ORIGINAL ARTICLE

Total intravenous anesthesia or volatile anesthesia in pediatric neuroanesthesia applications: retrospective study

Anestesia total intravenosa o anestesia volátil en aplicaciones de neuroanestesia pediátrica: estudio retrospectivo

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Abstract

Objective: *The primary objective of this study was to assess the effects of preferred anesthesia methods on perioperative hemodynamics in pediatric patients undergoing neurosurgery.* **Method:** *This retrospective and cross-sectional study included all pediatric patients undergoing brain surgery at Dicle University Hospital between January 2018 and December 2023. Group 1 received sevoflurane and remifentanil anesthesia, whereas Group 2 received propofol and remifentanil anesthesia. Perioperative hemodynamic parameters, post-operative outcomes, mortality rates, use of inotropic agents, and laboratory values of the patients were collected.* **Results:** *A total of 840 patients were included in the study. When comparing perioperative heart rate values between the groups, patients in Group 1 exhibited significantly higher heart rates. In addition, when evaluating mean arterial pressure (MAP), it was found that patients in Group 1 had lower MAP values compared to those in Group 2.* **Conclusions:** *Based on the results obtained in the present study, we recommend the use of total intravenous anesthesia in pediatric patients undergoing brain surgery due to its ability to provide more stable hemodynamics during the perioperative period.*

Keywords: *Total intravenous anesthesia. Volatile anesthesia. Pediatric patients.*

Resumen

Objetivo: *El objetivo principal de este estudio fue evaluar los efectos de los métodos de anestesia preferidos en la hemodinámica perioperatoria en pacientes pediátricos sometidos a neurocirugía.* **Método:** *Este estudio retrospectivo y transversal incluyó a todos los pacientes pediátricos sometidos a cirugía cerebral en el Hospital Universitario de Dicle entre enero de 2018 y diciembre de 2023. El grupo 1 recibió anestesia con sevoflurano y remifentanilo, mientras que el grupo 2 recibió anestesia con propofol y remifentanilo. Se recopilaron los parámetros hemodinámicos perioperatorios, los resultados posoperatorios, las tasas de mortalidad, el uso de agentes inotrópicos y los valores analíticos de los pacientes.* **Resultados:** *Un total de 840 pacientes fueron incluidos en el estudio. Al comparar la frecuencia cardiaca perioperatoria entre los grupos, los pacientes del grupo 1 mostraron frecuencias cardiacas significativamente más altas. Además, al evaluar la presión arterial media se encontró que los pacientes del grupo 1 tenían valores más bajos que los del grupo 2.* **Conclusiones:** *Basándonos en los resultados obtenidos en el presente estudio, recomendamos el uso de anestesia total intravenosa en pacientes pediátricos sometidos a cirugía cerebral debido a su capacidad para proporcionar una hemodinámica más estable durante el periodo perioperatorio.*

Palabras clave: *Anestesia total intravenosa. Anestesia volátil. Pacientes pediátricos.*

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Introduction

Recent advancements in pediatric neurosurgical anesthesia have significantly improved outcomes for infants and children affected by central nervous system lesions. Inhalation anesthesia and total intravenous anesthesia (TIVA) techniques are widely used in pediatric anesthesia practice.

Inhalation anesthetics have been a standard choice for general anesthesia in clinical practice since the mid-19th century, when diethyl ether was first introduced[1]. Sevoflurane was first synthesized in 1971 and became widely available in the 1990s. Due to its favorable pharmacodynamic and pharmacokinetic properties, sevoflurane is a particularly popular anesthetic agent, particularly in pediatric patients[1]. Sevoflurane is a stable, colorless, non-irritating, and non-flammable substance at room temperature with a characteristic sweet odor[2,3]. Although sevoflurane has long been popular, its short-term and long-term effects on neurological function are still under investigation. In recent years, there has been a significant increase in pre-clinical studies investigating the toxic effects of anesthetics on the developing brain[4]. Numerous calls have been made for more precise research to determine whether exposure to anesthesia during early childhood has clinically significant effects on neurodevelopment in humans[5,6].

TIVA has been used in adult practice since 1982, whereas its practical application in pediatric patients is relatively new. A previous study showed that only 10% of pediatric anesthetists utilize TIVA at least once a week[7]. The use of TIVA has increased despite certain barriers such as interindividual pharmacokinetic and pharmacodynamic variability and safety concerns related to propofol infusion syndrome[8-10].

The primary objective of this study was to assess the effects of preferred anesthesia methods on perioperative hemodynamics in pediatric patients undergoing neurosurgery. The secondary aim of this study was to investigate the effects of anesthesia techniques on post-operative outcomes, mortality rates, use of inotropic agents, and laboratory values.

Method

This retrospective, cross-sectional study included all pediatric patients undergoing brain surgery at Dicle University Hospital between January 2018 and December 2023. A total of 840 patients were initially assessed. Fifty-nine patients were excluded due to incomplete or missing data, and 781 patients were included in the final analysis. This study was initiated after obtaining the necessary ethical approvals. Pediatric patients undergoing brain surgery were documented for their American Society of Anesthesiologists (ASA) classification, perioperative hemodynamic data, intraoperative need for blood transfusion, intraoperative use of inotropic agents, type of anesthesia administered, anesthetic agent used, post-operative status of patients (intubated or extubated), and duration of stay in the intensive care unit (ICU) between the specified dates. Patients aged ≥ 15 years as well as those with incomplete records were excluded from the study.

All surgical procedures were performed under general anesthesia. The choice between inhalation and intravenous anesthesia induction techniques was determined by the responsible anesthesiologist based on the presence or absence of signs of intracranial hypertension in the patient. Following endotracheal intubation and induction of general anesthesia, anesthesia was maintained with an intravenous infusion of remifentanil (0.02-0.2 µg/kg/min) combined with either propofol (Propofol Fresenius Kabi, Sweden) at 6-12 mg/kg/h or sevoflurane (Sevoflurane® Liquid 100%, Queenborough) at a concentration below 1%. The solutions we prepared were sent with the infusion pump MDT SN-S1 model (Sino Medical-Device Technology Co., Ltd, Shenzhen, China) (Fig. 1). Routine intraoperative monitoring included electrocardiography, non-invasive arterial blood pressure monitoring, capnography, pulse oximetry, body temperature monitoring, and urinary output through a catheter. An arterial catheter and central venous line were placed after the induction of general anesthesia.

Demographic data, including age, sex, and body weight, along with ASA classification, pre-operative hemoglobin (Hb) level, coagulation parameters, and intracranial mass localization, were recorded. Intraoperative data, including duration and year of operation, intraoperative position, intraoperative inotrope use, whether blood transfusion was performed, and whether central venous and arterial catheters were applied, were recorded. All patients were transferred to the ICU for post-operative follow-up. During the post-operative period, records regarding post-operative Hb and hematocrit values, whether patients were intubated or extubated, duration of stay in the ICU, and length of hospital stay were kept. Saturation and mean arterial pressure (MAP) of the patients were measured at the entrance, intraoperative 30th min, and

Figure 1. *Infusion pump device.*

in the post-extubation period. Routine blood samples were taken in the ICU from patients scheduled for surgery 1 day before and immediately after the operation.

We divided the patients into two groups and evaluated the results. Group 1 consisted of patients who received sevoflurane as the inhalation agent, whereas Group 2 consisted of patients who underwent TIVA as the anesthetic method.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) 16.0 software for Windows (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Continuous data are expressed as mean and standard deviation; categorical data are expressed as frequency and percentage. The categorical data of the groups were compared using the χ^2 and Fisher's exact tests. The Kolmogorov-Smirnov test was used to determine whether the numerical data were normally distributed. Student's *t*-test was used to analyze data with a normal distribution, whereas the Mann-Whitney U test was used to analyze non-normally distributed data. The Wilcoxon W test was performed for evaluations within groups. In all comparisons, $p < 0.05$ was considered significant.

Results

A total of 840 patients were included in this study. Fifty-nine patients were excluded from the study due to the unavailability of records or incomplete information, resulting in a total of 781 patients included in the study. Patients were divided into two groups according to the anesthetic agent administered. The TIVA group consisted of 159 (20.4%) patients, and the other group consisted of 622/781 (79.6%) (Fig. 2).

Demographic data, pre-operative laboratory values, intraoperative hemodynamic data, and other characteristics were compared between the groups. Demographic data revealed that mean age and body weight were significantly lower in Group 1 than in Group 2 ($p < 0.001$ for both variables), and the incidence of comorbidities was higher in Group 1 ($p = 0.005$). There were no statistically significant differences between the two groups in terms of sex and ASA classification (Table 1).

When comparing emergency and elective surgical procedures, sevoflurane was more commonly used as the anesthetic agent in patients undergoing emergency surgery ($p < 0.001$). When the groups were compared in terms of anesthesia and surgical duration, it was found that anesthesia and surgical duration were significantly longer in Group 2 than in Group 1 ($p < 0.001$ for both variables). Upon examining the post-operative admission to the ICU, it was found that patients in Group 2 had a higher rate of extubation compared with those in Group 1 ($p = 0.004$) (Table 1).

When both groups were compared in terms of mortality, it was found that the mortality rate was significantly higher in Group 2 compared to Group 1 (Group 1: 13 patients, 2.09%; Group 2: 14 patients, 8.80%, $p < 0.001$) (Table 1).

When comparing the saturation values between the groups, it was found that patients in Group 2 had significantly higher pre-operative and post-operative saturation values than those in Group 1 ($p = 0.026$, $p < 0.001$). Comparing the groups in terms of perioperative heart rate values, it was found that patients in Group 1 had significantly higher heart rates ($p < 0.001$ for all heart rate values). In addition, when evaluated for MAP, it was found that patients in Group 1 had lower MAP values compared to those in Group 2 (p values were < 0.001, 0.003, and < 0.001, respectively). The details of the comparison between both groups are presented in table 2.

When pre-operative and post-operative laboratory values were compared within the groups, Hb and hematocrit values significantly decreased in both groups during the post-operative period ($p < 0.001$ for both variables for Hb, $p < 0.001$ and $p = 0.011$ for heat

Table 1. Demographic data of patients

Variables	Group 1 (n = 622)		Group 2 (n = 159)		p
	Mean	SD	Mean	SD	
Age	4.53	4.41	8.59	4.47	< 0.001
Weight	17.44	13.65	31.45	15.9	< 0.001
Intensive care hospitalization period	15.91	17.25	16.16	14.52	0.308
Anesthesia time	147.27	120.61	466.13	253.09	< 0.001
Surgery time	130.51	113.30	427.30	247.47	< 0.001
	Frequency	Percent	Frequenccy	Percent	
Sex					
Male	331	42.4	71	9.1	0.15
Female	292	37.4	88	11.3	
ASA*					
ASA 1	139	17.8	44	5.6	0.054
ASA 2	294	37.6	75	9.6	
ASA 3	163	20.9	33	4.2	
ASA 4	23	2.9	6	0.8	
Surgery type					
Emergency surgery	347	44.4	41	5.2	< 0.001
Elective surgery	276	35.3	50	6.4	
Comorbidity					
Yes	106	13.6	17	2.2	< 0.001
No	516	66.1	142	18.2	
Intraoperative inotrope usage					
Yes	18	2.3	2	0.3	< 0.001
No	605	77.5	157	20.1	
Postoperative airway status					
Extubated	493	63.1	62	7.9	0.004
Intubated	130	16.6	97	12.4	
Mortality					
Death	13	1.7	14	1.8	< 0.001
Survive	609	78	145	18.6	
Intraoperative blood transfusion need					
Yes	82	10.5	57	7.3	< 0.001
No	541	69.3	102	13.1	

The bold values represent statistically significant results ($p < 0.05$).
*ASA: American society of anesthesiologist.
TIVA: total intravenous anesthesia; SD: standard deviation.

hematocrit [Htc]). When pre-operative and post-operative white blood cell (WBC) values were compared within the group, it was found that WBC values significantly increased in patients in Group 1 ($p = 0.024$). It was observed that chloride (Cl) levels were significantly elevated in both groups during the post-operative period ($p < 0.001$, $p = 0.001$). Furthermore, post-operative urea and alanine transaminase (ALT) values decreased significantly and increased significantly in Group 2 patients ($p = 0.024$ and $p = 0.014$) (Figs. 3 and 4, Table 3).

Intra-group before and after comparisons are given in tables 4 and 5.

Discussion

The results obtained in this retrospective study examining the use of sevoflurane or TIVA with propofol-remifentanil in pediatric patients undergoing brain surgery revealed that perioperative heart rate was higher and MAP was significantly lower in the sevoflurane group. Similarly, Chui et al. in a systematic study comparing TIVA and inhalation agents for

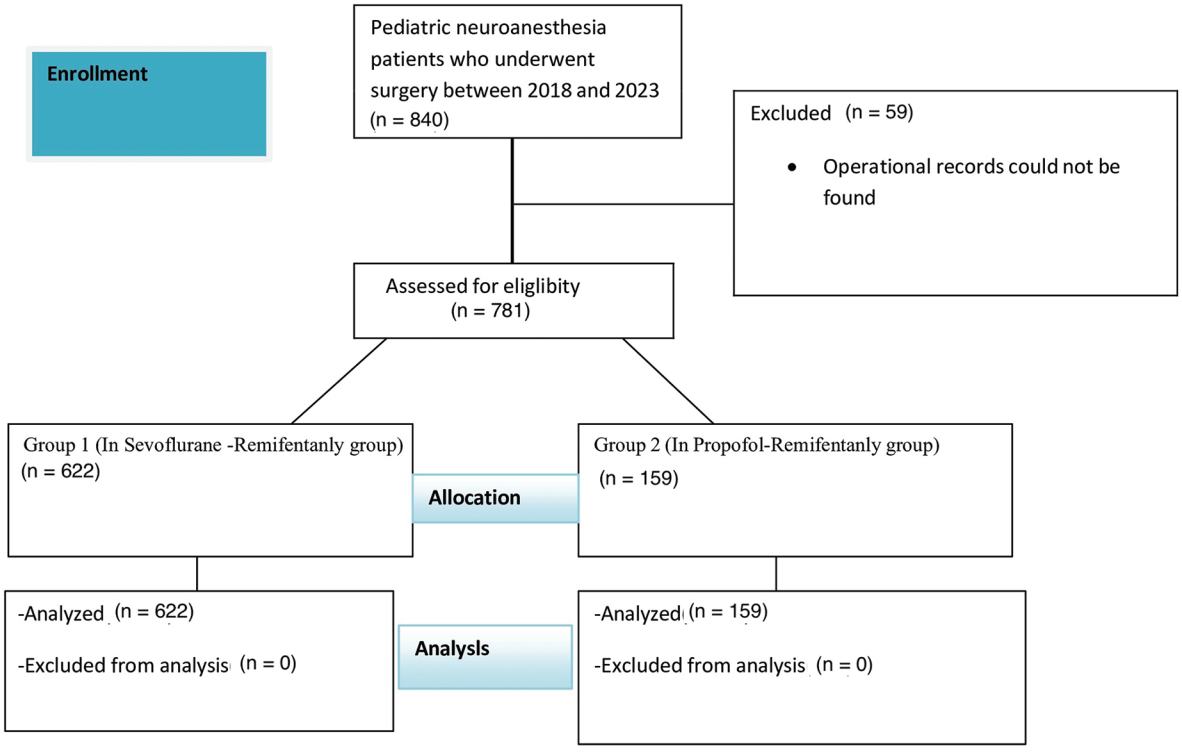

Figure 2. *Recruitment and flow of patients.*

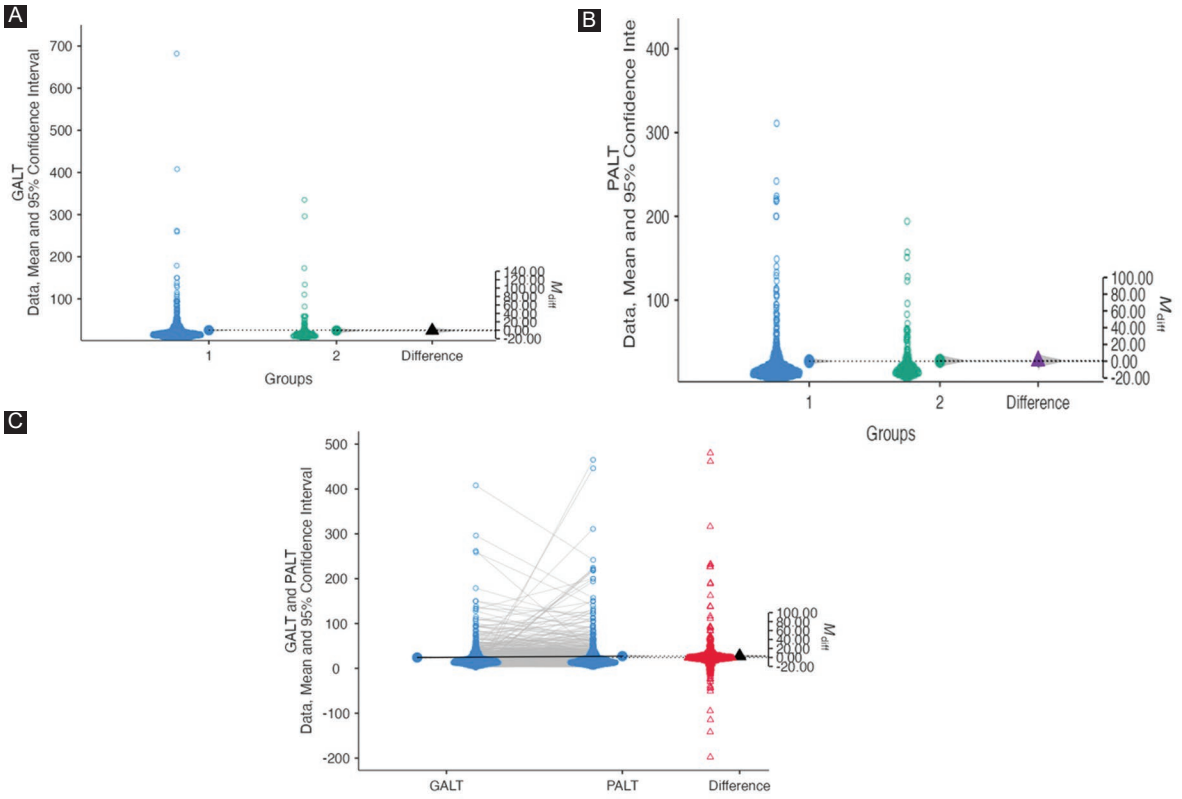

Figure 3. *Comparison of pre-operative and post-operative alanine aminotransferase (ALT) values of the groups* **A:** *comparison of pre-operative ALT values between groups,* **B:** *comparison of post-operative ALT values between groups, and* **C:** *change of per-operative ALT values.*

Table 2. Perioperative hemodynamics in pediatric neuroanesthesia applications

Variables	Group 1 Sevoflurane (n = 622)		Group 2 TIVA (n = 159)		p
SpO_2 (1)	97.78	1.89	98.16	1.94	0.026
SpO_2 (2)	98.74	3.72	99.24	0.84	0.097
SpO_2 (3)	98.15	1.52	98.68	1.27	< 0.001
Heart rate (1)*	120.02	21.54	103.49	20.69	< 0.001
Heart rate (2)	114.38	19.40	96.12	19.42	< 0.001
Heart rate (3)	114.90	19.28	97.06	22.61	< 0.001
MAP (1)	68.08	11.35	77.46	10.29	< 0.001
MAP (2)	66.08	8,81	72.71	10.29	0.003
MAP (3)	67	9.88	72.48	9.19	< 0.001

*heart rate.
SPO_2: oxygen saturation; MAP: mean arterial pressure; TIVA: total intravenous anesthesia.

anesthesia maintenance during elective craniotomy, concluded that TIVA administration was associated with less intraoperative hypotension compared to inhalation agents, and there was no significant difference in the incidence of intraoperative hypertension, bradycardia, or tachycardia[11]. In a prospective study, Sneyd et al. administered TIVA and sevoflurane anesthesia to 24 and 26 patients, respectively, and noted that the sevoflurane group had more hypotensive events than the TIVA group[12]. Consistent with the present study, the use of inotropic agents was also higher in the sevoflurane group[12]. In a prospective study, Chen et al.[13] compared TIVA and sevoflurane in pediatric patients and found that the TIVA group induced less pronounced hemodynamic changes[13,14]. It is possible that the sevoflurane group received a deeper anesthesia.

In the present study, the use of sevoflurane or TIVA with propofol-remifentanil in pediatric patients was examined, and a large proportion of patients (73.5%) were maintained with sevoflurane anesthesia.

When comparing the post-operative outcomes of patients, extubation was performed more frequently in the sevoflurane group compared with the TIVA group. Consistent with the present study, Raeder et al. reported earlier extubation in the sevoflurane group compared to TIVA[14].

When the pre-operative and post-operative laboratory values of the patients were compared in the present study, as expected, Hb and hematocrit values were significantly lower. Furthermore, although the

Table 3. Comparison of pre-operative and post-operative laboratory values between groups

Variables	Pre-operative		Post-operative		p
	Mean	SD	Mean	SD	
Group 1 Hb	11.7	2.16	10.7	1.99	**< 0.001**
Group 2 Hb	12.2	1.56	11.5	1.91	**< 0.001**
Group 1 Htc	35.65	6.29	32.87	5.74	**< 0.001**
Group 2 Htc	36.65	4.44	35.24	5.31	**0.011**
Group 1 WBC	13.44	8.05	14.37	7.24	**0.024**
Group 2 WBC	13.06	27.55	16.01	7.3	0.357
Group 1 Üre	22.46	13.76	21.74	14.98	0.157
Group 2 Üre	24.7	8.8	22.95	7.97	**0.024**
Group 1 Creatinine	0.5	0.1	0.51	0.1	0.78
Group 2 Creatinine	0.68	0.02	0.58	0.09	0.2
Group 1 Na	135.47	5.67	135.58	6.09	0.587
Group 2 Na	136.68	3.56	137.85	4.86	0.014
Group 1 K	4.33	0.615	4.34	0.598	0.934
Group 2 K	4.03	0.35	4.1	0.31	0.794
Group 1 Cl	104.19	4.26	105.21	6.58	**0.001**
Group 2 Cl	103.97	3.8	108.25	6.65	**< 0.001**
Group 1 AST	47.01	77.66	46.09	73.62	0.807
Group 2 AST	32.5	24.81	38	32.48	0.087
Group 1 ALT	25.74	31.7	27.98	43.09	0.232
Group 2 ALT	22.57	29.29	28.63	29.47	**0.014**
Group 1 Lactate	3	0	9	9.89	0.549
Group 2 Lactate	1.37	0.55	2.03	0.95	0.184

The bold values represent statistically significant results ($p < 0.05$).
Hb: hemoglobin; Htc: hematocrit; WBC: white blood cell; ALT: alanine transaminase; AST: aspartate transaminase; Cl: chloride.

WBC values increased in both groups, there was a significant increase in the sevoflurane group. In contrast to the present study, Soto et al. conducted a prospective study involving adult patients and compared WBC counts during sevoflurane and TIVA anesthesia to baseline, and they did not observe a significant change[15]. Similarly, Kim et al. conducted a prospective study involving adult patients and found that while the WBC count increased more in the sevoflurane group, the difference between the groups was not statistically significant. In the present study, Cl values increased in both groups. We attribute this result to the use of 0.9% NaCl solution in our study. We observed that patients in the TIVA group had

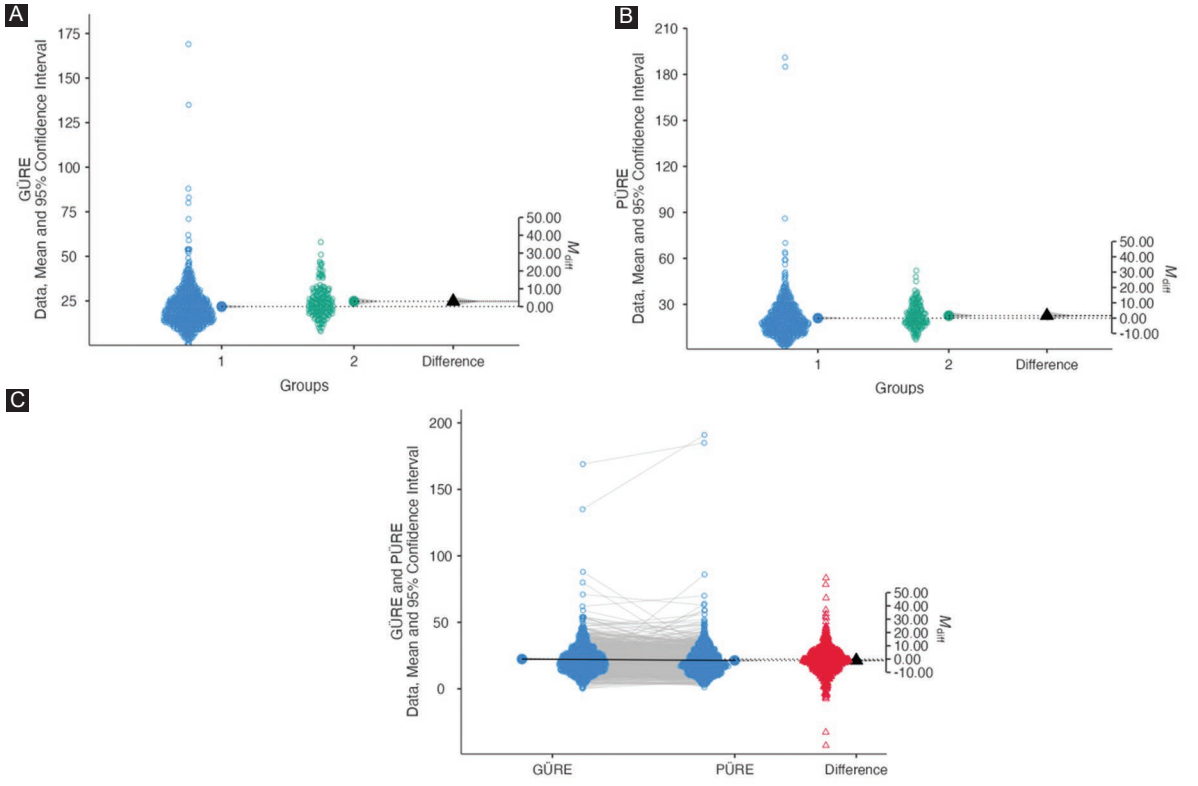

Figure 4. *Comparison of pre-operative and post-operative urea values of the groups:* **(A)** *comparison of pre-operative urea values between groups,* **(B)** *comparison of post-operative urea values between groups,* **(C)** *change in perioperative urea values. Güre: pre-operative urea, Püre: post-operative urea.*

Table 4. Group 1 before and after comparison

Pre-operative-post-operative	Statistic	p	Mean difference	SE difference
Hb	89161	<0.001	1.1500	0.0798
Htc	104108	< 0.001	3.1800	0.6127
WBC	56127	0.004	−0.8000	0.3099
ÜRE	70127	0.013	1.0000	0.4717
Creatinin	54075	0.011	0.0150	0.0192
NA	56094	0.948	−6.53e-5	0.1902
Potassium	70722	< 0.001	0.1500	0.2851
PCI	40458	< 0.001	−1.4000	209.2010
AST	77515	< 0.001	2.5000	3.6729
ALT	70709	< 0.001	1.5000	1.7983

Hb: hemoglobin; Htc: hematocrit; Wbc: white blood cell; ALT: alanine transaminase; AST: aspartate transaminase.

Table 5. Group 2 before and after comparisons

Pre-operative-post-operative	Statistic	p	Mean difference	SE difference
Hb	6402	< 0.001	0.9500	0.16940
Htc	7691	< 0.001	2.5000	0.46509
WBC	1193	< 0.001	−5.2000	1.73740
ÜRE	6135	0.013	1.9999	0.71996
Creatinin	4258	0.017	0.0250	0.00954
NA	3282	0.012	−1.5000	0.45331
Potassium	6548	< 0.001	0.3000	0.04996
PCI	1549	< 0.001	−4.5000	0.57951
AST	3753	0.087	−2.0000	3.07967
ALT	3003	< 0.001	−2.5000	2.23551

Hb: hemoglobin; Htc: hematocrit; Wbc: white blood cell; ALT: alanine transaminase; AST: aspartate transaminase.

significantly elevated ALT values when ALT values were evaluated. Contrary to the present study, one study in the literature conducted by Kang et al. retrospectively compared pre-operative and post-operative ALT values in patients under 3 years of age over 3 years and found no significant difference[16].

Considering the longer duration of surgery in the TIVA group in the present study, we believe that further prospective studies are needed. A decrease in urea levels was observed in both groups of patients, but this decrease was significantly greater in the TIVA group. Ebert et al. compared the laboratory values of desflurane, sevoflurane, and TIVA groups in 52 patients and found that urea significantly decreased in all three groups[17].

It should be noted that our study has some limitations. The primary limitation of this study is its single-center and retrospective design. Since TIVA is generally used in mass surgery in our clinical practice, the duration of anesthesia and surgery was quite long in this group. The demographic parameters were also different. The number of patients was not evenly distributed. There is a need for further prospective and multicenter studies on this subject.

Conclusions

Based on the results obtained in the present study, we recommend the use of TIVA in pediatric patients undergoing brain surgery due to its ability to provide more stable hemodynamics during the perioperative period.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely collected and anonymized clinical data; therefore, individual informed consent was not required. Relevant ethical recommendations have been followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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