Delirium: a diagnostic dilemma

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#### Abstract

Effective symptom management for a patient with a palliative

diagnosis can be challenging. There are some symptoms that may be more difficult to control and understand than others. Delirium, as a symptom, may well prove to be a significant challenge for all involved, leaving family and professionals perplexed and exhausted.

Understanding the predisposing factors and the manifestations may aid the health professional in the assessment and identification of this distressing symptom facilitating more effective management and care of those who are approaching the end of life. This article attempta to address some of the challenges and offer a number of suggestions that may aid in identifying delirium in patients at the end of life but also examines some of the dilemmas when attempting to treat delirium.

Key words: Delirium ■ End of life ■ Diagnosis ■ Patient with cancer and reversibility

Ensuring those reaching the end of life receive proactive, evidence-based care is paramount and symptom management is crucial in facilitating a dignified, peaceful death. Providing effective relief

from symptoms that are perceived as distressing should be a key priority for health professionals (Brown, 2012). The health professional needs to ensure that a patient-centred approach is adopted with an attempt to maintain patient autonomy, The patient should be encouraged to prioritise problems and symptoms that are distressing or important to him or her during the assessment and care planning process. Unfortunately, patients may have complex needs or symptoms that are difficult to manage e.g. intractable vomiting, neuropathic or bone pain. Delirium is one symptom at the end of life that may also pose a management dilemma.

This article aims to clarify and substantiate existing knowledge surrounding delirium, to help in the management of delirium for a patient with cancer who is reaching the end of life. A clear understanding of delirium, its presentation and the many pre-disposing factors can help health professionals identify the condition and address the impact it has on the patient and his or her loved ones.

Within palliative care, more recently referred to as supportive and palliative care, knowledge and expertise in symptom management for those with life limiting illness, such as cancer or heart failure is an intrinsic aspect of the service provided (Twycross, 1997; World Health Organization, 2007, National Cancer Action Team, 2007 [AQ1: See ref list]; National Council for Palliative Care, 2012). The pressure of expectation from patients, lay carers and loved ones of ensuring that this is in place can leave supportive care teams feeling exhausted (Spiller and Keen 2006). As a consequence, it is important for any member of a supportive care team to study any element of care delivery or symptom management that is not understood, but also to maintain their knowledge and understanding as encompassed by the health professional's duty of care (Nursing and Midwifery Council, 2015 and Care Quality Commission (CQC) 2013.

## Background

Delirium or acute confusional state, is a generalised disturbance of cognitive function, perception and/or consciousness, and may be as a consequence of a number of predisposing factors e.g. post-operative confusion, intensive care (ICU) delirium (formally referred to as ICU psychosis) or infection (Meagher and Leonard, 2008, National Institute for Health and Care Excellence (NICE) 2010). NICE has produced guidelines surrounding the assessment and treatment of delirium but makes it clear that the guidance does not look at those receiving end of life care (NICE 2010).

Delirium has been under-reported in all healthcare settings, which has been attributed to a poor knowledge base and difficulties in identifying delirium (NICE, 2010). Dementia and delirium are often confused as they may present with similar features e.g. dementia may be associated with a confusional state and poor perception, which is generally of a progressive nature, while delirium is an acute and rapidly progressing condition with sudden changes to the patient's presentation. The key difference between the two, in addition to the rate of progression, is the reversibility, delirium may have some potential for reversibility but dementia, in its progressive state, has no reversibility (NICE 2010). One must be cautious, however, as a patient who has a dementia diagnosis could also have reversible delirium due to another underlying condition e.g. infection.

It has been suggested that 70% of patients presenting with delirium fail to be diagnosed and some of these may be patients approaching the end of life (Waszinski, 2004). In the UK, the initial release of recognised guidelines developed by NICE in 2010 initiated and renewed a degree of interest in the management of delirium. These guidelines followed five reviews from the Cochrane Collaboration based on the problems surrounding delirium [Note: on checking the citations of the reviews they were not all first published in 2009, have reworded] but these do not address end of life for patients with cancer. Four of the reviews cover prevention of delirium in hospitalised patients (Siddiqi et al, 2007), the use of antipsychotics (Lonergan et al, 2007), the use of benzodiazepines (Lonergan et al, 2009) and the effectiveness of cholinesterase inhibitors for delirium (Overshott et al, 2008). The fifth was not applicable to this discussion as it related solely to dementia. The four Cochrane reviews do contain some valuable information and practicalities for trying to establish best practice in the management of delirium.

A more recent review by the Cochrane Collaboration (2014) examines the prevention of delirium, which is extremely important as it may increase the risk of premature mortality and the length of stay but also for patients with a dementia diagnosis, it can exacerbate the condition (CC 2014). It also reports that the prevention is of the upmost importance, as delirium itself carries a substantial financial cost but also has a significant effect on quality of life for those with a terminal diagnosis Additionally it also continues to be underdiagnosed in this patient group (CC 2012)

NICE (2010) and NHS Scotland (2011have identified that haloperidol should be the drug of choice for patients presenting with irreversible delirium. Despite the fact that both NICE (2010) and NHS Scotland (2011) advocate that haloperidol is useful in the treatment of delirium the Cochrane researchers acknowledged (2012) that it was useful in the short term but one needs to consider that it may cause adverse extra pyramidal symptoms among some patients (Lonergan et al, 2007). When they compared haloperidol with chlorpromazine both groups initially experienced cognitive improvement, however, those treated with chlorpromazine experienced a deterioration in their cognitive function 48 hours after initiating treatment. Within this review, the only study they could identify was one by Breitbart (1996) despite this review taking place in 2012, which demonstrates the lack of current available evidence upon which to base out clinical practice. Limitations identified are that it was a small study and its focus was on patients with Auto Immune Deficiency Syndrome

but they were at the advanced stage of their disease so there may be transferable and generalizable aspects despite this review specifically focusing on cancer patients.

The Cochrane reviews reported it was evident that although there had been some studies and several randomised controlled trials undertaken, more should be done to ensure the prevention of delirium (Lonergan et al, 2007; Siddiqi et al, 2007; Overshott et al, 2008; Lonergan et al, 2009; ). The subsequent Cochrane review (2014) did not examine terminal care but care of those in long-term care so again limited application to the focus of this paper. Again, the researchers could only identify two papers for their review as they either failed to focus on delirium or its treatment, some examined other health conditions rather than delirium and two were not in the long-term setting therefore excluded (one was based at home and the other was acute care. Neither were treated for delirium at the end of life.

NICE released the guidelines Delirium: diagnosis, prevention and management in 2010, which discuss the importance of preventing delirium. The guidance is primarily focused on preventing delirium in adults in hospital and long-term care establishments, aiming to reduce the length of hospital stays. Although this guidance does provide positive information to ensure best practice is upheld, it provides a disclaimer that the guidelines do not cover, children, people withdrawing from alcohol and people receiving end of life care.

With the Cochrane reviews and the guidance from NICE surrounding delirium it was hoped that some direction would be located in relation to patients at the end of life with cancer, but as NICE did not include patients at the end of life it is evident that this has yet to be addressed (Siddiqi et al, 2007; Agar et al, 2008).

Although identifying positive interventions for those suffering with delirium at the end of life with cancer would be a great benefit, this requires valid research studies in order to provide robust evidence on which to underpin practice. The difficulty in completing research in palliative care with the use of reliable and validated randomised controlled trials is an ethical one, when dealing with those who are dying, an instinct for most is to protect the terminally ill rather than burden them with questions or cause distress (Ross and Cornbleet, 2003).

# Literature review

Reliable evidence on which to underpin care surrounding delirium at the end of life for a cancer patient, one may argue, is not widely available, or suitably explored. During the author's search for evidence, which incorporated a Medline, CINAHL and PsychInfo database search, there appeared to be a limited number of comparable studies, other than by the same author (Meager et al 2007, 2008), which affects the reliability as partiality is likely to be evident, making it difficult to effectively compare and contrast. Despite the paucity of national guidance on delirium at the end of life for a cancer patient, delirium was being discussed in the 1980s-90s by reputable authors in palliative care, such as Robert Twycross (1997). Various researchers internationally have also taken an interest in the complexities of delirium, such as Morita et al (2007), Trzepacz et al (1999), Meagher and Leonard (2008) and more recently Boettger et al (2012). The effort made by such researchers has enabled a greater understanding of delirium, for example, the causes and reversibility potential but also its sub-categories e.g. the hypoactive and hyperactive associations, which in turn have facilitated progression in the management and treatment. One may argue that there is still limited data to suggest clearly, how to apply assessments and best practice to patients at the end of life with cancer (Agar et al, 2008).

Definition of delirium at the end of life for a cancer patient

Although this discussion will focus on patients with cancer at the end of life it is important to be cognisant that delirium can affect anyone at any time of life. What one can acknowledge are some of the predisposing factors in non-end-of-life care as some of these may be predisposing factors in those reaching the end of life e.g. a period of ill health, or increasing age (Meagher and Leonard, 2008; NICE, 2010). Delirium is thought by many to be reversible if the episode is identified early enough, through improved assessment and identification but as already established earlier, this tends to not be the case for those approaching the end of life (CC 2012). They estimate that it is reversible in a maximum of 50% of cases for those with a terminal diagnosis (Gagnon, 2012) [AQ14: missing from list] but with the risk that the longer it is left untreated, the more difficult and improbable the reversibility becomes (George and Lee 2005). Delirium at the end of life may present a diagnostic challenge, as its presentation may be similar or the same as reversible delirium, with no clear indication to suggest which the patient is suffering from (Spiller and Keen, 2006). The difficulty then arises when attempts are being made to define what delirium is at the end of life. Boettger et al (2012) attempted to define delirium as a neuropsychiatric disorder, suggesting it is characterised by an array of attributes, varying from cognitive disturbances and underlying causes e.g. infection, hypercalcaemia, opioid toxicity. In addition it may incorporate not simply physical symptoms but also spiritual or emotional distress. This delirium may be termed, 'agitated delirium, terminal delirium, terminal restlessness, terminal agitation, existential distress or terminal distress' (CC 2012 pg 3)

In concurrence to some degree, but equally in comparison to this, it has been concluded by Brooker and Nicol (2007 [AQ15: see ref list]) that delirium, is neurological but presents in two variances; cerebral and extracerebral.

The suggestion that the cerebral characteristic is inclusive of all conditions that are primarily 'post event' such as encephalitis, transient ischaemic attacks, raised intracranial pressure or post seizure would certainly attribute to an onset of delirium (Twycross, 1997) [AQ16: I don't understand what you mean here, needs rewording]. But this theory would not always apply to a patient who is in the end stages of life as a result of cancer as there may be a number of contributing factors (highlighted earlier) which could be difficult to determine when considering a patients with a limited life expectancy. Extracerebral incidences, however, such as drug/alcohol withdrawal, constipation and infection are increasingly identified as a major cause of delirium for the patient with cancer; infection risks increase as the body is deteriorating and constipation becomes prevalent as the patient becomes less mobile and takes a significantly reduced diet (Spiller and Keen, 2006). Both of these features present with similar traits; poor attention to external stimuli, hallucinations, mood changes and paranoia (Brooker and Nicol, 2007), notably these may be indicative of many conditions affecting the wellbeing of one's mind but as suggested these may be numerous in a patient suffering with cancer at the end of life (Pessin et al, 2002). It is fair to say a cancer patient at the end of life may well be experiencing these symptoms but not as a result of delirium, it may also be due to a loss of hope and control (Pessin et al, 2002, Holloway et al, 2010).

Another conjecture that may aid with the definition of delirium is based on the work of Spiller and Keen (2006). They have clearly reinforced the idea that there are two types of delirium; their focus is predominantly hypoactive delirium, which leaves the patient feeling lethargic and withdrawn, but does also refer to the better understood hyperactive delirium (presence of hallucinations and agitation). Although the authors report significant correlation within the results, empowering the

use of assessment tools, it is clear that the data from this study does not clearly coalesce; also it does not consider which of the patients with delirium came from home or hospital, as it would be expected, when considering evidence brought up by Siddiqi et al (2007) and NICE (2010), that those from hospital should be at a higher risk of developing delirium. In relation to the areas explored, it may be fair to suggest that delirium can be defined as an acute confusional state or altered consciousness that can be triggered by either intrinsic or extrinsic elements (Spiller and Keen, 2006).

### The dissimilarity of reversible and irreversible delirium

As already identified, delirium can be reversible or irreversible (Leonard et al, 2008), hypoactive or hyperactive (Spiller and Keen, 2006) and caused by intrinsic or extrinsic factors (Spiller and Keen, 2006; Brooker and Nicol, 2007). Although acclaimed already as a challenge, being able to recognise and diagnose which variant the patient is suffering from should facilitate appropriate treatment but a patient presenting with [AQ17: both?] hypo and hyperactive delirium may be an additional challenge (NICE, 2010).

A study carried out by Leonard et al (2008) suggests that reversible delirium presents with either one or sometimes, a number of intrinsic and extrinsic factors (however, the study examines patients with a number of diseases and illnesses therefore its transferability to end of life care may be questioned and may indeed be limited). Intrinsic elements include metabolic problems, central nervous systems (CNS) infections, systemic neoplasm, CNS neoplasm, organ failure, cerebrovascular and systemic infections (Leonard et al, 2008). Despite the fact that this paper does not focus on end of life care specifically, the intrinsic elements described can be associated with some of the presentations seen. Drug intoxication, drug/alcohol withdrawal and traumatic brain injury were listed as the extrinsic elements, and these have little resemblance to end of life care issues (Leonard et al, 2008). Although this study investigated the differences between the two types of delirium, it is appears that both types of delirium may share similar symptoms and as a result there may be similar causes. If a patient is approaching the end of life, one has to consider the dilemmas associated with spending time trying to assess for reversibility rather than simply treating the delirium. Delays in treatment while assessing the patient may result in distress for both the the person and their family. Assessing the patient individually and recognising when the end of life is approaching may be factors to consider when presented with a patient who appears to be suffering from delirium. One could suggest that focusing on providing an effective nursing environment i.e. quiet and calm, may be more beneficial than managing and diagnosing the cause at this stage in the patients journey. What is evident in Leonard et al's (2008) study is that the intrinsic and extrinsic factors are evident at some point in all cases and types of delirium, but the question surrounding the reversibility is unclear with the exception of organ failure, this is predominantly irreversible. However, it is clear that there are significant predisposing factors to delirium (Siddiqi et al, 2007) which include; bone metastases, haematological malignancy, advanced age, cognitive impairment, and low albumin level (Ljubisavljevic and Kelly, 2003), therefore taking a more proactive approach and recognising these risk factors may result in more prompt treatment.

Delirium may be a manifestation from an underlying cause such as cancer and exacerbated by another intrinsic element for example, an infection. But it is still not clear if delirium at the end of life is reversible or an innate part of the dying process.

#### Conclusion

What is apparent within the evidence examined is that delirium manifests in a number of ways and consequently, may leave health professionals confused in relation to its diagnosis and management. Hypoactive delirium can usually present with traits similar to depression, for example, withdrawal from day to day activities, family and eating and drinking (Spiller and Keen, 2006). It is also thought that health professionals with specific expertise in the field of palliative care may also miss the symptoms of hypoactive delirium, believing that the patient is either depressed or just generally deteriorating in condition (Spiller and Keen, 2006).

Future work should be undertaken to examine and identify best practice in managing delirium. Developing tools to aid assessment and treatment of delirium would benefit practice but currently we should endeavor to raise awareness and assessment skills in order to recognise and treat it as a serious symptom promoting dignity in patients approaching the end of life.

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