ISSN: 0976-3031

Available Online at http://www.recentscientific.com

CODEN: IJRSFP (USA)

International Journal of Recent Scientific Research
Vol. 9, Issue, 12(B), pp. 29881-29884, December, 2018

International Journal of Recent Scientific Research

DOI: 10.24327/IJRSR

Research Article

CAN MPV AND NLR BE USED AS ALTERNATIVE INDICATORS IN THE DIAGNOSIS AND TREATMENT OF CHRONIC OSTEOMYELITIS?

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DOI: http://dx.doi.org/10.24327/ijrsr.2018.0912.2951

ARTICLE INFO

Article History:

Received 13th September, 2018
Received in revised form 11th October, 2018
Accepted 8th November, 2018
Published online 28th December, 2018

Key Words:

Osteomyelitis , Mean Platelet Volume, C-Reactive Protein

ABSTRACT

Background: Osteomyelitis is a chronic recurrent disease of the bone that can be seen in all age groups. The most important factor accepted in the treatment of chronic osteomyelitis is total excision of dead tissues. Treatment response is followed by clinical recovery and reductions in inflammatory markers such as, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and white blood cell count (WBC). In this study, we compared pre-operative ESR, CRP, WBC, mean platelet volume (MPV), neutrophil to lymphocyte ratio (NLR), hemoglobin, hematocrit, and neutrophil and lymphocyte counts of patients with chronic osteomyelitis with those in post-treatment period.

Methods: In this retrospective study, pre- and post-treatment blood parameters of 71 (69% [n=49] male), 31% [n=22] female) patients with pathologic diagnosis of chronic osteomyelitis who were operated due to osteomyelitis in our orthopedics service between 2010 and 2017 were investigated. Numerical data were compared with Student's t test and p values less than 0.05 were considered statistically significant.

Results: Mean age of the patients recruited to the study was 31.1 ± 17.0 (3-80) years, and mean follow-up period duration was 9.3 ± 11.7 (1-46) months. There was no statistically significant difference between pre-op and post-treatment values of hematocrit, lymphocyte count and NLR ($p < 0.05$). While, post-treatment ESR, CRP, WBC, neutrophil count, hemoglobin and MPV were significantly different compared to pre-op values ($p<0.05$ for all).

Conclusion: These results suggest that MPV may be a useful and readily available inflammatory marker for follow-up the treatment response in patients with chronic osteomyelitis.

INTRODUCTION

Osteomyelitis is defined as the infection of the bone. The disease results from the involvement of the bone by microorganisms through direct or indirect pathways. It covers a wide range of clinical scenarios such as chronic hematogenous osteomyelitis, post-traumatic osteomyelitis, periprosthetic infections and contagious osteomyelitis. Chronic osteomyelitis lesions have been detected in Egyptian mummies 4000 years ago. It has been reported that the overall incidence of osteomyelitis is 15-170 at 100,000 which is more common in males. Despite the increasing diversity and effectiveness of treatment modalities, management of osteomyelitis is still challenging and the cure rates are not satisfactory. Therefore, chronic osteomyelitis treatment continues to be a serious problem today (1-5). The diagnosis of chronic osteomyelitis is based on clinical symptoms, physical examination findings, and laboratory and imaging modalities. However, the most important factor in the diagnosis establishment is histopathological examination of the samples taken and the microbiological identification of the infectious agent. Laboratory findings are usually nonspecific. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are usually elevated in patients with osteomyelitis. The white blood cell count can be found as normal or elevated (6,7). ESR and CRP are the parameters used in the evaluation of the response to treatment and follow-up of the patient. WBC, MPV, neutrophil count and NLR are being used as markers of inflammation process and their diagnostic value is increasing day by day (8,9). There are many studies investigating MPV and NLR from hematological parameters, which are markers of inflammation in many rheumatologic diseases, cancers and infectious diseases (10,11,12,13,14). In this study, we aimed to investigate the utility of MPV and NLR as alternative to other hematological markers (ESR, WBC, and CRP) which are used in the follow-up of in chronic osteomyelitis, an inflammatory process.

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MATERIALS AND METHODS

In this retrospective study, preoperative and post-treatment blood parameters of chronic osteomyelitis patients were compared who were admitted to and treated in Orthopedics Department of Dursun Odabaş Medical Center Hospital of Van Yüzüncü Yıl University between 2010 and 2017. Blood parameters including white blood cell count, neutrophil count, lymphocyte count, hemoglobin (Hb), hematocrit (Htc), mean platelet volume (MPV), and neutrophil to lymphocyte ratio (NLR) were examined in all patients in the study. NLR was obtained by dividing the neutrophil count by the lymphocyte count in peripheral blood. Complete blood count (CBC), ESR and CRP parameters were assessed. Hematological parameters were measured with Beckman Coulter LH 780 instrument, ESR values with ALS -100 auto ESR analyzer and CRP with BNR II SYSTEM SN 442176 instrument. Patients with a diagnosis of diabetes mellitus, an immunological disease, or any systemic disease that may affect inflammatory parameters were not included.

Statistical Analysis: Descriptive statistics for continuous variables are expressed as mean, standard deviation, minimum and maximum values; for categorical variables as number and percentage. In terms of continuous variables, the pre - and post-treatment values of the patients were compared using the Matching t - test. Statistical significance level was accepted as 0.05 in the calculations and SPSS statistical package program was used for the statistical analysis.

RESULTS

Of the total 71 patient included in the study, n=49 were male (69%), and n=22 were female (31%), the mean age was 31.1 ± 17.0 years and the mean follow up period was 9.3 ± 11.7 months.

Table 1 Demographical data of the study population

Preop and postop Parameters	Mean values	Count (n)	*Standard Deviation*. SD	P value
WBC¥	9.732	71	3.8739	0.019
WBC£	8.392	71	2.5256	
HB¥	12.801	71	2.2991	0.023
HB£	13.345	71	2.0891	
HTC¥	39.017	71	6.5008	0.210
HTC£	39.959	71	6.7348	
MPV¥	7.742	71	1.0112	0.001
MPV£	8.075	71	1.0163	
NEUTROPHIL¥	6.297	71	3.5493	0.028
NEUTROPHIL£	5.076	71	2.3216	
LYMPHOCYTE¥	2.521	71	1.1231	0.899
LYMPHOCYTE £	2.535	71	1.1767	
ESR¥(mm/hour)	34.453	55	20.6845	0.001
ESR£(mm/hour)	18.85	55	17.123	
CRP¥(mg/dl)	37.2054	69	63.84253	0.001
CRP£(mg/dl)	9.33	69	12.919	
NLR¥	2.9771	71	2.16252	0.994
NLR£	2.9733	71	3.72851	

¥;shows pre-op values, £; shows post-treatment values

There was no statistically significant difference between preoperative and postoperative hematocrit, lymphocyte counts and NLR values of the patients as shown on Table 1 ($p>0.05$). Mean WBC, hemoglobin, neutrophil count, ESR, CRP and MPV values of patients were compared in pre- and post-operative period and statistically significant difference was found ($p<0.05$).

The study population was consist of 71 patients who were diagnosed as osteomyelitis histopathologically; 49 of them were male (69%) and 22 of them were female (31%), the mean age was 31.1 ± 17.0 years and the mean follow up period was 9.3 ± 11.7 months.

DISCUSSION

Osteomyelitis is a serious infection of the bone, usually caused by pyogenic organisms, resulting in inflammatory bone destruction, bone necrosis and new bone formation. Chronic osteomyelitis is still an important medical problem today. The long lasting, costly treatment of the disease and the long-term restriction of the patient's daily activity further increase the importance of this disease (15).

Chronic osteomyelitis is diagnosed by using hematological parameters, cultures of the samples from affected region, radiography, nuclear imaging, CT, MRI and histopathological methods. WBC, CRP and ESR values are not diagnostic. The definitive diagnosis is made only by histopathological examination (16). The most important factor accepted in the treatment of chronic osteomyelitis is total excision of dead tissues (17). Following the treatment of chronic osteomyelitis, an inflammatory process, clinical examination and some laboratory tests give us useful information about the effectiveness of the treatment. As reported in many studies, these inflammatory markers have led many experienced physicians and surgeons in the decision-making process for surgery(18). It is known that chronic infections cause many changes in the hematopoietic system; including reduced erythrocyte count, reduced amount of iron used for erythropoiesis, and increased tendency to anemia due to decreased bone marrow activity(19). In our study, when the hemoglobin and hematocrit values were compared before and after treatment, these two parameters had increased after treatment. The increase in mean hemoglobin level of the patients was statistically significant while the increase in hematocrit levels was not. This may be due to the improvement of the chronic osteomyelitis causing chronic disease anemia.

Erythrocyte sedimentation rate (ESR) is one of the oldest laboratory tests used which usually increases in case of inflammatory conditions, pregnancy, anemia, paraproteinemia, high fibrinogen level and a number of disorders with unknown etiology (20). However, ESR increase is also associated with infectious causes such as rheumatoid arthritis, systemic lupus erythematosus, tissue necrosis, and inflammatory bowel disease (21-22). ESR was used as a prognostic tool in monitoring the treatment response in patients treated for infectious diseases (23). It has been reported that ESR continues to increase until an appropriate treatment is started in patients with infectious diseases (24). In our study, there was a statistically significant difference between preoperative values and post-treatment ESR values of patients with chronic osteomyelitis, and ESR decreased significantly ($p<0.05$). This significant difference suggests that ESR, the oldest used laboratory method, still retains its validity in monitoring the treatment response in chronic osteomyelitis, an inflammatory process, and that is a highly valued marker with high accuracy in monitoring treatment response in such inflammatory processes.

C-reactive protein (CRP) is an acute phase reactant that increases in serum in response to inflammation (25). There are

previous studies showing the importance of ESR and CRP values in determining the severity of the disease and therefore the length of stay in the hospital, and in identifying and monitoring post-operative infections(23). In our study, there was a statistically significant difference between pre- and post-treatment CRP levels of chronic osteomyelitis patients ($p<0.05$). These results suggest that CRP, which we use in following up inflammatory processes and in response to treatment, is still a safe marker to use, such as ESR.

A study by Orimolade *et al*. reported that the WBC was high in patients with chronic osteomyelitis cases but this difference was not significant (26). It has been reported that neutrophil count increases in chronic osteomyelitis(27). In our study, the neutrophil and WBC counts decreased significantly after treatment compared to pre-treatment values. It is well known that neutrophil count and WBC increase in acute inflammatory processes, and decrease in these two parameters during follow-up has prognostic significance in monitoring the response to treatment. Consistent with previous studies showing that WBC and neutrophil count increase in chronic osteomyelitis, a chronic inflammatory process, in our study we found these parameters high and they decreased significantly after treatment. Although the results of the study by Orimolade EA *et al*. in Nigeria(26) has proposed that post-treatment decline in WBC values was not statistically significant, we found a statistically significant decrease in WBC and neutrophil count after treatment compared to those in pre-op period which may be related to treatment efficacy, patient compliance and patient prototype. The results of our study suggest that WBC and neutrophil count can also be used as inflammatory markers in chronic osteomyelitis.

MPV is measured and NLR can easily be calculated at no additional cost as part of routine complete blood count examination hematology laboratories(28). MPV has been shown to be a marker of platelet size, synthesis and function, and has been shown to be associated with platelet activation under inflammatory conditions. MPV, which has been shown as an initial indicator of an inflammatory process, is measured in many laboratories as part of a routine complete blood count with no additional cost. MPV acts as an acute phase reactant in some inflammatory conditions according to the severity of systemic inflammation. It has been shown to increase in low grade inflammations, but in case of severe inflammatory conditions, MPV has been shown to decrease due to intensive degradation of platelets in inflammatory regions (28,29,30,31,32).

Tanrıkulu *et al*. compared acute appendicitis patients were with the healthy controls and reported that WBC, MPV and RDW values and neutrophil ratio were significantly higher in patients with acute appendicitis(33). Post-treatment MPV values of patients with chronic osteomyelitis participated in our study increased significantly compared to pre-treatment values. This result supports the hypothesis that the MPV values are reduced due to intensive consumption of platelets in the inflammatory processes. We thought that during following-up the response to treatment, the consumption of platelets decreased as the inflammatory process subsides, thus MPV values increased after treatment. Therefore, we suggest that MPV values can be used as a useful parameter in the diagnosis and monitoring the response to treatment in chronic osteomyelitis.

NLR has increasingly been used as a marker of systemic inflammation recently. NLR, which is used as a useful marker in the diagnosis of inflammatory conditions, is also useful in predicting mortality and prognosis. NLR is a good indicator of the severity in some diseases. The underlying mechanism of the relationship between NLR and disease severity has not been fully elucidated and is still controversial. This may be due to increased circulating neutrophil count, activated IL-1β, fever, and migration of neutrophils to the tissue. First publications on NLR have been made by cardiologists in myocardial ischemia, and NLR has been reported to increase in case of myocardial ischemia (9,28,29,32,33,34). In our study, we showed that pre-treatment NLR values of patients with chronic osteomyelitis were high and decreased after the treatment. However, this difference was not statistically significant. Despite the pre-treatment neutrophil values were significantly higher than the post-treatment neutrophil counts, the NLR results did not reduce significantly after treatment probably due to the lack of a statistically significant difference between pre-treatment and post-treatment circulating lymphocyte count. We did not find any previous study in the English literature suggesting that MPV and NLR could be used to show the efficacy of treatment and follow-up of chronic osteomyelitis.

In conclusion, we suggest that MPV can be used as a supportive indicator together with other commonly used inflammatory markers (ESR, CRP, and WBC) in evaluation of treatment efficacy and follow-up in chronic osteomyelitis. Further large scale, randomized-controlled trials are needed to clarify this issue.

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How to cite this article:

Sezai ÖZKAN and Cihan ADANAŞ.2018, Can Mpv and Nlr Be Used as Alternative Indicators in the Diagnosis And Treatment of Chronic Osteomyelitis?. *Int J Recent Sci Res.* 9(11), pp. 29881-29884. DOI: http://dx.doi.org/10.24327/ijrsr.2018.0912.2951

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