



## Plateletcrit Could Be A Marker of Inflammation in Cesarean Section Sezaryen Operasyonlarında Plateletcrit İnflamasyon Belirteci Olabilir

Ibrahim Karagoz<sup>1</sup>, Ayhan Ekici<sup>2</sup>

<sup>1</sup>Abant İzzet Baysal University Hospital, Department of Anesthesiology and Reanimation, Bolu, Turkey.

<sup>2</sup>Abant İzzet Baysal University Hospital, Department of Obstetrics and Gynecology, Bolu, Turkey.

### Abstract

**Objective:** We aimed to compare preoperative and postoperative values of novel inflammatory markers of hemogram; especially neutrophil to lymphocyte ratio (NLR), mean platelet volume (MPV), red cell distribution width (RDW), MPV to platelet ratio (MPR), RDW to platelet ratio (RPR) and plateletcrit (PCT) in pregnant women undergone cesarean section by either general or spinal anesthesia.

**Material-Method:** Patients who had elective caesarean section in our institution that had no contraindications for general and regional anesthesia, with a single fetus pregnancy, 18-40 years old women were included in the study. The subjects were randomly divided into two groups. Group I (n=30) patients underwent general anesthesia and Group II (n=30) patients underwent spinal anesthesia. Preoperative and postoperative hemogram parameters were compared.

**Results:** Postoperative PCT values of spinal and general anesthesia groups were 0.16 (0.05)% and 0.19 (0.07)%, respectively. The difference in postoperative PCT was statistically significant (p=0.03).

**Conclusions:** We suggest that PCT could be used as a marker of inflammation after cesarean section surgery. If not contraindicated, spinal anesthesia should be preferred for those pregnant women in cesarean delivery.

**Keywords:** Plateletcrit, Inflammation, Cesarean Section Surgery.

### Özet

**Amaç:** Hemogram kökenli yeni inflamatuvar belirteçlerin; özellikle nötrofil / lenfosit oranı (NLR), ortalama trombosit hacmi (MPV), kırmızı hücre dağılım genişliği (RDW), MPV-trombosit oranı (MPR), RDW / trombosit oranı (RPR) ve trombosit oranı (MPT) preoperatif ve postoperatif değerlerini genel veya spinal anestezi ile sezaryen yapılan gebelerde karşılaştırmayı amaçladık.

**Materyal-Metot:** Çalışmamızda genel ve bölgesel anestezi için herhangi bir kontrendikasyonu olmayan, tek bir fetüs gebeliği olan, 18-40 yaşları arasındaki seçmeli sezaryen bölümü olan hastalar çalışmaya alındı. Denekler rastgele iki gruba ayrıldı. Grup I (n =30) hastalara genel anestezi, Grup II (n=30) hastalara spinal anestezi uygulandı. Preoperatif ve postoperatif hemogram parametreleri karşılaştırıldı.

**Bulgular:** Spinal ve genel anestezi gruplarının postoperatif PCT değerleri sırasıyla %0,16 (0,05) ve %0,19 (0,07) idi. Postoperatif PCT'deki fark istatistiksel olarak anlamlıydı (p=0,03).

**Sonuç:** Sezaryen ameliyatı sonrası PCT'nin inflamasyon belirteci olarak kullanılabileceğini düşünüyoruz. Kontrendike değilse, sezaryen doğumundaki gebe kadınlar için spinal anestezi tercih edilmelidir.

**Anahtar kelimeler:** Plateletcrit, İnflamasyon, Sezaryen Cerrahisi.

### Introduction

Surgical intervention is a source of inflammatory stress for the patients (1). Inflammatory stress causes leukocytosis together with lymphopenia and depresses the reticuloendothelial system (2). Differences occur in leukocyte counts and subgroups due to immune depression (3).

Cesarean surgery is an operation that is frequently applied in obstetrics practice (4). General anesthesia usually preferred as well as proven regional techniques for anesthesia in cesarean section (5). Numerous studies have been carried about surgical stress by different anesthesia methods which caused metabolic and inflammatory responses. It is known that general anesthesia and regional anesthesia differently effect the leukocyte distribution (6). Autonomic, neurohumoral and immunological mechanisms are responsible of inflammatory response in anesthesia (1, 7).

Hemogram parameters, such as, mean platelet volume (MPV), red cell distribution width (RDW) and platelet distribution width are considered as novel inflammatory markers in recent studies (8-10). Moreover, hemogram derived inflammatory indices; including, neutrophil to lymphocyte ratio (NLR), MPV to lymphocyte ratio (MLR), MPV to platelet ratio (MPR) and RDW to platelet ratio (RPR), were also suggested as predictors of inflammatory burden (11-15). Another important indice in hemogram test, plateletcrit (PCT) was also being considered as an inflammatory marker in various diseases, recently (16-18).

In this prospective study, we aimed to compare preoperative and postoperative values of hemogram parameters; especially NLR, MPV, MPR, RPR and PCT in pregnant women undergone cesarean section by either general or spinal anesthesia.

## Material and Methods

After the approval of the ethics committee (IRB Approval date: 25/05/2017 and number: 2017/20) and the informed consent of the patients, the patients who had elective caesarean section in Obstetrics and Gynecology Clinic of University Hospital, that had no contraindications for general and regional anesthesia, A total of 60 patients with a single fetus pregnancy, 18-40 years old with ASA (American Society of Anesthesiologists) I-II, were included in the study. Patients with diabetes mellitus, chronic obstructive pulmonary disease, allergy history for local anesthesia, bleeding clotting time abnormalities, liver disease, renal failure (creatinine level 2.5 mg and over), preeclampsia, eclampsia, patients with pre-existing metabolic disorders, planned emergency surgery patients and patients who did not agree to participate in the study were excluded from the study. All cesarean procedures were performed by experienced obstetricians. No premedication was applied to the cases. All patients were allowed to lie on their left side until they were transferred to the operating room and the baby was labored. All patients were taken to the operating room with an 18-20 G cannula from the back of the hand or the antecubital area. All patients were hydrated by intravenous (i.v.) 15ml/kg of 0.9% isotonic electrolyte solution 20 to 30 minutes before the operation. Electrocardiography (ECG), noninvasive blood pressure, pulse and peripheral oxygen saturation monitoring were performed in all patients. The subjects were randomly divided into two groups. Group I (n=30) patients underwent general anesthesia and Group II (n=30) patients underwent spinal anesthesia.

Group I cases were treated with 2 mg/kg of propofol and 0.6mg/kg of rocuronium in anesthesia induction. Endotracheal intubation was performed after muscle relaxation. Tidal volume was adjusted to 8-10 ml/kg and respiratory frequency was 10-12 per minute. Anesthesia was maintained with 50% oxygen and 50% air mixture and 1 MAC desflurane. An additional dose of 0.15mg/kg of rocuronium was administered for muscle relaxation. In this group, fentanyl 1-1.5 µg/kg was administered as an analgesic after labor.

The sterile conditions were achieved by placing the sitting position in Group II cases. Local anesthesia was performed with 1-2 cc of 2% lidocaine from L4-5 or L3-4 levels. Free CSF flow was observed by entering the subarachnoid space with spinal needle (25 G Quincke) at the same levels. 2.1-2.2 ml of 0.5% hypertonic bupivacaine (marcaine heavy) was administered to the subarachnoid space and spinal anesthesia was performed. Sensory block level was evaluated with "pin-prick" test and motor block level was measured with Bromage scale. The sensory block was allowed to operate when a sufficient level (T6-8) was achieved. From the beginning until the end of the operation 3 liters per minute of 100% oxygen support was provided.

Maternal hemogram, white blood cell count (WBC), platelet count (PLT), RDW, MPV, PDW, and PCT values were recorded in the blood samples taken within the last 24 hours before the operation and within the first 8 hours postoperatively. NLR

was calculated by dividing of neutrophil count to lymphocyte count, MPR was calculated by dividing of MPV to PLT, and RPR was calculated by dividing RDW to PLT.

In conduction of statistical analysis, SPSS software (SPSS 15.0 for Windows, IBM Co, Chicago, IL, USA) was used. Distribution of study parameters in study groups was analyzed by Kolmogorov-Smirnov test. Comparison of homogenously distributed variables was done with independent samples t test and expressed as mean  $\pm$  standard deviation. Variables without homogenous distribution were compared in study groups by Mann-Whitney U test and expressed as median (interquartile range). Preoperative and postoperative variables were compared with paired samples t test. A p value lower than 0.05 was considered as statistically significant.

## Results

A total of 60 patients; 30 each in spinal and general anesthesia group were enrolled to the study. Mean age of spinal and general anesthesia groups were 30 $\pm$ 6 and 31 $\pm$ 6 years, respectively.

There were no significant difference between spinal and general anesthesia groups in terms of preoperative WBC(p=0.98), postoperative WBC(p=0.71), preoperative PLT(p=0.79), postoperative PLT(p=0.11), preoperative MPV(p=0.68), postoperative MPV(p=0.43), preoperative RDW(p=0.40), postoperative RDW(p=0.61), preoperative NLR(p=0.98), postoperative NLR(p=0.71), preoperative PDW(p=0.2), postoperative PDW(p=0.60), preoperative MPR(p=0.68), postoperative MPR(p=0.14), preoperative RPR(p=0.79), postoperative RPR(p=0.32) and preoperative PCT(p=0.28) values. Postoperative PCT values of spinal and general anesthesia groups were 0.16 (0.05)% and 0.19 (0.07)%, respectively. The difference in postoperative PCT was statistically significant (p=0.03).

Only preoperative WBC value was significantly different from postoperative WBC in spinal anesthesia group (p=0.02). Other hematologic values were not different in preoperative compared to postoperative period in this group (all p>0.05). In general anesthesia group, none of the hematological markers were different in preoperative period compared to postoperative values (p>0.05 for all).

## Discussion

Present study showed that higher PCT in postoperative period could be a marker of greater inflammatory burden caused by general anesthesia.

Plateletcrit has been supposed as an inflammatory marker in various conditions. For example; patients with normal coronary blood flow have significantly lower PCT levels compared to those with slow coronary blood flow (19). It has also been associated with pulmonary tuberculosis (18). Other inflammatory conditions which PCT was found to be related include; inflammatory bowel disease (16), endotoxemia (20), gastritis (21), and non-ST elevation myocardial infarction (22). Similarly, we reported higher PCT values in patients undergone general anesthesia compared to spinal anesthesia

in present study.

Plateletcrit was also suggested to be related with different obstetric problems. It is considered as a predictor of recurrent pregnancy loss in a study by Aynioglu et al (23). Moreover, it could be a marker of preterm labor in pregnant women (24). PCT was also supposed to be a predictor of severe preeclampsia during pregnancy (25). Accordingly, we showed that first time in literature that PCT could reflect the greater inflammatory burden in pregnant women undergone caesarean section with general anesthesia compared to those with spinal anesthesia.

Tissue damage during surgery is responsible of inflammation during anesthesia (26). Released inflammatory mediators during surgery trigger the systemic inflammatory response (27). The choice of anesthetic or the type of anesthesia can change the inflammatory response of the body (28). Inflammation during surgery may lead to tissue infarction, lung damage, increased capillary permeability, pain and reperfusion damage. New anesthesia and surgical techniques may reduce the morbidity of inflammatory stimuli during surgery (26).

Not only inflammation, but also postoperative delirium is more common in general anesthesia compared to regional anesthesia (29). It is also possible general anesthesia might be associated with greater inflammatory burden than local anesthesia. Indeed, both human and animal studies showed anti-inflammatory properties of local anesthetics by influencing mediators of leukocytes, free radical production, and leukocyte migration (26). Authors believe that benefits of local anesthetics could be due to their anti-inflammatory effects (30). Moreover, administration of local anesthetics during epidural analgesia regulate the postoperative inflammatory status (26). These data in literature suggest the findings in present study that relieved more inflammatory burden in general anesthesia compared to spinal anesthesia group, since the latter received local anesthetic bupivacaine.

There are controversial studies about the anti-inflammatory effects of local anesthetics recently. For instance, ropivacaine was failed to ameliorate inflammation in inflammatory bowel disease (26). Furthermore, patients undergone general anesthesia in present report were received propofol, which has anti-inflammatory effects via regulating hepatic blood supply, and increasing the production of anti-inflammatory cytokines (31, 32).

Limitation of present study are relatively small study population and lack of other surgery types that undergone general or spinal anesthesia. However, to the best of our knowledge, this is the first study in literature that found association between PCT and the type of anesthesia in cesarean section surgery.

## Conclusion

We suggest that PCT could be used as a marker of inflammation after cesarean section surgery. If not contraindicated, spinal anesthesia should be preferred for those pregnant women in cesarean delivery.

## References

1. Acar D, Karakaş Erkiş E, Gümüş T, Şahin D, Sepici Dinçel A, Kanbak O. The Effects of Different Anaesthetic Techniques on Surgical Stress Response During Inguinal Hernia Operations. *Turkish Journal of Anesthesiology and Reanimation*. 2015; 43(2): 91-9.
2. Akkaya A, Yıldız I, Tekelioğlu UY, Demirhan A, Bayir H, Özlü T, et al. Dexamethasone added to levobupivacaine in ultrasound-guided transversus abdominis plain block increased the duration of postoperative analgesia after caesarean section: a randomized, double blind, controlled trial. *European review for medical and pharmacological sciences*. 2014; 18(5): 717-22.
3. Dogan N, Kursad H, Alici HA, Cesur M. The Effects of General and Epidural Anaesthesia on the number of Leukocytes and the distribution of Leukocyte subtypes. *Medical Journal of Ataturk University*. 2003; 35: 37-41.
4. Aydın M, Şenol DK, Erdoğan S. Determination of Preoperative Anxiety Levels on Women Scheduled for Caesarean Delivery. *ACU Sağlık Bil Derg*. 2014; 2014(1): 54-8.
5. Aksoy M, Aksoy AN, Dostbil A, Gürsaç Çelik M, Ahıskalıoğlu A. Anaesthesia Techniques for Caesarean Operations: Retrospective Analysis of Last Decade. *Turk J Anaesth Reanim* 2014; 42: 128-32.
6. Salo M. Effects of anaesthesia and surgery on the immune response. *Acta anaesthesiologica Scandinavica*. 1992; 36(3): 201-20.
7. Kelbel I, Weiss M. Anaesthetics and immune function. *Current opinion in anaesthesiology*. 2001; 14(6): 685-91.
8. Atak BM, Duman TT, Aktas G, Kocak MZ, Savli H. Platelet Distribution Width is Associated with Type 2 Diabetes Mellitus and Diabetic Nephropathy and Neuropathy. *National Journal of Health Sciences* 2018; 3: 95-8.
9. Aktas G, Kocak MZ, Duman TT, Erkus E, Atak BM, Sit M, et al. Mean Platelet Volume (MPV) as an inflammatory marker in type 2 diabetes mellitus and obesity. *Bali Medical Journal*. 2018; 7(3): 650-3.
10. Aktas G, Sit M, Karagoz I, Erkus E, Ozer B, Kocak MZ, et al. Could Red Cell Distribution Width be a Marker of Thyroid Cancer? *Journal of the College of Physicians and Surgeons--Pakistan : JCPSP*. 2017; 27(9): 556-8.
11. Kocak MZ, Aktas G, Erkus E, Duman TT, Atak BM, Savli H. Mean Platelet Volume to Lymphocyte Ratio as a Novel Marker for Diabetic Nephropathy. *Journal of the College of Physicians and Surgeons--Pakistan : JCPSP*. 2018; 28(11): 844-7.
12. Duman TT, Aktas G, Atak B, Kocak MZ. Is Mean Platelet Volume to Platelet ratio a promising indicator of diabetic regulation in type 2 diabetes mellitus? *Journal of Medical Research*. 2018; 4(3): 137-9.
13. Aktas G, Sit M, Dikbas O, Erkol H, Altinordu R, Erkus E, et al. Elevated neutrophil-to-lymphocyte ratio in the diagnosis of Hashimoto's thyroiditis. *Revista da Associacao Medica*

Brasileira (1992). 2017; 63(12): 1065-8.

14. Kosekli MA, Erkus E, Kocak MZ. Mean Platelet Volume to Platelet ratio as a promising marker of hepatosteatosis. *Experimental Biomedical Research*. 2018; 1(2): 55-9.

15. Atak BM, Erkus E, Duman TT, Kocak MZ, Kosekli MA. Mean Platelet volume to platelet and red cell distribution width to platelet ratios in Irritable Bowel Syndrome. *Experimental Biomedical Research*. 2018; 1(2): 60-4.

16. Tang J, Gao X, Zhi M, Zhou HM, Zhang M, Chen HW, et al. Plateletcrit: a sensitive biomarker for evaluating disease activity in Crohn's disease with low hs-CRP. *Journal of digestive diseases*. 2015; 16(3): 118-24.

17. Ergelen M, Uyarel H. Plateletcrit: a novel prognostic marker for acute coronary syndrome. *International journal of cardiology*. 2014; 177(1): 161.

18. Sahin F, Yazar E, Yildiz P. Prominent features of platelet count, plateletcrit, mean platelet volume and platelet distribution width in pulmonary tuberculosis. *Multidisciplinary respiratory medicine*. 2012; 7(1): 38.

19. Akpınar I, Sayın MR, Gursöy YC, Aktop Z, Karabag T, Kucuk E, et al. Plateletcrit and red cell distribution width are independent predictors of the slow coronary flow phenomenon. *Journal of cardiology*. 2014; 63(2): 112-8.

20. Yılmaz Z, Eralp O, İlcol YO. Evaluation of platelet count and its association with plateletcrit, mean platelet volume, and platelet size distribution width in a canine model of endotoxemia. *Veterinary clinical pathology*. 2008; 37(2): 159-63.

21. Tuzun A, Keskin O, Yakut M, Kalkan C, Soykan I. The predictive value of mean platelet volume, plateletcrit and red cell distribution width in the differentiation of autoimmune gastritis patients with and without type I gastric carcinoid tumors. *Platelets*. 2014; 25(5): 363-6.

22. Gul M, Uyarel H, Akgul O, Akkaya E, Surgit O, Cakmak HA, et al. Long-term prognostic significance of admission plateletcrit values in patients with non-ST elevation myocardial infarction. *Blood coagulation & fibrinolysis : an international journal in haemostasis and thrombosis*. 2016; 27(6): 696-701.

23. Aynioğlu O, Isik H, Sahbaz A, Harma MI, Isik M, Kokturk F. Can Plateletcrit be a Marker for Recurrent Pregnancy

Loss? *Clinical and applied thrombosis/hemostasis : official journal of the International Academy of Clinical and Applied Thrombosis/Hemostasis*. 2016; 22(5): 447-52.

24. Isik H, Aynioğlu O, Sahbaz A, Arıkan I, Karcaaltınçaba D, Sahin H, et al. Can plateletcrit, an underestimated platelet parameter, be related with preterm labour? *Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology*. 2015; 35(7): 676-80.

25. Yucel B, Ustun B. Neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, mean platelet volume, red cell distribution width and plateletcrit in preeclampsia. *Pregnancy hypertension*. 2017; 7: 29-32.

26. Torres LM, Martínez Ruiz A. Inflammation and anesthesia, is there anything new? *Revista española de anestesiología y reanimación*. 2017; 64(7): 365-8.

27. Baki ED, Sivaci RG, Kokulu S, Ela Y, Aldemir M. Effects of anesthetic choice on inflammatory response in cardiac surgery. *Inflammation and Cell Signaling*. 2014; 1: e75.

28. Galley HF, Dubbels AM, Webster NR. The effect of midazolam and propofol on interleukin-8 from human polymorphonuclear leukocytes. *Anesthesia & Analgesia*. 1998; 86(6): 1289-93.

29. Patel V, Champaneria R, Dretzke J, Yeung J. Effect of regional versus general anaesthesia on postoperative delirium in elderly patients undergoing surgery for hip fracture: a systematic review. *BMJ open*. 2018; 8(12): e020757.

30. Ata N, Erdur O, Görgülü M, Yılmaz E. Effects of two different local anaesthetic methods vs no anaesthesia on pain scores for intratympanic injections. *The Journal of Laryngology & Otology*. 2016; 130(12): 1153-7.

31. Brix-Christensen V, Tonnesen E, Sorensen IJ, Bilfinger TV, Sanchez RG, Stefano GB. Effects of anaesthesia based on high versus low doses of opioids on the cytokine and acute-phase protein responses in patients undergoing cardiac surgery. *Acta anaesthesiologica Scandinavica*. 1998; 42(1): 63-70.

32. Winterhalter M, Brandl K, Rahe-Meyer N, Osthaus A, Hecker H, Hagl C, et al. Endocrine stress response and inflammatory activation during CABG surgery. A randomized trial comparing remifentanyl infusion to intermittent fentanyl. *European journal of anaesthesiology*. 2008; 25(4): 326-35.