: 1616-1622).