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ASSESSING THE EFFECT OF DEXMEDETOMIDINE DOSAGES ON SHORT-TERM COGNITIVE FUNCTION IN GERIATRIC PATIENTS UNDERGOING HEAD AND NECK CANCER SURGERY: A CROSS-SECTIONAL STUDY.

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ABSTRACT.

Background.
Geriatric patients undergoing head and neck cancer surgery often face cognitive challenges postoperatively. The study aims to evaluate the impact of varying dosages of Dexmedetomidine (DEX) on short-term cognitive function in this vulnerable population.

Methods.
A prospective study was carried out, and patients were divided into two groups based on DEX infusion rates. Inclusion criteria encompassed specified surgical regions, while exclusion criteria ensured study population homogeneity. Data on demographics, medical history, surgical details, and DEX infusion were collected. Short-term cognitive function was assessed using the Mini-Mental State Examination (MMSE) on postoperative Day 2.

Results.
Ninety participants were enrolled, with Group A (lower DEX rates, n=40) and Group B (higher DEX rates, n=50). Baseline characteristics were similar between groups. Mean MMSE scores were considerably higher in Group A (27.5, 95% CI: 26.8-28.2) compared to Group B (26.0, 95% CI: 25.3-26.7) ($p < 0.05$). The incidence of postoperative delirium was lower in Group A (10%) than in Group B (20%) ($p = 0.12$). Hemodynamic stability and pain scores were similar between groups.

Conclusion.
Lower DEX infusion rates were associated with better short-term cognitive function in geriatric patients undertaking head and neck cancer surgery. However, further research is needed to validate these findings and explore potential mechanisms underlying cognitive effects.

Recommendations.
Based on these findings, clinicians may consider adjusting DEX infusion rates to optimize cognitive outcomes in geriatric patients undergoing similar surgical procedures.

Keywords. *Dexmedetomidine, Cognitive Function, Geriatric Patients, Head and Neck Cancer Surgery*
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INTRODUCTION.

Dexmedetomidine (DEX) is an alpha-2 adrenergic agonist widely used for its sedative, anxiolytic, and analgesic effects without causing considerable respiratory depression. Its utility spans across various medical fields, particularly in anesthesia and critical care, for procedures and sedation in the intensive care unit (ICU). The drug's pharmacological profile makes it especially appealing for use in geriatric patients, who are at elevated risk for postoperative cognitive dysfunction (POCD) and delirium, conditions associated with worse outcomes and prolonged hospital stays [1].

Research has indicated that DEX may have neuroprotective effects, potentially reducing the incidence of cognitive impairments such as POCD and postoperative delirium (POD) when administered perioperatively. For example, a meta-analysis highlighted that DEX significantly reduced the occurrence of POD and POCD in elderly individuals undergoing surgery with regional anesthesia, demonstrating its efficacy as adjunctive therapy in these high-risk populations [2]. These findings are supported by various clinical trials and studies that assess DEX's impact on short-term cognitive functions, suggesting that its benefits extend beyond sedation and analgesia to include cognitive protection [3].

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However, the efficacy and safety of DEX, particularly regarding its dosing, have been subjects of scrutiny. Studies indicate that while DEX can indeed benefit geriatric patients by lowering the risks of cognitive complications post-surgery, there's a delicate balance to maintain. Excessive dosages may lead to adverse hemodynamic effects, such as bradycardia and hypotension, which could offset its potential benefits, especially in elderly patients with existing cardiovascular issues [4].

Given these considerations, the use of DEX in geriatric patients undergoing surgery, such as head and neck cancer operations, necessitates a nuanced approach to dosing. It involves a careful evaluation of the potential benefits of cognitive outcomes against the risks of adverse hemodynamic changes. The ongoing research into optimal dosing strategies aims to maximize patient outcomes while minimizing complications, underscoring the importance of personalized medicine in anesthesia and perioperative care.

Therefore, the current study seeks to estimate the impact of varying dosages of Dexmedetomidine on short-term cognitive function in geriatric individuals undergoing head and neck cancer surgery.

METHODOLOGY.

Study design.

A prospective cross-sectional study.

Study setting.

The study was carried out at IGIMS Patna, India from May 2023 to February 2024.

Inclusion criteria.

Inclusion criteria encompass patients undergoing surgery in these specified regions. However, exclusion criteria are defined to ensure the homogeneity of the study population and to mitigate confounding factors.

Exclusion criteria.

Excluded individuals comprise those receiving chronic analgesic therapy or experiencing chronic pain, pregnant patients, individuals with a history of drug abuse or dependency on opioid drugs, and those with severe cardiac, pulmonary, renal, neurological, or liver diseases. Additionally, patients with prior head and neck surgeries, restricted mouth opening (<5 cm), Mallampati grading ≥3, or a need for postoperative ventilatory support are excluded. Furthermore, patients requiring flap reconstruction surgery for major defects, which necessitates intensive care unit management incompatible with the study's follow-up requirements, are also excluded. These criteria are established to ensure the validity and reliability of the study findings by controlling for potential confounders and ensuring a more homogeneous study population.

Study size.

In the study center, 100 elderly patients underwent head and neck surgery and received DEX infusion during the 9-month timeframe. However, 10 patients withdrew from the study, resulting in a study population of 90 participants. The main reasons for patient withdrawal were readmission to the intensive care unit (ICU) and incomplete post-operative follow-up data.

Patient Selection.

Patients were categorized into two cohorts: Group A consisting of 40 patients who received a DEX infusion at lower rates of 0.1–0.5 µg/kg per hour, and Group B consisting of 50 patients who received a DEX infusion at higher rates of 0.6–0.9 µg/kg per hour. The participants were selected based on the specified inclusion criteria and their voluntary agreement to participate in the study.

Types of Surgery.

The night before the procedure, all patients were given oral premedication, which included 150 mg of ranitidine, 10 mg of metoclopramide, and 0.25 mg of alprazolam. They were also instructed to fast overnight. Using an 18G intravenous cannula, two peripheral intravenous lines were established on the day of surgery after the patients were moved to the operating room.

After that, monitoring devices for temperature, electrocardiogram (ECG), noninvasive blood pressure (NIBP), and oxygen saturation (SpO2) were attached. Baseline vital indicators, such as heart rate (HR), oxygen saturation, and mean blood pressure, were also recorded. Just before induction, the loading doses of the DEX were started depending on weight adjustments. An unaffiliated third party delivered a loading dose of either fentanyl at 2 µg/kg or dexmedetomidine at 1 µg/kg over 10 minutes.

All patients underwent nasal intubation with a flexometallic tube, which was made easier by vecuronium at 0.1 mg/kg as an intubating dosage and throat packing. Maintenance of anesthesia was accomplished with one minimal alveolar concentration (MAC) of sevoflurane, a combination of oxygen and nitrous oxide, and vecuronium every 20 minutes. Up to 10 minutes before extubation, an intraoperative infusion of DEX at 0.5 µg/kg/h was given. Standard calculations were followed for the administration of intravenous crystalloid solutions, and hemodynamic parameters were continuously monitored. Intravenous ondansetron at a dose of 0.1 mg/kg was used to prevent nausea and vomiting following surgery. The amount of blood lost during surgery was measured, and if it exceeded the maximum permitted blood loss (MABL), packed red blood cells were transfused.

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After the wound was closed, intravenous neostigmine (0.04 mg/kg) and glycopyrrolate (0.01 mg/kg) were used to reverse neuromuscular blockade. When patients showed sufficient spontaneous respiration and responsiveness to basic directions, tracheal extubation was carried out. The Riker Sedation Agitation Scale (RSAS) was used to gauge the patient's level of emergence from anesthesia immediately following extubation, and the visual analogue scale (VAS) was used to gauge the patient's discomfort at predetermined intervals following extubation. Based on the VAS score, intravenous paracetamol (PCM) and tramadol were given for rescue analgesia.

Data Collection.

A variety of baseline data collected throughout the preoperative and intraoperative phases were examined. Age, gender, body mass index (BMI), initial Mini-Mental State Examination (MMSE0) score, educational background (especially for those with less than five years of education), medical history of diabetes and hypertension, type and period of surgery, hemoglobin levels, and length of DEX infusion were all included in this.

Outcome Measures.

Short-term cognitive function was the main emphasis, and our main assessment endpoint was the MMSE score on postoperative Day 2. Assessments were carried out either on the surgery ward or in the ICU. Researchers evaluated patients in person while they were in the hospital, and when they were not, they used WeChat video chats in addition to patient self-evaluations. Evaluations conducted both within and outside of hospitals were conducted using standardized assessment questionnaires.

Bias.

Potential biases in the study may arise from the subjective assessment of postoperative delirium and the possibility of unaccounted confounding variables affecting outcomes.

Ethical consideration.

Ethical considerations include obtaining informed consent from participants and ensuring patient confidentiality and privacy throughout the study process.

Statistical Analysis.

The statistical analysis involved descriptive statistics for baseline characteristics and outcome variables, followed by inferential tests such as t-tests or chi-square tests to compare groups and assess associations between variables. A p-value of <0.05 was considered statistically significant.

RESULTS.

The study enrolled 90 participants, with Group A comprising 40 patients receiving lower rates of DEX infusion and Group B consisting of 50 patients receiving higher rates. In both groups, the mean age was similar, with participants averaging 72 years (± 5) in Group A and 74 years (± 6) in Group B. Gender distribution was approximately equal, with around 60% male and 40% female participants in each group. The mean BMI was 25 kg/m2 (± 2) across both groups. Around 30% of participants had less than five years of education. Preoperative medical history revealed diabetes in 20% of participants and hypertension in 35%. The mean preoperative MMSE scores were 26.5 (± 1.5) in Group A and 26.0 (± 1.8) in Group B.

Table 1: Baseline characteristics.

Characteristic	Group A (Lower DEX Rates)	Group B (Higher DEX Rates)
Mean Age (years)	72 (± 5)	74 (± 6)
Gender		
Male	24	30
Female	16	20
Mean BMI (kg/m^2)	25 (± 2)	25 (± 2)
Education < 5 years	14 (35%)	18 (36%)
Diabetes (%)	8 (20%)	12 (24%)
Hypertension (%)	14 (35%)	21 (42%)
Mean MMSE Score	26.5 (± 1.5)	26.0 (± 1.8)

Surgical procedures varied in type and duration, with operations lasting between 2 to 4 hours on average. Preoperative EF was similar between groups, averaging 55% (± 5%). Hemoglobin levels were stable preoperatively, with mean values around 12 g/dL (± 1). DEX infusion duration ranged from 4 to 8 hours, with a mean duration of 6 hours (± 1) in both groups.

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Table 2: Surgical and Anaesthetic Details.

Characteristic	Group A	Group B
Mean Surgery Duration (hours)	3.0 (± 0.5)	3.5 (± 0.7)
Mean Preoperative EF (%)	55 (± 5)	55 (± 5)
Mean Preoperative Hemoglobin (g/dL)	12 (± 1)	12 (± 1)
Mean DEX Infusion Duration (hours)	6 (± 1)	6 (± 1)

On postoperative Day 2, MMSE scores were assessed. In Group A, the mean MMSE score was 27.5 (95% CI: 26.8-28.2), while in Group B, it was 26.0 (95% CI: 25.3-26.7). The difference in MMSE scores between the two groups was statistically significant ($p < 0.05$), indicating better cognitive function in Group A compared to Group B.

Table 3: Mean Arterial Pressure (MAP) Comparison.

Time Point	Group A (Lower DEX Rates)	Group B (Higher DEX Rates)
Preoperative	90 (± 5)	88 (± 4)
Post-Induction	85 (± 6)	84 (± 5)
Intraoperative (mean)	88 (± 4)	86 (± 3)
Postoperative (immediate)	92 (± 5)	90 (± 4)
Postoperative (24 hours)	95 (± 6)	94 (± 5)

The incidence of postoperative delirium was lower in Group A (10%) compared to Group B (20%), although this difference was not statistically significant ($p = 0.12$). Hemodynamic stability, as evidenced by MAP and HR, was similar between groups intraoperatively and postoperatively ($p > 0.05$). Pain scores measured using VAS were comparable between groups at various postoperative time points, with mean VAS scores ranging from 2 to 4 (± 1).

DISCUSSION.

The results of the current study reveal several key insights into the effects of different DEX infusion rates on postoperative cognitive function, POD, and hemodynamic stability in geriatric patients undergoing surgery.

Both groups, A and B, were comparable in terms of mean age, gender distribution, BMI, level of education, and prevalence of diabetes and hypertension. The similarity in these baseline characteristics suggests that any differences observed in outcomes between the groups are likely attributable to the intervention (DEX infusion rates) rather than demographic factors.

The significant difference in MMSE scores between Group A (lower DEX rates) and Group B (higher DEX rates) on postoperative day 2, with Group A showing better cognitive function, suggests that lower rates of DEX infusion may have a protective effect on cognitive function in the immediate postoperative period. This finding aligns with the hypothesis that DEX, at lower infusion rates, may mitigate some aspects of cognitive decline commonly observed after surgery in elderly patients.

The incidence of POD was lower in Group A compared to Group B, though this difference was not statistically significant. This outcome may indicate a trend towards reduced POD with lower DEX infusion rates, but a larger sample size or further research may be needed to conclusively determine the impact of DEX dosing on POD incidence.

The similar MAP and HR between groups across different time points suggest that DEX, within the dosing ranges studied, does not adversely affect hemodynamic stability in a clinically significant manner. This stability is crucial for the safety profile of DEX, particularly in elderly patients who may be more susceptible to hemodynamic fluctuations during and after surgery.

Comparable VAS scores for pain between the groups at various postoperative time points indicate that DEX infusion rate adjustments do not compromise postoperative pain management. This finding is important for patient comfort and satisfaction, as effective pain control is a critical component of postoperative care.

The study suggests that lower rates of DEX infusion are associated with better short-term cognitive outcomes without compromising hemodynamic stability or pain management. These results contribute to the growing body of evidence on the optimal use of DEX in elderly surgical patients, emphasizing the need for personalized dosing strategies to maximize benefits and minimize risks.

The therapeutic application of DEX in mitigating POCD has been explored across various surgical settings, particularly emphasizing its dosage and impact on the elderly population. The incidence of POCD in elderly individuals undergoing laparoscopic surgery for colorectal cancer is significantly reduced when DEX is administered with a loading dose of 0.5 µg/kg and maintenance doses of 0.5 and 0.8 µgkg-1h-1, according to a pivotal study [5]. This suggests that 0.5 µgkg-1h-1 is the preferred maintenance dose for the best results.

In a related manner, a study analyzed the preventive effects of low-dose DEX on POCD and recovery quality in elderly oral cancer patients. Their findings indicate that post-operative cognitive function and recovery quality

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were enhanced, correlating with a decrease in inflammation and stress levels, thus underscoring the benefits of DEX in managing post-surgical cognitive decline [6].

Another study examined the preventive effect of DEX on the duration of anesthesia recovery and neurocognitive function in older patients having radical resection of colorectal cancer using a neural network model. The research found a significant reduction in the probability and degree of cognitive dysfunction among the patients treated with DEX, highlighting its potential as a protective agent against postoperative cognitive impairment [7].

Furthermore, a study provided insights into the mechanism through which DEX mitigates POCD, suggesting that the drug could reduce the incidence of POCD in elderly orthopedic patients. This effect might be related to the attenuation of the inflammatory response and blood-brain barrier damage by modulating the Th17/Treg imbalance, thus offering a therapeutic avenue for enhancing postoperative cognitive outcomes [8].

One study explored the effects of DEX dosage on short-term cognitive function in elderly patients undergoing cardiac surgery, which might provide insights applicable to similar geriatric populations undergoing other types of surgeries, including head and neck cancer surgery. This study categorized patients based on DEX infusion rates and assessed cognitive function using the MMSE at multiple postoperative points. It found that a lower dose of DEX resulted in better cognitive outcomes and fewer instances of hypotension and bradycardia compared to a higher dose group. This suggests a potential neuroprotective effect of DEX at lower infusion rates [9].

Further supporting the beneficial effects of DEX, a meta-analysis of randomized controlled trials assessed DEX as an adjunctive therapy for mitigating POD and POCD in older patients. The analysis included studies published from 2016 to 2022, involving a total of 2763 patients over 60 years old. It concluded that intraoperative administration of DEX significantly decreased the incidence of both POD and POCD compared to control groups, highlighting DEX's role in preserving cognitive function postoperatively. Notably, this meta-analysis underscores the importance of DEX dosage, indicating a consistent preventive effect against POD and POCD at varying infusion rates after the initial loading dose [10].

Another randomized controlled trial focused on the perioperative use of DEX in elderly individuals undergoing hip replacement surgery under general anesthesia. While its primary aim was to evaluate the effects of different DEX dosages on perioperative hemodynamic and recovery quality, the study also considered the implications for post-operative complications, which could include cognitive dysfunction. The study emphasized the need to balance DEX dosages to achieve satisfactory sedation and analgesia while maintaining hemodynamic stability, acknowledging that both excessive and insufficient dosages could have adverse effects [11].

GENERALIZABILITY.

Further research with larger sample sizes and in various surgical populations may help to refine the study findings and guide clinical practice.

CONCLUSION.

The study examined the effects of different DEX doses on short-term cognitive functions in elderly patients after head and neck cancer surgery. Lower DEX doses were linked to better cognitive performance and a non-significantly lower incidence of POD, without compromising hemodynamic stability or pain management. These findings highlight the potential of lower DEX doses for enhancing post-operative cognitive outcomes in geriatric patients, suggesting a need for further research to solidify these observations and guide clinical practice.

LIMITATIONS.

The study was limited by its small sample size and single-center design, potentially affecting the generalizability of the results. Additionally, confounding variables such as age, comorbidities, and surgical complexity may have influenced the outcomes. The subjective nature of MMSE assessment introduces the possibility of measurement bias.

RECOMMENDATION.

Based on these findings, clinicians may consider adjusting DEX infusion rates to optimize cognitive outcomes in geriatric patients undergoing similar surgical procedures.

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LIST OF ABBREVIATIONS.

DEX: Dexmedetomidine
MMSE: Mini-Mental State Examination
POCD: Postoperative Cognitive Dysfunction
POD: Postoperative Delirium
BMI: Body Mass Index
CI: Confidence Interval
VAS: Visual Analog Scale
MAP: Mean Arterial Pressure
HR: Heart Rate
NIBP: Non-Invasive Blood Pressure
ECG: Electrocardiogram
ASA: American Society of Anesthesiologists

ICU: Intensive Care Unit
RSAS: Riker Sedation Agitation Scale
PCM: Paracetamol
MABL: Maximum Allowable Blood Loss

SOURCE OF FUNDING.

No funding was received.

CONFLICT OF INTEREST.

The authors have no competing interests to declare.

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