



## Delirium Risk in ICU Patients Cut by Melatonin Agonist



New research findings, published online in the February 19 edition of *JAMA Psychiatry*, show that delirium in older patients hospitalised for acute medical illness could be prevented with nightly administration of a melatonin agonist.

A team of researchers led by Kotaro Hatta, MD, PhD, University of Amsterdam in the Netherlands, conducted a multicenter, randomised, placebo-controlled trial. It showed that in comparison with placebo, ramelteon was associated with a lower risk for delirium at 3% vs 32%.

The authors write that ramelteon administered nightly to elderly patients admitted for acute care may provide protection against delirium, a finding which supports a possible pathogenic role of melatonin neurotransmission in delirium.

It is estimated that the incidence of delirium in elderly patients during hospitalisation lies between 3% and 56%, and it has independently been associated with impaired physical and cognitive recovery, increased mortality and increased healthcare costs. Despite this, there is no US Food and Drug Administration (FDA)-approved medication for delirium prevention.

While a number of agents have been tested for delirium and antipsychotic agents having shown some benefit, it is believed that the associated risk for adverse effects, in particular for acutely ill patients, may be cause for concern.

Findings of one previous randomised controlled trial suggested that melatonin, the pineal gland hormone responsible for regulating the sleep-wake rhythm, was associated with a lower risk for delirium. Additionally, case series have suggested that ramelteon, FDA approved in 2005 for the treatment of insomnia, may help prevent delirium in elderly patients.

In their efforts to examine the preventive effect of the drug, the investigators conducted the trial and included 67 eligible patients between 65 and 89 years old.

All participants were admitted to hospital because of serious medical problems and were able to take medications orally. Patients were randomly assigned to receive ramelteon (8 mg/d, n = 33) or placebo (n = 34) every night for the duration of 7 days.

The study results revealed that ramelteon was associated with a lower risk for delirium at 3% vs 32%; with a relative risk of 0.09 (95% confidence interval [CI], 0.01 - 0.69). This association remained even after controlling for risk factors.

While Sophia E. de Rooij, MD, PhD, and colleagues from the University of Amsterdam note in an accompanying editorial that this study was the first to show a significant prophylactic effect on the incidence of delirium in elderly ICU patients treated with ramelteon, they also write that further research was needed to determine the strategy's effectiveness in the prevention of delirium in other high-risk populations such as dementia patients or elderly patients undergoing hip surgery.

They also list the pathophysiologic mechanisms responsible for the development of delirium and the effects of melatonin and/or melatonin receptor agonists on the long-term sequelae of delirium as other issues that remain to be addressed.

Source: [Medscape](#)

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