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A Comparative Study of Brain Injury Biomarker S100β During General and Spinal Anesthesia for Caesarean Delivery: A Prospective Study

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Abstract: *Background and Objectives*: Anaesthesia is a medical procedure that involves the use of drugs to induce a state of unconsciousness or reduced awareness. A biomarker of pathological conditions is elevated S100β levels found in biological fluids. In order to investigate it, this study aims to differentiate brain injury in general along with spinal anaesthesia during C-section. *Materials and Methods*: The 60 parturient women underwent a C-section from July 1, 2021 to Dec 30, 2023 had been evenly distributed into 2 groups General anaesthesia (n=30), and Spinal anaesthesia group (n=30). The prospective observational study effectively compared the changes in the S100β brain damage biomarker ratio in maternal blood (preoperative and postoperative) and umbilical artery blood during a C-section, using either general or spinal anaesthesia. *Results*: S100β concentrations slightly increased once the C-section was over in both the SA and GA group, but without notable differences. In the SA and GA groups, preoperative S100 β concentration in maternal blood was 195.1±36.2 ng/L, 193.0±54.3 ng/L, then increased to 200.9±42.9ng/L, 197.0±42.7 at the end of operation. Although there was no major statistical difference (p=0.86), S100B concentrations in the postoperative stage and umbilical artery in the spinal anaesthesia group clearly tended to be higher than that in the general anaesthesia group. *Conclusions*: S100β concentrations slightly increased after C-section in both groups. General anaesthesia faint impacts S100β levels in umbilical cord blood during C-section. Spinal and general anesthesia are considered safe for the maternal and fetal brain during cesarean sections when administered appropriately, with no evidence suggesting harmful effects. Further studies is needed to study associations between anaesthesia, perioperative release of brain injury biomarker, and perioperative clinical outcomes.

Keywords: Anesthesia; maternal; brain damage

Introduction

In the obstetrics department, caesarean section is the most common surgery. World Health Organization (WHO) research shows that global caesarean section (C-section) delivery has risen to over 21% of all childbirths [1]. According to a study by the Center for Health Development, the C-section rate in Mongolia has been increasing over the years from 22.4% in 2012 to 25.4% in 2016 [2,3]. Anaesthesiologists must decide whether general or regional anaesthesia is optimal for caesarean section delivery based on the specific condition and clinical circumstances of each patient.

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A classical method of anaesthesia for C-sections delivery is spinal anaesthesia (SA) and through relevant and rigorous guidelines can be recommended to patients. Spinal anaesthesia is rapid, providing quick onset of bilateral, dense, and reliable anaesthesia using minimal drug dosages with low risk of both material toxicity and fetal drug transfer. One drawback of spinal anaesthesia is its fixed duration after a single injection. A major adverse fetal effect of SA is maternal sympathetic blockade resulting in uteroplacental hypoperfusion causing hypotension and a decrease in the intervillous blood flow potentially leading to acidemia [5,6]. General anaesthesia (GA) provides a rapid and reliable onset, with steady control over the airway and ventilation, potentially reducing the risk of hypotension. GA may be more suitable in certain conditions (e.g., profound fetal bradycardia, ruptured uterus, severe haemorrhage, severe placental abruption, umbilical cord prolapse, and preterm footling breech) [7]. Traditionally, there was a belief that exposure to general anaesthesia (GA) during a Caesarean section could lead to birth asphyxia [8]. However, current understanding suggests that brief exposure to GA is generally safe for the foetus. Short-acting anaesthetics like propofol are preferred to minimize exposure time and reduce potential risks [9].

Propofol offers a rapid reliable loss of consciousness [10]. It is an intravenous sedative-hypnotic agent, containing amnestic properties for induction of GA. It also lowers cerebral blood flow, intracranial pressure, and cerebral metabolic rate whilst preserving static autoregulation [11] and vascular responsiveness to carbon dioxide [12]. Propofol's neuroprotective effects are thought to stem from its antioxidant capabilities, its enhancement of γ-aminobutyric acid (GABAA)-mediated inhibition of synaptic transmission, and its suppression of glutamate release in cerebral ventricles [13]. On the other hand, GA has been demonstrated to be neurotoxic for certain animals' developing brains in a dose and time manner and may be associated with both long-term learning and development disorders [14,15]. However, these effects of GA cannot be confirmed for the human species. The mechanisms underlying general anaesthesia-mediated effects, including neuroprotection and neurotoxicity, remain unclear despite various proposed hypotheses. The development of a reliable biomarker to detect acute anaesthesia neurotoxicity in the brain could significantly enhance research progress. However, uncertainties persist regarding its effectiveness in reflecting anaesthesia-related brain injury in humans.

The calcium-binding protein S100β serves as a widely employed biomarker for identifying brain damage resulting from various stressors, such as ischemia [16] and trauma [17,18]. Notably sensitive, S100β, primarily found in astrocytes due to its affinity for calcium, plays a pivotal role in regulating diverse intra- and extracellular physiological processes. It functions both as a marker and a signal, activating detection and protective mechanisms upon central nervous system (CNS) damage [19]. Studies indicate S100β's established specificity as a marker for CNS tissue damage [20]. Its presence in biological fluids, including cerebrospinal fluid, peripheral and cord blood, urine, saliva, and amniotic fluid, signifies active neural distress [21]. Moreover, S100β serves as a reliable biomarker for fetal hypoxia and ischemic damage in pregnant patients. Investigations have demonstrated the correlation between elevated S100β plasma levels and brain damage in foetuses exposed to general anaesthetics, particularly reflecting apoptosis levels [22]. This protein proves effective in detecting severe neurological damage in developing animal brains and can also identify the effects of prenatal drug exposure [21–23].

The umbilical artery carries deoxygenated blood from the developing foetus's circulation and demonstrates fetal changes whereas the umbilical vein holds oxygenated blood originating in the placenta and shows changes from the mother [24]. Utilizing the brain damage biomarker S100β, we compared the ratio of S100β levels between maternal arterial blood and umbilical artery blood immediately post-delivery, and assayed fetal S100β levels. All patients underwent a C-section using SA or GA. Our hypothesis suggests that the brain damage biomarker S100β would exhibit no elevation in the cord arterial blood of foetuses who experienced brief exposure to general anaesthetics compared to those who underwent C-section using spinal anaesthesia.

2. Materials and Methods

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2.1. Study Design and Participants

The study was a single-centre prospective, controlled study. In accordance with the inclusion and exclusion criteria, the parturient women who undergo C-section in The Obstetrics and Gynaecology Hospital of The National Center of the Maternal and Child Health of Mongolia from July 2021 to December 2023 enrolled in this study. All procedures performed in the study complied with the Declaration of Helsinki and adhered to the Consolidated Standards of Reporting Trials (CONSORT) guidelines. The terms general anaesthesia (GA) and spinal anaesthesia (SA) were used to designate two distinct groups. Women giving birth by caesarean-section in hospital granted permission to take part in the study and were registered. Figure 1 shows patient recruitment and flow. The sample size of the study was calculated using Open Epi software. The sample size was calculated based on the difference in means under the hypothesis of a difference between the two groups. A minimum of 29 subjects was required per study group. The study adhered to the following specific inclusion and exclusion criteria for the participants. The inclusion criteria were as follows: (1) aged between 18-40 (2) American Society of Anaesthesiologists physical status I or II (3) term gestation at 37 weeks (4) patients whose haemoglobin >100 g/L (5) women with uncomplicated singleton pregnancies who were advised to undergo elective caesarean sections due to factors such as a previous caesarean delivery, a history of primary infertility, or other reasons. Exclusion criteria were as follows: (1) less than height 150 cm (2) body mass index (BMI) ≥ 30 kg/m2 (3) parturient women who suffered from severe internal, surgical, or obstetric comorbidities (4) preeclampsia (5) known fetal neurologic deficit, intrauterine growth retardation (6) patients who received analgesic and sedative medicine before C-section (7) patients who suffering from a severe mental illness (8) emergency C-section for delivery (9) classification as ASA status ≥ III (10) patients who were unwilling to partake in the study (11) patients who were allergic to anaesthetics (12) patients who had contraindications to general/ or spinal anaesthesia.

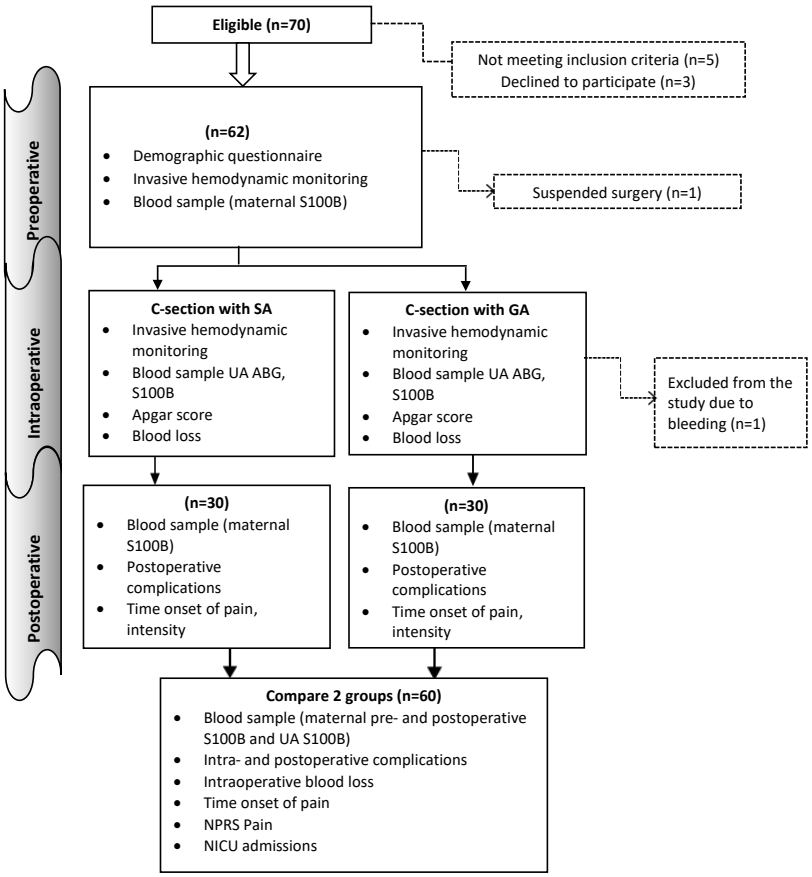

Figure 1. Flowchart detailing of the study. GA: General anaesthesia, SA: Spinal anaesthesia, ABG: Arterial blood gas, UA: Umbilical artery, NPRS: Numeric pain rating scale, NICU: Neonatal intensive care.

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2.2. Methods of Anaesthesia

In preparation, Ranitidine 150 mg orally (H2-blocker), and metoclopramide 10 mg intravenously. To avoid supine hypotension syndrome, women in both groups were maintained in a 15-degree left lateral tilt position until birth. An observer gathered all the intraoperative data. Hypoxia was defined as SpO2 <95%. A 20% decrease in systolic arterial pressure below the baseline value was defined as hypotension in this study and treated with intravenous ephedrine. Additionally, oxygen was administered at a rate of approximately five L/min through a transparent face mask during the operation. The anaesthetists performing the anaesthesia had similar levels of expertise and were unaware of the study protocol.

GA procedure: In the instances in the general anaesthesia group, pre-oxygenation was carried out using 100% oxygen for five minutes before the administration of general anaesthetic. Patients were induced with propofol 2 mg/kg (manufacturer: Guangdong Jiabo Pharmaceutical Co., Ltd.; specification: 20 ml/ 200 mg) and succinylcholine 2 mg/kg intravenously. After anaesthesia was induced tracheal intubation was performed. After intubation the patients were administered 0.5 mg/kg of atracurium besylate (manufacturer: Flagship Biotech International, India; specification: 2.5 ml/25 mg), 2.0 μg/kg of fentanyl (manufacturer: IVCO, Mongolia, specification: 0.005%-2 ml) and infusions of propofol at 2.5 mg/kg per and fentanyl at 0.05 mg/kg per minute. Surgery began after verification that the endotracheal tube was appropriately placed and positioned through capnography. After delivery, the patients received intravenous injection of five units of oxytocin then continuous pump infusion 15 units (manufacturer: HBM Pharma, Slovakia, specifications: 1 ml/5 mg). Anaesthesia maintained with continuous inhalation of 1 MAC of isoflurane and propofol intravenously at a dosage of 1.5 mg/kg.

SA procedure: With the patient lying in a left lateral position, spinal anaesthesia was performed at the L2–L3 or L3–L4 interspace with 10 mg of 0.5% heavy bupivacaine (manufacturer: Troikaa, Pharmaceuticals Ltd, India specification: 4 ml/20 mg) plus 10 micrograms of fentanyl. The level of the sensory block was modified to be approximately T5–T6.

2.3. Follow-Up

Preoperative: Eligible patients were contacted and provided with written informed consent prior to surgery. Preoperative assessments were carried out by main investigators, the researchers gathered demographics data and basal health questionnaires.

Intraoperative: Radial arterial cannulation was performed for all the patients using 20G Surflo® (Terumo China holding Co., Ltd.) under local anaesthesia (2% lidocaine), and arterial blood pressure was monitored. Invasive blood pressure readings including systolic, diastolic, and mean blood pressures were obtained. Heart rate and SpO2 were measured by the fingertip photoelectric sensor (manufactured: Guangzhou Sichuang Hongyi Electronic Technology Co., Ltd.). Time from anaesthesia induction to delivery, total operative time, intraoperative blood loss, urine output, and complications during surgery were recorded in both groups. All vital signs were recorded.

Postoperative: For the two hours of the postoperative stage, patients were monitored in the recovery room. Complications after C-section within two hours were recorded in both groups including postoperative nausea, vomiting, headache, fever, and pain. The patients were assessed using the Numeric pain rating scale (NPS), which showed the severity of the postoperative level of pain from a scale of 0 to 10, with 0 = no pain and 10 being the worst pain ever. The onset time was also recorded.

Neonatal assessment: Following the delivery of the baby, pediatricians assessed the neonatal condition, assigned Apgar scores at one and five minutes, and determined the need for admission to the Neonatal intensive care unit (NICU). An Apgar score of 7 to 10 was considered normal; 4 to 6, mild neonatal asphyxia; and 3 and below, severe neonatal asphyxia. The Apgar score was assessed based on 5 criteria: activity, pulse rate, grimace (reflex irritability), skin color, and respiratory effort. Following the delivery of the baby, the cord was cut between the two clamps placed approximately 10 to 12 cm apart and away from the placenta and newborn. One to three ml of blood was collected

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from the umbilical artery from between the clamps immediately following placental delivery. This protocol was designed to prevent contamination of S100β levels in the cord arterial blood by placental S100β, ensuring that the measured concentrations accurately reflect those originating from the newborn.

2.4. Laboratories Outcome Measurements

Measurement of serum s100 β: The maternal serum S100β protein levels of the 30 patients from each group were analyzed before and at the end of the operation, with 5 ml of blood was withdrawn from the mother via the arterial line. The blood samples were immediately centrifuged at 2500 RPM for 10 minutes and the supernatant was gathered and stored at minus 80-degree temperature until the measurement of S100β levels. The concentration of S100β protein in the blood serum was determined by the enzyme-linked antibody reaction (ELISA) using the Human S100 calcium binding protein B (S100B) ELISA kit (Catalog Number SL2183Hu) album of Sunlong Biotech CO., Ltd (China). According to the manufacturer's protocol, each sample was incubated with the tracer from the kit for 2 hours, following the instructions precisely to maintain intra-batch variation below 10% and inter-batch variation below 15%.

Arterial blood gas analysis: The blood gas analysis was performed from umbilical cord blood immediately drawn after the delivery. A sample of the blood was immediately inserted to a blood gas/electrolyte analyzing system. (COBAS B-221, ROSHE) for pH, pCO2, pO2, Hb, Hct, O2Hb, COHb, Ca2+, K+, Na+, CI-, SO2, BB, BE, HCO3, Osm measure and compared between the 2 groups, and the remaining blood sample was then used for the S100β study assay.

2.5. Statistical Analysis

The primary outcome of the study involved collecting blood samples for the analysis of brain injury biomarker S100β. These samples were obtained from the arterial line of maternal blood, both preoperative and postoperative, as well as from the umbilical artery of C-section deliveries performed under either spinal or general anaesthesia. The secondary outcomes were invasive hemodynamic monitoring, surgery and anaesthesia outcomes, umbilical cord blood gas values, Apgar scores, neonatal asphyxia rate, and maternal postoperative numeric pain rating scale (NPRS) compared in two groups. Categorical variables were expressed as frequency and percentages. Continuous variables were assessed for distribution using the Shapiro-Wilk test, and dependent variables were normally distributed. Differences between the two groups were calculated using a parametric test. Differences between the means of two groups were evaluated by the T test. Proportional differences between groups were calculated using the Chi-square test. In case of abnormal distribution, differences between three groups were determined by Friedman's test, and Wilson Signed Rank test was used for differences between two groups

3. Results

Sixty patients were recruited for the study. This study included a total of 60 pregnant women undergoing caesarean section, equally divided into two anaesthesia groups: Spinal Anaesthesia (SA) and General Anaesthesia (GA) (n=30 per group). To ensure comparability before assessing anesthetic effects on fetal outcomes, maternal demographic and obstetric characteristics were analyzed between the two groups. They were comparable among the study groups, with no statistically significant differences ($p > 0.05$), as shown in Table 1.

Table 1. Participants general characteristics by anaesthesia group (n=60).

Variables	Anaesthesia groups				p value	Total	
	SA group		GA group				
	n	%	n	%		n	%
Maternal age, y, mean±std	30.1±5.0		31.2±5.1		0.302+	30.6±5.1	

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Weight, kg, mean±std	69.6±9.7		70.0±18.3		0.203+	69.8±14.5	
Height, cm, mean±std	160.2±3.4		156.4±17.9		0.519+	158.3±12.9	
Location (Urban)	16	53.3	14	46.7	0.606	30	50.0%
Education status					0.375		
<High school degree	3	10.0	2	6.7		5	8.3%
High school graduate	7	23.3	12	40.0		19	31.7%
≥ Bachelor's degree	20	66.7	16	53.3		36	60.0%
Working conditions					0.601		
Normal	28	93.3	29	96.7		57	95.0%
Abnormal	2	6.6	0	0.0		3	5.0%
Abdominal surgery, yes	13	43.3	13	44.8	0.908	26	44.1%
Allergy, yes	3	10.0	2	6.7	0.640	5	8.3%
Gestation age at 1st prenatal visit					0.583		
≤ 8 weeks	20	66.7	17	56.7		37	61.7%
8-12 weeks	8	26.7	9	30.0		17	28.3%
12-16 weeks	2	6.7	2	6.7		4	6.7%
≥16 weeks	0	0.0	2	6.7		2	3.3%
Gestational age					0.633		
37-38 weeks	8	26.7	5	16.7		13	21.7%
38-39 weeks	10	33.3	12	40.0		22	36.7%
39-40 weeks	12	40.0	13	43.3		25	41.7%
Previous Births					0.372		
1-2 births	15	50.0	13	43.3		28	46.7%
3-4 births	14	46.7	13	43.3		27	45.0%
5≤ births	1	3.3	4	13.3		5	8.3%

+Group differences were compared using Student t test. Values are mean (SD), number of observations (n), and 95% confidence intervals. SA: spinal anaesthesia, GA: general anaesthesia.

3.1. S100β Marker and Methods of Anaesthesia

The mean serum S100β levels was 194.1 ± 45.8 ng/L in all women pre-operatively with no significant difference observed between the two groups (p=0.231). Furthermore, there were no significant difference between SA and GA group S100β protein levels post-surgery (p=0.375) and in newborn blood serum (p=0.143) (Table 2).

Table 2. Brain injury markers in 2 groups (N=60).

Variables	Groups		p value‡	Total
	Spinal	General		
	Mean, std	Mean, std		
S100β, ng/L				
Pre-operative	195.1±36.2	193.0±54.3	0.231	194.1±45.8
Post-operative	200.9±42.9	197.0±42.7	0.375	198.9±42.5
Umbilical cord blood	221.2±52.8	203.1±60.6	0.143	214.9±57.1

‡-Wilcoxon signed rank test.

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The changes in S100β protein levels before and after surgery were different for each group. The maternal blood S100β post-surgery and neonatal umbilical cord blood protein levels were different in the GA group (p=0.047), there were lacked a difference in the SA group. In the SA group, preoperative S100β concentration in maternal blood was 195.1±36.2 ng/L, then increased to 200.9±42.9ng/L at the end of operation. Also, in the GA group, preoperative S100β concentration in maternal blood was 193.0±54.3 ng/L, then increased to 197.0±42.7 at the end of operation (Figure 2).

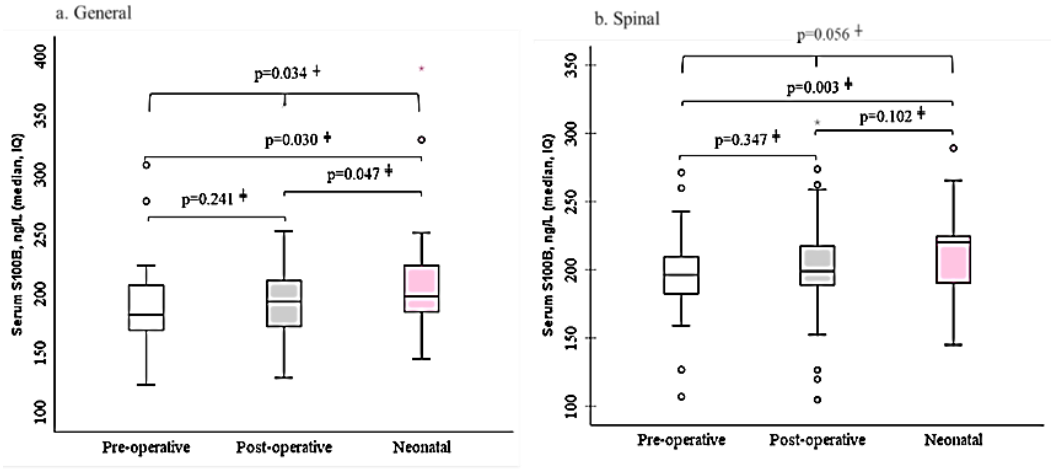

Figure 2. Changes in maternal and neonatal S100β protein by each anaesthesia group, a. General anaesthesia group, b. Spinal anaesthesia group, ┼Repeated measure ANOVA, ǂWilcoxon signed rank test.

3.2. Perioperative Characteristics by Anaesthesia Groups

The perioperative outcomes, intraoperative time, drug dosage and postoperative complications between the 2 groups, are shown in Tables 3 and 4. There were zero noteworthy differences in time from anaesthesia to incision, the operation duration, infused crystalloid volume, blood loss, and urine output (Table 3).

Table 3. Surgery time and drug doses by study groups (N=60).

Variables	Groups				p value	Total	
	SA		GA				
	Mean	Std	Mean	Std		Mean	Std
Surgery time (min)	49.9	8.0	51.6	10.4	0.471	50.7	9.2
Dosage of drugs							
Fentanyl dose (mcg)	14.3	2.2	231.7	58.8	0.0001*	123.0	117.1
Succinylcholine (mg)			104.7	12.5		104.7	12.5
Tracrium dose (mg)			43.1	40.2		43.1	40.2
Bupivacaine dose (mg)	10.3	0.5				10.3	0.5
Ephedrine dose (mg)	17.9	9.0				17.9	9.0
Oxytocin dose (iu)	21.5	3.5	22.8	3.1		22.2	3.4
Isotonic solution (ml)	1563.3	237.1	1561.7	235.9	0.972	1562.5	234.5

Std – Standart deviations, number of observations (n), and 95% confidence intervals, *Significant difference between 2 groups.

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Table 4. Caesarean Surgery Intraoperative and Postoperative Complications by Anaesthesia Method.

Variables	Groups				P value	Total	
	SA		GA				
	n	%	n	%		n	%
Complications during surgery							
Hypotension	5	16.7%	1	3.3%	0.085	6	10.0%
Hypertension	0	0.0%	12	40.0%	0.0001	12	20.0%
Bradycardia	0	0.0%	2	6.7%	0.0001	2	3.3%
Tachycardia	5	16.7%	11	36.7%	0.079	16	26.7%
Nausea	15	50.0%	0	0.0%	0.0001	15	25.0%
Headache	2	6.7%	0	0.0%	0.0001	2	3.3%
Complications after surgery							
Nausea	11	36.7%	9	30.0%	0.075	20	33.3%
Vomiting	2	6.7%	1	3.3%	0.553	3	5.0%
Headache	5	16.7%	1	3.3%	0.085	6	10.0%
Shivering	4	13.3%	3	10.0%	0.677	7	11.7%
Weakness	1	3.3%	6	20.0%	0.044	7	11.7%
Tinnitus	3	10.0%	0	0.0%	0.237	3	5.0%
Shortness of breath	4	13.3%	2	6.7%	0.671	6	10.0%
Time of onset of pain					0.0001		
≤ 60 min	1	3.3%	13	43.3%		14	23.3%
61-119 min	16	53.3%	14	46.7%		30	50.0%
120-179 min	13	43.3%	2	6.7%		15	25.0%
≥180 min	0	0.0%	1	3.3%		1	1.7%
Blood loss during surgery, ml (mean, std)	431.7±72		456.0±83		0.105	443.8±78	
Urine output, ml (mean, std)	155.0±95		195.0±93		0.232	175.0±78	

†Group differences were compared using Student t test. Values are mean (SD), number of observations (n), and 95% confidence intervals. SA: spinal anaesthesia, GA: general anaesthesia.

However the frequency of headache and nausea were more common in the SA group ($p<0.0001$, $p<0.0001$) while hypertension and tachycardia were more frequent in the GA group ($p=0.079$, $p<0.0001$) during surgery. Postoperative complications such as nausea, headache and weakness were significantly difference in the SA and GA groups ($p=0.044$). We detected that the time of onset of pain was significantly shorter in GA group was 13 (43.3%) patients felt pain after surgery within ≤ 60 minutes. The NPRScore and length of stay in hospital between the two groups were also alike. ($p=0.105$, $p=0.232$) (Table 4)

3.3. Neonatal Clinical and Laboratory Outcomes Following Spinal Versus General Anaesthesia

No significant differences were found in Apgar scores and neonatal asphyxia rates between the two groups ($p=0.476$) and blood gas outcomes of the umbilical artery (UA) in Table 5. It shows pH and Ca^{2+} levels of UA were lower in the GA group ($p=0.009$, $p=0.0001$).

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Table 5. Neonatal Arterial Blood Gas Profiles and Clinical Outcomes Following Spinal versus General Anaesthesia (n=60).

ABG values	Total		Groups				p value
			SA		GA		
	Mean	SD	Mean	SD	Mean	SD	
pH	7.30	0.04	7.31	0.04	7.28	0.04	**0.009**
pCO_2 (mmHg)	42.8	8.0	41.3	9.6	44.3	5.9	0.157
PO_2 (mmHg)	48.2	29.2	45.5	27.3	51.0	31.2	0.476
Hb (g/L)	146.5	28.1	142.2	37.0	150.9	14.2	0.237
Hct (%)	44.3	6.6	43.8	8.6	44.8	3.8	0.588
O_2Hb (%)	73.1	15.9	70.1	14.6	76.1	16.9	0.146
HHb (%)	23.2	15.6	25.0	14.6	21.5	16.7	0.385
MetHb (%)	0.8	0.1	0.8	0.1	0.9	0.2	0.389
Ca^{2+} (mmol/L)	1.41	0.15	1.34	0.15	1.47	0.12	**0.0001**
K^+ (mmol/L)	5.80	1.74	5.91	1.93	5.70	1.55	0.643
Na^+ (mmol/L)	134.9	5.0	133.5	6.7	136.3	1.8	0.029
Cl^- (mmol/L)	103.5	2.0	103.2	2.1	103.8	1.9	0.263
SO_2 (%)	75.3	16.7	72.6	16.1	78.0	17.2	0.216
BB (mmol/L)	42.1	2.0	42.1	2.2	42.1	1.8	0.923
BE (mmol/L)	-5.9	1.9	-5.8	2.2	-5.9	1.6	0.864
$ctCO_2$	18.3	2.0	18.0	2.3	18.5	1.5	0.341
HCO_3^-	20.4	2.1	20.1	2.4	20.7	1.7	0.263
Osm (mOsm/kg)	271	4	269	5	272	3	**0.004**
Hospital length (d)	4	1	4.1	0.9	3.6	0.5	0.351
Apgar score, n,%							0.476
4-6 score	12	20.3	7	24.1%	5	16.7%	
7< score	47	79.7	22	75.9%	25	83.3%	

p value is calculate Student T test.

4. Discussion

The stress response to surgery triggers various physiological and biochemical changes, including sympathetic nervous system activation, the release of stress hormones such as cortisol and catecholamines, and modulation of immune function [25]. Exposure to anaesthetic agents has been shown to induce programmed cell death (apoptosis) in glial and neuronal cells of the central nervous system, potentially leading to neurotoxicity and brain injury. Numerous animal and in vitro studies have reported that anaesthetic agents can exert harmful effects on the developing brain [26], particularly barbiturates, ketamine, propofol, and inhaled anaesthetics [27].

This study examined the brain injury biomarker S100β during cesarean section under general anaesthesia (GA; propofol, fentanyl, isoflurane) and spinal anaesthesia (SA; bupivacaine, fentanyl). Perioperative measurement of S100β levels, which reflects glial cell activity and possible neuroinjury, was performed before and after surgery [28]. Our primary finding was a slight, non-significant increase in maternal arterial S100β concentrations following C-section in both GA and SA groups. This finding aligns with those of Zhendong Xu et al., who reported no significant change in maternal venous S100β levels following epidural or general anaesthesia during C-section [29].

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Additionally, our results indicated that cesarean delivery itself does not appear to significantly influence maternal S100β concentrations. However, some studies have reported higher S100β levels in vaginal deliveries compared to elective C-sections, suggesting delivery-mode dependency [30,31]. One previous study observed a significant decrease in the umbilical artery/umbilical vein (UA/UV) S100β ratio after GA compared to epidural anaesthesia, while maternal venous S100β levels remained largely unchanged [32]. In our dataset, UA S100β concentrations were consistently higher than maternal levels in both GA and SA groups, with a slightly lower level observed in the GA group.

We also established a reference range for serum S100β in third-trimester pregnant Mongolian women, identifying a baseline of 194.1 ± 45.8 ng/L. Notably, S100β levels measured beyond 37 weeks of gestation exceeded this normal range [33]. We propose two primary interpretations for our findings. Neither general nor spinal anaesthesia caused detectable neuronal injury during cesarean delivery. This may be attributed to the short duration of surgery and, consequently, limited exposure to anaesthetic agents. In fact, brief GA exposure might confer some neuroprotection under stress conditions [34], possibly explaining the slightly lower post-operative S100β levels in the GA group. The absence of maternal (e.g., CNS disorders), obstetric (e.g., diabetes, hypertension, placental insufficiency), or fetal (e.g., acute/chronic hypoxia) complications—conditions known to elevate S100β—may have influenced our results. Moreover, previous studies support the concept that fetal-origin S100β can pass into maternal circulation via a physiological gradient [35], consistent with our finding that UA S100β levels exceeded maternal concentrations. Although we did not find a significant association between S100β concentrations and perioperative variables, we observed moderate correlations with some umbilical artery blood gas parameters. In conclusion, our findings suggest that cesarean delivery under either anaesthetic technique does not significantly alter maternal S100β levels, and thus may not be associated with acute brain injury. However, the anaesthetic agents used could influence biomarker profiles.

Our study's strengths include the use of a newly biomarker that allows for a comprehensive evaluation of the effects of two anesthesia methods on both maternal and fetal brain damage during C section. Firstly, this is the first known investigation to assess S100β levels in the maternal and umbilical circulation among pregnant Mongolian women undergoing cesarean section, thus contributing unique regional data to the global literature. Secondly, the study provides a direct comparison between general and spinal anaesthesia, offering valuable insights into their respective impacts on neonatal biochemical outcomes and maternal neurobiological markers. Thirdly, by including both maternal and fetal (umbilical arterial) blood samples, we were able to explore the potential fetal origin of S100β more comprehensively. Additionally, the use of standardized anaesthetic protocols and perioperative care ensured internal consistency, while the integration of neonatal Apgar scores and arterial blood gas analysis allowed for a broader evaluation of neonatal well-being. These elements collectively strengthen the scientific value and clinical relevance of our findings. But this study has several limitations. First, the relatively small sample size limits the statistical power and generalizability of our findings. Second, the study population consisted exclusively of pregnant women from a single tertiary hospital in Mongolia's capital city, further restricting external applicability. Additionally, the lack of long-term follow-up prevents conclusions regarding the potential delayed neurological effects of anaesthetic exposure.

5. Conclusions

In conclusion, S100β concentrations slightly increased after C-section in both the SA and GA group. General anaesthesia has a faint impact on the umbilical cord blood's S100β levels during C-section. Spinal and general anesthesia are considered safe for the maternal and fetal brain during cesarean sections when administered appropriately, with no evidence suggesting harmful effects. Further research needed to study associations between anaesthetic drugs, perioperative release of brain injury biomarker, and perioperative clinical outcomes are warranted.

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Data Availability Statement: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Abbreviations

The following abbreviations are used in this manuscript:

MDPI	Multidisciplinary Digital Publishing Institute
BMI	Body mass index
ABG	Arterial blood gas
CNS	Central nervous system
GA	General anesthesia
SA	Spinal anesthesia
UA	Umbilical artery

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