

Evaluation of Perioperative Melatonin's Potential to Prevent and Treat Postoperative Delirium in Older Patients Following Hip Arthroplasty under Spinal Anesthesia

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Abstract

Background: Tryptophan is converted into the hormone melatonin (N-acetyl-5-methoxytryptamine) by the pineal gland in the brain. Supplements containing synthetic melatonin have been utilized for several medical ailments, most prominently sleep disturbances. When taken as a premedication to reduce anxiety and sedate patients before surgery, it has been shown to be effective and have a good cognitive profile.

Material and Method: Four groups were assigned to the patients. Nothing was given to Group 1 (control) as premedication. One 5 mg melatonin capsule was given to Group 2 (melatonin) at bedtime and an additional 5 mg capsule was given 90 minutes before to surgery. One 7.5 mg pill of midazolam was given to Group 3 at bedtime, and another 7.5 mg was given 90 minutes before to surgery. Group 4 was given one tablet containing 100 µg at bedtime and an additional 100 µg 90 minutes prior to surgery.

Result: The melatonin group differed significantly compared with all groups, having less number of patients developed delirium. The total number of patients prescribed postoperative melatonin for treatment of delirium was 62 patients. Treatment was successful in 36 (58.06%) with no significant group differences.

Conclusion: Testing various preoperative sedatives demonstrated the role that sedative drug sharing plays in the delirium issue. Melatonin significantly reduced the incidence of postoperative delirium, but midazolam and clonidine induced an insignificantly greater incidence of delirium.

Keywords: Perioperative, Melatonin, Delirium, Hip Arthroplasty and Midazolam.

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Introduction

Acute confusional state, another name for delirium, is a syndrome marked by altered consciousness (i.e., less clarity in awareness of the surroundings), altered cognition (including attention), disordered thinking, disturbed psychomotor activity, and an irregular sleep-wake cycle. In people 65 years of age or older, 10% to 61% experience postoperative delirium. Compared to patients having general surgery, orthopedic patients are more prone to have delirium. Compared to 10% to 14% of patients undergoing general surgery, 44% to 55% of hip surgery patients experience delirium. After delirium sets in, fatality rates from 10% to 75% are reported; however, mortality may be more closely linked to advanced age and severe illness than to delirium itself. [1]

The most often reversible cause of delirium is medication. Between 22% and 39% of delirium instances are thought to be caused by drugs. According to a study conducted on older persons hospitalized, medication use was most likely the main cause of delirium in the sample population. [2]

Tryptophan is converted into the hormone melatonin (N-acetyl-5-methoxytryptamine) by the pineal gland in the brain. Supplements containing synthetic melatonin have been utilized for several medical ailments, most prominently sleep disturbances. When taken as a premedication to reduce anxiety and sedate patients before surgery, it has been shown to be effective and have a good cognitive profile. [3] It was also thought to be beneficial for treating postoperative delirium. In

this study, we attempt to establish a baseline for postoperative delirium in individuals having hip replacement surgery while sedated from the spine. Additionally, the impact of three distinct sedative medications, including melatonin, on this incidence will be investigated. In a trial to reduce symptoms, postoperative melatonin was given to patients who might develop postoperative delirium. [4]

Material and Methods

In this study, 300 participants were enrolled. All patients or their responsible families gave their informed consent once the departmental committee gave its approval. The study included ASA I-III patients 65 years of age or older who were scheduled for hip replacement surgery. An anesthesia resident has seen and examined patients during the night before the operation. The hospital pharmacy manufactured and randomized a closed envelope with an enclosed brochure with the medication's dosage, time, and precautions, which was provided to the ward nurse along with the prescription medications that were part of the trial. The medication within the sealed envelope was invisible to the resident anesthetist. At that time, every patient underwent an Abbreviated Mental Test (AMT). The British Geriatric Society and the

Royal College of Physicians recommend this test for routine evaluation of cognitive function in the elderly. Individuals who received a score of less than eight were not allowed to continue in the research.

Four groups were assigned to the patients. Nothing was given to Group 1 (control) as premedication. One 5 mg melatonin capsule was given to Group 2 (melatonin) at bedtime and an additional 5 mg capsule was given 90 minutes before to surgery. One 7.5 mg pill of midazolam was given to Group 3 at bedtime, and another 7.5 mg was given 90 minutes before to surgery. Group 4 was given one tablet containing 100 µg at bedtime and an additional 100 µg 90 minutes prior to surgery.

Results

An attempt was made to enroll 300 patients in the research. Of them, 78 had an AMT score of less than 8. This indicates a preoperative delirium incidence of 26%. The remaining patients, numbering 222, were included to the trial. Due to the requirement to induce general anesthesia for various reasons, eleven individuals were further disqualified, and eight more patients were admitted to the intensive care unit after surgery. The study was finished by the remaining 203 patients.

Table 1: Distributions of cases, demographic, and surgical data between groups.

	Control	Melatonin	Midazolam	Clonidine
No. of Patients	49	53	50	51
Age (Yrs)	72.3±6.4	70.4±7.1	69.9±8.2	71.5±6.8
Gender (M/F)	22/27	24/29	26/24	27/24
Weight (Kg)	74.68±12.23	72.75±11.67	88.2±7.9	78.5±11.3
Duration of surgery (min)	1197±36.7	126.8±44.9	110.7±40.8	133.8±33.2
Blood Transfused (ml)	6554±112.5	703.4±98.2	588.8±133.6	684.8±106.6

Out of 203 patients 99 were male and 104 were female. Average weight of Group 1 was 74.68±12.23 kg and Group 2 was 72.75±11.67. Duration of surgery was higher in Control Group i.e. 1197±36.7 min and lowest in Midazolam 110.7±40.8 min.

Table 2: Number of patients developed delirium in different postoperative days

	Control	Melatonin	Midazolam	Clonidine
POD-0	0	0	2	0
POD-1	4	1	8	5
POD-2	8	1	10	9
POD-3	4	3	2	5
Total (%)	16 (32.65)	5 (9.43)	22 (44)	19 (37.25)
No. of Patients Treated with Melatonin	9	2	14	11

The melatonin group differed significantly compared with all groups, having less number of patients developed delirium. The total number of patients prescribed postoperative melatonin for treatment of delirium was 62 patients. Treatment was successful in 36 (58.06%) with no significant group differences.

Discussion

Healthcare professionals tend to underestimate the issue of postoperative delirium. Patients who are elderly in particular are more likely to experience postoperative delirium. Because of population aging and an increase in senior patients undergoing major surgery, postoperative delirium will probably become increasingly common.

Postoperative delirium's pathogenesis is still poorly understood. Prior research findings have not always been entirely consistent. Investigates delirium in individuals undergoing surgery as well as medical conditions. Preexisting patient factors, as well as intraoperative and postoperative causes, are particularly relevant to older surgical patients. Important pre- and intraoperative factors that have not been demonstrated to promote delirium have also been noted in several studies. Preoperative patient-related factors are immutable among the myriad variables linked to delirium. This explains why delirium and "preoperative" delirium occur in hospital medical wards. [5]

The reason behind the increased incidence of postoperative delirium observed in our study with midazolam and clonidine (albeit statistically insignificant) compared to the control group, and the statistically significant lower incidence observed with melatonin, is not easily explained. The symptoms of delirium include altered consciousness (i.e., less focused awareness of the surroundings), altered cognition (including attentional changes), disordered thinking, disrupted psychomotor activity, and an irregular sleep-wake cycle. Given this criteria, it could be simpler to comprehend the clinical variations with regard to postoperative delirium if the mechanism of action and clinical effects of these medications are reviewed. All that midazolam is is a GABA receptor agonist. Psychomotor functions are significantly impaired when midazolam is used. Antrograde amnesia is a common side effect of midazolam. [6]

The human body, on the other hand, naturally produces melatonin, which is crucial for controlling the sleep-wake cycle. Its natural circadian cycle of secretion is triggered by the hypothalamic suprachiasmatic nuclei. Degeneration of these nuclei is more common in the elderly. As a result, older people's baseline serum melatonin levels are lowered. [7] Additionally, surgery causes the serum melatonin to drop even further. This results in postoperative REM sleep disturbance and a condition of sleep disorders. It is well known that exogenous melatonin treatment speeds up the beginning of sleep and enhances its quality. In terms of clinical use, it lacks amnesic qualities and does not affect cognitive, psychomotor, memory, or visual sensitivity tests. [8]

Conclusion

In conclusion, most doctors underestimate the risk of postoperative delirium following anesthesia and surgery. We faced a significant rate of postoperative and "preoperative" delirium. Testing various preoperative sedatives demonstrated the role that sedative drug sharing plays in the delirium issue. Melatonin significantly reduced the incidence of postoperative delirium, but midazolam and clonidine induced an insignificantly greater incidence of delirium. When given postoperatively to individuals experiencing postoperative delirium, melatonin proved effective in treating over half of the cases of delirium.

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