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The Perioperative Utilization of Dexmedetomidine vs. Melatonin to Reduce Postoperative Delirium: An Educational Module

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The Perioperative Utilization of Dexmedetomidine vs. Melatonin to Reduce Postoperative Delirium: An Educational Module

Nicole Wertheim College of Nursing and Health Sciences

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Abstract

Background: Elderly individuals undergoing general anesthesia commonly experience postoperative delirium (POD), which has been linked to increased morbidity and mortality rates. Recent evidence shows that POD is associated with increased complications, prolonged hospital stays, decreased long-term cognitive function, and poor functional recovery. This condition's complex and multifactorial nature contributes to the difficulty in identifying effective preventive or treatment options. To date, emphasis is placed on risk stratification and interventions that may alter the physiological processes associated with POD. While controversial data exists, melatonin and dexmedetomidine remain two common pharmacologic agents utilized for the prevention of postoperative delirium. Hence, this DNP project aimed to inform anesthesia providers of current, evidence-based research that can be utilized to transform clinical practice and improve patient outcomes.

Methods: A comprehensive literature review was conducted to identify randomized controlled trials published within the last 6 years that evaluated the effectiveness of either Melatonin or Dexmedetomidine for preventing POD and compared to a placebo. The relevant evidence obtained was utilized to develop an online educational module comprised of a pre-test to evaluate anesthesia providers' baseline knowledge and attitudes regarding POD, dexmedetomidine, and melatonin, and a voiceover PowerPoint presentation on current statistics and evidenced-based practices, followed by a post-module assessment to determine the degree of knowledge gained and providers' inclination to implement these research findings into practice. This educational model was distributed via an anonymous link with randomized identifiers. Qualtrics software was used to collect data and generate the study's results.

Results: The results indicated a statistical difference between the pre- and post-survey responses. The average number of correct responses on the pre-test was 59.5%, and an average of 87.63% correct responses were reflected on the post-test. The calculated percent change of these results, 47.28%, signifies the knowledge improvement acquired from this module. The average amount of anesthesia providers inclined to utilize melatonin for POD prevention in high-risk patients was 22% in the pre-test and 63% in the post-test. A drastic increase in the inclination to use melatonin for POD prevention was observed, with a percent change of 186.36%.

Discussion: The higher means for the post-test survey showed that the educational module improved knowledge regarding POD and effective interventions to prevent or mitigate its occurrence among elderly patients. Participants' attitudes and inclinations toward implementing melatonin to prevent POD also improved after completing this educational module. The number of respondents and the module's delivery were 2 major limitations of this study. While this study does not distinctly point to a superior agent for this condition, the positive results obtained offer hope for a transformation of clinical practice. Anesthesia providers are at the forefront of this condition and can reduce the incidence of POD and improve patient outcomes. As advanced practice nurses, certified registered nurse anesthetists (CRNAs) are responsible for generating new research findings and translating them into clinical practice to improve patient care. The information obtained from this project will hopefully spark interest in this topic and provide a foundation for future research.

Key Words: Postoperative delirium, delirium, dexmedetomidine, Precedex, melatonin

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I. Introduction

Delirium is a clinical syndrome characterized by cognitive disturbances, altered levels of consciousness, abnormal psychomotor behavior, and disorganized thinking.[1] Postoperative delirium (POD) is a common complication affecting more than 2.6 million adults each year and accumulates an average healthcare expenditure of more than $164 billion annually.[2] Evidence shows that postoperative delirium is associated with increased complications, prolonged hospital stays, decreased long-term cognitive function, and poor functional recovery.[2] The pathophysiology of POD is not well understood and is presumed to be a complex syndrome with many precipitating and predisposing factors.[3] Some common risk factors linked to the development of POD include pain, advanced age, dementia, intraoperative fluctuation of blood pressure, electrolyte imbalances, alcoholism, smoking, and benzodiazepine usage.[1]

The prolonged life expectancy and growth of the elderly population have led to an increased need for geriatric surgeries.[4] This population expansion, coupled with their comorbidities, is a confounding factor that increases the risk of developing POD.[4] Current research shows that advanced age (>70 years old) is an independent predictor of developing POD and presents with a four-fold increase in experiencing POD.[5,6] As the aging population continues to expand, the incidence of POD is likely to exhibit a linear relationship. To date, no single pharmacological intervention has been identified to prevent or treat POD, and therefore, current research focuses on interventions that may reduce the incidence and/or the severity of POD. Dexmedetomidine (Dex) and melatonin are two commonly studied pharmacologic agents utilized to mitigate the occurrence of POD. Hence, this project aimed to determine which agent is superior at reducing the incidence and/or severity of POD in elderly patients.

Melatonin and dexmedetomidine are pharmacological agents that produce anxiolytic, sedative, and analgesic effects without causing respiratory depression. Melatonin is a natural hormone produced by the pineal gland.[4,7] Exogenous melatonin administration is favorable for its sedative effects and large safety profile.[5,7] The reduction of postoperative delirium following melatonin administration may be associated with its anti-vasospasm effects, improvements in vascular endothelial cell functions, antineuronal apoptosis, and improvements in cerebral perfusion and sleep quality.[4] Dexmedetomidine is a popular alpha$_2$ selective agonist with anxiolysis, sedative, and analgesic properties.[2] Dexmedetomidine's mechanism of action for reducing postoperative delirium may be explained by its ability to improve sleep quality, its lack of anticholinergic effects, which have been shown to attenuate the inflammatory response, and its significant opioid-sparing effects.[2] Dexmedetomidine has the potential to produce unwanted side effects such as hypertension, hypotension, and bradycardia, which may limit its use in the elderly population.

Purpose and PICO Question

The development of postoperative delirium has negative consequences and may be associated with long-term cognitive dysfunction and poor functional recovery.[2] While the treatment of POD remains unclear, pharmacological interventions such as melatonin or dexmedetomidine may reduce the incidence and/or severity of POD.[2-6] Finding a solution to prevent or reduce the severity of POD supports the following PICO question: In elderly patients undergoing general anesthesia, how does administering melatonin versus dexmedetomidine affect the occurrence and/or severity of postoperative delirium? This study placed focus on elderly patients, as POD is more prevalent and detrimental in this population. Melatonin and

dexmedetomidine are two of the most studied pharmacologic agents utilized for the prevention of POD.

Population (P): Elderly patients undergoing general anesthesia

Intervention (I): Melatonin

Comparison (C): Dexmedetomidine

Outcomes (O): Incidence/severity of postoperative delirium

Problem Identification

Delirium is a clinical syndrome characterized by cognitive disturbances, altered levels of consciousness, abnormal psychomotor behavior, and disorganized thinking.[1] The development of postoperative delirium (POD) occurs in up to 60% of patients older than 65 who undergo major surgery and is associated with a mortality rate of up to 75%.[1,8] Current research shows that the development of postoperative delirium is associated with increased complications, prolonged hospital stays, decreased long-term cognitive function, and worsened functional recovery.[2]

To date, no single pharmacological intervention has been identified to prevent or treat POD, and therefore, current research focuses on interventions that may reduce the incidence and/or the severity of POD. Dexmedetomidine and melatonin are 2 commonly studied pharmacologic agents for this concern. Hence, this project aimed to determine which agent was superior at reducing the incidence and/or severity of POD in elderly patients.

Background

The prolonged life expectancy and growth of the elderly population have led to an increase in geriatric surgeries.[4] This population expansion, coupled with their comorbidities, are

confounding factors that increase the risk of developing POD.[4] Commonly used anesthetic agents such as sedatives, anxiolytics, and analgesics may be associated with the development of POD and are, therefore, frequently withheld in high-risk patients. Certain surgical procedures also pose a higher risk for developing POD, including major gastrointestinal or cardiac surgeries, trauma, orthopedics, and any procedure requiring prolonged anesthetic times.[1] Since the type of surgery, anesthetic time, and comorbidities are typically nonmodifiable, POD is mitigated by risk reduction strategies.

Melatonin is a natural hormone produced by the pineal gland.[4,7] Exogenous melatonin administration is favorable for its sedative effects and large safety profile.[5,7] A recent study reports that melatonin is as efficacious as midazolam at reducing preoperative anxiety and may be a safer alternative for elderly patients.[7] It has been proposed that there is a link between melatonin concentrations and the development of delirium.[7] Melatonin is a potent free-radical scavenger and broad-spectrum antioxidant that freely crosses the blood-brain barrier.[4] The properties of melatonin and its ability to cross the blood-brain barrier have proven to attenuate acute brain injury, cerebrovascular spasms, cerebral edema, and the consequent inflammatory response in the brain.[7] The reduction of postoperative delirium following melatonin administration may be associated with its anti-vasospasm effects, improvements in vascular endothelial cell functions, antineuronal apoptosis, and improvements in cerebral perfusion and sleep quality.[4]

Dexmedetomidine is a popular alpha$_2$ selective agonist with anxiolysis, sedative, and analgesic properties.[2] Dexmedetomidine's mechanism of action for reducing postoperative delirium may be explained by its ability to improve sleep quality, its lack of anticholinergic effects, which have been shown to attenuate the inflammatory response, and its significant

opioid-sparing effects.[2] Dexmedetomidine has the potential to produce unwanted side effects such as hypertension, hypotension, and bradycardia, which may limit its use in the elderly population.

Scope of the Problem

In the United States alone, more than 2.6 million adults develop delirium each year.[2] Risk factors for developing postoperative delirium include but are not limited to age, dementia, fluctuation of blood pressure intraoperatively, electrolyte imbalances, alcoholism, smoking, and benzodiazepine usage.[1] Current research shows that advanced age (>70 years old) is an independent predictor of developing POD, and this age population presents with a 4-fold increase in developing POD.[5,6] As the aging population continues to expand, the incidence of POD is likely to exhibit a linear relationship. The astonishing incidence of POD and its detrimental effects on patients, families, and healthcare systems should raise concern and hasten research on the identification of preventative or treatment options.

Consequences of the Problem

Once delirium develops, patients are faced with morbidity and mortality rates of up to 75%.[1] Postoperative delirium can be associated with delayed functional recovery, prolonged hospital stays, and increased healthcare costs.[5] In the United States, the annual healthcare expenditure associated with the development of delirium averages more than $164 billion.[2]

While the diagnosis of POD is presumed to be transient, research shows that a small percentage of patients achieve full recovery by discharge, and approximately 80% of patients have remaining defects for up to 6 months postoperatively.[9] Evidence suggests that there is an association between POD and dementia up to 5 years after the diagnosis of POD .[3] Research

also suggests a potential association between the duration of POD and the degree of cognitive and functional recovery.[3]

Knowledge Gaps

The development of POD is not associated with a single mechanism but rather a combination of many predisposing and precipitating factors.[3] This complex, multifactorial pathophysiology presents many uncertainties for the prevention and treatment of POD. Evidence suggests that the inflammatory process following surgery and neurochemical imbalances are major contributing factors for the development of POD.[3] Therefore, many studies focus on interventions that may alter these processes. Melatonin and Dexmedetomidine are 2 commonly studied medications to mitigate POD. While their mechanism of action remains unknown, researchers believe it is due to their anti-inflammatory properties and ability to improve sleep quality.[2,4] While current research supports the use of melatonin and dexmedetomidine for reducing the incidence, severity, and/or duration of POD, the lowest effective dose remains unclear.[2,4,7]

Proposed Solution

Current literature regarding melatonin and dexmedetomidine for postoperative delirium point to a common outcome. The administration of both agents has been associated with a reduction in postoperative delirium.[1,2,4,5,7,8] Identification of interventions that safely reduce the incidence, severity, and/or duration of POD can result in improved patient outcomes, decreased length of hospital stays, reduced healthcare costs, and long-term complications associated with postoperative delirium. The results of this study can be utilized to transform clinical practice and improve patient outcomes.

Summary

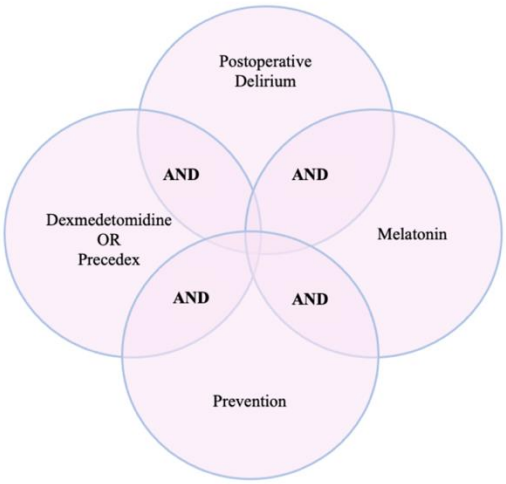
Postoperative delirium is a common complication in elderly patients that has been linked to increased morbidity and mortality.[1,8] There is no known cure for POD; therefore, emphasis is placed on preventive strategies. Current research shows that melatonin and dexmedetomidine effectively reduce the occurrence and/or duration of POD.[1,2,4,5,7,8] Melatonin and dexmedetomidine are pharmacological agents that produce anxiolytic, sedative, and analgesic effects without causing respiratory depression.[1,2,4,5,7,8] Melatonin is favorable for its large safety profile when compared to dexmedetomidine. Dexmedetomidine may present unwanted cardiovascular side effects in the elderly population. Overall, the goal of this study was to identify a safe and effective method to reduce postoperative delirium in elderly patients and to transform clinical practice.

II: Literature Review

Literature Search Process

The following health-science-related databases were accessed to conduct a literature review for this study: Cumulative Index to Nursing and Allied Health Literature (CINAHL), Embase, PubMed, and Medline. The basis of the PICO question was utilized to identify the following search terms: postoperative delirium, prevention, dexmedetomidine or Precedex, and melatonin.

Figure 1. Search Keywords



The databases were analyzed for randomized controlled trials (RCT) published within the last 6 years. The inclusion criteria consisted of RCTs written or transcribed in English, studying the effectiveness of either melatonin or dexmedetomidine for preventing POD and compared to a placebo. Studies that failed to highlight the potential effect of these medications on the incidence or severity of POD and studies in which full-text documents were unavailable were excluded. Studies that consisted of participants under the age of 18 were also excluded. The initial search with the above-mentioned keywords yielded 186 articles. Three duplicates were identified, and the search was refined using the inclusion and exclusion criteria mentioned above. In total, 15 articles were utilized in the literature review.

Literature Appraisal and Literature Matrix

The articles analyzed in this literature review evaluated the medication's effect as a preventative and/or treatment modality to reduce the incidence or severity of POD. The effects of melatonin on POD were investigated by Mohamed et al, Sharaf et al, Fazel et al, Aldujaili et al, Fan et al, Zedah et al, and Ford et al.[1,5-7,9-11] In contrast, the effects of dexmedetomidine on POD were investigated by Xaun et al, Li et al, Li et al, Likhvantsev et al, Wang et al, Kim et al, and

Liu et al.[2,12-17] All studies comprising this literature review were double-blinded, randomized controlled trials, which constituted level II evidence.[1,2,5-7,9-17]

Characteristics of the Included Studies

In an investigation by Mohamed et al,[1] 80 individuals were evenly divided and randomized to receive melatonin (40 patients) or a placebo (40 patients). The presence of delirium was evaluated using the Abbreviated Mental Test (AMT) by an anesthesiologist who was blinded to the groups. The Statistical Package for Social Sciences (SPSS) was utilized for data analysis. The independent *t*-test was utilized to compare the mean values of each group. The study showed a significant reduction in the development of POD in the melatonin group compared to the control group, as evidenced by a *p*-value < 0.001. Ten patients (25%) in the melatonin group and 25 patients (52.5%) in the control group experienced delirium in the immediate postoperative period and up to 6 hours after surgery.

Sharaf et al[5] conducted a study that analyzed 50 patients randomly treated with melatonin (n = 25) or a placebo (n = 25) who were undergoing coronary artery bypass graft (CABG) surgery. This study aimed to determine melatonin's effectiveness as a preventative and curative measure for POD. An Intensive Care Delirium Screening Checklist was utilized to determine the presence and severity of POD. SPSS was utilized for data analysis. Cronbach's alpha score was utilized to signify the reliability of the results. *P*-values of <.05 were considered significant, and values <.01 were considered highly significant. *T*-test and chi-square test were used to compare mean values between the groups. The results of this study supported melatonin as a preventative measure to reduce POD, as there was a significant reduction in delirium in the melatonin group (8%) compared to the control group (28%) as evidenced by a *p*-value of 0.046. Of the 9 patients who developed POD, 5 (56%) were cured by the continuation of melatonin therapy, 2 patients

(22%) improved but were not cured, and 2 (22%) did not respond to the continued therapy. The authors concluded that melatonin is effective as a preventative method for POD in patients undergoing CABG and was also successful as a treatment for POD in more than 50% of cases.

Fazel et al[6] randomized 72 patients over the age of 60 to receive melatonin (n = 36) or a placebo (n = 36). The presence of delirium was assessed for 3 postoperative days by using the AMT tool. A Chi-square test was utilized to compare data between the two groups. The generalized estimating equations model (GEE) was utilized for multivariate analysis. SPSS was used for statistical analysis, and a p-value of <0.05 was considered statistically significant. On the initial postoperative day (POD), 8 patients (22.2%) in the melanin group experienced delirium compared to 16 (44.4%) in the placebo group. The melatonin group produced similar outcomes on POD2 and POD3, with 6 patients (16.7%) and 2 (5.6%) patients developing delirium compared to 14 (38.9%) and 11 (30.6) in the control group. The present study concluded that the incidence of postoperative delirium was significantly reduced (p-value <0.05), up to 3 days post-procedure) by melatonin administration.

Aldujaili et al[7] conducted a multicenter study that analyzed 36 patients randomized to receive melatonin (n = 11), midazolam (n = 12), or a placebo (n = 12). Delirium was assessed at 30, 60, and 90 minutes postoperatively by the Memorial Delirium Assessment Scale. The chi-square test was used for statistical analysis, and SPSS was utilized for descriptive and analytic statistics. The study showed only slight differences in the occurrence of POD at 0 and 30 minutes between groups. In contrast, at 60 minutes, 2 patients (16.6%) in the melatonin group compared to 8 patients (66.6%) in the midazolam group and 9 patients (75%) in the control group presented with signs of delirium, which signified statistical significance evidenced by a p-value <0.05. At 90 minutes postoperative, zero patients who had received melatonin displayed signs of POD

compared to 5 patients (41.6%) in the midazolam group and 7 patients (58.3%) in the control group, which also signified statistical significance ($P < 0.05$). The authors concluded that melatonin was superior at reducing the incidence of POD compared to no prophylactic treatment (placebo) and midazolam.

In a prospective study by Fan et al,[10] 139 patients over 65 years of age were randomly divided to receive melatonin ($n = 69$) or a placebo ($n = 70$). The presence of delirium was based on results from the Mini-Mental State Examination (MMSE), administered by a trained investigator blind to the study. SPSS was used for statistical analysis, and a p-value of <0.05 was considered statistically significant. A two-way ANOVA analyzed the differences between the groups in MMSE scores and the subjective assessment. Intergroup comparisons were made using t-tests. Chi-square or Fisher exact tests were used to analyze categorical variables such as age, American Society of Anesthesiologists (ASA) classification, and side effects. Cognitive function was assessed preoperatively and postoperative on days 1, 3, 5, and 7. No differences were noted in the baseline score between the melatonin and control group. MMSE scores remained unchanged during the 7 days of observation in patients who received melatonin, while the placebo group experienced significant decreases at postoperative days 1, 3, and 5, signifying statistical significance as evidenced by p-values <0.05. Results of subjective assessments by the participants revealed postoperative impairments in sleep quality, general well-being, and fatigue in the control group when compared with the melatonin group. From these results, the authors concluded that melatonin improves sleep quality and can be beneficial in reducing POD.

In an investigation by Zadeh et al,[9] 60 patients undergoing CABG were randomly assigned to receive either melatonin ($n = 30$) or a placebo ($n = 30$). The occurrence of delirium was assessed by the Confusion Assessment Method for Intensive Care Unit (CAM-ICU), and the

severity of delirium was assessed using the Memorial Delirium Assessment Scale (MDAS). SPSS was utilized for data analysis. *T*-test and chi-square test were used to compare mean values between the groups. Assessments were completed every 12 hours for up to 48 hours after extubation. On postoperative day 1, 4 patients (13.3%) who received melatonin developed delirium compared to 11 patients (36.6%) in the control group. Similar results were noted on the second postoperative day, with 3 patients (10%) in the melatonin group and 14 (46.6) in the control group experiencing delirium. The results from POD1 and POD2 yielded statistical significance, as evidenced by *p*-values < 0.05. The severity of delirium was significantly worse in patients who did not receive melatonin ($p = 0.003$). From this work, the authors concluded that melatonin reduces the incidence and severity of POD. The authors also reported a direct correlation between age and the incidence and severity of POD.

Ford et al[11] conducted a multicenter study that consisted of 202 patients undergoing major cardiac surgery who were randomly assigned to receive melatonin ($n = 98$) or a placebo ($n = 104$). Of the participants being analyzed, 84 in the melatonin group and 82 in the control group were available for a 3-month follow-up assessment. The CAM and MDAS tools were utilized to evaluate the presence and severity of delirium. Stata v13.1 software was utilized for data analysis. *T*-tests and Mann-Whitney tests were utilized for ordinal data analysis. Logistics regression was used to determine the odds of the primary and secondary outcomes. Cronbach's alpha score was utilized to signify the reliability of the results. In the immediate postoperative period, the incidence of delirium was similar between the groups, with an occurrence rate of 21.4% in the melatonin group and 20.2% in the control group. The duration of delirium failed to yield significant results between the groups ($p = 0.304$), with a median duration of 3 days in the melatonin group and 2 days in the control group. The severity of delirium was similar between

the groups, with severe episodes occurring in 42.9% of patients who received melatonin and 28.5% in the control group, which also did not yield statistical significance ($p = 0.221$). Of the patients who developed POD ($n = 42$), 95.2% experienced postoperative complications. According to results from the 3-month follow-ups, no differences in cognitive function between the groups were noted. The authors of this investigation conclude that their findings do not support the use of melatonin as a prophylactic intervention for POD in patients undergoing major cardiac surgery.

Xaun et al[2] conducted a multicenter study that consisted of 453 patients who were randomly assigned to dexmedetomidine ($n = 227$) or a placebo ($n = 226$). The presence of delirium was assessed using the CAM score. SPSS was utilized to analyze and process all data. Categorical variables were analyzed with the X2 test, *t*-test, or Mann-Whitney U test analyzed numerical data, and data between the groups were calculated with the Hodges-Lehmann estimator. Statistically significant results were represented by *p*-values less than 0.05. During the first 7 postoperative days, 30 (13.2%) of patients in the dexmedetomidine group experienced POD compared to 64 (28.3%) in the placebo group, which signified statistical significance ($p < 0.0001$). Patients in the placebo group experienced significantly longer hospital stays (16.5 ± 5.5 vs 15.4 ± 4.2) and hospital expenses ($p = 0.001$). From this study, the authors concluded that dexmedetomidine is effective at reducing POD, improving analgesic quality, and decreasing the length of hospital stays and expenses. It was also noted that postoperative complications such as hypertension and tachycardia were similar between the groups.

In an investigation by Li et al,[13] 260 patients undergoing brain tumor resection were randomly assigned to receive dexmedetomidine ($n = 130$) or placebo ($n = 130$). The Mini-Mental State Exam was utilized to assess baseline cognitive function. Multiple scales, including CAM-

ICU, 3D-CAM, and RASS, evaluated the presence of delirium. A numerical rating scale (NRS) was utilized to quantify pain, and the Richards-Campbell sleep questionnaire evaluated sleep quality. Statistical analysis and group comparisons were completed using Stata/SE 16.0, two-tailed X^2 tests, Fischer's exact tests, student *t*-tests, Mann-Whitney tests, and Kaplan-Meier curves. Statistical significance was considered for *p*-values < 0.05. Statistical significance was noted between the incidence of POD in patients who received the placebo (46%) and the dexmedetomidine (22%), as evidenced by a *p*-value < 0.001. The duration of delirium, however, was similar among the groups. Secondary outcomes such as pain scores, sleep quality, and postoperative complications were analyzed and recorded. The study concluded that dexmedetomidine reduces the incidence of POD in this high-risk patient population and improves sleep quality and pain control without causing hemodynamic complications.

Li et al[14] conducted a randomized, double-blind placebo trial on elderly patients (≥60 years old) undergoing major non-cardiac surgery to evaluate the impact of intraoperative dexmedetomidine on the incidence of postoperative delirium. The Mini-Mental State Exam (MMSE) was utilized to evaluate cognitive function, and delirium was assessed using the Confusion Assessment Method (CAM). SPSS software was utilized for statistical analysis. Independent *t*-tests and Mann-Whitney U tests were used to compare the groups' data. Six hundred and nineteen patients were randomly assigned to receive dexmedetomidine (*n* =309) or a placebo (*n* = 310). Patients who received dexmedetomidine had a lower incidence of delirium (17/309; 5.5%) than the control group (32/310; 10.3%), which yielded statistical significance as evidenced by *p* = 0.026. While the dexmedetomidine group experienced a lower incidence (2.3% vs 6.5%) of surgery-related complications such as gastrointestinal hemorrhage, ileus, anastomotic leak, surgical site infection, and sepsis, admission to the ICU after surgery, ICU and

hospital durations ($p < 0.005$), and 30-day mortality did not differ between the groups ($p > 0.05$). The authors concluded that dexmedetomidine is effective at reducing POD in elderly patients undergoing non-cardiac surgery and was associated with fewer postoperative surgical complications.

In a study conducted by Likhvantsev et al,[12] 169 patients undergoing cardiac surgery requiring cardiopulmonary bypass were randomly assigned to receive dexmedetomidine ($n = 84$) or a placebo ($n = 85$). The presence of delirium was evaluated with the CAM-ICU score, and the severity was assessed with the Intensive Care Delirium Screening Checklist. Variable distribution was evaluated with the D'Agostino- Pearson test. Student *t*-tests or Mann-Whitney U tests were utilized for between-group comparisons. The Chi-square or Fisher exact test was used to compare categorical variables. Of these patients, 6 (7.1%) in the dexmedetomidine group, compared to 16 (18.8%) in the control group, developed POD, which yielded statistical significance as evidenced by a *p*-value of 0.02. While patients in the dexmedetomidine group experienced a shorter duration and severity of delirium, the differences between the 2 groups were clinically insignificant ($p > 0.05$). After comparing dexmedetomidine with a placebo, the authors concluded that initiating an infusion of dexmedetomidine at the time of anesthesia induction and continuing until ventilator weaning results in lower incidences of POD. The authors believe that the timing of dexmedetomidine infusion is crucial for delirium prevention as its action may be mediated by preconditioning properties, which require some time to establish.

Wang et al[17] randomized 652 patients to receive dexmedetomidine ($n = 326$) or a placebo ($n = 326$). The Mini-Mental State Exam and Pittsburgh sleep quality index were utilized pre- and postoperatively to evaluate sleep quality and cognitive function. Sedation and agitation were assessed in the ICU with the Richmond agitation-sedation score (RASS), and the presence of

delirium was determined by the confusion assessment method (CAM; CAM-ICU). SPSS was utilized for data analysis. Cox regression was used for incidence analysis. The incidence of POD was statistically insignificant, with 47 participants (14%) in the dexmedetomidine group and 51 (16%) in the control group developing delirium, as evidenced by a *p*-value of 0.62. The presence of POD occurred more frequently in patients over the age of 65 (31%) compared to 12% in patients less than 65, which yielded statistical significance ($p < 0.001$). No significant difference was noted in the duration of delirium, ICU, and hospital stays between the groups ($p = 0.99$). From the results, the authors concluded that the administration of dexmedetomidine is not beneficial for reducing the incidence of POD. The authors also noted a potential correlation between dexmedetomidine administration and acute postoperative kidney injury. This is likely attributed to its mechanism of action resulting in hypotension and decreased renal perfusion.

In a prospective, randomized controlled study conducted by Kim et al,[15] 120 patients were analyzed following dexmedetomidine ($n = 60$) or placebo ($n = 60$) administration. The Riker sedation agitation scale was used immediately after extubation and in the recovery room to assess for emergence delirium. The CAM/CAM-ICU scale was used to evaluate the presence of postoperative delirium. Data analysis was completed with SAS and SigmaPlot software. A chi-square test with an alpha of 5% signified statistical significance. The pre-and postop lab values were compared using the Wilcoxon rank-sum test. The incidence of POD between the groups was statistically insignificant, with 25% of participants from each group developing delirium. Pro- and anti-inflammatory cytokines were analyzed as a secondary outcome to determine dexmedetomidine's physiological effects. The results were statistically significant and showed that dex administration alters various cytokines, ultimately placing the patient at an increased risk of developing a pro-inflammatory state ($p < 0.05$). These cytokine imbalances may explain

Dexmedetomidine's ability to reduce emergence agitation without producing anti-delirium effects. The authors concluded that dexmedetomidine administration did not reduce the incidence of POD in patients undergoing thoracoscopic lung surgery. However, dexmedetomidine was associated with a statistically significant reduction in intraoperative inhaled anesthetics and postoperative opioid requirements, as evidenced by a p-value < 0.001. These results also supported that there is no association between the reduction of emergence agitation and the incidence of POD.

In an investigation by Liu et al,[16] 120 patients were randomly assigned to receive dexmedetomidine (n = 60) or a placebo (n = 60). Patients were assessed for the presence of delirium using the 3-Minute Diagnostic Interview for CAM (3D-CAM). Visual Analog Scores (VAS) were utilized to assess postoperative pain levels. Sleep quality was assessed using the Richards-Campbell Sleep Questionnaire (RCSQ). SPSS was utilized to analyze and process all data. Independent t-test and ANOVA were used to compare data between the groups. The Chi-square or Fisher exact test was used for the ratio between groups. Of the participants, 5 (8.3%) in the dex group versus 8 (13.3%) in the control group developed POD. These results and the duration of delirium were statistically insignificant, as evidenced by p >0.05. The dex group, however, was associated with statistically significant lower postoperative pain scores and improved postoperative sleep quality compared to the control, as evidenced by p < 0.05. The authors concluded that dexmedetomidine is not effective at reducing the incidence and duration of POD but may improve pain scores and sleep quality. While dex may be effective at improving sleep quality, its inability to alter sleep cycles limits its effectiveness at reducing delirium symptoms.

Synthesis of the Literature

Due to its physiologic alterations, patients who experience POD are faced with increased morbidity and mortality rates.[1] While POD is generally considered to be an acute complication, research suggests that cognitive defects may persist up to 6 months postoperatively.[9] Current literature also suggests a potential association between the duration of delirium and the degree of cognitive and functional recovery.[3] The complex mechanism of POD presents many uncertainties for identifying effective preventive and treatment options.

Melatonin's ability to antagonize the pathophysiological causes of POD can be explained by its biochemical properties.[1,4-7] Circadian rhythm disturbances are among the many risk factors for developing POD. Current studies report that prophylactic administration of melatonin improves sleep quality while reducing the incidence of POD by 20%.[6,10] While melatonin is not commonly studied as a treatment for POD, Sharaf et al[5] found it to be effective at treating more than 50% of patients diagnosed with POD. Melatonin's usefulness in reducing POD in patients undergoing cardiopulmonary bypass remains controversial.[9,11]

Dexmedetomidine is one of the most frequently studied pharmacological interventions for POD. The use of dex during surgical procedures decreases anesthetic requirements and adequately addresses pain, both of which are important risk factors for developing POD.[2,12-17] These benefits would seemingly contribute to a reduction in POD. However, research is controversial, even in the presence of decreased anesthetics requirements and adequate pain control.[2,12-17] The variable outcomes associated with dex may be attributed to the timing of its administration.[12,15,17] Dex exhibits preconditioning properties, which are associated with delirium prevention. However, ample time is required for dexmedetomidine to produce these effects, especially in patients requiring cardiopulmonary bypass.[12]

Most recent studies focus on melatonin and dexmedetomidine as separate preventative options for POD. However, Javaherforooshzadeh et al[18] reported that these 2 agents produced significant results when used in conjunction. The combination of melatonin and dexmedetomidine produced a lower incidence and duration of delirium and mitigated the impact of many risk factors observed in those not receiving melatonin.[18]

Definition of Terms

General anesthesia

According to Siddiqui et al,[19] general anesthesia is defined as a medically induced, reversible, and controlled loss of consciousness with concurrent loss of protective reflexes due to anesthetic agents. General anesthesia is required for many surgical procedures. It often entails a variety of anesthetic agents, including inhalational anesthetics, analgesics, amnestics, and muscle relaxants to obtain and maintain an adequate depth of anesthesia.

Delirium

According to Echeverria et al,[20] delirium is defined as a clinical syndrome that usually develops in the elderly and is characterized by an alteration of attention, consciousness, and cognition, with a reduced ability to focus, sustain, or shift attention. By definition, delirium is caused by an underlying medical condition and is not better explained by another preexisting, evolving, or established neurocognitive disorder.[20]

Elderly

The term elderly is commonly defined as an individual who is 65 years of age or older. While it is frequently quantified with a number, individuals younger than 65 who present with declining functional or cognitive status may also be described as elderly.

Summary

Postoperative delirium is a common complication that is more prevalent in the elderly population. The complex and multifactorial nature of this condition contributes to the difficulty in identifying effective preventive or treatment options. To date, emphasis is placed on risk stratification and interventions that may alter the physiological processes associated with POD. The development of POD increases patients' risk for complications and may associated with long-term functional and cognitive impairments. While controversial data exists, melatonin and dexmedetomidine remain 2 common pharmacologic agents utilized for the prevention of postoperative delirium.

III: Methodology

Primary DNP Project Goal

Postoperative delirium (POD) is a common complication in elderly patients that has been linked to increased morbidity and mortality.[1,8] This condition's complex and multifactorial nature contributes to the difficulty in identifying effective preventive or treatment options. To date, emphasis is placed on risk stratification and interventions that may alter the physiological processes associated with POD. While controversial data exists, melatonin and dexmedetomidine remain 2 common pharmacologic agents utilized for the prevention of postoperative delirium. This DNP project aimed to inform anesthesia providers of current, evidence-based research on melatonin and dexmedetomidine's effect on POD. An educational model was created and presented to nurse anesthesia alumni nationally. The overall goal was to present relevant information on this topic that certified registered nurse anesthetists (CRNAs) can utilize and implement to transform clinical practice and improve patient outcomes.

SMART Objectives

Specific

FIU's Nurse Anesthesia program alumni participated in this online education module. After completing this course, the anesthesia providers should understand the pathophysiology and risk factors for postoperative delirium. The participants should also be able to formulate an anesthetic plan for patients at high risk for developing POD.

Measurable

The success of this educational module was determined through the analysis of surveys provided to the study participants. The participants were asked to complete a pre- and post-test questionnaire, which was used to determine the degree of knowledge gained from this module. Qualtrics software was utilized to generate the surveys and evaluate data points.

Achievable

The anesthesia providers participating in this module were educated on the causes of POD in surgical patients, risk factors that contribute to its development, the impact of POD on patient outcomes, and current evidence-based practices to mitigate its occurrence.

Relevant

The astonishing and steady rise in the incidence of POD was presented within the educational module, along with the multidimensional impact that POD projects on patients, families, and healthcare systems.

Time-Based

This 10-minute online educational program was distributed on April 1, 2024, and participants were asked to complete the module along with the pre- and post-test questionnaires by June 30, 2024. By successfully completing this module, anesthesia providers should

demonstrate improved comprehension of POD and potential pharmacologic interventions to mitigate its occurrence.

Organizational SWOT Analysis

Strengths and Opportunities

Strengths are internal elements within an organization that facilitate reaching a goal, while opportunities are external elements that help achieve this goal.[21] The primary stakeholders for this QI Project were FIU nurse anesthesia alumni practicing nationally as certified registered nurse anesthetists. Prolonged life expectancy creates an increased demand for surgical procedures in the elderly population, placing anesthesia providers at the forefront of their care affording them the ability to positively impact patient outcomes and reduce the occurrence of POD. It is anticipated that incorporating melatonin for POD prevention can enhance patients' functional recovery, underscoring a pivotal opportunity.

Weakness and Threats

Many internal and external factors may hinder the success of this project, including the participants' lack of knowledge and willingness to change, limited resources, and organizational support. Successful implementation of new protocols and practices relies heavily on the organization's and providers' adaptability. Ensuring that providers are well-informed and have the tools necessary for change enhanced the likelihood of success.

While symptoms of POD may present in the immediate postoperative period, the diagnosis is commonly made in the late postoperative period. Because of this, CRNAs may be unaware of its profound and detrimental impact on patient outcomes. Completion of this module will ensure that participants understand the incidence, pathophysiology, risk factors, complications, and current evidence-based practices to reduce the occurrence of POD.

Conceptual Underpinning and Theoretical Framework

The evolution of evidence-based research into practice is crucial to ensure patients receive high-quality care. However, this is a very dynamic and complex process. Even in present times, there is a wide variation in the rate at which research and evidence are obtained and implemented into practice.[22] Theoretical frameworks guide this process by evaluating the determinants of implementation.[22] Kurt Lewin's theoretical framework, formally reported as one of the most influential approaches to organizational change, was utilized for this project.

Theory Overview

Kurt Lewin, also known as the father of social psychology, proposed a three-step change theory in the mid-1900s.[23] This classic theory appears deceptively simple. However, the components are quite complex. Lewin describes change as a balance or a "quasi-stationary equilibrium" between 2 opposing forces.[23] The driving forces promote change, while the restraining forces inhibit change.[22] The complexity of this theory occurs when organizations are faced with identifying and understanding the opposing forces.

The first step of Lewin's theory is *unfreezing*.[22,23] For this step to occur, individuals or organizations must recognize that their current practices no longer align with the advancements in evidence-based research. During this phase, the driving forces must outweigh restraining forces, disrupting the quasi-equilibrium.[23] If the opposite occurs, the process of change will be unsuccessful. A thorough evaluation of all driving and restraining forces must be made. The magnitude of obstacles an organization must overcome will determine if the proposed change is possible and sustainable. The next step is *moving* or *changing*.[22,23] This is where the implementation of change occurs. Diligent planning and communication are required to ensure a smooth, successful transition phase. After the change has been made, *refreezing* must occur to

ensure sustainability. During this stage, the implemented change becomes the new “quasi-stationary equilibrium.” This stage also encourages individuals within the organization to develop a new outlook and ensures patients receive the highest quality of care.

The ever-changing field of healthcare supports the need for doctoral-prepared nurses. This level of education is obtained to foster the translation of research into clinical practice. The utilization of nursing theories provides a foundation and guides this translation to reduce the gap between new evidence and its implementation into clinical practice. Doctoral-prepared anesthesia providers are responsible for bridging this gap by remaining current on research trends and supporting evidence.

Setting and Participants

The participants of this study included approximately 20 alumni of a nurse anesthesiology program who graduated and are currently practicing nationwide in office-based and hospital settings. The participants will engage in an educational module on POD and potential preventative interventions backed by evidence-based research. This sample population is integral to this study as these providers frequently administer anesthesia to elderly patients who are at the highest risk for developing POD. The sample demographics included male and female, full- or part-time employees of various ages, levels of education, and ethnic groups. This sample also included variations of novices to experts within the nurse anesthesia profession.

Procedures

The methodology utilized for the delivery of this project included a virtual educational module that was preceded and followed by 10-15 question anonymous qualitative surveys. The initial survey was generated after informed consent and delivered via Qualtrics software to assess the participants' baseline understanding of POD and to collect demographic information. An

educational module was then presented as a Voiceover PowerPoint presentation concentrating on the etiology, incidence, consequences, diagnosis, and prevention of POD. A post-test was administered using the same template and software as the pre-test to assess learning acquisition on this topic. All responses to this virtual educational model remained anonymous.

In pre-and post-interventional studies, a variable of interest is evaluated and measured before and after an intervention in the same participants.[24] Results derived from this type of study describe the relationship of the measurements to the intervention.[24] For example, the post-test results will reflect the efficacy of the virtual educational module. Current research suggests that virtual platforms are favored for fostering a dynamic and autonomous approach to learning.[25] Additional benefits of virtual learning modalities include maximizing access to information, respecting participants' time, and facilitating a personalized learning experience.[25]

Participant Recruitment

Following approval from the university and the Institutional Review Board (IRB), email addresses were obtained from the university's program director. A recruitment letter was sent with brief details of the quality improvement project and enrollment instructions. Contact information for the private investigator and the co-private investigator was provided in the event that future communication was needed. Participants who enrolled then received information regarding the topic of the educational module and detailed instructions on how to access and complete the course. Access to pre-and post-test questionnaires and the educational module was granted through a nontransferable link sent directly to the email addresses provided by the participants. All participation in this study was anonymous and voluntary.

Data Collection

The data obtained from this study were collected from the pre-and post-test questionnaires. Demographic information was included in the pre-questionnaire. Each survey consisted of 10-15 questions focusing on the etiology, prevalence, diagnosis, and prevention of POD. The surveys were generated and distributed via Qualtrics software. IRB standards were followed to ensure the validity and reliability of the results. Data obtained from questionnaires were secured via password-protected software and only accessible by the principal investigator (PI), Dr. Campbell, and co-PI, Logan Newberry.

Data Management/Analysis

The data obtained from this study was stored in a password-protected database accessible only by the PI and co-PI. Results from the pre-and post-surveys were randomized and analyzed using Qualtrics software. This allowed the authors to determine the participants' baseline understanding of POD and the degree of learning acquired from the educational module. The primary author manually tracked and recorded responses and initiated follow-up emails when appropriate to facilitate maximal efforts and results of this study. To ensure data security and protection of the participants, no direct identifiers were collected during this investigation.

Protection of Human Subjects

While demographic information was collected in the pre-test questionnaire, specific participant identifiers were not obtained. Personal data or medical records were not accessed or utilized in this study. To protect the rights and privacy of all participants, all survey responses remained anonymous. Potential benefits to the participants include a greater comprehension of postoperative delirium, its effect on patient outcomes, and possible preventative or treatment options. While any form of harm or discomfort is not anticipated from any of the participants, possible risks include emotional distress, feelings of self-doubt, headache, and back pain.

Following a comprehensive disclosure of the project and its intended purpose and procedures, informed consent was obtained from all participants. This demonstrated an understanding of the project and acknowledgment of the potential risks and benefits of participating in this study.

International Review Board approval was obtained for this quality improvement project. To ensure the protection of all participants, all standards and protocols mandated by the IRB were strictly followed. All material presented in this module, including the pre- and post-test surveys, was submitted to the IRB for a thorough evaluation.

IV: Results

This education module was distributed via email over a 12 week time span. One hundred sixty-nine participants were invited to participate. Reminder emails were scheduled and delivered every 2 weeks throughout the 2-month response window. The number of respondents is a major limitation of this study, with an overall response rate of 5%. Nine participants completed the pre-test survey, while only 8 completed the module. The premature completion of the module by one participant contributed to the completion rate of 88.9%. Due to postoperative delirium being specific to anesthesia and the postoperative period, the generalizability of these results to other professions is limited.

Pre-test Demographics

The results of this project included 9 alumni of the FIU nurse anesthesiology program who are actively practicing in the hospital setting. Seven of these respondents identified as females, representing 78.78%, while 2 were males, representing 22.22%. The participants' ages were classified between 29 and 53, with the median age being 34. Most of the participants identified as Caucasian (67%), followed by Hispanic (22%) and African American (11%). Regarding practice experience, most respondents had less than 2 years, representing 56%, while

33% had 2 to 5 years, and 11% had more than 10 years of experience. Of the 9 participants, most (88.89%) have a doctorate in anesthesia, while only 1 (11.11%) have a master's degree. Pre-test demographics are displayed in Table 1.

Table 1. Pre-Test Demographics

Gender	Percentage
Male	22.22%
Female	77.78%
Prefer not to say	0.00%

Ethnicity	Percentage
Hispanic	22%
Caucasian	67%
African American	11%
Asian	0%
Other	0%

Experience	Percentage
1-2 years	56%
2-5 years	33%
5-10 years	0%
>10 years	11%

Education Level	Percentage
MSN	11.11%
DNP	88.89%
PhD	0.00%
Other	0.00%

Pre-Test Knowledge

Pre-test knowledge of POD revealed that 8 participants (89%) knew that POD is commonly identified as a multifactorial disease process, while only 11% did not. A more significant variation in results regarding the incidence of POD was identified. Forty-five percent correctly identified that the annual incidence of POD in the United States is approximately 2.5 million. Therefore, most participants (55%) were unaware of the clinical incidence. When asked

to identify which independent risk factor is associated with a four-fold increase in the risk of developing POD, 4 participants (45%) selected age as the correct answer. Regarding the consequences of POD, only 33% of participants were able to identify the correct response that included decreased long-term cognitive function, prolonged hospital stays, increased morbidity rates, delayed functional recovery, and increased risk for developing dementia.

The following questions were used to assess the participants' baseline understanding of the pathophysiology and pharmacology of melatonin and dexmedetomidine. When asked to identify the production site of Melatonin, 4 individuals (45%) correctly selected the pineal gland, while 55% chose the following incorrect answers: medulla oblongata (11%), adrenal gland (11%), locus coeruleus (33%). Most participants (n = 8; 88%) could not correctly identify melatonin's mechanisms of action, contributing to its clinical effects in reducing POD. All participants identified dexmedetomidine's drug classification as a highly selective alpha$_2$ agonist. All participants also correctly identified bradycardia, analgesia, and anxiolysis as physiological effects associated with the administration of dexmedetomidine. The results indicated that participants have a better baseline understanding of dexmedetomidine.

The inclination to implement melatonin for POD prevention into anesthesia practice before completing the educational module was low. Five participants (56%) were either extremely unlikely or somewhat unlikely to use melatonin as a preventative option for high-risk patients. Twenty-two percent were unbiased and reported being neither likely nor unlikely, while the remaining 22% reported being somewhat likely to implement melatonin into their practice.

Post-Test Knowledge

Premature completion of the educational module by 1 participant led to 8 post-test responses, compared to 9 pre-test responses. After completing the module, the post-test results

indicated improved knowledge of POD. All participants (100%) correctly identified that POD is a multifactorial disease process with an annual incidence of 2.5 million. All 8 participants (100%) correctly selected age as the appropriate independent risk factor associated with a 4-fold increase in developing POD. Regarding the consequences of POD, 7 participants (88%) identified the 5 correct responses, while only 1 (13%) did not.

After completing the module, the anesthesia providers' knowledge of the pharmacologic management for POD utilizing melatonin and dexmedetomidine improved overall. All participants (100%) correctly identified the pineal gland as the production site for melatonin. Two participants (25%) recognized the mechanisms by which melatonin attenuates POD. Most participants (88%) correctly identified dexmedetomidine's drug classification. All participants correctly identified bradycardia, analgesia, and anxiolysis as physiological effects associated with the administration of dexmedetomidine.

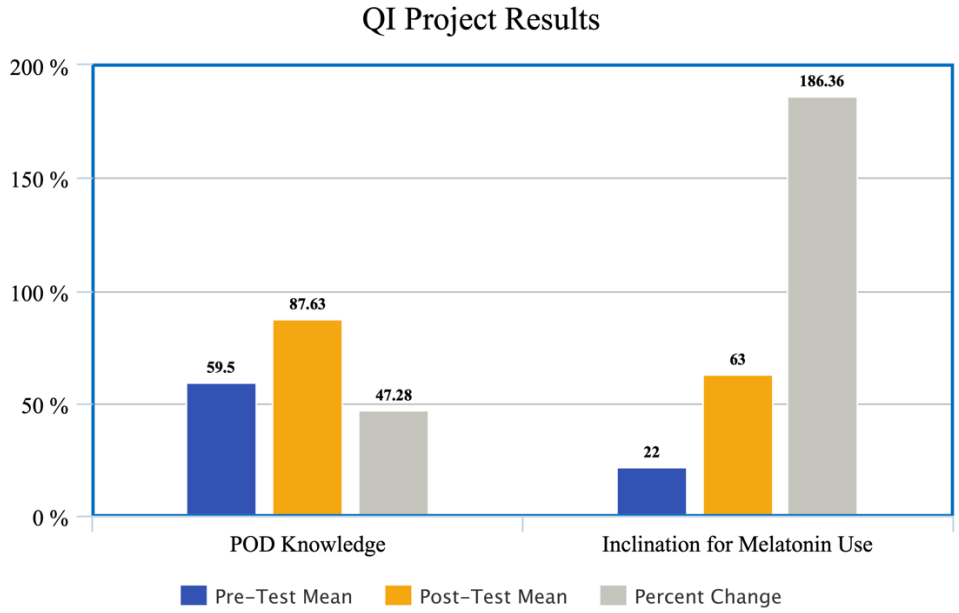
After completing the educational module, providers' inclination to implement melatonin for POD prevention increased. Twenty-six percent were extremely unlikely or somewhat unlikely to implement the practice change, while 63% were somewhat or extremely likely. One participant (13%) remained unbiased and reported being neither likely nor unlikely to utilize melatonin for POD prevention in high-risk patients.

Summary

The results indicated a statistical difference between the pre-and post-survey responses. The average number of correct responses on the pre-test was 59.5%, and an average of 87.63% correct responses were reflected on the post-test. The calculated percent change of these results, 47.28%, signifies the knowledge improvement acquired from this module (Figure 1). The average amount of anesthesia providers inclined to utilize melatonin for POD prevention in high-

risk patients was 22% in the pre-test and 63% in the post-test. A drastic increase in the inclination to use melatonin for POD prevention was observed, with a percent change of 186.36% (Figure 1).

Figure 1. QI Project Results



V: Discussion

Timeline

Evidenced-based, quality improvement projects require careful planning and organization. The estimated timeline for the creation, dissemination, data analysis, and finalization of this QI project was 12 months. Approximately 7 months were devoted to planning and creating the project, followed by IRB approval. The educational module was distributed with a response window of approximately 2 months. The data analysis process was estimated to take 2 months, while the project's finalization should take approximately 1 month. This was not a definitive timeline, as many factors related to the research process, dissemination of the module, and/or participants may impact the project’s progression.

Interpretation of Results

The higher means for the post-test survey showed that the educational module improved knowledge regarding POD and effective interventions to prevent or mitigate its occurrence among elderly patients. Of the 8 questions presented in the pre-and post-test, 6 had a positive percentage change in the post-test results, 1 had no change, and 1 had a negative percentage change. Participants were asked to identify 3 effects of dexmedetomidine administration, and all answered correctly on the pre-and post-test, reflecting the 0% percentage change for this question. On the pre-test, all participants correctly identified dexmedetomidine's drug class as a selective alpha$_2$ agonist. One participant selected the incorrect answer on the post-test as a selective alpha$_2$ antagonist. Due to all participants answering correctly on the pre-test, the selection of the wrong answer on the post-test may have been accidental, but this cannot be proven. The pre-and post-test results and their percentage differences are listed below in Table 2.

Participants' attitudes and inclinations toward implementing melatonin to prevent POD improved after this educational module. The percentage of participants who reported being "extremely unlikely" to utilize melatonin in the pre-test decreased by 31% compared to the post-survey results. A less significant change was noticed in the providers who reported being "somewhat unlikely" to implement melatonin into their practice, with only a 3% change noted between the pre- and post-test results. The percentage of unbiased participants who reported being "neither likely nor unlikely" to utilize melatonin for POD decreased by 9%. The 41% increase in the "somewhat likely" and "extremely likely" post-survey responses supports the participants' positive inclination toward using melatonin. The pre-and post-test results and percentage differences regarding the utilization of melatonin as a preventative option of POD are displayed in Table 3 below.

Table 2. Pre vs. Post-Test Results

Question	Correct in Pre-Test	Correct in Post-Test	Difference
The diagnosis of postoperative delirium can frequently be connected to a single mechanism/factor	89%	100%	+11%
The annual incidence of postoperative delirium in the United States is approximately:	44%	100%	+66%
Which of the following risk factors for postoperative delirium is considered an independent predictor and is associated with a 4-fold increase in the risk of developing postoperative delirium?	44%	100%	+66%
Consequences of postoperative delirium include all the following except:	33%	88%	+55%
Melatonin is a natural hormone produced by the:	44%	100%	+66%
Dexmedetomidine belongs to which drug class?	100%	88%	-12%
The administration of Dexmedetomidine may produce (select 3)	100%	100%	0
Melatonin's ability to attenuate POD may be described by which of the following properties (select 3)	22%	25%	+3%

Table 3. Utilization and Attitudes of Melatonin POD Prophylaxis Pre- and Post-Test

Question	Pre-Test	Post-Test	Difference
How likely are you to utilize Melatonin as a preventative option for patients at high risk for developing POD?			
Extremely unlikely	44%	13%	-31%
Somewhat unlikely	11%	13%	+3%
Neither likely nor unlikely	22%	13%	-9%
Somewhat likely	22%	50%	+28%
Extremely likely	0%	13%	+13%

Limitations

Obstacles and limitations were encountered when conducting this QI project. Despite the large number of email invitations delivered to potential participants, the number of respondents remains a significant limitation of this study. More than 150 email invitations were distributed to

FIU alumni. Of these, 9 CRNAs completed the pre-test, while only 8 CRNAs completed the entire module, including the post-test. Reminder emails were scheduled and delivered to all potential participants every 2 weeks, with a participation window of 2 months. While the online modality of this educational module is intended to offer a sense of convenience and promote participation, it inadvertently contributed to the study's limitations. Delivery of this educational module via a live presentation format would facilitate recruitment and participation, mitigating the limitations encountered.

Future Implications for Advanced Nursing Practice

Identifying an effective method for preventing postoperative delirium is detrimental to patient outcomes, particularly in high-risk patients. While this study did not distinctly point to a superior agent for this condition, the positive results reported from melatonin administration are sufficient to set the stage for a new paradigm. Prophylactically administering melatonin to patients at moderate or high risks of developing POD could become a standard of care and halt the growing incidence of POD. As the elderly population expands, finding a solution to this problem is imperative. Melatonin's accessibility and feasibility make it an appealing option.

As advanced practice nurses, CRNAs are responsible for generating new research findings and translating them into clinical practice to improve patient care. Hopefully, the information obtained from this project will spark interest in this topic and provide a foundation for future research. As medical technologies and pharmaceuticals continue to advance, more definitive treatment or preventative options for POD may arise. The bridge between new research findings and implementation into clinical practice rests in the hands of doctoral-prepared advanced practice nurses.

Conclusion

Unrecognized, undiagnosed, and untreated postoperative delirium results in poor patient outcomes and delayed cognitive and functional recovery. Anesthesia providers are at the forefront of this condition and have the ability to reduce the incidence of POD and improve patient outcomes. Current practices focus on risk stratification techniques. However, many studies show that pharmacological interventions such as melatonin and dexmedetomidine offer promising effects on the incidence of POD.

Acknowledging and defining a problem are the first steps in problem resolution, both of which were addressed in this module. This educational module also gave anesthesia practitioners the information and resources to implement a change in their practice. It also provided insight into the incidence of POD and its associated morbidity and mortality rates.

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Appendix

Appendix A: IRB Approval

FIU | Research & Economic Development
FLORIDA INTERNATIONAL UNIVERSITY

MEMORANDUM

To: Dr. Yasmine Campbell

CC: Erica Newberry

From: Carrie Bassols, BA, IRB Coordinator CeB

Date: February 2, 2024

Proposal Title: "The Perioperative Utilization of Dexmedetomidine vs Melatonin to Reduce Postoperative Delirium: An Educational Module"

The Florida International University Office of Research Integrity has reviewed your research study for the use of human subjects and deemed it Exempt via the **Exempt Review** process.

IRB Protocol Exemption #:	IRB-24-0035	**IRB Exemption Date:**	02/02/24
TOPAZ Reference #:	113902		

As a requirement of IRB Exemption you are required to:

1) Submit an IRB Exempt Amendment Form for all proposed additions or changes in the procedures involving human subjects. All additions and changes must be reviewed and approved prior to implementation.
2) Promptly submit an IRB Exempt Event Report Form for every serious or unusual or unanticipated adverse event, problems with the rights or welfare of the human subjects, and/or deviations from the approved protocol.
1) Submit an IRB Exempt Project Completion Report Form when the study is finished or discontinued.

Special Conditions: N/A

For further information, you may visit the IRB website at http://research.fiu.edu/irb.

Appendix B: Informed Consent

CONSENT TO PARTICIPATE IN A QUALITY IMPROVEMENT PROJECT
The Perioperative Utilization of Dexmedetomidine vs Melatonin to Reduce Postoperative Delirium: An Educational Module

SUMMARY INFORMATION
Things you should know about this study:

- **Purpose:** Educational module to increase providers' awareness of postoperative delirium and current evidence-based practices to reduce the incidence or severity to improve patient outcomes.
- **Procedures**: If the participant chooses to participate, they will be asked to complete a pretest, 5 minutes watch a voice PowerPoint 15 minutes, and then a post-test 5 minutes
- **Duration:** This will take about a total of 25 minutes total.
- **Risks**: There will be minimal risks involved with this project, as would be expected in any type of educational intervention, which may include mild emotional stress or mild physical discomfort from sitting on a chair for an extended period.
- **Benefits:** The main benefit to you from this research is increasing in the participant's knowledge of preventative measures to reduce the occurrence of postoperative delirium.
- **Alternatives:** There are no known alternatives available to the participant other than not taking part in this quality improvement project.
- **Participation:** Taking part in this quality improvement project is voluntary.

Please carefully read the entire document before agreeing to participate.

NUMBER OF STUDY PARTICIPANTS:
If the participant decides to be in this study, they will be approximately 1 of 20 people in this research study.

PURPOSE OF THE PROJECT
The participant is being asked to be in a quality improvement project. The goal of this project is to increase providers' knowledge of postoperative delirium and potential complications associated with POD, along with current evidence-based practices, to reduce the occurrence. If you decide to participate, you will be 1 of approximately 20 participants.

DURATION OF THE PROJECT
The participation will require about 25 minutes

PROCEDURES
If the participant agrees to be in the project, PI will ask you to do the following things after informed consent is obtained virtually:
1. Complete an online 10 question pre-test survey via Qualtrics, an Online survey product for which the URL link is provided 5 minutes
2. Review the educational PowerPoint Module lasting 15 minutes via Qualtrics, an Online survey product

for which the URL link is provided.
3. Complete the online 10 question post-test survey via Qualtrics, an Online survey product for which the URL link is provided. 5 minutes

RISKS AND/OR DISCOMFORTS
The main risk or discomfort from this research is minimal. There will be minimal risks involved with this project, as would be expected in any type of educational intervention, which may include mild emotional stress or mild physical discomfort from sitting on a chair for an extended period.

BENEFITS
The following benefits may be associated with participation in this project:
An increased knowledge of the negative effects that postoperative delirium has on patient outcomes, as well as current evidence-based interventions to reduce the occurrence. The program's overall objective is to increase the providers' knowledge based on the current literature.

ALTERNATIVES
There are no known alternatives available to the participant other than not taking part in this project. However, if the participant would like to receive the educational material, it will be provided to them at no cost.

CONFIDENTIALITY
The records of this project will be kept private and will be protected to the fullest extent provided by law. If, in any sort of report, PI might publish, it will not include any information that will make it possible to identify the participant. Records will be stored securely, and only the project team will have access to the records.

PARTICIPATION: Taking part in this quality improvement project is voluntary.

COMPENSATION & COSTS
There is no cost or payment to the participant for receiving the health education and/or for participating in this project.

RIGHT TO DECLINE OR WITHDRAW
The participation in this project is voluntary. The participant is free to participate in the project or withdraw the consent at any time during the project. The participant's withdrawal or lack of participation will not affect any benefits to which you are otherwise entitled. The investigator reserves the right to remove the participant without their consent at such time that they feel it is in their best interest.

RESEARCHER CONTACT INFORMATION
If you have any questions about the purpose, procedures, or any other issues relating to this research project, you may contact Erica "Logan" Newberry at 912-424-1765/ Enewb004@fiu.edu OR Yasmine Campbell, DNP, CRNA, ARNP, CNE, CHSE / Ycampbel@fiu.edu.

IRB CONTACT INFORMATION
If the participant would like to talk with someone about their rights pertaining to being a

subject in this project or about ethical issues with this project, the participant may contact the FIU Office of Research Integrity by phone at 305-348-2494 or by email at ori@fiu.edu.

PARTICIPANT AGREEMENT
I have read the information in this consent form and agree to participate in this study. I have had a chance to ask any questions I have about this study, and they have been answered for me. By clicking on the "consent to participate" button below I am providing my informed consent.

Appendix C: Pre- and Post-Test Survey

Pretest and Posttest Questionnaire:

Dexmedetomidine vs. Melatonin to Reduce Postoperative Delirium

Introduction

The primary aim of this QI project is to increase providers' awareness of postoperative delirium and current evidence-based practices to reduce its incidence or severity and improve patient outcomes.

Please answer the questions below to the best of your ability. The questions are either multiple-choice or true/false and are meant to measure knowledge of postoperative delirium.

Demographic Information

1. **Gender:** Male_____ Female_____ Other_____
2. **Age:** _____
3. **Ethnicity:**

   Hispanic____ Caucasian____ African American_____

   Asian____ Other____
4. **How many years have you been a CRNA?**

   10+____ 5-10____ 2-5____ 1-2____
5. **Highest Level of Education:** MSN____ DNP____ PhD____

Questionnaire

1. **The diagnosis of postoperative delirium can frequently be connected to a single mechanism/factor.**
    a. True
    b. False
2. **The annual incidence of postoperative delirium in the United States is approximately:**
    a. 1.1 million
    b. 2.5 million
    c. 5 million
    d. 1 billion
3. **Which of the following risk factors for postoperative delirium is considered an independent predictor and is associated with a 4-fold increase in the risk of developing postoperative delirium?**
    a. Age
    b. Electrolyte imbalances
    c. Intraoperative blood pressure fluctuations
    d. Benzodiazepine use
    e. Dementia
    f. Cardiac surgery
4. **Consequences of postoperative delirium include all the following except**
    a. Decreased long-term cognitive function
    b. Transient ischemic attacks
    c. Prolonged hospital stays
    d. Increased morbidity rates

e. Delayed functional recovery

f. Increased risk of developing dementia

5. To date, no single pharmacological intervention has been identified to prevent or treat postoperative delirium.

a. True

b. False

6. Melatonin is a natural hormone produced by the

a. Medulla Oblongata

b. Pineal gland

c. Adrenal gland

d. Locus coeruleus

7. Dexmedetomidine belongs to which drug class?

a. Selective alpha$_2$ agonist

b. Selective alpha$_2$ antagonist

c. Non-selective alpha agonist

d. Anticholinesterase inhibitor

e. Calcium channel blocker

8. The administration of Dexmedetomidine may produce (select 3)

a. Bradycardia

b. Anxiolysis

c. Analgesia

d. Increased salivation

e. Ventricular tachycardia

9. **Melatonin's ability to attenuate POD may be described by which of the following properties (select 3)**
    a. Potent free-radical scavenger
    b. Inability to cross the blood-brain barrier
    c. Broad spectrum antioxidant
    d. Apoptosis
    e. Alters the sleep cycle
    f. Reduces cerebral oxygen demands
10. **How likely are you to utilize Melatonin as a preventative option for patients at high risk for developing POD?**
    a. Most likely
    b. Somewhat likely
    c. Most unlikely
    d. Somewhat unlikely

Appendix D: Recruitment Letter

Nicole Wertheim College of Nursing & Health Sciences

The Perioperative Utilization of Dexmedetomidine vs Melatonin to Reduce Postoperative Delirium: An Educational Module

Dear FIU ALUMNI Perioperative Providers:

My name is Erica Logan Newberry RN, BSN, and I am a student from the Anesthesiology Nursing Program Department of Nurse Anesthesiology at Florida International University. I am writing to invite you to participate in my quality improvement project. The goal of this project is to increase healthcare providers' awareness of postoperative delirium and pharmacological interventions to reduce its occurrence. You are eligible to participate in this project because you are a part of the FIU ALUMNI perioperative provider.

If you decide to participate in this project, you will be asked to complete and sign a consent form for participation. Next, you will complete a pre-test questionnaire, which is expected to take approximately 5 minutes. You will then be asked to view an approximately 15 minutes long educational presentation online. After going through the educational module, you will be asked to complete the post-test questionnaire, which is expected to take approximately 5 minutes. No compensation will be provided.

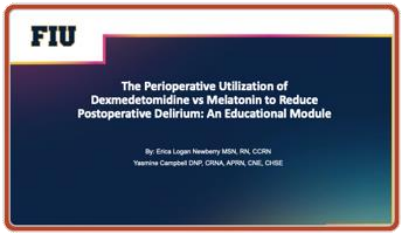
Remember, this is completely voluntary. You can choose to be in the study or not. If you'd like to participate or have any questions about the study, please email or contact me at 912-424-1765 / enewb004@fiu.edu

Thank you very much.

Sincerely,

Erica Logan Newberry RN, BSN / 912-424-1765 / Enewb004@fiu.edu

Appendix E: PowerPoint Presentation for Educational Module



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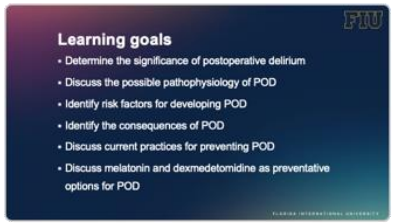

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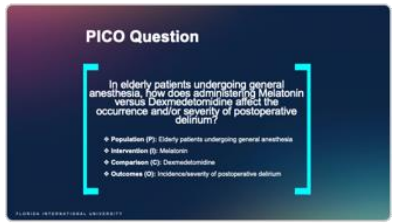

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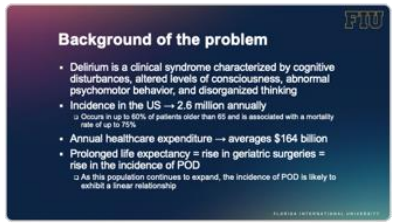

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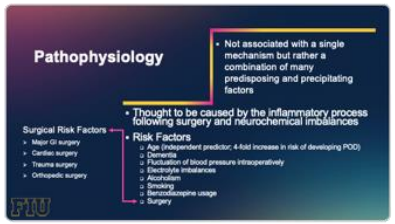

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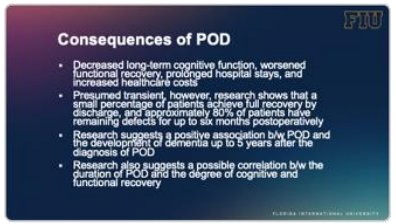

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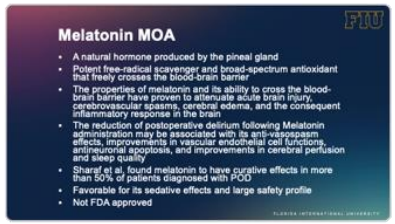

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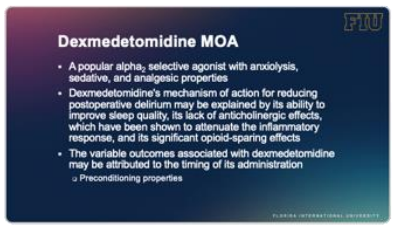

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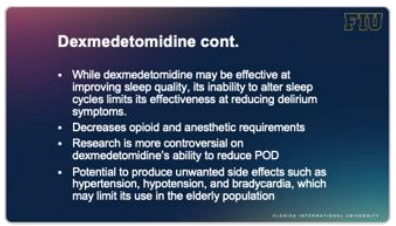

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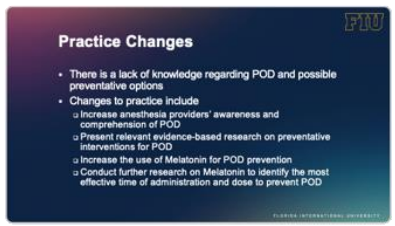

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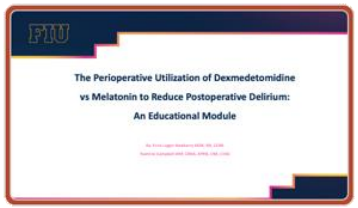
Appendix F: PowerPoint Presentation for Dissemination of Project



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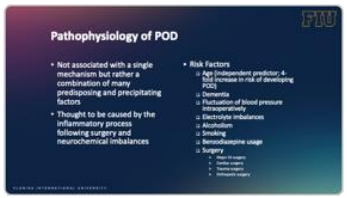

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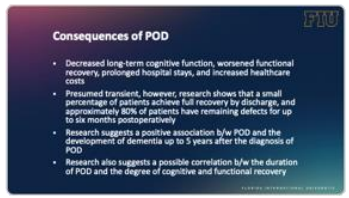

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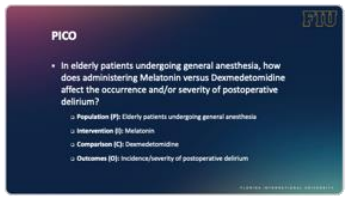

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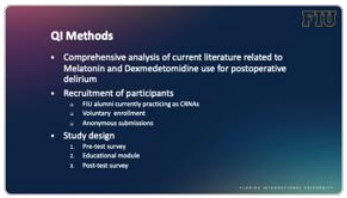

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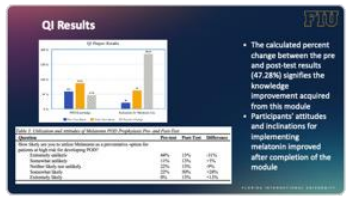

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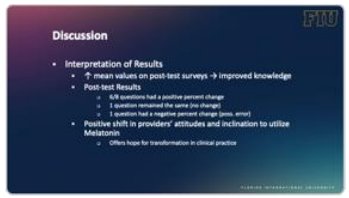

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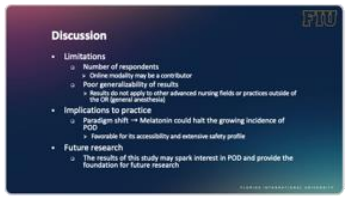

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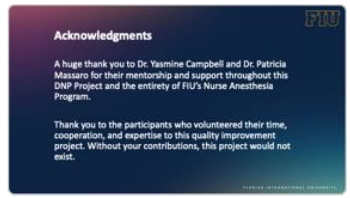

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Appendix G: DNP Poster

Erica Logan Newberry, MSN, RN; Yasmine Campbell DNP, CRNA, APRN, CNE, CHSE

Introduction

- POD affects more than 2.6 million adults each year and is associated with complications and poor outcomes
- There is no known cure for POD; therefore, emphasis is placed on preventive strategies. Current research shows that melatonin and dexmedetomidine effectively reduce the occurrence and/or duration of POD.
- Melatonin is favorable for its large safety profile when compared to dexmedetomidine. Dexmedetomidine may present unwanted cardiovascular side effects in the elderly population.

Methods

- IRB approval requested and approved for FIU and teaching hospital
- Anesthesia Providers at teaching facility recruited via Email to participate in Quality Improvement Project
- Educational Module created by a voiceover Powerpoint
- Consents obtained, surveys and educational module distributed to participants via Qualtrics
- Data gathered and stored in Qualtrics for analysis

PICO Question

In elderly patients undergoing general anesthesia, how does administering Melatonin versus Dexmedetomidine affect the occurrence and/or severity of postoperative delirium?

Research and Learning Outcomes

Prolonged life expectancy → ↑ elderly population → ↑ need for geriatric surgeries → ↑ incidence of POD

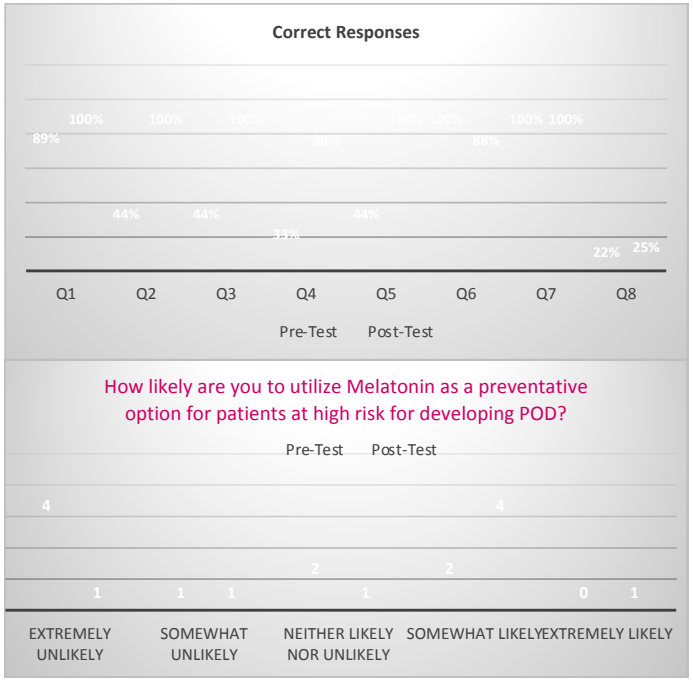
Growing topics in research on POD include:

Early identification	Acute and long-term complications	Preventative / treatment options

Project Purpose

- To educate anesthesia providers on current evidence-based practices regarding POD
- To promote discussion of preventative options for POD

Results



Limitations

- Sample Size
- Incompletes
- Distribution

References:

Appendix H: Literature Review Tables

Citation	Design/Method	Sample/Setting	Major Variables Studied and Their Definitions	Measurement And Data Analysis	Findings	Results	Conclusions	Appraisal: Worth to Practice/Level
Mohamed et al,[1] 2022	This article is a double-blinded prospective randomized comparative study. The study compared the incidence of postoperative delirium (POD) in elderly patients who received Melatonin vs a placebo.	This study was conducted at Cairo University Hospital between July and December 2020. The study consisted of 80 elderly patients undergoing orthopedic surgeries with general anesthesia. Of the one hundred patients enrolled, 80 completed the study. Inability to contact patients after discharge, refusal to consent, and admission to the ICU were the factors that contributed to the attrition rate.	IV= Melatonin IV2= Placebo DV= Incidence of POD	The Abbreviated Mental Test (AMT) was used to evaluate for delirium. The Pain Assessment in Advanced Dementia, sedation scores, and hemodynamic status was also recorded. All scales utilized in this study are qualitative, ordinal scales. Cronbach's alpha score was utilized to signify the reliability of the results. Quantitative methods were used to answer the research question.	The Statistical Package for Social Sciences (SPSS) was utilized for data analysis. Qualitative statistics were expressed as standard deviations and conveyed as a number and percent. The independent T-test was utilized to compare the mean values of each group. *P*-value of less than 0.5 was utilized to signify statistical significance.	The incidence of POD was significantly lower in the Melatonin group as evident by *p*-value <.001, odds ratio (OR) of 2.3, and a 95% confidence interval (CI) of -0.44, + 1.23 No significant difference was noted in the risk variables between the groups as evident by *p*>.05 Statistical significance was noted between AMT scores with the Melatonin group at PACU (P=.001) and postoperative day 0 (P=.035) The incidence of POD was significantly less (25%) in the Melatonin group compared to the Non-Melatonin group ((52.5%)	The administration of Melatonin significantly reduces the occurrence of POD in the recovery period and Day 0 (6 hours after surgery). Since there was no significant difference noted by the presence of multiple risk variables, the higher incidence of POD in the non-melatonin group cannot be attributed to these risk factors (sx duration, blood transfusion requirements, BP fluctuations, hypoxia, age, gender, BMI, ASA score). No significant difference was found in pain score or hemodynamics.	This double-blinded randomized control study classifies as level II evidence. The size of the study population was sufficient to produce strong, reliable results. Limitations to the study include failure to use different doses of Melatonin, the utilization of only the AMT score for POD evaluation and was only conducted for orthopedic surgeries. Due to Melatonin's large safety profile, the risk associated with its administration is minimal making it a feasible intervention to implement into anesthesia practice.
Aldujail et al,[7] 2023	The primary goal of this randomized control trail was to determine the efficacy of Melatonin on POD.	This study was conducted at Al-Kadhimiya Private Hospital and Ghazi Al-Hariri Teaching hospital from July	IV= Melatonin IV2= Non-medicated IV3= Midazolam DV= Incidence of POD	The Memorial Delirium Assessment Scale was utilized to evaluate the	Chi square test was used for statistical analysis and SPSS was utilized for	The incidence of POD in the non-medicated group at 0, 30, 60, & 90 mins did not yield statistically	Approx 60% of patients that received no premedication experienced delirium at 90	This double-blinded randomized control study classifies as level II evidence. The

		to October 2020. The study consisted of 36 patients undergoing orthopedic surgeries with general anesthesia. Of the 50 patients enrolled, 36 completed the study. Fourteen patients were excluded for neurological disorders, acute/chronic confusion, taking centrally acting drugs, or alcohol abuse which contributed to the attrition rate.		presence of POD. This assessment tool consists of 10 items which allows the clinician to interact and observe patient behaviors. This scale is an ordinal scale.	descriptive and analytic statistics. *P*-values <.05 signifies statistical significance.	significant results as evident by a *p*-value > .05. The incidence of POD in the Melatonin group had a statistically significant reduction in POD at 30, 60 and 90 mins postoperatively as evident by a *p*-value <.05. The Midazolam group also did not yield significant results in the reduction of POD as evident by a *p*-value >.05. When comparison is made between the three groups, there are no significant differences in POD at 0 and 30 mins (*p*>.05). At 30 mins, the Melatonin group was significantly lower (*p*<.05) when compared to the control group and the Midazolam group. At 90 mins, the Melatonin group yielded highly significant results in the reduction of POD which was 0%. The odds ratio for the Melatonin group at 30, 60, & 90 mins was 0.06,0.08, and 0). The Chi square test results indicated that preoperative administration of Melatonin is dependent on the outcome (occurrence of POD).	mins postop. While Midazolam administration resulted in a 42% incidence of POD at 90 mins postop, these results were significantly insignificant (*p*>.05). Preoperative administration of Melatonin was the only group that produced statistically significant results (*p*=.01) and yielding a 0% incidence of POD at 90 mins postop. Overall, Melatonin has proven superior at reducing the incidence of POD.	utilization of, and results from the Chi Square test in this study demonstrate the statistically significant data. Limitations to the study include the sample size of 36 patients which may limit generalizability. Melatonin has statistically and clinically been proven as a reliable, safe intervention to decrease the occurrence of POD.

Fazel et al,[6] 2022	This randomized control trail was conducted to determine the effectiveness of Melatonin on the prevention and treatment of POD in elderly patients undergoing orthopedic surgeries with spinal anesthesia.	This study was conducted between May and November 2019 at Kashan Shahid Beheshti Hospital in Iran. The study consisted of 72 patients over 60 years of age. Of the 80 patients enrolled in the study, eight did not complete the study due to the need for general anesthesia instead of spinal anesthesia (6) or admission to the ICU (2) postoperatively.	IV= Melatonin IV2= Placebo DV= Incidence of POD	The Abbreviated Mental Test (AMT) was used to evaluate the occurrence of delirium. The AMT classifies an ordinal scale.	A Chi-square test was utilized to compare data between the two groups. The generalized estimating equations model (GEE) was utilized for multivariate analysis. SPSS was used for statistical analysis, and a *p*-value of <0.05 was considered statistically significant.	No significant difference on POD was found between the two groups regarding patient demographics (age, sex). Significant differences were noted in the Melatonin group on all 3 days following the surgery as evidenced by the following *p*-values 0.046, 0.035, 0.006.	After 60 years of age, there is no statistical significance of increased age on the incidence of POD. The administration of Melatonin preoperatively reduced the incidence of POD up to 3 days postoperatively. Melatonin administration improves sleep quality and regulates circadian sleep disturbances, which are hypothesized to contribute to POD.	This double-blinded randomized control study classifies as level II evidence. The utilization of the Chi-Square test in this study demonstrates the statistically significant data. The small sample size and age requirements for included participants limit the generalizability of this study. Another limitation includes the lack of long-term follow-up, as some patients may develop POD after the study period. Melatonin has statistically and clinically been proven as a reliable, safe intervention to decrease the occurrence of POD.
Fan, et al,[10] 2017	This randomized control trial was executed to determine if Melatonin administration could ameliorate early postoperative cognitive decline in patients >65 years old undergoing hip arthroscopy with spinal anesthesia.	This study took place in Jinling Hospital, Nanjing China. Of the 148 patients enrolled in this trial, 9 did not complete the study due to the inability to follow up postoperatively.	IV= Melatonin IV2= Placebo DV= Incidence of POD	Subjective assessment regarding sleep quality, general well-being, postoperative fatigue, and pain was determined using visual analog scales (VAS). A 30 question assessment tool,	SPSS was used for statistical analysis, and a *p*-value of <0.05 was considered statistically significant. A two-way ANOVA analyzed the differences in MMSE	Baseline MMSE scores between the two groups revealed no difference signifying the absence of cognitive dysfunction preoperatively. In the Melatonin group, there was no statistically significantly decline in MMSE scores from baseline at days	The results of this study demonstrated that the administration of Melatonin improved sleep quality which is a factor linked to the development of POCD. Melatonin administration is not associated with unwanted side effects or	This double-blinded randomized control study classifies as level II evidence. The subjective assessments utilize within this study may be viewed as limitations. Objective sleep measurements

				the Folstein MMSE, was utilized to determine cognitive function preoperatively and at days 1,3,5, and 7 postoperatively. These scales classify as ordinal scales.	scores and the subjective assessment between the groups. Intergroup comparisons were compared using t-tests. Chi square test of fisher exact tests were used to analyze categorial variables such as age, ASA classification, and side effects.	1,3,5,& 7 postoperative as evident by *p*-value > 0.05. A statistically significant decline in MMSE scores were noted in the control group at days 1,3, & 5 postop as evident by a *p*-value <0.05. A significant decrease in MMSE scores were also noted in the control group when compared with the Melatonin group for the corresponding date. The subjective assessment results revealed a significant decline in reported sleep quality, well-being, and fatigue in the control group when compared to the Melatonin group.	cognitive or psychomotor impairment. The results of this study revealed that poor subjective sleep quality coexisted with postoperative cognitive decline.	may produce more precise results on Melatonin's role in sleep regulation. This study also reported no differences in side effects between the groups signifying the safe, practical use of Melatonin for prevention of POD.
Sharaf et al,[5] 2018	This randomized, controlled, double-blinded study aimed to determine the effectiveness of Melatonin in producing preoperative sedation as well as its preventative and curative effects on postop delirium in elderly patients undergoing coronary artery bypass surgery.	This study was conducted in Ain Shams University Hospital.[5] Fifty patients over the age of 60 were enrolled. The attrition rate was not discussed.	IV= Melatonin IV2= Placebo DV= Incidence of POD	The Mini-Mental State Examination (MMSE) was utilized to determine patient baseline (pts with a score of 24 or less were excluded from the study). A preoperative sedation assessment was obtained by a clinical global impression (CGI) sedation score. An Intensive Care Delirium Screening Checklist	SPSS was utilized for data analysis. Cronbach's alpha score was utilized to signify the reliability of the results. *P*-values of <.05 was considered significant and values <.01 was considered highly significant. T-test and chi-square test were used to compare	Regarding patient demographics, no significant difference was noted in the incidence of POD between the 2 groups. The Melatonin group produced statistically significant levels of preoperative sedation 30 mins after the administration when compared to the placebo as evidenced by a *p*-value of.022. A significant decrease in the incidence of POD was noted in the Melatonin group (P=0.046). Only	Prophylactic Melatonin administration produced sedative effects and decreased the incidence of POD from 28% to 8%. Melatonin administration successfully treated 56% of patients who developed POD.	This double-blinded randomized control study classifies as level II evidence. Limitations to this study was not discussed. Melatonin is a safe alternative to many other anxiolytics and sedatives as it lacks the unwanted side effects such as PONV, POD, and respiratory depression.

				(ICDSC) was utilized to determine the presence of POD (score of 4 or higher). The scales utilized classify as ordinal scales.	mean values between the groups.	2/25 patients in the Melatonin group developed POD which was cured with continued Melatonin administration.7/25 patients in the control group developed POD, 3 were cured with Melatonin administration, 2 improved but were not cured, and 2 had no response. These results were statistically significant. All of the following independent variables produced statistically significant associations with POD; age >70, bypass time >60 mins, cross clamp time >45 mins, EF <55%, and fentanyl dose >1200mcg.		
Zadeh et al,[9] 2021	The primary goal of this RCT was to determine the effect of Melatonin on the occurrence and intensity of POD. The secondary goals evaluated postoperative mechanical ventilation times and length of ICU stay.	The study took place between September 2018 and March 2019 at Golestan Hospital in Iran. Sixty patients were enrolled in this study, and it has a 0% attrition rate.	IV= Melatonin IV2= Placebo DV= Incidence of POD	The presence of delirium was assessed by the Confusion Assessment Method for ICU (CAM-ICU) scale, and the intensity of POD was evaluated using the Memorial Delirium Assessment Scale (MDAS). The scales utilized classify as ordinal scales.	SPSS was utilized for data analysis. T-test and chi-square test were used to compare mean values between the groups. *P*-values of <.05 was considered significant.	The presence of delirium on the POD1 was statistically significant between the Melatonin (4/30) and control (11/30) group (P=0.037). The development on delirium on POD2 also yielded statistically significant results; Melatonin group (3/30) control group (14/30) P=0.029. The severity of the delirium between the two groups was also	The administration of Melatonin reduced the incidence and severity of POD in patients undergoing CABG. Melatonin was also affecting at reducing postoperative mechanical ventilation time as well as ICU admission duration.	This double-blinded randomized control study classifies as level II evidence. Limitations to this study include the duration of the study which consisted of 2 days postoperative, failure to evaluate surgical complications as a cause of delirium, and failure to perform baseline

						statistically significant P=0.003. The secondary outcomes of this study, mechanical ventilation time postoperatively and duration of ICU stay, were both reduced in the Melatonin group and produced statistically significant results as evidenced by *P*-values 0.032 and 0.04.		psychiatric screenings. Melatonin has statistically and clinically been proven as a reliable, safe intervention to decrease the occurrence of POD.
Ford et al,[11] 2020	The primary goal of this randomized control trial was to determine the effectiveness of Melatonin in reducing the incidence of POD after major cardiac surgeries.	The study took place in Perth, Western Australia, between January 2016 and October 2018 and consisted of 210 patients, 50 years or older, undergoing CABG or valve replacement surgery. Of the 210 patients enrolled, 44 did not complete the study due to lack of follow-up, withdrawal of consent, intraoperative death, or cancellation of surgery.	IV= Melatonin(M) IV2= Placebo (C) DV= Incidence of POD	The Confusion Assessment Method (CAM) was utilized to evaluate the presence of delirium. The severity of delirium was assessed with the Memorial Delirium Assessment Scale (MDAS). The Hospital Anxiety and Depression Scale was used to assess mood and anxiety. Cognitive function was measured with the TICS-M. The scales utilized are classified as ordinal scales.	Stata v13.1 software was utilized to for data analysis. T tests and Mann-Whitney tests were utilized for ordinal data analysis. Logistics regression was used to determine the odds of the primary and secondary outcomes. Cronbach's alpha score was utilized to signify the reliability of the results.	Forty-two patients developed POD in the immediate post-op period. Of these patients, they were evenly disbursed between the Melatonin (21.4%) and control (20.2%) groups [OR=1.08]. The duration of delirium between the two groups (M 3 days & C 2 days) did not yield statistically significant results (P=0.304). The severity of POD between the groups, as based on MDAS scores, also did not yield significant results (P=0.221), as the severity score was similar in each group (M=9; C=8.5). While Melatonin's median LOS was longer, the association was no longer significant after adjustments were made for age, heart failure, DM,	The results from this study did not favor the use of Melatonin as a prophylactic to prevent or reduce POD in patients undergoing major cardiac surgeries. The risk of developing POD increased 12% yearly with age. In patients with baseline cognitive dysfunction, the administration of melatonin may increase the risk of POD. It was also noted that the odds of developing a medical or surgical complication was not affected by melatonin administration.	This double-blinded randomized control study classifies as level II evidence. One limitation to this study is the study population which included relatively healthy and physically fit participants when compared to medical/surgical populations (ex: pts w/ hip fx). Many factors that have been associated with the development of POD were not accounted for in this study analysis, including CPB time, transfusion requirements, EF, home medication use, and type/dose of perioperative analgesia/sedation. The generalizability of

						baseline cognitive dysfunction, and surgical procedure. Between the groups, no difference was noted in mood, anxiety, and cognitive function at discharge and 3 months post-op. Patients with impaired baseline cognitive function, based on TICS-M scores, had a 16-fold increase in the odds of developing POD (OR=16.47). The odds of these patients treated with Melatonin developing POD increased 60% as evidenced by OR=1.60.		these results may be limited because the results focused on a specific surgery type and population.
Li et al,[14] 2020	The goal of this randomized clinical trial was to determine the effect of intraoperative dexmedetomidine on the incidence of POD in elderly patients undergoing major non-cardiac surgery.	This study took place between December 2015 and March 2018 at Peking University First Hospital. The study included 620 patients 60 years or older who were undergoing general anesthesia for major non-cardiac surgery. Of the 620 patients enrolled, one patient withdrew consent and did not complete the study.	IV= Dexmedetomidine IV2= Placebo DV= Incidence of POD	The Barthel Index was utilized to assess the baseline function of performing activities of daily living (ADLs). The Mini-Mental State Exam (MMSE) was utilized to evaluate cognitive function and delirium was assessed using the Confusion Assessment Method (CAM). The scales utilized are	SPSS software was utilized for statistical analysis. Independent T-test and Mann-Whitney U test were utilized to compare data between the groups. The Kaplan-Meier survival analysis evaluated 'time to event' data. Odds ratios were used to quantify the estimated	The Dex group produced a statistically significant decrease in the developed POD compared to in control group as evidenced by a *P*-value of 0.026. The Dex group was also associated with a lower incidence of non-delirium (p=0.047) and surgical (p=0.011) complications when compared to the control. ICU admissions, length of hospital stays, and 30-day mortality rates were not significant among the two groups. Statistically	Dexmedetomidine proved effective in reducing the incidence of POD in elderly patients undergoing major non-cardiac surgeries. Dexmedetomidine also reduced the incidence of agitation, tachycardia, PONV, and non-delirium complications postoperatively. Using Dexmedetomidine reduces intraoperative anesthetic requirement which may be one mechanism of its	This double-blinded randomized control study classifies as level II evidence. Limitations to study may be attributed to the hemodynamic effects of Dex which may have weakened the blinding to the anesthesia provider. While Dex may be a feasible option, one must be cautious of the side effects associated with its administration.

				classified as ordinal scales.	effect size. *P*-values of less than 0.05 were considered statistically significant.	significant results were found in the Dex group regarding lower incidences of acute agitation (p=0.007), tachycardia (p=0.038), and PONV (p=0.021). The rate of bradycardia, however, was significantly increased (p=0.014) in the Dex group.	delirium-sparing effects. Another mechanism may be attributed to its ability to attenuate the surgical stress response which is also associated with an increased risk of POD. The attenuation of the stress response by Dex administration may also be the reason for the reduced surgical complications found in this study.	
Liu et al,[16] 2022,	This study was conducted to determine the effect of Dexmedetomidine on the development of POD in patients undergoing oral surgery. A dexmedetomidine infusion was administered from 10 mins before induction to 30 mins before the end of surgery. The control group received normal saline for the same time intervals.	The study was conducted from December 2021 to March 2022 in Cangzhou Central Hospital. 120 patients were enrolled in this study and there was a 0% attrition rate.	IV= Dexmedetomidine IV2= Placebo DV= Incidence of POD	Patients were assessed for the presence of delirium using the 3-Minute Diagnostic Interview for CAM (3D-CAM). Visual Analog Scores (VAS) were utilized to assess postoperative pain levels. Sleep quality was assessed using Richards Campbell Sleep Questionnaire (RCSQ). The scales utilized are classified as ordinal scales.	SPSS was utilized to analyze and process all data. Independent T-test and ANOVA were used to compare data between the groups. Chi-square tests or Fisher exact text was used for the ratio between groups. Statistically significant results were represented by p-values less than 0.05.	There was no significant difference in the development of POD between the Dex (8.3%) and control (13.3) groups [p=0.387]. All 13 patients developed delirium on the first postoperative day, and there was no statistically significant difference in the duration of the delirium between the groups (p=0.7). The Dex group did produce statistically significant lower VAS scores at 6, 12, and 24 hours postop, as evidenced by *p*-values less than 0.05.Postoperative sleep quality was statistically significant, with the Dex group reporting higher scores (*p*<0.001). No	Dexmedetomidine was not effective at reducing the occurrence or duration of POD in elderly patients undergoing oral/maxillofacial procedures. The explanation for the Dex group having higher sleep quality score but no improvement in POD may be described by Dex's ability to mimic natural sleep without altering the sleep cycle. Dex did improve postoperative pain score and reduce intraoperative anesthetic requirements both of which may be risk factors for POD.	This double-blinded randomized control study classifies as level II evidence. Limitations to this study include the study size and the dose of Dex that was administered throughout the surgery. While Dex may be a feasible option, one must be cautious of the side effects associated with its administration.

						significant difference was noted in blood loss, urine output, anesthesia time, BIS, hospital stays, or bradycardic or hypotensive episodes between the groups as evidenced by *p*-values > 0.05.		
Xaun et al,[2] 2018	This double-blinded placebo clinical trial was conducted to determine if Dexmedetomidine could reduce the incidence of POD. The Dex group received an IV infusion of Dex at 0.1mcg/kg/hr that was initiated 1 hour postop and continued for three days. The control group received normal saline at the same dose.	This study took place between August 2015 and August 2017 in three hospitals in Jiangsu and Anhui, China. A total of 453 participants were enrolled in this study, and 9 patients withdrew consent.	IV= Dexmedetomidine IV2= Placebo DV= Incidence of POD	The CAM and CAM-ICU scale was utilized to assess the presence of POD. Sedation and agitation were assessed by using RASS. The scales utilized are classified as ordinal scales.	SPSS was utilized to analyze and process all data. Categorical variables were analyzed with X^2 test, t-test or Mann-Whitney U test analyzed numerical data, and data between the groups were calculated with the Hodges-Lehmann estimator. Statistically significant results were represented by *p*-values less than 0.05.	The development of POD in the Dex group was significantly reduced when compared to the control group ($p<0.0001$). The length of hospital stay and hospital expenses were significantly increased in the placebo group compared to the dex group (p=0.001). Postoperative hypertension was lower in the Dex group (p=0.034) while the occurrence of hypotension (p=0.1) and tachycardia (p=0.06) between the groups were not significantly different.	A prophylactic low dose of Dexmedetomidine may reduce the incidence of POD in elderly patients undergoing joint replacements. Dexmedetomidine.	This double-blinded randomized control study classifies as level II evidence. Limitations to this study are as follows; only included joint replacement procedures, a baseline delirium screening was not conducted, a single dose of dex was utilized. While the Dex and control group did not produce statistically significant differences in side effects, that cannot be disregarded if one plans to implement Dex for POD prevention.
Li et al,[13] 2023	This study was conducted to determine if dexmedetomidine reduces POD in patients undergoing intracerebral tumor resection. The intervention group was given a loading dose of Dex (0.6mcg/kg)	The study took place between January and December 2021 in two tertiary care hospitals in Beijing. Of the 260 patients enrolled in the study, 3 did not complete it due to	IV= Dexmedetomidine IV2= Placebo DV= Incidence of POD	The Mini-Mental State Exam was utilized to assess baseline cognitive function. The presence of delirium was evaluated by	Statistical analysis and group comparisons were completed by utilizing Stata/SE 16.0, two-tailed X^2	No participant presented with delirium or delirium features according to baseline/preoperative MMSE scores. Postoperative requirements for rescue analgesic was significantly reduced	Dexmedetomidine produced a 50% reduction in the incidence of POD in patients undergoing intracerebral tumor resection. Dexmedetomidine also reduced pain	This double-blinded randomized control study classifies as level II evidence. Limitations to this study are as follows; relatively young and healthy

	followed by a continuous infusion at 0.4mcg/kg/hr until dural closure. Normal saline was administered at the same rate for the control group. Patients were assessed for the presence of delirium twice a day during the initial 5 postoperative days.	being in a comatose state or being discharged before the 5th postoperative day.		multiple scales including CAM-ICU, 3D-CAM, and RASS. A numerical rating scale (NRS) was utilized to quantify pain and sleep quality was evaluated by the Richards Campbell sleep questionnaire. The scales utilized are classified as ordinal scales.	tests, Fischer's exact tests, student t-tests, Mann-Whitney tests, and Kaplan-Meier curves. Statistical significance was considered for *p*-values < 0.05. Risk ratios and confidence intervals were calculated for categorical variables.	in the Dex group (p=0.0.11). The incidence of POD in the Dex group was significantly less (22%) than the control group (46%), as evidenced by a *p*-value of less than 0.001. The Dex group had lower incidences of all 3 subtypes of delirium including hypoactive, hyperactive, and mixed delirium. However, there was only a statistically significant decrease associated with the hypoactive type ($p<0.001$). Between the groups, the duration of delirium did not differ significantly. Pain scores were with the Dex group and the control group required more postop analgesia.The NRS scores for sleep quality was significantly greater in the Dex group ($p<0.001$) at 24 hours postop. No statistical significance was noted on CV side effects b/w the groups (hypotension p=0.642; bradycardia p=0.473)	intensity and improved sleep quality. Pain and poor sleep quality are two important risk factors for the development of POD and may be part of the reason Dexmedetomidine reduces the occurrence of POD. Dex is known for its cardiovascular side effects esp bradycardia and hypotension. The absence of significant differences in hemodynamics between the Dex and control group may be attributed to the study population being young and healthy and should therefore not be disregarded or portrayed as negligible.	study population, failure to evaluate the severity of delirium, and failure to evaluate the mechanism of the POD. The generalizability of these results may be limited as this was conducted on relatively young, healthy patients with minimal comorbidities.
Likhvantsev et al,[12] 2021	This study was performed to evaluate Dexmedetomidine's effect on the rate of	This study took place between December 2016 and March 2019 at a	IV= Dexmedetomidine IV2= Placebo	The presence of delirium was evaluated with the CAM-ICU	Variable distribution was evaluated	There were significantly fewer patients in the Dex group that developed	Perioperative infusion of Dexmedetomidine from induction to	This double-blinded randomized control study

	POD after cardiac surgery. Patients in the intervention group received a Dex infusion at 0.7mcg/kg/hr beginning at induction of anesthesia and continued to the ICU until ventilation weaning occurred. Patients in the control group received normal saline at the same rate.	University Hospital in Moscow, Russia. Of the 175 patients enrolled in the study, 169 patients completed the study. Six patients had to return to surgery, which led them to be excluded from the study.	DV= Incidence of POD	score and the severity was assessed with the Intensive Care Delirium Screening Checklist.	with the D'Agostino-Pearson test. Student T or Mann-Whitney was utilized for between-group comparisons. Chi-square or Fisher exact test was used to compare categorical variables. The primary outcome was also expressed as an odds ratio. *P*-values < 0.05 represented statistical significance. Data analysis was performed with Statistica and MedCalc software.	POD compared to the control group (p=0.02). No significant difference was noted in the duration (p=0.44) and severity (p=0.24) of delirium between the groups. No difference was noted in 30 day mortality or in major adverse cardiac or cerebral events between the groups. The Dex group had significantly shorter mechanical ventilation time (p=0.001), ICU stays (p=0.002) and hospital stays (p=0.04) when compared to the control group. A logistic regression analysis revealed that Dex administration and bypass time were independently associated with the development of delirium.	vent weaning in the ICU reduces the risk of POD in patients undergoing cardiac surgeries. Length of ICU and hospital stays were also reduced which can result in decreased healthcare costs. Timing of the initiation of the Dex infusion plays a crucial role in its ability to reduce POD. The proposed mechanism is that if Dex is initiated prior to CPB, its preconditioning properties will have time to produce effects.	classifies as level II evidence. Limitations to this study are as follows: the differences in mortality could not be determined bc the study was not powered enough to do so, only 18 total patients developed delirium (fragility index of 2- meaning the statistical significance would be reversed if 2 fewer pts didn't develop POD) so the results should be interpreted with caution, and baseline cognitive status was not reported preoperatively. While the results of this study favor the use of Dexmedetomidine as a preventative to reduce the incidence of POD, the timing of the administration may play a crucial role in its effectiveness in reducing POD.
Wang et al,[17] 2023	This randomized control trial was conducted to assess Dexmedetomidine's effectiveness in reducing the incidence of POD. The Dex group received a loading dose of	This RTC was conducted at Fuwai Hospital in China. Of the 652 patients enrolled in the study, 10 were lost for the following reasons: death (5), deep	IV= Dexmedetomidine IV2= Placebo DV= Incidence of POD	The Mini-Mental State Exam and Pittsburgh sleep quality index were utilized pre- and postoperatively to evaluate	SPSS was utilized for data analysis. Cox regression was used for incidence analysis. Interaction	No significant difference was noted between the incidence of delirium in the Dex (14%) and control (16%) group as evidenced by a *p*-value of 0.62. The duration of	Dexmedetomidine is not effective in reducing the incidence of POD in patients undergoing heart valve surgery and CPB. The administration of	This double-blinded randomized control study classifies as level II evidence. Limitations to this study are as follows: limited

	0.6mcg/kg over 10 mins followed by a continuous infusion at 0.4mcg/kg/hr until the end of surgery. The control group received normal saline at the same intervals and rates.	sedation/comatose state (2), and required reoperation (3).		sleep quality and cognitive function. Sedation and agitation were assessed in the ICU with the Richmond agitation-sedation score (RASS) and the presence of delirium was determined by the confusion assessment method (CAM; CAM-ICU).	analyses were conducted on participants >65 years old. *P*-values < 0.05 represented statistical significance.	delirium was 2 days in both groups and therefore did not yield statistical significance (p=0.99). Statistical significance was noted related to age and the development of delirium. There was a significant increase in the incidence of POD in patients >65 yrs old (*p*<0.001). The Dex group yielded significantly more diagnoses of acute postoperative kidney injury than the control group (*p*=0.04). No significant difference was noted in mechanical ventilation time, ICU, or hospital length of stays. The incidence of hypotension and ventricular arrhythmias were insignificant between the Dex control group.	Dex may also be associated with an increased risk for postoperative kidney injury.	generalizability of results and the frequency at which the incidence of delirium was evaluated. More frequent assessment may increase the detection of and provide more precise results on the duration of delirium. The results of this study did not favor the use of Dexmedetomidine for reducing POD. The results of this study warrant further research on Dex and other potential ways to reduce the incidence of POD.
Kim et al,[15] 2019	This study was conducted to determine if Dexmedetomidine, used as a preventative, is effective at reducing emergence delirium and postoperative delirium in patients undergoing VATs lobectomy. The intervention group received a continuous infusion of Dex starting after induction until the end of surgery at a	This study was conducted between April and July of 2016 and consisted of 143 participants. Of the 143 patients enrolled, 23 did not complete the study for the following reasons: protocol violation (2) or requiring wedge resection/conversion to open thoracotomy (21).	IV= Dexmedetomidine IV2= Placebo DV= Incidence of POD	The Riker sedation agitation scale was used immediately after extubation and in the recovery room to assess for emergence delirium. The CAM/CAM-ICU scale was used to evaluate the presence of	Data analysis was completed with SAS and SigmaPlot software. Chi-square test with an alpha of 5% signified statistical significance. The pre- and postop lab	The Dex group had a significantly lower incidence of emergence agitation (*p*=0.011). The Dex group had more favorable results (calm, follows commands) according to the Riker sedation agitation scale (*p*=0.05). Pro- and anti-inflammatory cytokines were	Dexmedetomidine is not effective at reducing POD but did reduce the incidence of emergence agitation. Therefore, it should be noted that the reduction of emergence agitation is not linked to a reduction in POD. The analysis of lab	This double-blinded randomized control study classifies as level II evidence. Limitations to this study include: early discontinuation of the Dex infusion may be associated with the lack of effect on delirium, lab values were

	fixed dose of 0.5mcg/kg/hr. The control group received saline at the same dose/rate.			postoperative delirium. Labs were collected pre- and postoperatively to evaluate pro- and anti-inflammatory cytokines and catecholamine levels. Complications encountered in the hospital were monitored based on the Clavien-Dindo classification.	values were compared using the Wilcoxon rank-sum test.	significantly reduced in the Dex group (p=0.024 & p<0.002). Epi and Norepi levels were significantly lower in the Dex group (p<0.001). All of the following categories were significantly reduced in the Dex group: intraoperative Sevo & Remifentanil requirements (p<0.001), pain scores and opioid dose requirements in PACU (p=0.021, p=0.004), and postoperative opioid consumption up to 6 hours postop (p=0.003). No significant different was noted in the rate of complications, ICU or hospital length of stays between the groups.	results leans towards Dex producing a pro-inflammatory state as it produced a reduction in all anti-inflammatory mediators. The decreased levels of Epi and Norepi by Dex causes analgesic, anxiolytic, and hypnotic effects which is supported by the reduction in agitation levels, intraoperative anesthetic requirements, and postop opioid requirements.	only assessed twice therefore in-depth analysis on the duration & overall effect of Dex on the inflammatory process was limited, effective dose of Dex to achieve anti-inflammatory action is unknown. The generalizability of the results may be limited due to the possibility of underlying pulmonary physiology & one-lung ventilation being confounding factors for the development of POD. While Dex's effect is controversial, this study may support that the timing & duration of Dex's administration plays a crucial role in its ability to effect POD.