

## Feasibility of Chronotherapy for Preventing Delirium in Patients with Cancer: An Idea for Future Clinical Trials

Sir,

Although delirium is a widespread neuropsychiatric complication within high dependency care units such as intensive care, its prevalence is increasing in patients who suffer from end-of-life situations. It is estimated that between 20% and 85% of patients with advanced cancer experience delirium.<sup>[1]</sup> This is while over 50% of these cases are

preventable and reversible.<sup>[2]</sup> The suggested factors associated with delirium in patients with advanced cancer are advanced illness, old age, opioid-induced neurotoxicity, central nervous system metastases, treatment with benzodiazepine, hematologic malignancy, sensory impairment, sleep disturbance, physical performance, cancer type, and albumin level.<sup>[1,3]</sup>

Delirium is a multifaceted syndrome characterized as an acute change in mental status, disturbance of consciousness, speaking, and attention as well as fluctuating impairment of cognition during the course of a day.<sup>[4]</sup> A possible mechanism leading to cognitive dysfunction and delirium is neuronal dysfunction, particularly cholinergic dysfunction, due to systemic disorders, loss of circadian rhythms, and environmental-related risk factors.<sup>[5]</sup> Based on this assumed mechanism, several interventions have been designed and implemented for its prevention and treatment with heterogeneous results to date. Elimination or correction of underlying causal factors, modification of predisposing risk factors and palliative care of symptoms are the current standard approaches to treat delirium in patients with cancer.<sup>[6]</sup> However, the effectiveness of these interventions is inconclusive and at this time, a specific intervention to target delirium in patients suffering from advanced cancer remains to be defined.<sup>[3,6]</sup> Whereas increasing evidence suggests that delirium has significant morbidity and mortality and untreated delirium can significantly impact clinical outcomes of patients with cancer.<sup>[4]</sup> Therefore, given the high prevalence rates and increased morbidity and mortality, effective preventive strategies need to be developed for reducing or treating delirium in patients with advanced cancer. In this regard, in recent years, most of the nonpharmacological interventions have focused on the restoration of the circadian rhythm in delirious patients.<sup>[7]</sup>

Chronotherapy is a therapeutic approach for purposeful modification and restoration of circadian rest-activity rhythms.<sup>[7,8]</sup> It includes interventions such as bright light therapy, music therapy, noise control, dynamic light applications, and use of eyeshades that moderate the environmental stimuli.<sup>[7,8]</sup> For many years, chronotherapy, in particular chronopharmacology, has been used to increase the effectiveness of cancer prevention and treatment interventions.<sup>[8]</sup> In addition, recent evidence suggests that chronotherapy, as a behavioral technique for sleep scheduling, appears to have a beneficial role in reducing the incidence of delirium within critical care.<sup>[7]</sup> However, to the best of our knowledge, no study has examined the effectiveness of chronotherapy on the reduction of delirium occurrence in cancer patients.

The research regarding the effect of chronotherapy on delirium mostly have been conducted on patients hospitalized in the intensive care units and the literature does not include any studies concerning the effect of chronotherapy on decreasing delirium incidence or preventing delirium among patients with advanced cancer. Considering the high incidence of delirium in patients with advanced cancer and potential benefits of chronotherapy on decreasing delirium incidence or preventing delirium, an interesting question arises that merits further investigation. Could chronotherapy reduce the delirium of patients with advanced cancer? However, because of inadequate evidence, the efficacy of chronotherapy is inconclusive and further research is needed. It seems that this nonpharmacological intervention can be used as an effective, inexpensive, innovative, and safe intervention for reducing the

delirium. Therefore, further well-designed clinical trials are necessary to determine the effectiveness of chronotherapy on delirium in patients with advanced cancer.

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The author certifies that she has participated sufficiently in the work to take public responsibility for the content, including participation in the concept, writing, or revision of the manuscript.

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#### Conflicts of interest

There are no conflicts of interest.

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## REFERENCES

1. Grandahl MG, Nielsen SE, Koerner EA, Schultz HH, Arnfred SM. Prevalence of delirium among patients at a cancer ward: Clinical risk factors and prediction by bedside cognitive tests. *Nord J Psychiatry* 2016;70:413-7.
2. Centeno C, Sanz A, Bruera E. Delirium in advanced cancer patients. *Palliat Med* 2004;18:184-94.
3. Lawley H, Hewison A. An integrative literature review exploring the clinical management of delirium in patients with advanced cancer. *J Clin Nurs* 2017;26:4172-83.
4. Edelstein A, Alici Y. Diagnosing and managing delirium in cancer patients. *Oncology (Williston Park)* 2017;31:686-692, III.
5. Hshieh TT, Inouye SK, Oh ES. Delirium in the elderly. *Psychiatr Clin North Am* 2018;41:1-7.
6. Breitbart W, Alici Y. Evidence-based treatment of delirium in patients with cancer. *J Clin Oncol* 2012;30:1206-14.
7. Luther R, McLeod A. The effect of chronotherapy on delirium in critical care – a systematic review. *Nurs Crit Care* 2017. Doi: doi.org/10.1111/nicc.12300.
8. Innominato PF, Lévi FA, Bjarnason GA. Chronotherapy and the molecular clock: Clinical implications in oncology. *Adv Drug Deliv Rev* 2010;62:979-1001.

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