

Palliative Medicine Grand Round

# Delirium in Palliative Care Setting

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## Introduction

Delirium is not a new disease entity. Hippocrates in 500 BC used the term “phrenitis” to describe acute mental abnormalities caused by fever, poisoning or head trauma.<sup>1</sup> Celsus in the 1<sup>st</sup> century was the first one to use “delirium” to describe such mental disorders. In a case of suppurative disease with fever, the delirious patient became more talkative and audacious than before. He might have experienced auditory hallucination and sleep-wake cycle disturbance in contemporary medical terms. Celsus also pointed out that delirium occurred when disease progressed or when death was imminent.<sup>2</sup>

2500 years later, not all about delirium has been unravelled. Classically delirium is described as acute onset, transient and reversible mental disturbance secondary to other medical illness. DSM-IV diagnostic criteria remains the gold standard for diagnosing delirium (Table1).<sup>3</sup> This concept is also subjected to challenge, as we find more and more irreversible delirium episodes, and superimposed delirium may account for the psychotic symptoms in dementia.<sup>4</sup>

Table 1: DSM-IV Diagnostic Criteria for Delirium

- A. Disturbance of consciousness (e.g. reduced clarity of awareness of the environment) with reduced ability to focus, sustain, or shift attention.
- 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.
- C. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day.
- D. There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiologic consequences of a general medical condition.

## Delirium is common

Delirium is prevalent in palliative care setting. Morita et al. found that delirium were present in 68% of hospice patients during their final 2 weeks of life.<sup>5</sup> It was the second commonest psychiatric diagnosis and accounted for 17.4% of psychiatric referral in a Japanese study, while the commonest diagnosis is adjustment disorder.<sup>6</sup> It was also the second commonest reason for specialist telephone consultation from general practitioners in the Netherlands.<sup>7</sup>

How about the situation in Chinese population? In a Taiwan study involving 228 terminal cancer patients who were screened by the Chinese Version of Delirium Rating Score, 109 patients were above the cut off score of 10 and regarded positive for delirium. Two patients were later excluded from the diagnosis after psychiatric assessment. The overall prevalence of delirium was 46.9%. Only 9 out of 38 patients with brain metastasis developed delirium. They also observed that mortality was higher in the delirium group (77.6% vs. 50.9%,  $p < 0.001$ ). The detection rate of delirium by palliative care team was around 44.9%.<sup>8</sup>

In one local study, Lam et al. reported an incidence of 40.2% of delirium in patients with advanced cancer, and 30 out of 51 deaths suffered from delirium. The mean number of causes of delirium was 2.1, similar to other overseas studies. The 30-day mortality was reported to be 80%, and significant association was found between delirium and mortality.<sup>9</sup>

## Delirium as Distress

Delirium is a distressing experience, not only to patients, but also to caregivers, health care workers as well as physicians. A study performed by Breitbart et al. found that 53.5% delirious hospice patients could recall their delirium experience. In a Numerical Rating Scale (NRS) of 0-4, 80% of patients described the delirium as “severe distressing”, and the overall mean NRS score was 3.2.<sup>10</sup> The

variables associated with patient distress included presence of perceptual disturbance, delusion, steroid as delirium etiology and the Karnofsky Performance Status (KPS).

Delirium is distressing to patient's formal and informal caregivers. The same study also showed that among patients, spouses and nurses, spouses experienced highest distress with a mean NRS of 3.75. Morita et al. interviewed the bereaved families, 54% reported that they felt "very distressed" or "distressed" about the experience of terminal delirium.<sup>5</sup> Buss showed that caregivers of patients with caregivers-perceived delirium were 12 times more likely to have generalized anxiety.<sup>11</sup>

Delirium episodes can be the source of conflicts between family members and health care workers. Presence of delirium was shown to be predictive of fall during hospitalization in palliative care unit.<sup>12</sup>

There are little evidence on the degree of distress experienced by palliative care physicians when facing delirious patients. Palliative care physicians are responsible for diagnosing the condition, ordering investigations and providing treatment for the patients. As a palliative care physician, I do have the following questions in my mind: Have I misdiagnosed an agitated patient as delirium? Or have I missed something important, like brain metastasis? Do I understand a delirious patient's symptoms burden and suffering? How far should I correct those contributing factors, even empirically? How far should I investigate in a dying patient? Have I provide the correct treatment? Is my "treatment" targeting the etiology of the patient's delirium?<sup>13</sup> Should I restrain the patient?

Different tools are available for screening, diagnosing and assessing severity of delirium.<sup>14</sup> The Confusion Assessment Method is gaining popularity.

### **Confusion Assessment Method**

Confusion Assessment Method (CAM) was developed by Dr. SK Inouye from Yale Medical School. The original aim is to allow non-psychiatric clinicians to diagnose delirium quickly and accurately after a brief formal cognitive testing. Four cardinal features of delirium will be assessed, including (1) acute onset and fluctuating course, (2) inattention, (3) disorganized thinking, (4) altered level of consciousness. The presence of criteria (1) and

(2) plus either (3) or (4) pointed to the diagnosis of delirium. Using CAM to diagnose delirium, the sensitivity was 94-100% and the specificity was 90-95%; with a positive predictive value of 91-94% and a negative predictive accuracy around 90-100%.<sup>15</sup>

Confusion Assessment Method has been validated in different settings, including nursing home, geriatric ward, ventilated patients in intensive care unit, acute and emergency department and in patients with dementia of Lewy Body.<sup>15</sup> It is now accepted as a screening tool by British Geriatric Society<sup>16</sup>, Society of Critical Care of Medicine<sup>17</sup> as well as Australian Health Ministers' Advisory Council<sup>18</sup>.

A Chinese version of CAM is available for intensive care setting.<sup>19</sup> In Hong Kong, Leung JLM et al. investigated the application of CAM among the Chinese geriatrics inpatients. English version was used as assessment was performed by clinicians in this study. The sensitivity of CAM was 0.76 and specificity was 1.00 in this study. They concluded that CAM is an accurate diagnostic instrument for detection of delirium in geriatric in-patient setting.<sup>20</sup>

### **CAM in palliative care setting**

CAM has been used in palliative care setting. In Caraceni's study<sup>21</sup>, 109 out of 393 consecutive palliative care patients gave positive results when screened by CAM. They found that delirium as detected by CAM was an independent factor associated with worse prognosis; the median survival of delirious patient was 21 days, while that of non-delirious patient was 39 days.

Confusion Assessment Method has been validated in palliative care setting recently.<sup>22</sup> Ryan et al. reported the implementation of CAM by non-consultant hospital doctors (NCHD) in a palliative care unit in Ireland. Patients were assessed by NCHDs for delirium within 24 hours of admission using CAM, while subsequent blinded and independent evaluations were performed by a psychiatrist. The study consisted of the pilot phase and the post-training phase. Results showed that with post-pilot phase reinforcement training to NCHDs, the sensitivity of detecting delirium by CAM was 88% and the specificity was 100% as compared with the gold standard of DSM-IV criteria. The quality of observations during clinical interview would directly affect the accuracy of CAM. The initial

The enhanced training program was provided as two 1-hour sessions, which included case-based learning and multiple-choice questions. The junior colleagues might have difficulty in recognizing the cardinal features of delirium as they often attributed the symptoms as a "normal" phenomenon of disease progression, such as fatigue, emotional stress or drowsiness. The training program was regarded as the most important parameter by the authors in enhancing the correct use of the screening tool.

### Treatment of Delirium

Half of the delirium episodes in palliative care setting can be reversed.<sup>24</sup> The framework provided by Pan-Glasgow Palliative Care Algorithms 2005 may serve as a useful guide in management of delirium patients in palliative care setting.<sup>25</sup> As the threshold for discomfort and disorientation is lowered in cachectic and anxious patients, the environment should be one that is stable, safe, quiet and comfortable. Soft lighting, attention by familiar faces, and frequent explanation to patients on what is happening help to reduce anxiety. The underlying causes of delirium should be elucidated. Potential contributing factors such as drugs, metabolic disturbance, anxiety/distress, uncontrolled pain, infection and immobility should be identified and rectified if possible.

A similar approach to delirium is adopted by the British Society of Geriatrics.<sup>18</sup> The guidelines suggest measures including withdrawal of incremental drugs, or adoption of opioid rotation in selected cases. Electrolyte disturbance should be corrected, and underlying infection should be treated appropriately. A quiet environment with appropriate lighting are also emphasized. Patient should be engaged in activities, with mobilization encouraged with aids.

Joceyln White has devised an acronym of CHIMBOP<sup>26</sup>, including seven reversible causes of delirium in hospice setting to assist the attending nursing staff and the resident in assessment of the modifiable factors and in provision of appropriate management. (Table 2)

### Pharmacological Treatment

Haloperidol remains the drug of choice in treating delirium as stated in various guidelines and recommendations, including that from American College of Critical Care Medicine and

**Table 2: CHIMBOP acronym<sup>26</sup>**

C = Constipation  
 H = hypovolemia, hypoglycaemia  
 I = Infection  
 M = Medications  
 B = Bladder catheter or outlet obstruction  
 O = Oxygen deficiency  
 P = Pain

and British Society of Geriatrics. In the Cochrane Systematic Review of drug treatment for delirium in terminally ill patients, the authors concluded that haloperidol was the most suitable drug therapy, while chlorpromazine might be an acceptable alternative if the small risk of cognitive impairment was not a concern. Haloperidol can be administered in various routes, including oral, intravenous, intramuscular and subcutaneous.<sup>27</sup>

### Typical or atypical antipsychotics?

The typical antipsychotics have side effects including extrapyramidal signs and symptoms, arrhythmia and sedation, they are still favoured because of the wider availability, accumulated experience and clinical evidence. Atypical antipsychotics have a more favourable side effect profile, but they are generally more expensive. In the Cochrane Systematic Review in 2007, the efficacy and incidence of adverse effects of haloperidol were compared with risperidone, olanzapine and quetiapine. The authors concluded that there was no evidence that haloperidol in low dosage (<3.0mg/day) had a lower efficacy or a higher incidence of adverse effects when compared with the atypical antipsychotics, namely olanzapine and risperidone. However, a higher dosage of haloperidol was associated with greater incidence of parkinsonism than the atypical antipsychotics.<sup>28</sup>

The role of benzodiazepines in treating delirium is still unsettled, awaiting more studies and systematic review. Methylphenidate has been suggested to be useful in palliation of hypoactive delirium.<sup>29</sup> However, the drug itself can be a cause of delirium. A randomized trial studying the effect of methylphenidate, rivastigmine and haloperidol in hypoactive delirium in intensive care patient swas unfortunately terminated in 2008.<sup>30</sup>

## Conclusion: Mental State as 6th vital sign

Half of the patients in palliative care unit suffer from delirium, and half of the delirious palliative patients remain undiagnosed. Delirium is distressing to patient, caregivers and health care workers. CAM may be a useful tool in helping non-psychiatric clinicians to diagnose delirium efficiently. Management should be targeted at the underlying cause. Both non-pharmacological interventions and drug treatment have their roles in calming the patient. While pain is being promoted as the fifth vital sign, Flaherty et al. suggested that mental status should be the sixth vital sign and delirium should be recognized.<sup>31</sup> Further studies are warranted to elucidate the best treatment of delirium in palliative care setting.

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