ORIGINAL ARTICLE

The effect of general and spinal anesthesia on neutrophil to lymphocyte ratio in patients undergoing cesarian section

Mesut Erbaş[1], Hüseyin Toman[1], Meryem Gencer[2], Hasan Şahin[1], Hasan Ali Kiraz[1], Tuncer Şimşek[1], Hatice Saylan[1], Tuğba Doğu[1], Uğur altınışık[1], H Betül Altınışık[1]

[1]*Department of Anesthesiology and Reanimation,*
[2]*Department of Obstetrics and Gynecology,*
Medical Faculty, Çanakkale Onsekiz Mart University, Çanakkale, (Turkey)

Correspondence: Mesut Erbaş, Departments of Anesthesiology and Reanimation, Medical Faculty, Çanakkale, Onsekiz Mart University, Çanakkale, *(Turkey);* Tel: +905324058309: E-mail: benimmesut@hotmail.com

ABSTRACT

Objective: Neutrophil to lymphocyte ratio (NLR) has become popular recently so that many studies have been done to find out the predictive value of NLR in many different aspects of clinical practice. The aim of this retrospective study was to evaluate the relationship between blood NLR and anesthetic techniques in patients undergoing cesarian section.

Methodology: In this study, eighty patients (American Society of Anesthesiologists physical status I~II) undergoing elective cesarian section using spinal (Group S: 40) or general anesthesia (Group G: 40) were retrospectively analyzed for neutrophil to lymphocyte ratio.

Results: The demographic characteristics of the groups, amount of bleeding, before the operation hemoglobin values, platelet counts, and NLR values were similar in both the spinal and general anesthesia groups. However, significant differences were observed with regard to NLR values in the postoperative period.

Conclusion: Postoperative neutrophil to lymphocyte ratio in patients undergoing cesarian section under spinal anesthesia was found to be significantly lower as compared to general anesthesia.

Key words: Anesthesia, Spinal; Anesthesia, general; Lymphocytes; Neutrophils

Citation: Mesut Erbaş M, Toman H, Gencer M, Şahin H, Kiraz HA, Şimşek T, Saylan H, Doğu T, altınışık U, Altınışık HB. The effect of general and spinal anesthesia on neutrophil to lymphocyte ratio in patients undergoing cesarian section. Anaesth Pain & Intensive Care 2015;19(4):485-488

INTRODUCTION

Neutrophil/lymphocyte ratio (NLR) has been proposed to be a simple marker for inflammatory response.[1] NLR in peripheral blood is used as a parameter providing information about the relationship between inflammatory environment and physiological stress. Currently NLR is accepted as a parameter showing both the high neutrophil count reflecting acute inflammatory response and the low lymphocyte count reflecting physiological stress response.[2] Neutrophil and lymphocyte counts are affected by a variety of hormones, cytokines and acute phase reactants in addition to surgical trauma. In addition it has been determined that they are also affected by anesthetic method in this situation.[3-5] Surgical stress and form of anesthetic cause different responses by affecting many systems; starting with the immune system. The formed responses are affected by factors such as direct pharmacological effect of anesthetic material, form, duration and depth of anesthesia, as well as the trauma. The stress response to the combination of anesthesia and surgical stres causes endocrine and metabolic changes.[4] During anesthesia and surgery there are changes in every stage of the immune system. These are the body's general physiological response, which changes linked to the extent of surgery, age of the patient, general health, medications used

and any blood transfusions performed. In addition it has been shown to be related to increased susceptibility to infection due to lymphopenia developing after surgery. As a result after surgery NLR measurements may be a useful method to evaluate any infection, prognosis and inflammatory response.[5-7] For cesarean anesthesia general and regional anesthetic techniques are used. In recent years regional anesthesia is chosen more often due to advantages such as patient request, patient awareness, no risk of aspiration, no respiratory depression in newborns and not causing uterus atony.[8]

In this study we aimed to retrospectively investigate the effects of general and spinal anesthesia for cesarean operations on NLR.

METHODOLOGY

Our study retrospectively investigated the NLR of 80 cases operated under elective conditions with spinal or general anesthesia at Canakkale 18 Mart University Medical Faculty Hospital between January 2013 to February 2014. The study was completed with permission from University Clinical Research Ethics Committee. Information was obtained from the patient files and anesthetic documents. Age, gender, height, weight and hemodynamic monitoring data were recorded from the files and documents. Non-elective cases, multiple pregnancies, preterm pregnancies; and cases associated with fetal anomalies, fetal development retardation, fetal birth weight below 2500 g, and infants with aspiration of meconium or amniotic fluid, were not included in the study. In addition data from patients, with inflammation or anemia in the preoperative period and more than expected hemorrhage during the operation, were not included in the study. All patients taken to the operating room were routinely monitored for electrocardiogram (ECG), peripheral oxygen saturation (SPO_2), and non-invasive blood pressure.

In the Group G propofol 2 mg/kg and rocuronium 0.6 mg/kg were administered IV for induction. During induction cases were oxygenized with 100% O_2 at 6 L/min through a mask. After 2 min of controlled ventilation through the mask, they were intubated with a suitable sized endotracheal tube. To maintain anesthesia, patients were ventilated with 2% sevoflurane in 50% air and 50% O_2 at 6 L/min. The patients were ventilated at a tidal volume of 6-8 ml/kg and respiration rate of 12/min, with an Avance S/5 anesthetic machine. After the baby was born inj. fentanyl 1 μg/kg was given. When the last skin suture was being completed the inhalation agents were stopped and manual ventilation with 100% O_2 was begun. In this period all parameters were measured. When spontaneous respiration began neuromuscular antagonization was achieved with atropine 0.01 mg/kg and neostigmine 0.03 mg/kg. After extubation the patient was taken to recovery.

For spinal anesthesia, patients chose to sit or lie on their side and a 26 G spinal needle was used in the L2-L3 or L3-L4 intervertebral space. When free cerebrospinal fluid flow was observed, slow injection of 0.5% hyperbaric bupivacaine (about 12.5 mg appropriate to the patient's height and weight) was completed for spinal anesthesia. After spinal injection the patients were placed in supine, raised head position and left until sensory block rose above T5 level. Sensory block was tested using the pinprick technique with a 22 G needle. When sensory block reached T5 the operation began. The maximum block height reached was recorded. Blood pressure was measured before spinal anesthesia, every 2 min in the 30 min after spinal anesthesia and every 5 min after this. If systolic blood pressure fell below 20% of initial value or below 90 mmHg, hypotension was recorded and 10 mg ephedrine IV was administered. Patients taken to the recovery room after operation were checked for block level. In both groups patients had blood taken in the 2nd hour postoperative and hemoglobin and platelet counts were measured with a Beckman Coulter LH 780 analyzer (Beckman Coulter, Inc. CA, USA) device and NLR were calculated.

Statistical Analysis

For statistical evaluation SPSS for Windows 15.1 version was used. Differences between the groups were tested with the chi-square test. Blood count parameters (leukocyte, neutrophil and lymphocyte) were found not to have normal distribution. NLR parameter was analyzed with the Mann Whitney U-test. All parameters are expressed as mean ± standard deviation. $P < 0.05$ was accepted as statistically significant.

RESULTS

From the point of view of demographic characteristics there was no significant difference between the Group G and Group S ($p > 0.05$) (Table 1). The amount of blood loss and the duration of surgery was also comparable in the two groups (Table 1).

In both groups there was no significant statistical

Table 1: Demographic characteristics of the group

Parameter	Group G	Group S	P
Age (years)	30.4 ± 5.3	29.7 ± 4.8	> 0.05
Height (cm)	161.9 ± 5.7	157.8 ± 8.3	
Weight (Kg)	80.9 ± 17.3	80.1 ± 15.8	
Amount of bleeding (ml)	620 ± 20	590 ± 30	
Duration of surgery (min)	66.5 ± 22.7	64.2 ± 12.5	

Table 2: The preoperative and postoperative hemoglobine and platelet values of both groups

	Grup G (pre-op / post-op)	P	Grup S (pre-op / post-op)	P
Hemoglobine (g/dL)	11.6 ± 1.3 / 10.3 ± 1.3	0.47	11.4 ± 1.3 / 10.1 ± 1.4	0.75
Platelets (/mm^3)	211 ± 65 / 198 ± 62	0.88	210 ± 61 / 183 ± 51	0.33

Table 3: The preoperative and postoperative neutrophil to lymphocyte ratio values of both groups

	NLR (preoperative)	NLR (postoperative)	P
Group G	4.44 ± 2.3	15.63 ± 11.1*	0.02*
Group S	4.41 ± 2.5	10.58 ± 4.3*	

P*: The significantly difference was observed with regard to NLR values in the postoperative period

difference between the hemoglobin and platelet values before and after the operation. The NLR values in the general anesthesia and spinal anesthesia groups were similar before the operation ($p > 0.05$) (Table 2).

However in the postoperative period while NLR was 15.63 ± 11.1 in the Group G, it was observed to be 10.58 ± 4.3 in the Group S ($p < 0.05$) (Table 3).

DISCUSSION

As a result of this study it was observed that comparing inhalation anesthesia with spinal anesthesia for cesarean operation the Group S had significantly lower NLR ratios. Studies on stress caused by surgical trauma have reported a suppression of cellular resistance and susceptibility to inflammation. In addition the increase in postoperative leukocyte values and reduction in lymphocyte values increase the tendency for infection.[9] These leukocyte changes have been proposed to cause inflammatory cytokines similar to IL-6. Studies have shown that total leukocyte count and changes in leukocyte subtypes are important markers for morbidity and mortality in cancer patients, renal failure patients and cardiovascular patients.[5,10,11] The neuroendocrine system is activated during and after surgery. Neuroendocrine hormones and cytokines are released linked to surgical stress. The effects of general or regional anesthesia in elective surgery on pro-inflammatory and antiinflammatory cytokines have been described by previous studies.[6,12] Regional anesthesia suppresses neuroendocrine activity linked to surgical procedure with sympathetic blockage. As a result while cortisol levels do not change, cytokine production reduces. While this effect is observed during high-level block (T4-S5), it is not observed at desired levels with lower-level block.[13] NLR provide information about the immune system and are an important morbidity marker in the postoperative period. Additionally in clinical application the measurement of NLR in peripheral blood is a cheap and simple test.[14] To research the effects of anesthetics on the immune system multi-modal anesthetic techniques have been applied. Studies with TIVA administration have found less effect on adrenergic and immune response in the postoperative period compared to inhalation anesthetics.[7] However there is no study found on the effect on NLR of inhalation anesthesia and spinal anesthesia. Some studies comparing spinal anesthesia with general anesthesia have

shown the reduction in neuroendocrine response to surgery as an advantage.[15] Another study reported that total intravenous anesthesia (TIVA) reduced stres hormones, cytokines and immune mediators by more compared to inhalation anesthesia.[5] As different anesthetic methods and anesthetics used in obstetrics affect the immunity of both mother and newborn the importance is greater. During pregnancy leukocytosis is an expected situation, leukocyte values may be 16,000/mcgL. In addition in normal pregnancies leukocytosis is accepted as a marker of an increasing inflammatory response.[16]

LIMITATIONS

There are some limitations to our study. First, other factors such as surgical stress or psychological state of the mothers may affect the differences in NLR between the groups. Additionally the variation in surgical factors may have an effect. Also the NLR measured at different periods during the first 24 hours, in addition to 2 hours after the operation, may be more significant.

CONCLUSİON

In conclusion spinal anesthesia, often chosen for elective cesarean sections, is associated with less rise in the neutrophil to lymphocyte ratio at two hours postoperative period than general anesthesia. This topic requires further prospective studies with a larger sample size and an extended period of measurement.

Conflict of interest: None declared by the authors.

Author contribution: All of the authors took part in the management of this patient and in manuscript preparation.

REFERENCES

1. Ateş F, Yaraş S, Sarıtaş B, Altıntaş E, Sezgin O, Orekici G. Does neutrophil to lymphocyte ratio in peripheral blood predict endoscopic erosive esophagitis? Endoscopy 2011;19(3):88-90
2. Gibson PH, Cuthbertson BH, Croal BL, Rae D, El-Shafei H, Gibson G, et al. Usefulness of neutrophil/lymphocyte ratio as predictor of new-onset atrial fibrillation after coronary artery bypass grafting. Am J Cardiol 2010;105:186-91. [PubMed] doi: 10.1016/j.amjcard.2009.09.007. Epub 2009 Dec 3.
3. Helmy SA, Wahby MA, El-Nawaway M. The effect of anaesthesia and surgery on plasma cytokine production. Anaesthesia 1999;54:733e8. [PubMed] [Free full text] DOI: 10.1046/j.1365-2044.1999.00947.x
4. Kılıç R, Yaşar M.A, Avcı L, Demirel İ, Yaşar D. The Effects of Using Epidural Anesthesia with General Anesthesia on Plasma Levels of Cytokins and Cortizol in Patients with Lower Abdominal Surgery. Fırat Tıp Dergisi 2005;10:59-63.
5. Kim WH, Jin HS, Ko JS, Hahm TS, Lee SM, Cho HS, Kim MH. The effect of anesthetic techniques on neutrophil-to-lymphocyte ratio after laparoscopy-assisted vaginal hysterectomy. Acta Anaesthesiol Taiwan. 2011 Sep;49(3):83-7.[PubMed] [Free full text] doi: 10.1016/j.aat.2011.08.004. Epub 2011 Sep 22.
6. Schneemilch CE, Ittenson A, Ansorge S, Hachenberg T, Bank U. Effect of 2 anesthetic techniques on the postoperative proinflammatory and antiinflammatory cytokine response and cellular immune function to minör surgery. J Clin Anesth 2005;17(7):517-27. [PubMed]
7. Ke JJ, Zhan J, Feng XB, Wu Y, Rao Y, Wang YL. A comparison of the effect of total intravenous anaesthesia with propofol and remifentanil and inhalational anaesthesia with isoflurane on the release of pro-and anti-inflammatory cytokines in patients undergoing open cholecystectomy. Anaesth Intensive Care 2008;36:74-8. [PubMed]
8. Keleş E, Yazgan H, Gebeşçe A, Pakır E. The Type of Anesthesia Used during Cesarean Section Is Related to the Transient Tachypnea of the Newborn. - ISRN Pediatr. 2013 Apr 24;2013:264340. [PubMed][Free full text] doi: 10.1155/2013/264340
9. Takahashi J, Shono Y, Hirabayashi H, Kamimura M, Nakagawa H, Ebara S, et al. Usefulness of white blood cell differential for early diagnosis of surgical wound infection following spinal instrumentation surgery. Spine 2006;31:1020-5. [PubMed]
10. Forget P, De Kock M. Perspectives in anaesthesia for cancer surgery. J Cancer Res Clin Oncol. 2014 Mar;140(3):353-9. [PubMed]
11. Ogawa K, Hirai M, Katsube T, Murayama M, Hamaguchi K, Shimakawa T, et al. Suppression of cellular immunity by surgical stress. Surgery 2000;127:329-36. [PubMed]
12. Žura M, Kozmar A, Šakić K, Malenica B, Hrgovic Z. Effect of spinal and general anesthesia on serum concentration of pro-inflammatory and anti-inflammatory cytokines. Immunobiology 2012;217:622-27. [PubMed] doi: 10.1016/j.imbio.2011.10.018. Epub 2011 Nov 3.
13. Yıldırım S, Aydoğan H, Yalçın Ş, Çiftçi H, Küçük A, Bilgiç T, Zeyrek FY. Comparison of the effects of regional and general anesthesia on the immune system via cytokines in urooncologic surgery. Journal of Clinical and Experimental Investigations 2013;4(1):51-55
14. Kurtoglu E, Kokcu A, Celik H, Tosun M, Malatyalioglu E. May ratio of neutrophil to lymphocyte be useful in predicting the risk of developing preeclampsia? A pilot study. J Matern Fetal Neonatal Med. 2014 Apr 9. [Epub ahead of print]
15. Bar-Yosef S, Melamed R, Page GG, Shakhar G, Shakhar K, Ben-Eliyahu S. Attenuation of the tumor-promoting effect of surgery by spinal blockade in rats. Anesthesiology 2001;94(6):1066–73 [PubMed] [Free full text]
16. Daniel AK, Brain JK. Maternal physiology during pregnancy. In: Decherney AH, Nathan L, Goodwin TM, Laufer N, eds. Current diagnosis and treatment obstetrics and gynecology. 10th ed. New York (NY): McGraw Hill Company:2007:156–71.

★★★★★