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ORIGINAL RESEARCH PERIOPERATIVE MEDICINE

Dexmedetomidine can reduce cognitive disorders after FESS; a quasi-experimental, randomized trial

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ABSTRACT

Background & objective: Functional endoscopic sinus surgery (FESS) needs a clear surgical field, which can be improved with controlled hypotension. This technique helps reduce bleeding during the procedure. However, hypotension may increase the risk of postoperative cognitive impairment. Dexmedetomidine is an α2-agonist that provides sedation, analgesia, and neuroprotection without affecting respiration. This study aims to evaluate the effect of dexmedetomidine on cognitive function after surgery.

Methods: A quasi-experimental study with a randomized pre-test–post-test design was conducted in patients undergoing FESS at RSUP Dr. Kariadi, Semarang. Subjects were divided into two groups, namely the dexmedetomidine and remifentanil groups. Cognitive function was assessed by MMSE examination, and S100B levels were measured before and within 24 hours after surgery. $P < 0.05$ was considered significant.

Results: A total of 28 patients were included in this study, with similar characteristics between the two groups. Pre- and postoperative Mini-Mental State Examination (MMSE) scores were found to be no different in the dexmedetomidine group (28.76 ± 5.02 vs 29.07 ± 1.84; $P > 0.05$), in the remifentanil group there was a significant difference (30.00 ± 00 vs 27.46 ± 1.12; $P < 0.001$), resulting in a greater MMSE difference compared with the dexmedetomidine group (0.30 ± 0.94 vs -2.5 ± 1.12; $P < 0.001$). Pre- and postoperative S100B levels showed no significant difference in the two groups.

Conclusions: Dexmedetomidine, as a hypotensive agent, is more effective in maintaining cognitive function based on MMSE scores and shows no significant difference from remifentanil in S100B level parameters.

Abbreviations: FESS: Functional endoscopic sinus surgery, MMSE: Mini-Mental State Examination, POCD: postoperative cognitive dysfunction

Keywords: FESS, Dexmedetomidine, Remifentanil, MMSE, S100B

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1. INTRODUCTION

Functional Endoscopic Sinus Surgery (FESS) has been a commonly performed procedure over the past 20 years for treating nasal and paranasal sinus pathologies.

Achieving optimal surgical visibility in FESS is critical, as the narrow operative field can easily be obscured by blood, which may also block the endoscope lens. Controlled hypotension is a technique used to improve

surgical visibility by deliberately lowering blood pressure to minimize bleeding. This involves reducing systolic blood pressure to 80–90 mmHg, mean arterial pressure (MAP) to 50–60 mmHg, or a 30% decrease from baseline MAP. Although effective in reducing bleeding, controlled hypotension poses risks, including reduced perfusion to vital organs like the brain.[1,2]

The use of controlled hypotension has been associated with potential complications such as postoperative cognitive dysfunction (POCD), which is linked to ischemic injuries and changes in brain biomarkers like S100B. S100B is a protein marker for neuronal damage, and its levels can rise following injury induced by controlled hypotension.[3–5] Additionally, postoperative cognitive function can be assessed using the Mini-Mental State Examination (MMSE), a widely used screening tool.[6]

Various hypotensive agents, such as remifentanil and dexmedetomidine, are utilized in controlled hypotension. Remifentanil, a short-acting opioid, is effective in achieving hemodynamic targets and controlling bleeding.[7] On the other hand, dexmedetomidine, a selective alpha-2 adrenergic receptor agonist, has neuroprotective effects and maintains stable hemodynamics without significantly increasing heart rate.[8,9] Both agents have been shown to blunt hemodynamic responses during surgery and may influence the risk of POCD differently. While prior studies have compared the efficacy of remifentanil and dexmedetomidine in achieving hemodynamic targets in FESS, their specific impact on MMSE scores and S100B levels remains unexplored. Thus, this study aims to evaluate the relationship between these agents and the incidence of POCD in FESS patients through MMSE scores and S100B levels.

2. METHODOLOGY

This quasi-experimental research used a randomized pre-test post-test design and involved patients who underwent FESS with controlled hypotension at RSUP Dr. Kariadi, Semarang, from May to August 2024. Patients aged 18-65 years old with ASA (American Society of Anesthesiologists) clinical status I–II, no history of allergies to both dexmedetomidine and/or remifentanil, hypertension, diabetes mellitus, and obesity, and no prior history of neuropsychiatric or cognitive disorders were enrolled for the study. Exclusion criteria included the patient's refusal, new postoperative neurological deficit, intraoperative bleeding of more than 350 mL, or in-hospital mortality. Sampling was done through a non-probability consecutive sampling technique. With a 95% confidence interval, 80% power, and an estimated 10% dropout rate, the minimum required sample size for each group was 11 patients.

The research ethical approval was granted by the Medical and Health Research Ethics Commission of the Faculty of Medicine, Diponegoro University. All participants provided written informed consent to participate in the study after being fully informed about its purpose and procedures. Before the operation, patients' cognitive status was evaluated using the Mini-Mental State Examination (MMSE), and blood samples were simultaneously collected for S100B level assessment. Randomization was performed using opaque envelopes containing the group allocation for each patient, which were opened by the anesthesiologist before induction.

General anesthesia was induced with propofol at a dose of 2 mg/kg IV, lidocaine at a dose of 1 mg/kg, and rocuronium at a dose of 0.6 mg/kg IV. After intubation, the patient was ventilated with 60% oxygen in air (tidal volume 8 mL/kg, respiratory rate 12 bpm). Remifentanil was used to maintain anesthesia, administered as a loading dose of 1 µg/kg followed by an infusion of 0.2–0.4 µg/kg/minute in the remifentanil group, while dexmedetomidine was given at 0.4–0.8 µg/kg/hour in the dexmedetomidine group. Systemic hypotension was achieved and kept at the target MAP of 50–60 mmHg. Blood samples for S100B assessment were taken 12 hours after surgery, while the MMSE assessment was done at 24 hours after surgery.

Statistical Product and Service Solutions (SPSS) for Windows was used for data analysis. Data distribution was assessed using the Shapiro-Wilk test. Independent t-test and Mann-Whitney test were used to compare the two groups, while paired samples t-tests and Wilcoxon signed-rank tests were used to compare changes within each group. Statistical significance was determined by $P < 0.05$.

3. RESULTS

A total of 28 patients undergoing FESS with controlled hypotension at Dr. Kariadi General Hospital, Semarang, Central Java, participated in this study, and all research subjects were included in the final analysis. The patient characteristics are presented in Table 1. Descriptive analysis revealed that the baseline characteristics of subjects in both groups were comparable.

Paired analysis using the Wilcoxon test showed no significant difference in MMSE scores before and after surgery in the dexmedetomidine group (28.76 ± 5.02 vs 29.07 ± 1.84; $P = 0.234$), whereas a significant difference was observed in the remifentanil group (30 vs 27.46 ± 1.12; $P < 0.001$). The Mann-Whitney test showed no difference in preoperative MMSE scores between the

Table 1: Demographic / Sample Characteristics

Variable	Dexmedetomidine Group (n = 14)	Remifentanil Group (n = 14)	P-value
Age (years)	41.53 ± 13.48	36.33 ± 14.25	0.330
Gender Male Female	 3 (23.1) 10 (76.9)	 5 (33.3) 10 (66.7)	0.544
Duration of operation (minute)	139.61 ± 25.59	167.33 ± 54.13	0.294
MAP changes (mmHg)	48.87 ± 13.00	45.40 ± 10.70	0.445
Ephedrine usage (times)	1.54 ± 1.12	1.80 ± 1.20	0.751

Data presented as n (%) or mean ± SD;
Notes: significant P < 0.05; ϕ-Wilcoxon test; ε - Mann-Whitney test

Table 2: Comparison of MMSE score

MMSE Score	Dexmedetomidine Group (n = 14)	Remifentanil Group (n = 14)	P-value
Pre-operation	28.76 ± 5.02	30.00 ± 0.00	0.170
Post-operation	29.07 ± 1.84	27.46 ± 1.12	0.004*
P-valueϕ	0.234	< 0.001*	
ΔMMSE	0.30 ± 0.94	-2.5 ± 1.12	< 0.001*

*Notes: *, significant (P < 0.05); ϕ, Wilcoxon test; ε, Mann-Whitney test*

Table 3: Comparison of S100B Levels

S100B (pg/mL)	Dexmedetomidine Group (n = 14)	Remifentanil Group (n = 14)	P-value
Pre-operation	36.32 ± 14.62	37.61 ± 1316	0.683ε
Post-operation	49.77 ± 26.89	53.40 ± 25.17	0.618ε
P-valueϕ	0.016*	0.004*	
ΔS100B (pg/mL)	13.44 ± 15.34	15.79 ± 20.30	0.786ε

*Notes: *, significant (P < 0.05); ϕ, Wilcoxon test; ε, Mann-Whitney test*

two groups (28.76 ± 1.84 vs 27.46 ± 1.12; P = 0.170), but postoperative MMSE scores were significantly higher in the dexmedetomidine group compared to the remifentanil group (29.07 ± 1.84 vs 27.46 ± 1.12; P = 0.004). Analysis of the difference between pre- and postoperative MMSE scores revealed that the use of remifentanil resulted in a greater MMSE score change compared to dexmedetomidine (0.30 ± 0.94 vs -2.5 ± 1.12; P < 0.001) (Table 2).

Paired analysis on S100B levels using the Wilcoxon test showed a significant difference before and after surgery in the dexmedetomidine group (36.63 ± 14.62 vs 49.77 ± 26.89 pg/mL; P = 0.016). as well as in the remifentanil group (37.61 ± 13.16 vs 53.40 ± 25.17 pg/mL; P = 0.004). The Mann-Whitney test showed no difference in preoperative (36,32 ± 14,62 vs 37,61 ± 13,16 pg/mL; P = 0,683) and postoperative (49.77 — 26.89 vs 53.40 ± 25.17 pg/mL) S100B levels between the two groups. Analysis of the difference between pre- and postoperative S100B levels revealed similar S100B levels change between the two groups (13.44 ± 15.24 vs 15.79 ± 20.30 pg/mL; P = 0.786) (Table 3).

4. DISCUSSION

This study aims to determine the effect of the use of dexmedetomidine compared to remifentanil on changes in MMSE scores and S100B levels in patients undergoing FESS surgery with the controlled hypotension technique. There are other sensitive tools to assess cognitive impairment than MMSE, such as the Montreal Cognitive Assessment (MoCA). When comparing the use of MoCA-INA with MMSE for assessing cognitive impairment, Athika et al. reported that MoCA-INA provides a more accurate description of cognitive deficits than MMSE, particularly in relation to the severity of head injury experienced by patients. However, one of the limitations of MoCA-INA is the need for special training before it can be used in daily practice, compared to MMSE, which is simpler and easier to do without training. Because this study assessed

cognitive comparisons before and after controlled hypotension, the use of the MMSE was quite sensitive and specific. S100B protein is a specific biomarker that can indicate intraoperative and postoperative nerve damage.

This study shows that the administration of dexmedetomidine to maintain hypotension during FESS provides a better cognitive result than the use of remifentanil. In the present study, Dexmedetomidine improved the MMSE scores, while on the other hand, Remifentanil reduced the scores. These findings are consistent with a previous study on cataract surgeries, which found that dexmedetomidine was associated with fewer cognitive impairments, likely due to its neuroprotective effects that may reduce postoperative delirium.[10] It is capable of affecting the NRF2 signaling pathway, making it possible to reduce inflammation, apoptosis, and autophagy, and to prevent the blood-brain barrier contraction through the prevention of ROS formation.[11,12]

POCD can be affiliated with neuroinflammation, cerebral hypoperfusion, ischemia, and neuronal apoptosis. Damage to brain cells can lead to the leakage of S100B biomarker into the blood.[13] S100B levels after surgery were higher in both groups, but the elevation was less pronounced in the dexmedetomidine group in comparison with the remifentanil group. This increase may be due to controlled hypotension.[14] One study involving ENT patients undergoing controlled hypotension reported elevated S100B levels in both normal and impaired cognitive outcomes, suggesting the timing of blood sampling post-procedure may influence results. In that study, samples were taken 12 hours after surgery, when S100B levels are expected to peak, whereas others were sampled earlier.[15] Another study also demonstrated significantly lower perioperative S100B levels in patients receiving dexmedetomidine during epilepsy surgery.[16]

No significant difference in S100B levels could be related to different factors. While the MMSE is a direct measure of the cognitive function, S100B is a biomarker of brain injury. These instruments assess diverse things. Meta-analyses quantifying S100B in psychiatric disorders indicate that S100B is increased in a number of diseases, and treatment does not affect these values.[17] This suggests that the neuroprotective property of dexmedetomidine may not change circulating S100B protein concentrations

Autoregulation may also play a role in maintaining cerebral blood flow across a range of mean arterial pressures (MAP) between 50 and 150 mmHg. In this study, controlled hypotension was maintained at a level not lower than 50 mmHg. Another study examined different levels of MAP reduction (100–90%, 90–80%, and 80–70% of baseline) and found that deeper hypotension levels were associated with lower MMSE scores, especially at the 80–70% level. Nevertheless, the 80–70% level always had lower MMSE score levels. The duration of hypotension also influences the percentage of cerebral oxygen saturation difference; controlled hypotension <90% MAP baseline data revealed significant differences.[18]

In this study, to prevent an excessive decrease in blood pressure, an intravenous injection of 5 mg ephedrine was administered as a rescue agent for controlled hypotension when MAP fell below 50 mmHg. This dose could be repeated if necessary. Complications related to hypotension were observed: among the 27 patients, three experienced prolonged recovery, two of whom had received remifentanil and one dexmedetomidine. Other complications, such as dizziness or delayed discharge, were not observed.

5. LIMITATIONS

This study has certain limitations. MMSE screening for POCD was conducted only 24 hours after the procedure. POCD events are categorized into three phases: postoperative delirium, which consists of acute disturbances in thinking, perception, and awareness lasting a few days; postoperative cognitive decline, which presents as cognitive dysfunction without altered consciousness from the 7th day up to the 1st year after surgery; and postoperative dementia, which refers to cognitive dysfunction occurring years after surgery.[5] Therefore, this study employed MMSE screening only up to 24 hours post-surgery because FESS patients are typically discharged within two days of hospitalization. Other screening tools, such as MoCA-INA, offer greater sensitivity but lower specificity for the diagnosis of POCD. However, the use of MoCA-INA requires administration by credentialed specialists.

6. CONCLUSION

In conclusion to our study, the use of dexmedetomidine maintained cognitive function based on better MMSE scores compared to remifentanil, but the effects of both regimens on S100B levels were found to be similar.

7. Ethical consideration

The research has obtained ethical approval from the Medical and Health Research Ethics Commission of the Faculty of Medicine, Diponegoro University, with No. 16138/EC/KEPK-RSDK/2024, and obtained permission to conduct research by Dr. Kariadi General Hospital, Semarang, with No. DP.04.01/D.X.2/2363/2024.

8. Conflict of interest

All authors declare that there was no conflict of interest.

9. Funding

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10. Authors' contribution

Conceptualization of the study was carried out by MA and MS. Data collection was performed by MA and TP. Data analysis was conducted by MA, MS, and TP. The first draft of the manuscript was prepared by MA, MS, and TP. All authors reviewed and approved the final version of this manuscript for submission.

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