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ISSN:2149-455X
Makale / Article

Changes in MPVand PDW Values in Patients Receiving Chemotherapy for Colon and Gastric Cancers

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Abstract

The increase of tendency to thrombosis along with chemotherapy in cancer patients is a well known issue today. In our study investigating the changes in MPV and PDW. 345 patients with the diagnosis of 169 gastric and 176 colorectal cancer to whom 6 different types of chemotherapy protocol were applied. Median age was 59 (23-80) and 155 patients were male. The platelet count, MPV and PDW values were measured before, during and after chemotherapy. It was found that while platelet count and MPV values significantly decreased, PDW increased in the patients receiving chemotherapy. Also, there is no statistically significant relationship between the changes of MPV, PDW values and vascular thrombosis, overall or progression-free survival.

Keywords: Gastric and colorectal cancers, Mean Platelet Volume, Platelet Distrubition Width

Özet

Kemoterapi alan kanser hastalarında tromboz eğiliminin arttığı günümüzde oldukça iyi bilinmektedir. Biz bu çalışmamızda bu hastalarda MPV ve PDW'daki değişiklikleri araştırdık. 169 gastrik ve 176 kolorektal kanser tanılı, 6 farklı kemoterapi protokolü uygulanan toplam 345 hasta çalışmamıza alındı. Medyan yaş 59 (23-80) olup 155'i erkekti. Kemoterapi öncesi, ortası ve sonrasında trombosit sayısı, MPV ve PDW değerleri ölçüldü. Kemoterapi alan hastalarda trombosit sayısı ve MPV değerleri belirgin olarak azalırken PDW değerlerinin arttığı saptandı. Ayrıca, MPV, PDW değerleri ve vasküler tromboz, genel veya progresyonsuz sağkalım değişiklikleri arasında istatistiksel olarak anlamlı bir ilişki olmadığı görüldü.

Anahtar Kelimeler: Mide Ve Kolorektal Kanserler, Ortalama Trombosit Hacmi, Trombosit Dağılım Aralığı

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Giriş

Cancer patients undergo a thrombotic event up to 78% in some studies during the course of the disease [1,2]. Mean platelet volume (MPV) is a parameter associated with platelet functions. Especially in recent years, it has gained much more importance and a correlation has been identified betweenMPV and many chronic diseases, and also it is known that there are still ongoing studies in this subject.In population-based studies of healthy individuals, a statistically significant relationship was found between increase of MPV values and thromboembolic event rate in those both with and without risk factors[3,4,5]. Like MPV, platelet distribution width (PDW) is also a simple platelet indice that shows platelet activity and is routinely run during a full blood count.With platelet activation, PDW and MPV similarly increase[6]. Increase of coagulation potential in a vaso-occlusive crisis is thought to be due to this PDW increase[7].

In our study, through chemotherapy regimens commonly used in patients with gastric and colorectal cancer, we aimed to investigatechanges inMPV, the number of platelets and PDW,which are thought to be related to staging and follow-up of cancer disease, length of life and also which have been shown to be associated with the risk of venous thromboembolism in the studies conducted[8,9,10].

Method

In the scope of the study, a retrospective file analysis of patient files of 654 patients diagnosed with gastric cancer and 704 patients diagnosed with colorectal cancer who applied to Zonguldak Bülent Ecevit University Health Research and Application center between 01.01.2008 and 30.04.2012. The patient files were thoroughly examined in terms of the type of chemotherapy the patientsgot, the number of chemotherapy cycles received, drugs they used, any chronic diseases or hematologic diseases they had. Demographic information such as age and gender was recorded. Progression-free survival (PFS) and overall survival (OS) durations in the patients were calculated. During the course of chemotherapy, it was examined whether or not a venous or arterial thromboembolic event was detected. Patients in both groups were classified according to the chemotherapy protocol given to them. The protocol was approwed by the Bülent Ecevit Üniversity Medical Faculty Ethics Committee.

Applied Chemotherapy Protocols (Regimen)
FUFA (fluorouracil, folic acid)
FOLFIRI (folinic Acid, fluorouracil (5FU), irinotecan)
DCF (docataxel, cisplatin, fluorourasil)
FOLFOX(fluorourasil, folinik asit, oksaliplatin)
FOLFIRI-B (fluorouracil, folinic acid, irinotecan-bevacizumab)

Exclusion Criteria

No patients with a thrombotic or hematologic disease, taking medications that affect platelet function,with chronic kidney or liver disease, with chronic infections, under the age of 18 and over 80 years were included in the study.

As a value prior to chemotherapy, recent full blood count measured before first chemotherapy treatment forall patients was taken into consideration. As chemotherapy median values, recent full blood count measured during answer evaluation process or before chemotherapy nearly in the middle of the chemotherapy protocols they received was taken. As to the value after chemotherapy, the first blood count measured under control conditions after the last chemotherapy was taken. Through full blood countsat specified times for each patient, MPV, PDW and platelet counts were recorded.

Statistical Analysis

In this study, all statistical analysis was performed using SPSS (The Statistical Package for the Social Sciences) for Windows software package (version 15.0). The results of all parameters on the cases were given as mean ± standard deviation.While student's t-testwas used in the intergroup comparisonsof normally distributedparameters., Mann-Whitney U test was used in the intergroup comparisons of non-normally distributed parameters for the comparison of quantitative data.Chi-square test was used for the comparison of qualitative data. The results were evaluated at a 95% confidence interval and a significance level of $p < 0.05$.

Results

169 gastric cancer patients and 176 colon cancer patients meeting the inclusion criteria were included in the study.The demographic and clinical characteristics of the patients are shown in the table 1. FUFA chemotherapy regimen for 108 patients with gastric cancer (63.9%), DCF regimen for 50 patients with gastric cancer (29.6%), FOLFIRI regimen for 11 patients with gastric cancer

(6.5%) were applied. While all patients receiving DCF and FOLFIRI were metastatic, 95 (88%) of 108 patients receiving FUFA were non-metastatic. FUFA chemotherapy regimen for 75 patients diagnosed with colorectal cancer (42.6%), FOLFOX regimen for the 63patients (35.8%) and FOLFIRI-B regimen for the 38 patients (21.6%) were applied. While all patients applied FUFA received adjuvant chemotherapy, 18 patients (10.2%) among the patients applied FOLFOX chemotherapy regimen were metastatic. All patients applied FOLFIRI-b chemotherapy regimen were those with metastatic.

Table 1: The demographic and clinical characteristics of the patients

	Gastric cancer	Colorectal cancer
Age	58.1+-12.55 (23-80)	59.9+-11.3 (25-80)
Male	111 (65.7%)	79 (44.9%)
Female	58 (34.3%)	97 (55.1%)
Diabetes mellitus	17	8
Hypertension	19	33
COPD	4	0
Other Chronic Diseases (Coronary failure, Coronary artery disease, etc.)	5	0
The number of patients who die during the study	45 (26.6%)	18 (10.2%)
The number of patients who are still alive at the end of the study	124 (73.4%)	158 (89.8%)
Number of patients with metastatic at the beginning of the study	74 (43.8%)	56 (31.8%)
Number of patients with non-metastatic at the beginning of the study	95 (56.2%)	120 (68.2%)

Before chemotherapy, mean platelet counts in patients with gastric cancer were detected as 288.343 +-108.064 (53.000-661.000), MPV8.33+-1.15 (6.00-11.60) PDW 16.72 +-0.74 (14.90-20.30) and mean platelet counts in colon cancer patients were detected as 291.744+-100.041, MPV 8.02+-1.05 (5.50-12.00) PDW 16.70+-0.57 (15.60-18.50).

During chemotherapy, mean platelet counts in patients with gastric cancer were detected as 235.597 +-94.299 (42.000-553.000), MPV 7.97+-1.07 (5.90-11.10) PDW 16.86 +-0.78 (13.80-19.00) and mean platelet counts in patients with colon cancer patients were detected as 234.712+-89.255(76.000-744.000), MPV 7.72+-1.02 (5.30-11.50) PDW 16.99+-0.57(15.40-19.00).

Whenpre- and during chemotherapy values were compared among patients with gastric cancer, there was a statistically significant decrease in platelet count (p= 0.00), MPV(p= 0.00) and there was a statistically significant increase in PDW(p=0.01). Similarly, in patients with colon cancer patients, there was a statistically significant decrease in platelet count (p= 0.00), MPV(p= 0.00) and there was a statistically significant increase in PDW(p=0.00).

When pre- and postchemotherapy values were compared among patients with gastric cancer, as in pre- and during chemotherapy values, there was a statistically significant decrease in platelet count (p= 0.001), MPV(p= 0.001) and there was a statistically significant increase in PDW(p=0.001). In patients with colon cancer patients, changes in pre- and postchemotherapy values were similar to the comparison of pre- and during chemotherapy values and similarity was found in the comparison results of patients with gastric cancer.

When pre- and postchemotherapy valueswere compared among 108 gastric cancer patients receiving FUFA chemotherapy regimen, while there was a statistically significant decrease in platelet count and MPV, there was an increase in PDW(p=0.00). While there was a 11.6 %+- 0.7 (p=0.00) decrease inplatelet counts between pre- and during chemotherapy, there was a 20.4%+-0.7 (p=0.001) decrease in platelet counts between pre- and postchemotherapy. There was a 2.9%+-0.1(p= 0.001) decrease in MPV values between pre- and during chemotherapy and a 5.7%+-0.1 (p=0.001) decrease in MPV values between pre- and postchemotherapy. In PDW values, there was a 1.3%+-0.5 (p= 0.001) increase between pre- and during chemotherapy and a 2.4%+-0.6 (p=0.001) increase between pre- and postchemotherapy

When pre- and postchemotherapy values were compared among patients receiving DCF chemotherapy regimen, there was a statistically significant decrease in platelet count (p=0.02) and MPV(p=0.001).There was a statistically insignificant increase in PDW values. (p=0.22). While there was a 2.1% +- 0.5 (p=0.02) decrease in platelet count in gastric cancerpatients receiving DCF chemotherapy regimen between pre- and during chemotherapy, there was a 7.1%+-0.5 (p=0.02) decrease in their platelet count between pre- and postchemotherapy. In MPVvalues there was a 5.4%+-0.6 (p=0.001) decrease between pre- and during chemot-

herapy and a 6.74%+-0.6 (p=0.001) decrease between pre- and postchemotherapy.In PDW values there was a0.3%+-0.1 (p=0.90) increase between pre- and during chemotherapy and a 0.8%+-0.180 (p 0.21) increase between pre- and postchemotherapy. While there was no statistically significant difference between the values noted between pre- and during chemotherapy and between pre- and postchemotherapy in PDW (p=0.90 ve p=0.21), there was a significant decrease in platelet count(p=0.02) MPV values(p=0.001)

When platelet parameters before and after chemotherapy were compared among gastric cancer patients receiving FOLFIRI chemotherapy regimen, there was a statistically insignificant decrease in platelet count (p=0.051) and PDW values and insignificant increase in MPVvalues. While there was a statistically significant decrease in platelet count between pre- and during chemotherapy, there was a statistically insignificant decrease in MPV and increase in PDW.

While there was a 22.9% +-0.4 (p<0.05) decrease in platelet count in patients receiving FOLFIRI between pre- and during chemotherapy and a 16.7%+-0.2 (p=0.51) decrease in platelet count between pre- and postchemotherapy.In MPVvaluesthere was a2.6%+-0.5 (p=0.37) decrease between pre- and during chemotherapy and a 3.7%+-0.7 (p=0.90) decrease between pre- and postchemotherapy. In PDWvaluesthere was a2.1%+-0.4 (p=0.09) increase between pre- and during chemotherapy and a2.1 %+-0.3 (p=0.37) increase between pre- and postchemotherapy.

When platelet parameters inthose receiving FUFA chemotherapy among patients with colorectal cancerwere examined before and after chemotherapy, similar results were found with the ones obtained from patients with gastric cancer. While there was a 6.26 %+-0.4 (p=0.001) decrease in platelet count in colorectal cancer patients receiving FUFA chemotherapy between pre- and during chemotherapy, there was a 11.8%+-0.3 (p=0.00) decrease between pre- and postchemotherapy. In MPVvalues there was a 2.7%+-0.1(p=0.001) decrease between pre- and during chemotherapy and a 3.1%+-0.1 (p=0.001) decrease between pre- and postchemotherapy. In PDWthere was a0.9%+-0.1(p=0.02) increase between pre- and during chemotherapy and a 1.7%+-0.1 (p=0.001) increase between pre- and postchemotherapy.

When thevalues between pre- and postchemotherapy in patients with colorectal cancer receiving FOLFOX chemotherapy were examined, a statistically significant decrease in platelet count (p=0.001) and MPV values (p=0.03) and a statistically significant increase in PDW(p= 0.001) were observed.

While there was a 23.3% +-0.3(p=0.00) decrease in platelet count in colorectal cancer patients receiving FOLFOX chemotherapy between pre- and during chemotherapy, there wasa 23.0%+-0.4 (p=0.001) decrease between pre- and postchemotherapy. In MPV values there was a 2.8%+-0.1(p=0.01) decrease between pre- and during chemotherapy and a 2.4%+-0.1 (p=0.03) decrease between pre- and postchemotherapy. In PDW there was a 2.6%+-0.1 (p=0.001) increase between pre- and during chemotherapy and a 3.1%+-0.1(p=0.001) increase between pre- and postchemotherapy.

Similarly, when the values between pre- and postchemotherapy in patients receiving FOLFIRI-b chemotherapy were compared, there was a statistically significant decrease in platelet count (p=0.00) and in MPVvalues (p=0.00) and there was a statistically significant increase in PDW (p=0.00). While there was a 15.9% +-0.3(p=0.00) decrease in platelet count in colorectal cancer patients receiving FOLFIRI-b chemotherapy between pre- and during chemotherapy, there was a 18.1%+-0.3 (p=0.00) decrease between pre- and postchemotherapy. In MPV values there was a 4.9%+-0.1(p=0.00) decrease between pre- and during chemotherapy and a 5.7%+-0.1(p=0.00) decrease between pre- and postchemotherapy. In PDW there was a 2.2%+-0.1(p=0.00) increase between pre- and during chemotherapy and a 3.7%+-0.1(p=0.00) increase between pre- and postchemotherapy.

In patients with gastric and colorectal cancer, the number of platelets noted before and during chemotherapy and before and after chemotherapy, changes in trombocyte count,MPV and PDW values are respectively shown in the table 2.

The median follow-up time for the patients with gastric and colorectal cancer who participated in our study was 18.60 + -11.40 months (range 3-52 months). During our study period, 92 (26.6%) patients died from cancer-related medical condition. The average life expectancy of these 92 patients after cancer diagnosis was14.46+-9.28 months. No statistically significant relationship

Table 2: The rate of change in trombocyte count, MPVand PDW observed in gastric and colorectal cancer patientsbefore and during chemotherapy and before and after chemotherapy.

Chemotherapy Protocols	Results	The rate of change in platelet counts before and after chemo-therapy.	The rate of change inMPV before and after chemotherapy	The rate of change inMPV before and after chemotherapy
FUFA Gastric Ca	Number of patients mean Standard deviation Minimum Maximum P	108 -0.2041 0.6597 -0.89 1.41 0.000	108 -0.0568 0.1044 -0.42 0.20 0.000	108 -0.0568 0.1044 -0.42 0.20 0.000
DCF Gastric Ca	Number of patients mean Standard deviation Minimum Maximum P	50 -0.0717 0.4632 -0.81 1.92 0.022	50 -0.0643 0.1326 -0.36 0.33 0.000	50 -0.0643 0.1326 -0.36 0.33 0.000
FOLFIRI Gastric Ca	Number of patients mean Standard deviation Minimum Maximum P	11 0.1712 0.2248 -0.23 0.55 0.051	11 0.0366 0.0670 -0.15 0.06 0.090	11 0.0366 0.0670 -0.15 0.06 0.090
FUFA Colorectal Ca	Number of patients mean Standard deviation Minimum Maximum P	75 -0.1182 0.2630 -0.69 1.08 0.000	75 -0.031 0.0965 -0.23 0.24 0.002	75 -0.031 0.0965 -0.23 0.24 0.002
FOLFOX Colorectal Ca	Number of patients mean Standard deviation Minimum Maximum P	63 -0.2289 0.3525 -0.76 1.10 0.000	63 -0.0238 0.1082 -0.24 0.30 0.031	63 -0.0238 0.1082 -0.24 0.30 0.031
FOLFIRI-B Colorectal Ca	Number of patients mean Standard deviation Minimum Maximum P	38 -0.1813 0.3373 -0.77 0.73 0.000	38 -0.0570 0.0954 -0.27 0.09 0.002	38 -0.0570 0.0954 -0.27 0.09 0.002
Total	Number of patients mean Standard deviation Minimum Maximum	345 -0.1564 0.4726 -0.89 1.92	345 -0.0456 0.1066 -0.42 0.33	345 -0.0456 0.1066 -0.42 0.33

between the median life expectancy and platelet count, MPV and PDWin these patients was observed. Moreover, when patients with metastatic were compared with those with non-metastatic, it was detected that there was no statistically significant difference between platelet parameters.

Discussion

At the end of our study, we saw that therewas a significant decrease in values of platelet activation markers such as platelet count and mean platelet volume in patients receiving chemotherapy. In patients with cancer, thrombotic diathesis is well known as well as increased bleeding tendency 3,11. Therefore, the issue of prophylactic treatment of thromboembolic events likea double-edged sword.The risk factors and necessity for prophylactic anticoagulant therapy planning should be probed very well. Although the risk scoring suggested by Khorana and colleagues for patients monitored during chemotherapy through ambulatory infusion is the best known in this area, it should be supported doing more extensive studies 12. While the platelet count was considered in this risk scoring, other platelet activation markers such as MPV and

PDW weren't taken into account. However, a number of recent studies in this area suggest that these platelet activation markers play important roles as well as platelet count in the development of thromboembolic events[6,13,14]. We also think that the values of MPVand PDW in patients undergoing chemotherapy, which are routinely noted at each control and require no additional costs or intervention at all, can be valuable in the diagnosis of thromboembolic events and calculation for developing risk.

When MPV and platelet count are considered platelet activation markers, in our study the degeneration of them both in patients receiving chemotherapy suggests that there may not be chemotherapy-induced platelet activation contrary to what's predicted in some studies[15,16,17].

Consequently, in the light of the findings we obtained, we think that the role of changes in the shape and size of platelets, among the reasons of the increase in the frequency of thromboembolic events due to chemotherapy, may be less important than supposed. In this case, drugs such as acetylsalicylic acid acting by modifying platelet functions may not be beneficial to thromboembolism prophylaxis. Moreover, such anticoagulant agents may increase the risk of bleeding in patients and may have additional negative effects on mortality and morbidity.In our study, we also observed that PDW values, another platelet activation marker, increased significantly in patients receiving chemotherapy. Further studies examining the role of PDW inincreasing thromboembolic risk due to chemotherapy will be helpful in elucidating this issue.

The retrospective nature of our study, the low number of patients in the study,not studyingplatelet activation markers with an advanced investigation like a p-selectin make it harder for us to reach more precise judgment on the issue.

There is a need for prospective studies to be conducted in larger populations including biochemical markers of platelet activation such as p-selectin and electron microscopy studies to better understand the enhancing effects of chemotherapy on the risk of thromboembolic events and to determine its effects on platelet functions.

References

1. Spencer FA, Lessard D, Emery C, Reed et al. Venous thromboembolism in the outpatient setting. Arch Intern Med. 2007;167:1471-1475.
2. Elting LS, Escalante CP, Cooksley C, et al. Outcomes and cost of deep venous thrombosis among patients with cancer. Arch Intern Med 2004; 164:1653.
3. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? Curr Pharm Des. 2011;17(1):47-58.
4. K. Brækkan, * E. B. Mathıesen, _ I. Njølstad, _ T. Wılsgaard, et al. Mean Platelet Volume İs A Risk Factor For Venous Thromboembolism: The Tromsø Studys. Journal Of Thrombosis And Haemostasis, 8: 157–162
5. Ferroni P, Guadagni F, Riondino S, et al. Evaluation of mean platelet volume as a predictive marker for cancer-associated venous thromboembolism during chemotherapy. Haematologica. 2014;99(10):1638-1644.
6. Vagdatli E, Gounari E, Lazaridou E, Katsibourlia E, et al. Platelet distribution width: a simple, practical and specific marker of activation of coagulation. Hippokratia. 2010;14(1):28-32.
7. Amin MA, Amin AP, Kulkarni HR. Platelet distribution width (PDW) is increased in -vaso-occlusive crisis in sickle cell dis- ease. Ann Hematol 2004; 83 (6): 331-335
8. Kaito, K., Otsubo, H., Usui, N., Yoshida, et al. Platelet size deviation width, platelet large cell ratio, and mean platelet volume have sufficient sensitivity and specificity in the diagnosis of immune thrombocytopenia. British journal of haematology 2005;128(5), 698-702.
9. Suppiah R, Shaheen PE, Elson P, et al. Thrombocytosis As A Prognostic Factor For Survival İn Patients With Metastatic Renal Cell Carcinoma. Cancer. 2006 Oct 15;107 (8):1793-800
10. Cil H, Yavuz C, Islamoglu Y, et al. Platelet count and mean platelet volume in patients with in-hospital deep venous thrombosis. Clin Appl Thromb Hemost 2012;18:650-3.
11. Lyman GH, Khorana AA, Falanga A, et al. American Society of Clinical Oncology guideline: recommendations for venous thromboembolism prophylaxis and treatment in patients with cancer. J Clin Oncol. 2007;25:5490-5505.
12. Khorana AA, Kuderer NM, Culakova E, Lyman GH, et al. Development and validation of a predictive model for chemotherapy-associated thrombosis. Blood. 2008;111(10):4902-4907.
13. Sev Sevuk U, Altindag R, Bahadir MV, Ay N, et al. Value of Platelet Indices in Identifying Complete Resolution of Thrombus in Deep Venous Thrombosis Patients. Indian Journal of Hematology & Blood Transfusion. 2015;31(1):71-76.
14. Khandekar MM, Khurana AS, Deshmukh SD, Kakrani AL, et al. Platelet volume indices in patients with coronary artery disease and acute myocardial infarction: an In- dian scena. J Clin Pathol 2006; 59 (2): 146-149.
15. Mutlu H, Artis Ta, Erden A, Akca Z. Alteration İn Mean Platelet Volume And Platicrit Values İn Patients With Cancer That Developed Thrombosis. Clin Appl Thromb Hemost 2012;19:331-3.
16. Scappaticci Fa, Skillings Jr, Holden Sn, et al. Arterial Thromboembolic Events İn Patients With Metastatic Carcinoma Treated With Chemotherapy And Bevacizumab. J Natl Cancer Inst. 2007; 99 (16):1232-1239.
17. H. Mutlu, V. Berk, H. Karaca, A. Erden, et al. Treatment Regimen With Bevacizumab Decreases Mean Platelet Volume İn Patients With Metastatic Colon Cancer Clın Appl Thromb Hemost 2012 18: 546