J Surg Med. 2022;6(7):700-704.
DOI: 10.28982/josam.1000340

Research article

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Comparison of thiol disulfide values in the cord blood of patients undergoing cesarean section under spinal or general anesthesia

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Ethics Committee Approval
Ethics Committee approval of the study was obtained from Yıldırım Beyazıt University Faculty of Medicine Clinical Research Ethics Committee on 26/10/2016 and it was approved with the number 26379996/252.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

Financial Disclosure
The authors declared that this study has received no financial support.

Published
2022 July 5

Abstract

Background/Aim: Oxidative stress is known to increase in patients receiving anesthesia before undergoing surgery. Since newborns are more sensitive to oxygen-free radicals, the effects and characteristics of anesthesia methods that are used for pregnant women require analysis. This study aimed to evaluate the effects of spinal and general anesthesia on oxidative stress by investigating thiol disulfide and ischemia modified albumin (IMA) concentrations in the cord blood of patients undergoing cesarean section (C-section) via spinal or general anesthesia.

Methods: This cross-sectional prospective study included 60 patients who were indicated for elective cesarean section. Patients with chronic disease, pregnancy complications and/or required emergency cesareans were not included. Group 1 (n = 30) underwent general anesthesia, and Group 2 (n = 30) underwent spinal anesthesia during their C-sections. Thiol–disulfide levels were evaluated concurrently in all blood samples taken from the umbilical artery remaining on the placental side.

Results: The mean age (SD) of the mothers was 30.6 (4.4) years and the mean gestational age (SD) was 39.0 (0.9) weeks. Gestational age, birth weight, and first and fifth min Apgar scores of the two groups were similar. The mean (SD) native thiol (362.4 [63.8]; 323.2 [45.8]), total thiol (409.6 [70.2]; 363.5 [46.1]), and disulfide values (23.6 (5.4); 20.2 (4.3)) were significantly higher in group 1 than group 2, while the median (interquartile range [IQR]) values of IMA (0.89 (0.85-max 0.92); 0.85 (min 0.82-max 0.879) were significantly higher in group 2 than group 1 ($P < 0.05$).

Conclusions: As general anesthesia may cause a higher degree of oxidative stress, selecting the appropriate anesthetic technique may be especially important for risky pregnancies in which increased oxidative stress in the mother and baby may be critical for the outcome.

Keywords: Thiol disulfide, Ischemia modified albumin, Cesarean section, Anesthesia

How to cite: Soysal Ç, Soysal Y, Döğer C, Yılmaz E, Özdemir O, Küçüközkan T, Erel Ö. Comparison of thiol disulfide values in the cord blood of patients undergoing cesarean section under spinal or general anesthesia. J Surg Med. 2022;6(7):700-704.

Introduction

Free oxygen radicals appear during normal metabolism. The levels of these substances are balanced by the action of various antioxidant systems present in the body. Disruption of this balance in favor of oxygen free radicals, which is called "oxidative stress" can causes cellular damage [1]. Thiols are among the molecules that are used for prevention of oxidative stress [2]. After oxidation, thiols form disulfide bonds called disulfide bridges. The formation of these bonds is reversible and when broken, provide thiols. The result is a dynamic thiol–disulfide homeostasis, which plays an important role in antioxidant protection against oxidative stress [3]. Since free radicals have an extremely short half-life, indirect markers are generally used for the determination of the levels of reactive oxygen species (ROS) and oxidative stress. Ischemia-modified albumin (IMA) has been suggested as a marker of nonspecific ischemia. Although recent studies suggest that various other mechanisms are involved in the formation of IMA, it is accepted that ischemic damage causes an alteration in the N-terminus of albumin, leading to increased IMA levels [4]. The levels have been shown to correlate with the degree of oxidative stress [5].

Oxidative stress is known to increase in patients receiving anesthesia before undergoing surgery [6]. Since newborns are more sensitive to oxygen free radicals, the effects and characteristics of anesthesia methods that are used with pregnant women require analysis. Previous studies have evaluated the relationship between thiol disulfide homeostasis and oxidative stress in cord blood [7]. Although no study on the effect of the type of anesthesia used at birth on the levels of oxidative stress in cord blood, it has been reported that general anesthesia has a considerably stronger negative effect on thiol disulfide homeostasis than does spinal anesthesia [8].

Therefore, the quantification of markers of oxidative stress in cord blood may be important in determining the extent of oxidative stress suffered by newborns during cesarean section surgery. It was hypothesized that umbilical cord thioldisulfide concentrations may be important in determining neonatal well-being and in ruling out suspected perinatal asphyxia. Tis study aimed to evaluate the effects of spinal and general anesthesia on oxidative stress by investigating thiol disulfide and IMA concentrations in the cord blood of patients undergoing cesarean section via spinal or general anesthesia.

Materials and methods

This cross-sectional prospective study was conducted in the Obstetrics and Gynecology Department of a hospital that is one of the primary maternity hospitals in Ankara, Turkey, between January 2019 and January 2020. The study included 60 patients between 18 and 40 years with an American Society of Anesthesiologists (ASA) group of I-II. Using the G-Power program, in the case in which the effect size was taken as moderate and bidirectional and $\alpha = 0.05$, power $(1\text{-}\beta) = 0.80$, the smallest sample size for each group was calculated as a minimum of 30 patients. Patients with diabetes mellitus, hypertension, chronic obstructive pulmonary disease, allergies to local anesthesia, bleeding-clotting time abnormality, liver disease, renal failure (creatinine levels ≥ 2.5 mg), preeclampsia, eclampsia, those who had children with metabolic disorders, patients who underwent emergency surgery, and/or those who refused to participate were excluded from the study. To prevent oxidative stress, emergency cesarean indications and additional systemic diseases were excluded.

The Ethics Committee approved the study. All individuals were informed about the study, and informed written consent was obtained.

All cesarean section procedures were performed by experienced obstetricians. Premedication was not used in any cases. All patients were allowed to lie on their left side while being transported to the operating room until the end of the operation. Electrocardiography, noninvasive mean arterial pressure, and peripheral oxygen saturation monitoring were performed for all patients after admission. The study patients were informed about spinal and general anesthesia and underwent cesarean section according to their preference. Because all patients had planned cesarean section, they were summoned to the hospital on the morning of surgery and hospitalized on the same day. The patients were followed in the hospital for 48 h post-operatively, and all patients were discharged 48 h later. Patients did not develop infections or complications.

Anesthesia protocols

Group 1 (n = 30) received spinal anesthesia, and Group 2 (n = 30) received general anesthesia. Spinal anesthesia was administered while the patient was in the left lateral position after appropriate antiseptic practice. Local anesthesia was performed with 1 cc 2% lidocaine in the L3-4 or L4-5 range. Spinal needle (22 G Quincke) advancement from the same level was continued until free cerebral spinal fluid (CSF) flow was observed. Spinal anesthesia was performed with previously prepared 2–2.2 ml 0.5% hypertonic bupivacaine (Marcain Heavy®). The sensory block level was evaluated with a pin-prick test, and motor block level was evaluated via the Bromage scale. When the sensory block reached a sufficient level (T10), the operation was started. From the beginning of the operation until the end, 100% oxygen support (3 L/min) was provided with a mask. Group 1 patients received 2 mg/kg propofol and 0.6 mg/kg rocuronium for anesthesia induction. After muscle relaxation, endotracheal intubation was performed by cricoid compression. Controlled ventilation (with Datex-Ohmeda S/5 Avance device) was achieved by adjusting tidal volume to 8 to 10 ml/kg and respiratory frequency to 10 to 12 /min. Anesthesia was maintained with 50% O_2 + 50% N_2O and included 1–1.5% sevoflurane.

Measurements

In both groups, maternal hemodynamic parameters (heart rate, mean arterial blood pressure) were recorded every 5 min for 45 min after anesthesia induction. In all cases, 5 ml blood samples were taken from the umbilical artery remaining on the placental side of the cord immediately after the cord was clamped and cut after delivery, and serum / plasma samples were separated and stored at −80 ºC. Thiol–disulfide levels were evaluated concurrently by spectrophotometric methods in all blood samples using a new technique developed by Erel [9]. Routine caesarean section and anesthesia procedures were performed during the operation; however, blood samples were also taken during the procedure. Blood samples were collected from the placental cord, which was discarded as medical waste after birth. Evaluation of the newborn was performed by a pediatric health and disease specialist and the Appearance/Pulse/Grimace/Activity/Respiration (APGAR) scores were recorded at the first and fifth minutes post-birth.

Statistical analysis

In the presentation of descriptive statistics, central and prevalence measures, such as number, percentage, median, mean, and standard deviation were used, and Pearson's chi-squared test was used to determine the difference between categorical variables. The distribution of continuous variables was evaluated using the Shapiro–Wilk test and histogram. An independent t-test was used for comparison of independent continuous variables with a normal distribution, and the Mann–Whitney U test was used for variables not having a normal distribution. Pearson's correlation analysis was used to determine the relationship between continuous variables. Data were analyzed using SPSS software (version 24, IBM, Chicago, IL, USA). *P*-values < 0.05 were considered statistically significant.

Results

In this study, 60 pregnant women (30 general anesthesia and 30 spinal anesthesia) who delivered their baby via elective cesarean section were evaluated. The mean age (SD) of the mothers was 30.6 (4.4) years, and the mean gestational age (SD) was 39.0 (0.9) weeks. The mean neonatal birth weight (SD) was 3230 (468.3) grams. No significant differences between characteristics of the mothers or newborns who comprised each group (*P* > 0.05, Table 1) were noted. APGAR scores at 1 and 5 min were similar between the two groups (Table 1).

Table 1: Maternal and neonatal characteristics

	General anesthesia (Group 1) (n = 30)	Spinal anesthesia (Group 2) (n = 30)	*P*-value
Maternal age (Years, Mean (SD)	30.7 (4.5)	30.5 (4.3)	0.815
Parity (Median [IQR])	1.0 (1.0-2.0)	1.0 (1.0-2.0)	0.677
Gender N (%)			
Female	19 (63.3)	17 (56.7)	0.598
Male	11 (36.7)	13 (43.3)	
Gestational age (Weeks, Median [IQR])	39.1 (38.7–39.6)	38.9 (38.6–39.3)	0.306
Birth weight (Grams, Mean (SD))	3188.2 (504.8)	3272.2 (433.3)	0.492
1 min Apgar score (Median [IQR])	8.0 (8.0–9.0)	9.0 (8.0–9.0)	0.354
5 min Apgar score (Median [IQR])	9.0 (9.0–10.0)	10.0 (9.0–10.0)	0.235

SD: standard deviation; IQR: interquartile range

When cesarean indications of the patients included in the study were evaluated, among those who underwent spinal anesthesia, the reason for non-urgent planned cesarean section was previous cesarean section for 28 patients and breech presentation in two patients. In the general anesthesia group, 29 patients underwent non-emergency planned cesarean section due to previous cesarean section, and one patient due to breech presentation. Among the patients who received general anesthesia, 24 (80%) had at least one living child, three (10.0%) had one miscarriage, and 24 (80%) had delivered by cesarean section. In the group receiving spinal anesthesia, 23 (76.7%) had at least one living child, 7(23.3%) had at least one miscarriage, and 22 (73.3%) had undergone a previous cesarean section.

Thiol–disulfide homeostasis values from cord blood are shown in Table 2. Albumin, disulfide/native thiol ratio, disulfide/total thiol ratio, and native thiol/total thiol ratio values were not statistically different between the two groups (*P* > 0.05). The mean native thiol value (SD) of the spinal anesthesia group was significantly higher than that of the general anesthesia group (362.4 (63.8); 323.2 (45.8); *P* = 0.009). Similarly, mean total thiol (SD) (409 (70.2); 363.5 (46.1); *P* = 0.004) and mean disulfide values (SD) (23.6 (5.4); 20.2 (4.3); *P* = 0.008) of the spinal anesthesia group were significantly higher than the corresponding values of the general anesthesia group. The median (IQR) values of IMA in the general anesthesia group were significantly higher than for those receiving spinal anesthesia (0.89 [0.85–0.92] versus 0.85 [0.82–0.87]; *P* = 0.046, Table 2). Finally, it was also found that disulfide and native thiol values (r = 0.27; *P* = 0.036), and disulfide and total thiol values (r = 0.45; *P* < 0.001) were positively correlated.

Table 2: Values of thiol–disulfide homeostasis in cord blood

	General anesthesia (Group 1) (n = 30)	Spinal anesthesia (Group 2) (n = 30)	*P*-value
Native thiol (μmol/Lt, Mean [SD])	323.2 (45.8)	362.4 (63.8)	0.009
Total thiol (μmol/Lt, Mean [SD])	363.5 (46.1)	409.6 (70.2)	0.004
Disulfide (μmol/Lt, Mean (SD))	20.2 (4.3)	23.6 (5.4)	0.008
Albumin (g/dL, Median [IQR])	4.02 (3.78–4.21)	4.23 (3.97–4.30)	0.084
Ischemia modified albumin (ABSU, Median [IQR])	0.89 (0.85–0.92)	0.85 (0.82–0.87]	0.046
Disulfide/ native thiol ratio (%, Mean [SD])	6.38 (1.69)	6.57 (1.41)	0.624
Disulfide/ total thiol ratio (%, Mean [SD])	5.62 (1.30)	5.78 (1.09)	0.594
Native thiol/ total thiol ratio (%, Mean [SD])	88.8 (2.6)	88.4 (2.9)	0.594

SD: standard deviation, IQR: interquartile range

Discussion

Thiols are involved in the neutralization of ROS that are formed normally (or abnormally) in the body. Therefore, a decrease in serum thiol levels in the event of oxidative stress is often observed [10, 11]. Thiol levels have been shown to decrease in diseases that demonstrate increased inflammatory activity, including many disease types of the renal, cardiovascular, and neurological systems, in addition to those that progress with elevated oxidative stress, such as diabetes mellitus, atherosclerosis, Alzheimer's disease and cirrhosis [10]. In our study, it was found that both native and total thiol levels of patients receiving general anesthesia were significantly lower than those receiving spinal anesthesia. The oxidative stress enhancing effect of various drugs used in general anesthesia may have led to this result, and therefore, the decrease of thiols in the general anesthesia group could be associated with this property of the drugs. Furthermore, considering that the oxidative balance of the body is not only associated with thiol concentration, IMA levels were also measured as an indirect marker of oxidation in cord blood. The increased levels of IMA in those receiving general anesthesia supported initial findings with thiol values. Overall, our results suggest that general anesthesia may lead to an increase in oxidative stress to a higher degree compared to spinal anesthesia.

In a recent and similarly planned study, the authors investigated the effect of anesthesia technique during cesarean section on thiol–disulfide homeostasis in maternal and cord blood. The authors showed that native thiols, total thiols, disulfide levels, disulfide / total thiol and native thiol/disulfide ratios were higher in the blood of mothers who delivered with general anesthesia compared to spinal anesthesia. In the cord blood of the patients under general anesthesia, native thiol and total thiol levels were significantly lower than those receiving spinal anesthesia, and other measurements were similar between the groups [8]. However, in contrast, Karabayırlı et al. [12] evaluated the oxidative stress index in the cord blood of women who underwent cesarean section using the same groups and found that oxidative stress was lower in recipients of general anesthesia. In contrast to our results, these authors suggested that general anesthesia should be preferred in cases in which lower fetal oxidative stress is desired. In the current study, cord blood native thiol, total thiol, and disulfide levels were found to be significantly higher in the spinal anesthesia group.

However, it appears to important to note that since thiols values were not measured in the cord blood before anesthesia, direct conclusions in regard to the nature of the differences found between the groups cannot be drawn. It is possible that the native thiol, total thiol, and disulfide values increased in the spinal anesthesia group or quite conversely, they may have decreased in the general anesthesia group. Despite this limitation, it is also apparent that it would be unreasonable to assume that patients undergoing any type of surgery with anesthesia would benefit from the procedure in terms of oxidative stress and/or antioxidant levels; thus, the differences found in our study seem to show that general anesthesia has significantly more adverse effects on the oxidative balance of women undergoing cesarean section.

In our study, disulfide values were significantly higher in the spinal anesthesia group compared to the general anesthesia group (23.6 [5.4]; 20.2 [4.3]). In the literature, disulfide values have been shown to increase in proliferative conditions, such as various cancer types [9, 13]. Factors, such as ongoing cell proliferation and development in newborns, may cause an increase in disulfide levels [13]. The mechanism leading to higher cord blood disulfide levels in the general anesthesia group could not be determined based on the available data; however, a positive correlation between the increase in disulfide level and the increase in native and total thiol levels directed us to the conclusion that this increase was mainly due to alterations in thiol levels and subsequent changes in oxidative homeostasis.

In studies evaluating the effect of anesthesia technique on oxidative stress by measuring different oxidative stress markers, it was found that various cytokines increased to a greater degree in cases in which general anesthesia was applied compared to those receiving local and spinal anesthesia [14, 15]. Another early indicator of hypoxia, ischemia, and oxidative stress is an increase in IMA levels, which was also evaluated in our study [16, 17]. Several studies have shown that IMA values rapidly increase immediately after the onset of surgery [16, 18]. In a study that compared the levels of IMA in the cord blood of women undergoing normal and cesarean deliveries without specifying anesthesia method, it was found that values were higher for those undergoing normal delivery [19]. In another study evaluating the effect of anesthesia technique on oxidative stress during cesarean section using IMA, a statistically significant difference was found between pre-operative and 30-min post-operative blood values of the mothers who received general anesthesia. This difference was not detected in the spinal anesthesia group. In the same study, it was stated that no statistically significant difference between general and spinal anesthesia groups in both maternal and cord blood could be found [20]. In contrast to this study, IMA values in the cord blood were found to be significantly higher in patients who underwent general anesthesia than those who underwent spinal anesthesia (0.89 versus 0.85). Although the number of variables assessed was low, our results appear to demonstrate that general anesthesia may be associated with higher oxidative stress compared to spinal anesthesia as determined by high IMA and low thiol levels in the cord blood of patients who received general anesthesia.

Thiol disulfide balance reacts rapidly and is affected by instant changes. Thiol and disulfide levels from cord blood were measured to determine intra-operative oxidative stress status. Since thiol–disulfide equilibrium shows the instantaneous state, it is not considered significant to evaluate any post-operative parameter or to use it as an indicator of surgery after the effect of anesthesia has disappeared. Oxidative stress can be confirmed by blood gas from the umbilical artery for the newborn, but blood gas was not examined in our study since in previous studies conducted for this purpose, the relationship between umbilical arterial blood gas and oxidative stress has already been investigated [21]. Although the newborn was not evaluated, in our study, it was found that under general anesthesia, the mother was exposed to greater oxidative stress. This finding may indicate that spinal anesthesia could be the preferred anesthesia technique for cesarean section since the mother is exposed to less oxidative stress.

Limitations

The cross-sectional nature of the study, the small number of participants, and the study being conducted with a homogeneous group can be considered as limitations of the study. Since levels of the related blood values in the cord blood before anesthesia were not measured, conclusive data regarding the influence of anesthesia type could not be provided. Furthermore, the mechanisms by which the anesthesia techniques affect thiol–disulfide homeostasis could not be evaluated. In addition, although the first and fifth minute APGAR scores of the newborns were determined, the lack of long-term well-being assessments can be considered as a limitation.

Conclusions

In conclusion, in our study, it was found that the values of native thiol, total thiol, and disulfide in cord blood were lower and IMA values were higher in the general anesthesia group. Based on these results, it can be said that general anesthesia may cause a higher degree of oxidative stress compared to spinal anesthesia. Deciding on the appropriate anesthetic technique may be especially important for risky pregnancies in which increased oxidative stress suffered by the mother and baby may be critical. In line with the results of this study, it would be important to determine the anesthesia approach for select groups through studies involving a higher number of patients and an extensive set of parameters associated with oxidative stress.

References

1. Sies H. Oxidative stress: oxidants and antioxidants. Experimental Physiology: Translation and Integration. 1997;82(2):291-5.
2. Cremers CM, Jakob U. Oxidant sensing by reversible disulfide bond formation. The Journal of Biological Chemistry. 2013;288(37):26489-96.
3. Jones DP, Liang Y. Measuring the poise of thiol/disulfide couples in vivo. Free Radical Biology & Medicine. 2009;47(10):1329-38.
4. Coverdale JP, Katundu KG, Sobczak AI, Arya S, Blindauer CA, Stewart AJ. Ischemia-modified albumin: Crosstalk between fatty acid and cobalt binding. Prostaglandins, Leukotrienes and Essential Fatty Acids. 2018;135:147-57
5. Bahinipati J, Mohapatra PC. Ischemia modified albumin as a marker of oxidative stress in normal pregnancy. JCDR. 2016;10(9):BC15.

6. Lee YM, Song BC, Yeum KJ. Impact of Volatile Anesthetics on Oxidative Stress and Inflammation. BioMed Research International. 2015;2015:242709.
7. Aktun LH, Aykanat Y, Erel O, Neselioglu S, Olmuscelik O. A Study Over Thiol Disulfide Homeostasis in Cord Blood in Women With Gestational Diabetes. Journal of Family & Reproductive Health. 2018;12(4):217-22.
8. Akin F, Kozanhan B, Deniz CD, Sahin O, Goktepe H, Neselioglu S, et al. Effects of the anesthesia technique used during cesarean section on maternal-neonatal thiol disulfide homeostasis. Minerva Anestesiologica. 2019;85(11):1175-83.
9. Erel O, Neselioglu S. A novel and automated assay for thiol/disulphide homeostasis. Clinical Biochemistry. 2014;47(18):326-32.
10. Mungli P, Shetty MS, Tilak P, Anwar N. Total thiols: biomedical importance and their alteration in various disorders. Online Journal of Health and Allied Sciences. 2009;8(2).
11. Erkus ME, Altiparmak IH, Akyuz AR, Demirbag R, Sezen Y, Gunebakmaz O, et al. The association between plasma thiol levels and left ventricular diastolic dysfunction in patient with hypertension. Scandinavian Journal of Clinical and Laboratory Investigation. 2015;75(8):667-73.
12. Karabayirli S, Keskin EA, Kaya A, Koca C, Erel O, Demircioglu RI, et al. Assessment of fetal antioxidant and oxidant status during different anesthesia techniques for elective cesarean sections. Journal of Research in Medical Sciences. 2015;20(8):739-44.
13. Ulubas Isik D, Akdas Reis Y, Bas AY, Unal S, Ozcan B, Mollamahmutoglu L, et al. The effect of the modes of delivery on the maternal and neonatal dynamic thiol-disulfide homeostasis. The Journal of Maternal-Fetal & Neonatal Medicine. 2019;32(23):3993-7.
14. Kulacoglu H, Ozdogan M, Gurer A, Ersoy EP, Onder Devay A, Duygulu Devay S, et al. Prospective comparison of local, spinal, and general types of anaesthesia regarding oxidative stress following Lichtenstein hernia repair. Bratislavske lekarske listy 2007;108(8):335-9.
15. Bravo-Cuellar A, Romero-Ramos JE, Hernandez-Flores G, Romo-Perez Fde J, Bravo-Cuellar L, Lerma-Diaz JM. [Comparison of two types of anesthesia on plasma levels of inflammatory markers]. Cirugia y Cirujanos. 2007;75(2):99-105.
16. Sinha MK, Gaze DC, Tippins JR, Collinson PO, Kaski JC. Ischemia modified albumin is a sensitive marker of myocardial ischemia after percutaneous coronary intervention. Circulation. 2003;107(19):2403-5.
17. Zapico-Muniz E, Santalo-Bel M, Merce-Muntanola J, Montiel JA, Martinez-Rubio A, Ordonez-Llanos J. Ischemia-modified albumin during skeletal muscle ischemia. Clinical Chemistry. 2004 Jun;50(6):1063-5.
18. Bar-Or D, Winkler JV, Vanbenthuysen K, Harris L, Lau E, Hetzel FW. Reduced albumin-cobalt binding with transient myocardial ischemia after elective percutaneous transluminal coronary angioplasty: a preliminary comparison to creatine kinase-MB, myoglobin, and troponin I. American Heart Journal. 2001;141(6):985-91.
19. Iacovidou N, Briana DD, Boutsikou M, Liosi S, Baka S, Boutsikou T, et al. Cord blood ischemia-modified albumin levels in normal and intrauterine growth restricted pregnancies. Mediators of inflammation 2008;2008:523081.
20. Omur D, Hacivelioglu SO, Oguzalp H, Uyan B, Kiraz HA, Duman C, et al. The effect of anaesthesia technique on maternal and cord blood ischaemia-modified albumin levels during caesarean section: a randomized controlled study. The Journal of International Medical Research. 2013;41(4):1111-9.
21. Noh EJ, Kim YH, Cho MK, Kim JW, Kim JW, Byun YJ, et al. Comparison of oxidative stress markers in umbilical cord blood after vaginal and cesarean delivery. Obstet Gynecol Sci. 2014;57(2):109-14.

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