

Comparison of the effect of propofol and desflurane on S-100 β and GFAP levels during controlled hypotension for functional endoscopic sinus surgery

A randomized controlled trial

Ji Su Jang, MD^a, Youngsuk Kwon, MD^b, Sung Mi Hwang, MD, PhD^{a,*}, Jae Jun Lee, MD^a, Jun Suck Lee, MD^c, Soo Kyoung Lee, MD, PhD^c, Ho Seok Lee, MD^a

Abstract

Background: Although surgical field visualization is important in functional endoscopic sinus surgery (FESS), the complications associated with controlled hypotension for surgery should be considered. Intraoperative hypotension is associated with postoperative stroke, leading to subsequent hypoxia with potential neurologic injury. We investigated the effect of propofol and desflurane anesthesia on S-100 β and glial fibrillary acidic protein (GFAP) levels which are early biomarkers for cerebral ischemic change during controlled hypotension for FESS.

Methods: For controlled hypotension during FESS, anesthesia was maintained with propofol/remifentanyl in propofol group (n=30) and with desflurane/remifentanyl in desflurane group (n=30). For S-100 β and GFAP assay, blood samples were taken at base, 20 and 60 minutes after achieving the target range of mean arterial pressure, and at 60 minutes after surgery.

Results: The base levels of S-100 β were 98.04 \pm 78.57 and 112.61 \pm 66.38 pg/mL in the propofol and desflurane groups, respectively. The base levels of GFAP were 0.997 \pm 0.486 and 0.898 \pm 0.472 ng/mL in the propofol and desflurane groups, respectively. The S-100 β and GFAP levels were significantly increased in the study period compared to the base levels in both groups ($P < .001$). There was no significant difference at each time point between the 2 groups.

Conclusion: On comparing the effects of propofol and desflurane anesthesia for controlled hypotension on the levels of S-100 β and GFAP, we noted that there was no significant difference in S-100 β and GFAP levels between the 2 study groups.

Clinical trial registration: Available at: <http://cris.nih.go.kr>, KCT0002698.

Abbreviations: BBB = blood-brain barrier, BIS = bispectral index, EtCO₂ = end tidal carbon dioxide, FESS = functional endoscopic sinus surgery, GFAP = glial fibrillary acidic protein, MAP = mean arterial blood pressure.

Keywords: cerebral ischemia, controlled hypotension, desflurane, functional endoscopic sinus surgery, propofol

Editor: Bernhard Schaller.

This work was supported by a grant from Hallym University Medical Center Research Fund (grant number HURF-2017-58).

The authors have no conflicts of interest to disclose.

^aDepartment of Anesthesiology and Pain medicine, Hallym University School of Medicine, Chuncheon Sacred Heart Hospital, ^bDepartment of Anesthesiology and Pain medicine, College of Medicine, Kangwon National University, Chuncheon, ^cDepartment of Anesthesiology and Pain medicine, Hallym University Sacred Heart Hospital, Anyang, South Korea.

* Correspondence: Sung Mi Hwang, Department of Anesthesiology and Pain medicine, Hallym University School of Medicine, Chuncheon Sacred Heart Hospital, 77 Sakju-ro, Chuncheon, 24253, South Korea (e-mail: h70sm@hallym.or.kr).

Copyright © 2019 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Jang JS, Kwon Y, Hwang SM, Lee JJ, Lee JS, Lee SK, Lee HS. Comparison of the effect of propofol and desflurane on S-100 β and GFAP levels during controlled hypotension for functional endoscopic sinus surgery. *Medicine* 2019;98:46(e17957).

Received: 4 April 2019 / Received in final form: 25 September 2019 / Accepted: 15 October 2019

<http://dx.doi.org/10.1097/MD.00000000000017957>

1. Introduction

Functional endoscopic sinus surgery (FESS) is an effective low-risk procedure and is performed commonly for chronic sinusitis. However, bleeding into the small surgical field can lead to serious complications. Providing optimal visualization of the surgical field is essential for adequate surgical exposure and for identification of crucial neurovascular structures.^[1] Controlled hypotension is one of the techniques used for minimizing bleeding during FESS.^[2-4] Controlled hypotension can be achieved by using various anesthetic agents, but there is no consensus on which agent is superior. However, a combination of propofol and remifentanyl infusion produces controlled hypotension without the need for additional hypotensive agents; further, it provides better surgical field visualization with less bleeding compared with traditional inhalational anesthetic techniques and is currently the preferred technique for FESS.^[1,2,5]

Although surgical field visualization is important, the complications associated with controlled hypotension should also be considered. Extreme hypotension may cause cognitive dysfunction, organ hypoperfusion, and subsequent ischemic injury.^[2,6-10] S-100 β and glial fibrillary acidic protein (GFAP) are early biomarkers for blood-brain barrier (BBB) damage and

cerebral ischemic change.^[11–14] Further, the effect of propofol/remifentanyl anesthesia for controlled hypotension on cerebral ischemia, apart from its effect on improving surgical field visualization, needs to be evaluated. In this study, we investigated the effect of propofol/remifentanyl and desflurane/remifentanyl anesthesia on S-100 β and GFAP levels during controlled hypotension for FESS.

2. Methods

2.1. Study design and patient selection

This prospective study protocol was approved by the Institutional Review Board of Chuncheon Sacred Heart Hospital, Chuncheon, South Korea (no: 2017-74) and was registered on the Clinical Information Service (available at: <http://cris.nih.go.kr>, KCT 0002698). Patients with a diagnosis of rhinosinusitis (defined as the presence of sinus symptoms persisting for at least 3 months despite medical therapy), aged over 20 years, and undergoing FESS were enrolled; written informed consent was obtained from all patients. Exclusion criteria included uncontrolled hypertension, diabetes, renal disease, history of cerebrovascular disease, and dementia. The included patients were divided into a propofol group and a desflurane group. The patients were randomly allocated to the groups using a computer-generated, permuted-block schedule (block size=4) by an independent nurse who prepared the anesthesia agent according to the assignment.

2.2. Anesthesia and controlled hypotension

No premedication was given. On arriving in the operating room, standard monitoring was performed using electrocardiography, pulse oximeter, noninvasive blood pressure monitoring, and bispectral index (BIS). Anesthesia was induced with propofol (target concentration 3–5 ng/mL), remifentanyl (0–0.2 μ g/kg/min), and rocuronium (0.8 mg/kg) in propofol group and with propofol (2 mg/kg), remifentanyl (0–0.2 μ g/kg/min), and rocuronium (0.8 mg/kg) in desflurane group. After endotracheal intubation, ventilation was controlled mechanically with a mixture of 50% oxygen in N₂O to maintain the end tidal carbon dioxide (EtCO₂) at 35 to 40 mm Hg. Anesthesia was maintained with propofol and remifentanyl (0–0.4 μ g/kg/min) in propofol group and with desflurane and remifentanyl (0–0.4 μ g/kg/min) in desflurane group. The dose of each agent was adjusted to maintain the mean arterial blood pressure (MAP) at 60 to 70 mm Hg and the BIS at 40 to 60. Propofol, desflurane and remifentanyl served mainly to control the target MAP, and nicardipine and phenylephrine were also used as needed. Patients were excluded if the target MAP could not be maintained within 5 minutes. A radial arterial catheter was inserted for continuous blood pressure monitoring and for taking a blood sample for measuring the levels of S-100 β and GFAP. The pressure transducer used for radial artery pressure measurement was zeroed at the level of the external auditory meatus throughout the surgery. After anesthesia induction and establishment of an arterial line, the patient was positioned in a reverse Trendelenburg position at 15°. Arterial blood gas analysis (ABGA) was performed 20 and 60 minutes after the patient was placed in the reverse Trendelenburg position and controlled hypotension were achieved. Surgery in all patients was performed by a single experienced surgeon.

After completion of the surgery, the patient was repositioned to be supine; then, anesthesia was discontinued and the neuromuscular block was reversed. After adequate awakening, the patient was extubated and transported to the recovery room, where the

MAP was monitored continuously to check for hypotension (20% of the preoperative value).

2.3. S-100 β and GFAP measurement

For S-100 β and GFAP assay, an arterial blood sample was taken after arterial line catheterization (baseline), at 20 (T_{20}) and 60 (T_{60}) minutes after placing the patient in the reverse Trendelenburg position and achieving the target range of MAP, and at 60 minutes after surgery (Post₆₀). If the surgery was completed before T_{60} , T_{60} was determined by the time at completion. The samples were centrifuged at 3000 rpm for 10 minutes, and serum was frozen within 30 minutes at -70°C until the end of this study. Serum S-100 β was measured using a commercially available Human S100B (S100 calcium binding protein B) ELISA kit (MBS2503148; MyBioSource, San Diego, CA). The sensitivity of the assay is 18.75 pg/mL and detection range is 31.25 to 2000 pg/mL. The GFAP assay was performed using the Human GFAP ELISA kit (MBS2506721; MyBioSource), which has a sensitivity of 0.188 ng/mL and detection range of 0.313 to 20 ng/mL.

2.4. PaCO₂ and EtCO₂

The ABGA was performed 20 and 60 minutes after placing the patient in the reverse Trendelenburg position and achieving the target range of MAP for comparison of PaCO₂. EtCO₂ was also recorded at the same time.

2.5. Statistical analysis

The sample size of this study was calculated using G-power (ver. 3.1, $\alpha=0.05$, power=0.8) for determination of a difference in S-100 β levels between the 2 groups at 60 minutes after the surgery, depending on our preliminary study results (propofol group; mean=265.89, standard deviation [SD]=70.67, desflurane group; mean=218.43, SD=55.54, effect size=0.75); a total of 30 patients were required in each group. Considering a 10% dropout rate, 34 patients per group were recruited. SPSS ver. 24.0 (SPSS Inc, Chicago, IL) was used for statistical analyses. Data are expressed as numbers or mean \pm SD. The Student *t* test was used for comparisons of age, height, weight, body mass index (BMI), duration of controlled hypotension, anesthesia, and surgery. The levels of S-100 β , GFAP, PaCO₂, and EtCO₂ at each time-point were also compared between the 2 groups using Student *t* test. The changes in S-100 β and GFAP levels within a group were compared using paired *t* test. The categorical data were analyzed using a Chi-squared test. A *P*-value <.05 was considered significant.

3. Results

A total of 68 patients undergoing FESS were allocated to the propofol and desflurane groups. Two patients in each group were excluded due to failure to maintain the target MAP during operation. In addition, 2 patients in the propofol group were excluded later owing to hemolysis of the blood samples; in the desflurane group, 1 patient was excluded owing to change in the surgical plan and 1 patient was excluded owing to hemolysis of the blood sample (Fig. 1). In the recovery room, there was no case of hypotension. Table 1 shows the demographic data of each group.

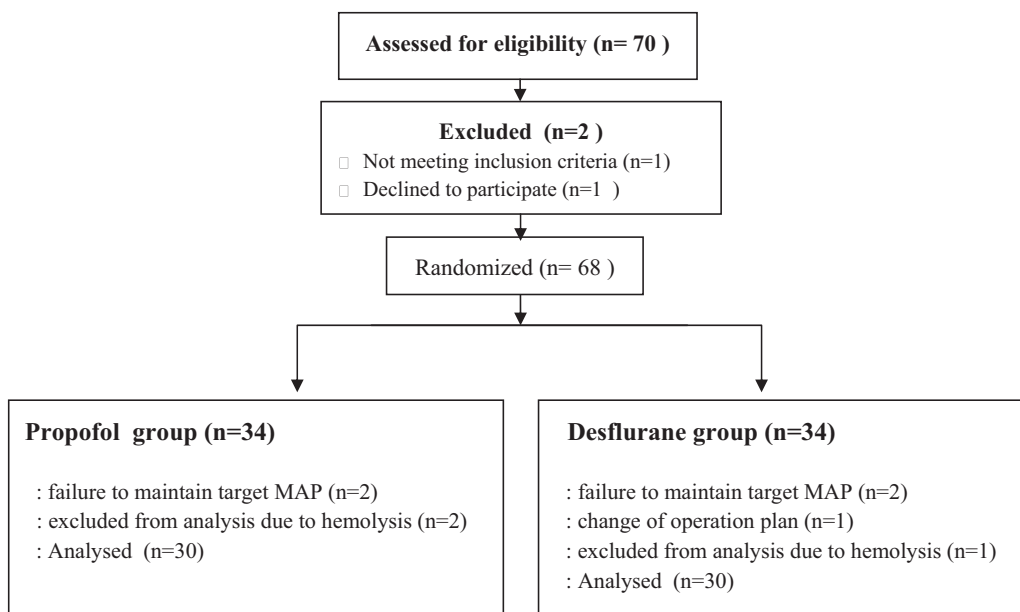


Figure 1. Flow of study. MAP=mean arterial blood pressure.

3.1. Levels of S-100β

The base levels of S-100β were 98.04±78.57 and 112.61±66.38 pg/mL in the propofol and desflurane groups, respectively. The S-100β levels were significantly increased in the intraoperative and postoperative periods compared to the baseline levels in both groups ($P \leq .001$) (Fig. 2). There was no significant difference at each time point between the 2 groups.

3.2. Levels of GFAP

The base levels of GFAP were 0.997±0.486 and 0.898±0.472 ng/mL in the propofol and desflurane groups, respectively. The GFAP levels were significantly increased in the intraoperative and postoperative periods compared to the baseline levels in both groups ($P \leq .001$) (Fig. 3). There was no significant difference at each time point between the 2 groups.

3.3. PaCO₂ and EtCO₂

The PaCO₂ at T₂₀ and T₆₀ was 35.3±3.4 and 35.1±5.5 mm Hg in the propofol group and 36.4±4.1 and 35.2±3.3 mm Hg in the desflurane group, respectively; EtCO₂ was 34.4±2.6 and 33.7±

2.9 mm Hg in the propofol group and 35.5±3.2 and 33.9±2.8 mm Hg in the desflurane group, respectively, at the 2 time points. There was no significant difference between the 2 groups for these parameters (Table 2).

4. Discussion

In this study, we evaluated the levels of S-100β and GFAP during controlled hypotension for FESS, which were observed to be raised in both the propofol and the desflurane groups. However, there were no significant differences between the groups regarding the measured parameters.

Table 1

Patient demographics and clinical characteristics.

	Propofol group (n=30)	Desflurane group (n=30)	P-value
Age, yr	47.3 (12.1)	44.1 (12.0)	.302
Gender, male/female	21/9	18/12	.417
BMI, kg/m ²	24.9 (3.3)	25.4 (3.2)	.530
Operation time, min	65 (28.9)	59.6 (34.2)	.517
Duration of controlled hypotension, min	75.1 (30.7)	68.8 (34.3)	.455
Duration of anesthesia, min	91.8 (31.3)	82.9 (35.7)	.310

Data presented as mean (standard deviation) or number. BMI=body mass index.

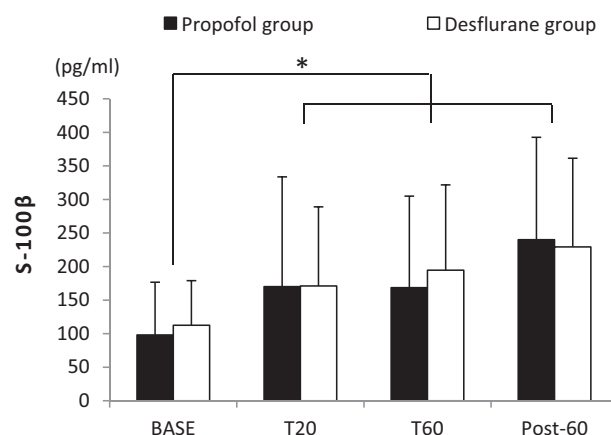


Figure 2. Comparison of the levels of S-100β. S-100β was significantly elevated at T₂₀, T₆₀, and Post₆₀ compared to base levels. * $P \leq .001$. There is no significant difference between the propofol group and desflurane group. BASE=before setting the reverse Trendelenburg position and achieving controlled hypotension, T₂₀ and T₆₀=time at 20 and 60 minutes after setting the reverse Trendelenburg position and achieving controlled hypotension, Post₆₀=time at 60 minutes after surgery.

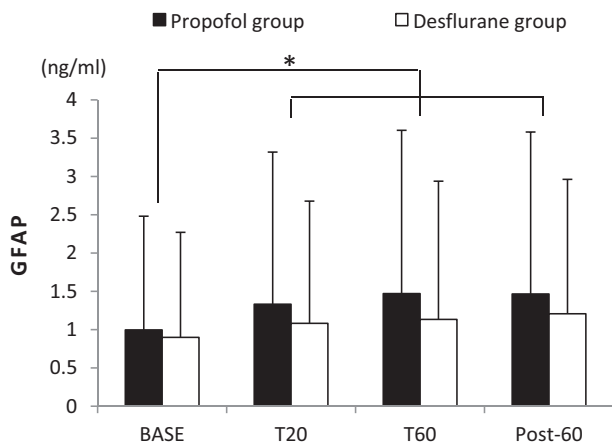


Figure 3. Comparison of the levels of glial fibrillary acidic protein (GFAP). GFAP was significantly elevated at T_{20} , T_{60} , and $Post_{60}$ compared to base levels. $^*P \leq .001$. There is no significant difference between the propofol groups and desflurane group. BASE=before setting the reverse Trendelenburg position and achieving controlled hypotension, T_{20} and T_{60} =time at 20 and 60 minutes after setting the reverse Trendelenburg position and achieving controlled hypotension, $Post_{60}$ =time at 60 minutes after surgery.

Controlled hypotensive anesthesia can be defined as the reduction of MAP to 50 to 70 mm Hg, with the primary aim to improve surgical visibility without compromising perfusion to vital organs.^[2] Although many agents can be used for controlled hypotension, total intravenous anesthesia (TIVA) with propofol and remifentanyl is the preferred anesthetic technique.^[11,2,5] In contrast to inhalational anesthetics, propofol infusion causes decreased perfusion pressure to the nasal cavity via the anterior and posterior ethmoid arteries by decreasing cerebral perfusion. Higher doses of inhalational anesthetics may cause additional vasodilation in the surgical field, increasing the likelihood of a worse visual field score.^[4]

On comparing propofol and sevoflurane anesthesia for FESS, propofol/remifentanyl anesthesia was observed to be associated with less blood loss and provide better surgical conditions.^[15] However, combined with remifentanyl, inhalational anesthetics can induce adequate controlled hypotension and provide effective surgical conditions and favorable hemodynamics.^[16] Therefore, it is difficult to determine which agent is better.

When controlled hypotension is induced, the associated complications as well as the importance of an optimal surgical field should be considered.^[2,9] Serious complications owing to organ hypoperfusion are uncommon, but intraoperative hypotension is associated with postoperative stroke, leading to subsequent hypoxia with potential neurologic injury.^[7,8,17,18] The mechanism of postoperative cerebral ischemia is multifactorial, and intraoperative hypotension may play a role in the

occurrence of postoperative stroke by compromising blood flow to a potentially ischemic brain area.^[18,19] Postoperative cognitive dysfunction is also considered when performing controlled hypotension; cognitive dysfunction is also associated with brain cellular injury.^[20] Intraoperative cerebral desaturation is known to be associated with a worse early cognitive outcome after on-pump cardiac surgery.^[21] One study reported that even when SpO_2 was in the normal range, cerebral desaturation was observed in 10% of the patients during controlled hypotension for rhinoplasty, and all patients with intraoperative cerebral desaturation showed decline in cognitive function after surgery. Therefore, the authors recommended monitoring cerebral oxygen saturation during controlled hypoperfusion.^[22]

The S-100 β is an early marker of BBB damage, and a large elevation in its level indicates prior brain damage.^[23] Serum S-100 β values in healthy individuals range from 0.02 to 0.15 $\mu\text{g/L}$, as determined by immunoluminometric analytical methods.^[24] Low (<0.34 ng/mL) serum levels are consistent with BBB opening without central nervous system damage.^[23] GFAP is also a brain-specific biomarker, and increased plasma GFAP concentrations are associated with decline in cognition after noncardiac surgery.^[20] The reported upper limit of GFAP in healthy subject was measured at <0.3 $\mu\text{g/L}$.^[14,25,26] The normal range of each biomarkers may vary depending on which analytic test is used as in the research of Wunderlich et al^[11] in which a new and 1st commercially available test kit was used and the GFAP levels differed from those of previous other studies. The ELISA kit used in this study has a sensitivity of 0.188 ng/mL and detection range of 0.313 to 20 ng/mL. Hence, we think that it is meaningful to compare the levels between the 2 groups and follow the levels and to predict the prognosis.

In stroke patients, S-100 β and GFAP release were significantly correlated and may be considered predictors of the early disease course and functional outcome.^[11,14] The rapid release within 3 to 6 hours after stroke onset and a continuous increase with maximal GFAP concentration 48 hours after stroke may be caused by continued subsequent cell death or persistent disturbance of the BBB; S-100 β can be elevated to 0.1 ng/mL as a result of BBB damage following and prior to neuronal damage.^[11-13] Early increase in S-100 β after surgery is associated with a cognitive dysfunction after surgery.^[27] Hence, evaluation of GFAP and S-100 β levels may be a useful approach for monitoring and evaluating the response to neuroprotective drugs.^[14]

Many recent studies have found that anesthetic agents may be neuroprotective and may provide cerebral protection in surgical patients.^[28] In cardiac surgery, the effects of propofol and inhalational anesthetics on cerebral protection remain unclear. However, propofol is considered an ideal anesthetic for neurosurgery because of its presumed beneficial effects on cerebral physiology including reduction of cerebral metabolic

Table 2
PaCO₂ and EtCO₂.

	T_{20}		P-value	T_{60}		P-value
	Propofol group (n=30)	Desflurane group (n=30)		Propofol group (n=20)	Desflurane group (n=18)	
PaCO ₂	35.3 (3.4)	36.4 (4.1)	.289	35.1 (5.5)	35.2 (3.3)	.896
EtCO ₂	34.4 (2.6)	35.53 (3.2)	.167	33.7 (2.9)	33.9 (2.8)	.796

Data presented as mean (standard deviation).

EtCO₂=end tidal carbon dioxide, T_{20} and T_{60} =time at 20 and 60 min after setting the reverse Trendelenburg position and achieving controlled hypotension.

rate and cerebral blood flow as well as brain relaxation.^[29] One study reported that a sevoflurane-based volatile anesthesia regimen might be associated with better cognitive function compared with a propofol-based anesthesia regimen.^[21] However, cerebral dysfunction and subtle cognitive changes after surgery are not readily detected in routine clinical examinations.^[30]

Evaluation of the level of a neurobiomarker such as S-100 β and GFAP may be helpful to diagnose and prospect of the patients' neurocognitive function. A meta-analysis showed that S-100 β levels assessed at the end of cardiopulmonary bypass and 24 hours postoperatively in cases of cardiac surgery, in which serious postoperative neuropsychologic complications were observed, were significantly lower in the inhalational anesthesia group than those in the TIVA group.^[31] The increase in GFAP was also reduced in the volatile anesthetics group compared with the midazolam-fentanyl infusion group after cardiac surgery.^[32] In this study, the increases in S-100 β and GFAP levels were not different between the propofol and desflurane groups.

Although extreme hypotension causes serious complications, some research reported that lowering the MAP to 2/3 of the initial value did not cause any damage^[33] and the degree of controlled intraoperative hypotension during FESS did not affect cognitive function after surgery.^[3] However, there are many case reports of serious cerebral ischemia after controlled hypotension. In this study, we controlled the MAP at 60 to 70 mm Hg, and there were no clinical neurogenic complications after surgery. Common predisposing factors for perioperative stroke in noncardiac surgery are age, a previous stroke, atrial fibrillation, obesity, and vascular and metabolic diseases.^[8,17] However, high-risk patients with cerebral ischemia were excluded in this study; hence, when choosing the anesthetic technique for controlled hypotension, it would be useful to consider the results of previous studies for surgical field visualization along with the results of the present study on the potential concerns of cerebral ischemia. The anesthesiologist and surgeon should keep in mind that marked hypotension (MAP < 60 mm Hg) is associated with a potential risk of ischemic injury to the cerebrum.^[2]

We have some limitations in this study. First, the sample size was small though it was statistically significant. Second, the surgical field condition and amount of blood loss were not compared between the study groups. It has been reported that controlled hypotension is one of the techniques used for minimizing bleeding during FESS.^[2-4,34] Third, the amount of remifentanyl infused during surgery was not compared between groups. We focused only on the effects of propofol and desflurane for controlled hypotension on the level of the biomarkers under conditions of routine anesthetic practice for controlled hypotension. Further, the biomarkers levels are compromised by extracranial injuries without brain injury. Hence, serial measuring and noting peripheral injury are important.^[35]

5. Conclusion

On comparing the effects of propofol/remifentanyl and desflurane/remifentanyl anesthesia for controlled hypotension on the levels of S-100 β and GFAP during FESS, we noted that the levels of these biomarkers increased compared to base values, but there was no significant difference in S-100 β and GFAP levels between the 2 study groups.

Author contributions

Conceptualization: Sung Mi Hwang, Jae Jun Lee.

Data curation: Ji Su Jang, Youngsuk Kwon, Sung Mi Hwang, Ho Seok Lee.

Formal analysis: Youngsuk Kwon, Jae Jun Lee.

Funding acquisition: Sung Mi Hwang.

Investigation: Ji Su Jang, Ho Seok Lee.

Resources: Jun Suck Lee, Ho Seok Lee.

Supervision: Sung Mi Hwang, Jae Jun Lee, Soo Kyoung Lee.

Writing – original draft: Ji Su Jang, Sung Mi Hwang, Jae Jun Lee.

Writing – review & editing: Ji Su Jang, Youngsuk Kwon, Sung Mi Hwang, Jae Jun Lee, Soo Kyoung Lee.

Sung Mi Hwang orcid: 0000-0001-6035-786X.

References

- Carlton DA, Govindaraj S. Anesthesia for functional endoscopic sinus surgery. *Curr Opin Otolaryngol Head Neck Surg* 2017;25:24–9.
- Ha TN, van Renen RG, Ludbrook GL, et al. The relationship between hypotension, cerebral flow, and the surgical field during endoscopic sinus surgery. *Laryngoscope* 2014;124:2224–30.
- Nowak S, Oldak A, Kluzik A, et al. Impact of controlled induced hypotension on cognitive functions of patients undergoing functional endoscopic sinus surgery. *Med Sci Monit* 2016;22:898–907.
- DeConde AS, Thompson CF, Wu EC, et al. Systematic review and metaanalysis of total intravenous anesthesia and endoscopic sinus surgery. *Int Forum Allergy Rhinol* 2013;3:848–54.
- Degoute CS, Ray MJ, Manchon M, et al. Remifentanyl and controlled hypotension: comparison with nitroprusside or esmolol during tympanoplasty. *Can J Anaesth* 2001;48:20–7.
- Boonmak S, Boonmak P, Laopaiaboon M. Deliberate hypotension with propofol under anaesthesia for functional endoscopic sinus surgery (FESS). *Cochrane Database Syst Rev* 2016;10:CD006623.
- Heller JA, DeMaria SJr, Govindaraj S, et al. Cerebral oximetry monitoring during sinus endoscopy. *Laryngoscope* 2015;125:E127–31.
- Pohl A, Cullen DJ. Cerebral ischemia during shoulder surgery in the upright position: a case series. *J Clin Anesth* 2005;17:463–9.
- Kim JS, Ko SB, Shin HE, et al. Perioperative stroke in the brain and spinal cord following an induced hypotension. *Yonsei Med J* 2003;44:143–5.
- Lindop MJ. Complications and morbidity of controlled hypotension. *Br J Anaesth* 1975;47:799–803.
- Wunderlich MT, Wallesch CW, Goertler M. Release of glial fibrillary acidic protein is related to the neurovascular status in acute ischemic stroke. *Eur J Neurol* 2006;13:1118–23.
- Kapural M, Krizanac-Bengez Lj, Barnett G, et al. Serum S-100 β as a possible marker of blood-brain barrier disruption. *Brain Res* 2002;940:102–4.
- Marchi N, Cavaglia M, Fazio V, et al. Peripheral markers of the blood-brain barrier damage. *Clin Chim Acta* 2004;342:1–2.
- Herrmann M, Vos P, Wunderlich MT, et al. Release of glial tissue-specific proteins after acute stroke. A comparative analysis of serum concentrations of protein S-100B and glial fibrillary acidic protein. *Stroke* 2000;31:2670–7.
- Ahn HJ, Chung SK, Dhong HJ, et al. Comparison of surgical conditions during propofol or sevoflurane anaesthesia for endoscopic sinus surgery. *Br J Anaesth* 2008;100:50–4.
- Dal D, Celiker V, Ozer E, et al. Induced hypotension for tympanoplasty: a comparison of desflurane, isoflurane and sevoflurane. *Eur J Anaesthesiol* 2004;21:902–6.
- Ng JL, Chan MT, Gelb AW. Perioperative stroke in noncardiac, nonneurologic surgery. *Anesthesiology* 2011;115:879–90.
- Bijker JB, Persoon S, Peelen LM, et al. Intraoperative hypotension and perioperative ischemic stroke after general surgery. A nested case-control study. *Anesthesiology* 2012;116:658–64.
- Caplan LR, Hennerici M. Impaired clearance of emboli (washout) is an important link between hypoperfusion, embolism, and ischemic stroke. *Arch Neurol* 1998;55:1475–82.
- Rappold T, Laflam A, Hori D, et al. Evidence of an association between brain cellular injury and cognitive decline after non-cardiac surgery. *Br J Anaesth* 2016;116:83–9.

- [21] Schoen J, Husemann L, Tiemeyer C, et al. Cognitive function after sevoflurane- vs propofol-based anaesthesia for on-pump cardiac surgery: a randomized controlled trial. *Br J Anaesth* 2011;106:840–50.
- [22] Erdem AF, Kayabasoglu G, Tas Tuna A, et al. Effect of controlled hypotension on regional cerebral oxygen saturation during rhinoplasty: a prospective study. *J Clin Monit Comput* 2016;30:655–60.
- [23] Marchi N, Rasmussen P, Kapural M, et al. Peripheral markers of brain damage and blood-brain barrier dysfunction. *Restor Neurol Neurosci* 2003;21:109–21.
- [24] Ben Abdesselam O, Vally J, Adem C, et al. Reference values for serum S-100B protein depend on the race of individuals. *Clin Chem* 2003;49:836–7.
- [25] Fassbender K, Schmidt R, Schreiner A, et al. Leakage of brain-originated proteins in peripheral blood: temporal profile and diagnostic value in early ischemic stroke. *J Neurol Sci* 1997;148:101–5.
- [26] Foerch C, Niessner M, Back T, et al. Diagnostic accuracy of plasma glial fibrillary acidic protein for differentiating intracerebral hemorrhage and cerebral ischemia in patients with symptoms of acute stroke. *Clin Chem* 2012;58:237–45.
- [27] Jönsson H, Johnsson P, Alling C, et al. S100 β after coronary artery surgery: release pattern, source of contamination, and relation to neuropsychological outcome. *Ann Thorac Surg* 1999;68:2202–8.
- [28] Wang H, Li P, Xu N, et al. Paradigms and mechanisms of inhalational anesthetics mediated neuroprotection against cerebral ischemic stroke. *Med Gas Res* 2016;6:194–205.
- [29] Kawaguchi M, Furuya H, Patel PM. Neuroprotective effects of anesthetic agents. *J Anesth* 2005;19:150–6.
- [30] Jeong H, Jeong S, Lim HJ, et al. Cerebral oxygen saturation measured by near-infrared spectroscopy and jugular venous bulb oxygen saturation during arthroscopic shoulder surgery in beach chair position under sevoflurane-nitrous oxide or propofol-remifentanyl anesthesia. *Anesthesiology* 2012;116:1047–56.
- [31] Chen F, Duan G, Wu Z, et al. Comparison of the cerebroprotective effect of inhalation anaesthesia and total intravenous anaesthesia in patients undergoing cardiac surgery with cardiopulmonary bypass: a systemic review and meta-analysis. *BMJ Open* 2017;7:e014629.
- [32] Dabrowski W, Rzecki Z, Czajkowski M, et al. Volatile anesthetics reduce biochemical markers of brain injury and brain magnesium disorders in patients undergoing coronary artery bypass graft surgery. *J Cardiothorac Vasc Anesth* 2012;26:395–402.
- [33] Townes BD, Dikmen SS, Bledsoe SW, et al. Neuropsychological changes in a young, healthy population after controlled hypotensive anesthesia. *Anesth Analg* 1986;65:955–9.
- [34] Sartcaoglu F, Celiker V, Basgul E, et al. The effect of hypotensive anaesthesia on cognitive functions and recovery at endoscopic sinus surgery. *Eur J Anaesthesiol* 2005;22:157–9.
- [35] Bloomfield SM, McKinney J, Smith L, et al. Reliability of S100 B in predicting severity of central nervous system injury. *Neurocrit Care* 2007;6:121–38.