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A review of Cost-effective pharmacotherapy prophylaxis in the prevention of elderly delirium in ICU

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ABSTRACT
Delirium's pathophysiology remains poorly understood, with many theories being overly simplistic. Given the multitude of etiologies, it's improbable that a single mechanism universally operates. Due to this, there is a great challenge and imitation phased in the ICU and other health care settings in terms of delirium prevention. This mixed-method study analysis investigates cost-effective pharmacological prophylaxis for delirium in critically ill patients.Both qualitative and quantitative data are utilized in order to understand the pattern of the disease and the effectiveness of the preventative plan in place. The study focused on ICU patients exclusively within the geriatric population (age >65) who were hospitalized in the ICU for a minimum of 5-7 days. Patients were randomly selected to receive prophylaxis intervention or placebo and were admitted to the ICU for post-surgical care and further evaluation and assessment. The participants were assessed using Confusion Assessment Method to assess and record the incidence of delirium. Result revealed that light therapy exhibits a modest benefit in ameliorating certain cognitive and non cognitive symptoms associated with dementia and delirium. Ramelteon, melatonin, and light therapy show the potential to minimize the incidence of delirium in post-surgical geriatric patients. Furthermore, a decrease in incidence, symptoms, and estimated development time of delirium were observed. Last, a short nighttime infusion of a low dose of dexmedetomidine exhibited higher efficacy, resulting in a 22% reduction in delirium incidence among post-surgical geriatric patients.

I. INTRODUCTION

Delirium is a sudden and severe change in brain function that causes a person to appear confused or disoriented. It can be triggered by a serious medical illness such as an infection, medication, and other causes. In general, delirium can be found whenever there are sick patients, and the incidence of delirium is even higher for patients 65 and older. Nearly 30 percent of older patients experience delirium at some time during hospitalization; the incidence is higher in intensive care units (Francis, 2020**)**. Among older patients who have had surgery, the risk of delirium varies from 10 to greater than 50 percent (S K Inouye, 1994). Many studies have examined its risk factors, but the results have been quite variable. Certain underlying conditions increase the risk of delirium. As of today, the known risk factors of delirium include sleep deprivation, limb fractures, immobilization, physical restraints, frailty, malnutrition, and immobility **(**SK Inouye & Zhang, 2007**)**.

Methods: This is a meta-analysis review of several clinical randomized, double-blind, placebo-controlled trials in several hospitals around the world. The study includes several clinical multicenter, rater-blinded, randomized placebo-controlled trials performed in intensive care units and regular acute wards of both university and general hospitals. The selected ICU patients were all in the geriatric population (>65 yo) and were admitted for at least 5- 7 days in the ICU. Several trials were conducted to compare the results of placebo vs pharmaceutical therapy alternatives to prevent delirium. Additionally, light therapy, and monitoring physiological systems including daily rhythms in core body temperature, melatonin secretion, cortisol, and appetite were studied to have a better correlation between circadian rhythms and the incidence of delirium.
Participants :ICU patient (>65 yo); selected geriatric patient admitted to the ICU

Apparatus and materials: EMR, CAM delirium scoring, DSM-IV-TR diagnostic criteria data were collected on standardized forms, and statistical analyses were performed.

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Médications : Ramelteon, melatonin 3mg, donepezil, risperidone, low dose dexmedetomidine, and placebo (330 mg of lactose powder).

Procedure: The participants were all patients aged 65 years or older, with informed consent, who were admitted to intensive care units after surgery or for intensive care. Patients were randomly selected to receive prophylaxis intervention or placebo and were admitted to the ICU for post-surgical care and further evaluation and assessment. Analyses were done by intention-to-treat and safety populations. The participants were assessed using Confusion Assessment Method to assess and record the incidence of delirium. The results of the trials will then be evaluated to understand the effectiveness of the prophylactic medications chosen and the relevance of preserving circadian rhythm.

Information sources : PubMed, Jama network, Stat Pearls Publishing, Wiley Online Library, and National Institute of Health.

Selection process and Search strategy: Keywords were used and entered the research database library to filter biomedical literature. Keywords used: Delirium, ICU, Delirium and circadian rhythm, Prophylaxis of delirium).

Data Analysis: Both qualitative and quantitative data collected from the study trials are utilized to understand the pattern of the disease and the effectiveness of the preventative plan in place. Additionally, a multivariate logistic regression model was constructed to control the risk factors and to estimate independent associations between the effects of holistic and pharmaceutical medication and the outcome of delirium.

Anticipated Ethical Issues in Study: The use of antipsychotics and the risk it introduces to the geriatric population admitted to the ICU.

II. RESULTS

Delirium and behavioral scales with light therapy and melatonin

With the main objective of utilizing two major synchronizers of the circadian timing system: bright light and melatonin to determine whether the progression of cognitive and non-cognitive symptoms may be ameliorated; Result shows that Melatonin treatment aggravated the withdrawn behavior rating by 1.02 points or 7%. on the Multi Observational Scale for Elderly Subjects (MOSES). Combined light and melatonin treatment ameliorated agitated behavior by 3.9 points or a relative 9%. on the Cohen-Mansfield Agitation Index (CMAI). Combined treatment also increased sleep efficiency by 3.5%; with increased sleep duration by 27 minutes with melatonin treatment and in addition by 10 minutes with light treatment. This suggests that synchronizing the circadian timing system through light and melatonin can be beneficial for managing dementia-related symptoms and improving sleep in long-term care residents.

Preventing Hospitalized Delirium with Melatonin

In a multicentre, double-blind, randomized controlled trial between November 2008 and May 2012, patients aged 65 years or older who were scheduled for acute hip surgery were eligible for inclusion received melatonin 3 mg or placebo. The study reveals that 55/186 (29.6%) in the melatonin group v. 49/192 (25.5%) in the placebo group; difference 4.1 (95% confidence interval -0.05 to 13.1) percentage points of incidence of delirium (De Jonghe A, 2014).

Dexmedetomidine Utilized as Delirium Prophylaxis

In 2016, A randomized, double-blind, placebo-controlled trial in two tertiary-care hospitals in Beijing, China was conducted. Selected ICU patients (at ages 65 and older) were given prophylactic low dose dexmedetomidine, a highly selective α2 adrenoceptor agonist in a computer-generated randomization sequence to randomly assign patients to receive intravenous dexmedetomidine. The overall incidence of postoperative delirium was reduced from 22.6% (79/350) with placebo to 9.1% (32/350) with dexmedetomidine. The result showed that prophylactic low-dose dexmedetomidine significantly decreases the occurrence of delirium during the first 7 days after surgery (Su& Meng, 2016). Additionally, the study confirmed that this therapy is safe for use in elderly and safe prophylactic treatment for postoperative delirium in this patient population.

Preventing Hospitalized Delirium with Ramelteon

In a Multicenter, rater-blinded, randomized placebo-controlled trial performed in intensive care units in Japan from September 1, 2011, through October 31, 2012, 67 patients (24 admitted to intensive care units and 43 admitted to regular acute wards) were included in the study. The 67 patients were randomly assigned to the 2 treatment groups. One group received ramelteon (8 mg/d; 33 patients) and the other group received

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placebo (34 patients) every night for 7 days. Results showed that Ramelteon was associated with 3% risk of delirium vs placebo with risk of 32%. Additionally, incidence of delirium, defined according to the Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition) were further evaluated using Delirium Rating Scale–Revised-98 (DRS-R98) to measure delirium symptoms (with a cutoff score of 14.5).

III. CONCLUSION:

Light has a modest benefit in improving some cognitive and non-cognitive symptoms of dementia and delirium. Exploring first, the potential role of non-pharmacological approaches such as light therapy and improving the patient's environment will play a key factor in balancing the circadian rhythm and promoting stability in the cognitive activity of geriatric patients in ICU. The need for research on neuroanatomic and neuropathy physiology components of delirium can transform the approach to preventative care. As mentioned earlier, with so many etiologies, it is highly unlikely that a single mechanism is universally operative. There is a great challenge in the ICU and other healthcare settings in terms of delirium prevention, but delirium is often preventable. Regulating the circadian rhythm with light therapy and melatonin has the potential to act as a non-invasive and cost-effective way to prevent delirium, however, randomized controlled trials employing melatonin agents have also resulted in mixed findings. A continuation of clinical trials focusing on a non-pharmacological approach with behavioral observation is vital to support this clinical intervention. In addition to this, early and recent studies have suggested the potential of pharmacologic drugs such as Risperidone and Dexmedetomidine as delirium prophylaxis. The clinical trial results revealed decreased risk and delays in the development of delirium. However, further studies with more evidence are crucial for these medications to be safely and routinely given.

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