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# A Holistic Approach to Delirium at the End of Life

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**Abstract**

Delirium at the end of life causes significant distress for patients, family and caregivers and its multi-factorial etiology makes management of this symptom challenging. Built around a case discussion of a delirious patient with terminal cancer at the end of life, a framework is proposed to aid healthcare teams tackle this problem holistically.

**Keywords:** Delirium; Palliative care; Terminal care

## Introduction

Delirium impairs the cognition and communication of patients, impairs effective care of patients at the end of life and bodes poorly upon their prognosis [1-2]. The manifestation of this complex neurocognitive syndrome often distresses family and care providers [3-5]. Within the palliative care setting, the reported prevalence of delirium ranges from 26%-62% upon admission and rising to 88% in the last days and hours of life [6]. The multifactorial nature of delirium at the end of life often sees it manifestations difficult to attenuate [7]. A holistic approach to management of this syndrome is required that must necessarily include consideration of the patient's burden of disease, goals of care, family concerns, social, cultural and religious sensitivities.

## Case Presentation

Soma was a 53 year old Indian gentleman with a background history of chronic obstructive pulmonary disease (COPD). He was diagnosed with Stage III cardio-esophageal adenocarcinoma in April 2014 and underwent a transhiatal total esophagogastrectomy. He was initially planned for adjuvant chemotherapy but defaulted follow up partially as a result of his faith in traditional medications and in part to his personal values and religious beliefs. When Soma represented with dysphagia and trimus in December 2015 he had an Eastern Cooperative Oncology Group (ECOG) performance status of 2 and was diagnosed with a tumour recurrence at the anastomosis with metastases to pleural, peritoneal and intramuscular sites.

Soma's pain which was attributed to the multiple soft tissue metastases within the masticator muscles, floor of the mouth, and submandibular spaces responded well to oral morphine 120 milligrams a day initiated by the palliative medicine team.

With palliative chemotherapy aiming for symptom control and prolongation of life planned.

Soma developed an infective exacerbation of his COPD. This precipitated a hyperactive delirious state that was distressing for both his family and the healthcare team. He was unable to communicate his symptoms properly although his facial expressions suggested fear and breathlessness and he constantly attempted to get out of bed and tug at his intravenous lines and oxygen mask.

Multiple factors were suspected of precipitating his delirium and all potentially reversible causes were addressed. He was treated for his pneumonia and COPD exacerbation with antibiotics, regular nebulizers, supplemental oxygen and steroids. Blood investigations revealed pre-renal acute kidney injury thus judicious hydration was carried out. Soma showed no signs of opioid induced neurotoxicity yet as a precaution his morphine was rotated to fentanyl due to its relative safety in renal impairment. A review of the drug chart showed no further medications that could precipitate an acute delirium. Haloperidol was initiated to attenuate his distress and confusion.

Soma was transferred to a private room to minimize excessive stimulation. His family were advised to stay by his side and were provided with regular updates, support and reassurance. Despite use of increasing doses of Haloperidol his symptoms worsened. Following a holistic review by the palliative care team and careful consideration of patient's and family's goals of care, the decision was made to add midazolam infusion for light sedation.

Soma passed away peacefully two days later. His management however drew significant discussion amongst the palliative care team. Here I share the fruits of our discussions as a team in the form of a holistic management of delirium in cancer at the end of life.

## Detecting and Diagnosing Delirium

The diagnosis of delirium is based on clinical assessment and is guided by standard criteria [8]. The DSM-5 diagnostic criteria for delirium [8] are as follows:

Disturbance in attention (i.e. reduced ability to direct, focus, sustain, and shift attention) and awareness.

Change in cognition (e.g. memory deficit, disorientation, language disturbance, perceptual disturbance) that is not better accounted for by a pre-existing, established or evolving dementia.

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

There is evidence from the history, physical examination or laboratory findings that the disturbance is caused by a direct

physiological consequence of a medical condition, an intoxicating substance, medication use, or more than one cause.

After diagnosing delirium, it is often classified into motor subtypes of hyperactive, hypoactive or mixed presentations. In clinical practice, a quick screening tool to assess for delirium before formal evaluation may be more practical. One common tool would be the Confusion Assessment Method (CAM) which is validated in the palliative care population [9]. It takes 5 minutes to complete and has reported sensitivity and specificity of 82% and 99% respectively [10]. It is important to be cognizant of the diagnostic and classification dilemmas in assessing delirium. The differential diagnoses to consider are wide and include pain, fatigue, mood disturbance, psychoactive medication effects and other causes of altered consciousness. In fact, hypoactive delirium in palliative care presents substantial diagnostic challenges as it is frequently undetected or misdiagnosed as depression [11,12].

Whilst delirium may also be associated with other comorbidities such as dementia which poses a diagnostic dilemma, I do not address this here given the context of the case.

### A contextualized approach

In order to provide individualized care, a holistic review is required. The loss of mental capacity renders the patient vulnerable and necessitates the need for best interest decisions based upon due consideration of the patient's particular situation, wishes, values and beliefs. In addition the wishes of the family and what can realistically be provided by the healthcare team should inform the decision making process.

### The relational rerspective

Within the Asian context, an individual possesses inextricable social, cultural, religious and familial ties. A careful consideration of these ties within the context of each case is vital. For example, Hindu culture believes in human interdependence and interconnectedness, which is understood to be the foundation of well-being. Interests in Asian families are often bi-directional - there is an equivalent concern about the impact of one's illness on the family [13,14].

### Religious rerspective

Generalization about Hindu patients at the end of life is difficult because their beliefs and attitudes will depend on education, class and religious tradition. However, hinduism provides key notions regarding a good death and such beliefs can influence care decisions. For example, a good death would include that it should be timely, in the right place, conscious and prepared, with the mind on God. All affairs should be set in order and last words are highly treasured. Bad deaths on the other hand are regarded as violent, premature and uncontrolled deaths in the wrong place at the wrong time, signified by vomit, faeces, urine and an unpleasant expression [15]. This would encourage a proactive approach towards symptom management of agitated delirium or even a pre-emptive exploration of the importance of a home demise.

### Sociocultural rerspective

Known sociocultural attitudes towards mental illnesses would suggest that the 'collectivist' nature of Asians leads to the perception that mental illnesses reflect flaws of the family. Similarly, 'bad deeds' and 'sins' committed in the present or past lives may be perceived as a cause of the mental illness leading to the stigmatization of those with these illnesses [16,17]. Equally important is awareness of our own attitudes towards delirium at the end of life. Delirium continues to be frequently underdiagnosed, misdiagnosed or undertreated by healthcare professionals, in part as a result of our own perceptions and as a result of premature labelling of delirium as "terminal" [18-20].

### Assessment of reversibility

The investigation of delirium requires a structured approach. Careful scrutiny of the timeline of events and its association with potential precipitating factors is sought. Studies of outcomes of delirium identify reversibility in up to 50% of cases [21,22].

It is important to balance investigative procedures against goals of care and the possibility of delirium reversal at all times. Only tests that will lead to specific management strategies should be ordered. For example, it may not be relevant to conduct brain imaging to identify brain metastases as the cause of delirium in a patient who is clearly nearing death and would not benefit from radiotherapy.

## Management of Delirium

Management of the symptoms of delirium must extend to care of the patient's family and caregivers [23,24].

### Non pharmacological interventions

Several evidence-based environmental interventions have been shown to minimize the risk and severity of symptoms associated with delirium [24-26]. These include:

reorientation and reassurance using familiar objects, family members, etc.

minimization of excessive stimulation e.g. loud music, bright lights, crowding around the bed

ensuring that hearing and vision aids are readily available if necessary

the presence of a hydration regime

an effective bladder and bowel regimen

avoidance of restraints and clinical interventions wherever possible

avoidance of disruption of the patient's normal sleep/wake cycle

### Pharmacological interventions

There is limited evidence to support the use of antipsychotics in palliative care patients with delirium. Much of prevailing management routines are guided by expert opinion and extrapolation from studies of delirium in non-palliative care settings. These studies describe some evidence of symptom resolution or improvement after starting of antipsychotics. There is no convincing evidence to suggest that any one agent or drug class is superior to another [27].

The only study of palliative care patients looked at 30 terminally ill AIDS patients, in which both haloperidol and chlorpromazine were found to be clinically effective [28]. In this study use of lorazepam was found to aggravate the symptoms of delirium. The published results of a phase III multicenter Australian study in palliative care patients

comparing orally administered haloperidol, risperidone and placebo is awaited [29].

Haloperidol remains the "practice standard" for short-term symptom control and regularly given to patients with hyperactive delirium. There is also data of its effectiveness in the treatment of hypoactive delirium [30]. There is however no convincing evidence to suggest that any one agent or drug class of antipsychotic is superior to another. A practical approach to the usage of haloperidol would be to start with 0.5 mg subcutaneously and increase the dosages progressively (e.g. 0.5 mg>1 mg>1.5 mg etc.) to obtain symptom control. The maintenance dose is based on the initial cumulative dose needed to settle the patient. Consideration should be made towards switching to a more sedating antipsychotic or adding on a benzodiazepine if delirium remains difficult to control [31].

Psychostimulants such as methylphenidate have been reported to help with hypoactive delirium but the evidence is limited [32]. As benzodiazepines may precipitate or exacerbate delirium, they are not routinely used unless the delirium is caused by benzodiazepine or alcohol withdrawal or is related to seizures. However they may play a limited role in combination with antipsychotics.

While deciding on pharmacotherapy, one should be aware of the possible harms and side effects. For example, Extrapyramidal Side Effects (EPS) of antipsychotics are the most commonly reported adverse events and are reported for both typical and atypical agents without any strong evidence of greater incidence or prevalence for one agent over another. Haloperidol can cause potentially fatal prolonged of QT interval and torsade de pointes. Caution is needed in patients with an underlying predisposition e.g. cardiac abnormalities, hypothyroidism, familial long QT syndrome, electrolyte imbalance (particularly hypokalemia or hypomagnesaemia) or taking drugs which prolong the QT interval.

### Additional considerations

**Impact on family and caregivers:** The family and caregivers of a delirious patient are often subject to severe distress and has been found to precipitate conflicts between family members and healthcare professionals caring for the patient family. Families experience a loss of the person that they know and love when behaviours become drastically out of character. Some struggle to interpret the meaning of delirious behaviours and are likely to feel profound helplessness [33-36]. Thus, it is important to regularly assess family member's perceptions and concerns regarding the delirium episode and to provide on-going counselling, emotional support and provide coping strategies.

**Palliative sedation at the end of life:** Refractory, intractable agitated delirium at the end of life may necessitate the use of more sedating medications to ensure patient symptomatic relief and comfort when other interventions have failed by inducing decreased or absent awareness. Whilst deeper considerations of the ethical considerations are vast and lie outside the scope of this paper, it is clear that the basic premise of reliance upon a holistic multi-professional assessment is called for when such option is exercised [37].

## Conclusion

Our holistic review of Soma's case replete with its sociocultural and clinical issues reaffirm the need for a holistic multipronged approach to care of patients with delirium at the end of life.

With a careful history, physical examination and investigation as appropriate, the causes of delirium are often discoverable even in patients with serious advanced illness. The subsequent diagnostic and management strategies must be delineated by context specific consideration of patient's burden of disease, goals of care, family concerns, social, cultural and religious sensitivities. Only by providing context sensitive care will health care professionals be able to provide effective care.

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