Introduction

Melatonin secretion decreases with age and in neurodegenerative diseases like Alzheimer’s Disease (AD). Sundown syndrome (“sundowning”), characterized by agitation, wandering, anxiety, aggression and confusion in the evening and at night is prevalent among demented patients [1,2]. Delirious state is a very common complication in severe dementia, dysregulation of the sleep-wake cycle is one characteristic finding during delirium. Melatonin is able to correct this circadian rhythm disorder [1,3]. Dysfunction of noradrenergic regulation and low tryptophan levels were found to be associated with delirium in the elderly, supporting the hypothesis of a possible role of tryptophan or tryptophan-like compounds such as melatonin in the pathogenesis of delirium [1,4].

Case study

H.E., female, aged 86 years, was admitted to our Department of Gerontology because of persisting agitation in the evening and during night time. A severe dementia was diagnosed (MMSE 4, Clock Drawing Test 0). Cranial CT-scan revealed leucaeraiosis and generalized atrophy, more pronounced in the temporal regions (Figure 1).
Routine laboratory tests were normal, no changes in sodium or potassium were found. Nocturnal agitation consecutively was treated with Seroquel® (Quetiapine 75 to 100 mg) without any effect. Treatment with Dominal® (Prothipendyl 40 to 120 mg) and Truxal® (Chlorprothixen 50 to 65 mg) likewise brought no relief, not even with additional medication of Midazolam® (Midazolam Hydrochlorid 1 to 4 ml) or Somnubene® (Flunitrazepam 1 to 2 mg).

Despite this medication our patient became even more agitated and consequently fell almost every other night, sometimes even repeatedly. To rule out intracranial bleeding, cerebral computed tomography had to be performed on four occasions.

As the treatment described above was unsuccessful, Circadin® (prolonged release melatonin) was established, 2 mg for 2 days, thereafter 4 mg at night; within four days no additive medication was needed and the patient no longer showed any agitation during nighttime. With the patient’s condition under control, she was discharged after eight weeks of institutional treatment.

Discussion

The circadian rhythm abnormality is a characteristic symptom in AD and becomes more marked with the progression of the disease [1]. This case study demonstrates successful treatment of a patient suffering severe dementia with persistent delirium by giving exogenous prolonged release melatonin in 4 mg dosage. In earlier studies lower doses were used in similar cases [5]. Melatonin was well tolerated, suggesting a probable role of tryptophan in the pathogenesis of delirium. Administration of melatonin or other chronobiotics might prevent delirium in patients at risk [1,6-11], since delirium worsens outcome in critically ill and non-critically ill hospitalised patients [12].

Additional controlled trials are required to find the optimal dosage of melatonin for different clinical situations and different subtypes of delirium in patients with dementia, and further to define the neuroprotective role of melatonin as an antidementia drug [1,11,13].

Conflict of interest: none

References