

The Relationship between Platelet Volume Indices (PVIs) and Epileptic Seizure

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Abstract

Background: Platelet volume indices (PVIs) are low on price and easily accessible criteria in today's medicine. However, the impact of PVIs on seizure characteristics in epileptic patients is not clear.

Aim: To assess the level of PVIs in seizure affected patients and to see if there is a relationship between these results and the clinical status of patients.

Methods: The current study enrolled patients with the epileptic seizure (ES) to evaluate the PVIs for investigating whether a relationship exists between PVIs levels with duration, frequency and type of seizure. In this survey, the platelet indices including mean platelet volume (MPV), platelet distribution width (PDW), and platelet count (PLT) were calculated for the patient.

Results: A total of 199 patients were included in the study period, for which 59 attacks were focal seizures and 149 attacks were generalized convulsive seizures. The platelet counts and PCT were significantly higher in focal seizure than in generalized convulsion seizure. In generalized onset, MPV was significantly higher as compared to the focal onset.

Conclusion: The acquired data indicated that the high level of MPV and low level of PLT and PCT in generalized seizures might substantially contribute to the clinical signs of epileptic patients.

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Introduction

Epilepsy is one of the most common neurologic disorders, which affects about 50 million persons all around the world. It can be identified by seizures but not all seizures are due to epilepsy (1). Seizure is an alteration in neurological function caused by synchronized high frequency discharge of neurons (2). Growing body of evidence suggests that inflammatory cells and proinflammatory cytokines are an important mechanism involved in seizure. Seizures and epilepsy can originate a cascade of events which foster an

inflammatory response in CNS. Seizure activity causes an increase in the expression level of IL-1, TNF- α , and IL-6 cytokines which in turn affect neuronal excitability, decrease seizure threshold, and induce molecular, structural, and synaptic changes revealing epileptogenesis (3, 4).

Platelet volume indices (PVIs) are biomarkers of potential platelet activity which are thought to be in relation with inflammatory reactions (5). Using various automated analyzers in whole blood counting, a number of platelet variables such as PVIs can be measured

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regularly. Among them, two important parameters that are commonly studied are the mean platelet volume (MPV) and platelet distribution width (PDW) (6). During recent years, many studies have been undertaken to estimate the PVIs levels in inflammatory disorders. Some scientific surveys have proposed that major inflammatory cytokines, such as IL-3 and IL-6, could have an impact on megakaryocyte ploidy, and cause the production of more reactive, larger platelets, leading to changes in the PVLs (3).

Since inflammation plays a substantial role in the advancement of cellular death following seizure, investigating the possible impact of PVIs is apparently useful in achieving therapeutic protocols. The intention of our study is to assess the level of PVIs in seizure affected patients and to see if there is a relationship between these results and the clinical status of patients.

Methods

This study was conducted retrospectively on 199 consecutive patients who were selected from those with a history of repeating seizures and were admitted to Emergency unit of Loghman Hakim Hospital (Tehran, Iran), during year 2017. The informed consent form was signed by all the patients on the day of admission, and routine tests were used for evaluation.

Age, sex, seizure types, and frequency as well as the history of medications were determined. Also, clinical and biochemical evaluation and complete blood cell count were done on the day of admission. Age of 18 years old with one or more convulsive seizures within 24 hours were the eligibility criteria to participate in this study. Exclusion criteria were ages younger than 18, pregnancy and history of maternity, active hemorrhage or history of hemorrhage; history of blood infusion or PLTs; use of anticoagulant drugs prior to their admission; and chemotherapy, radiotherapy or bone marrow transplantation one month before

admission. Patients with medical, neurologic or psychological situations; and those who had a history of recent head trauma were also eliminated from the study.

Our study was approved by the “Ethics Committee of Shahid Beheshti University of Medical Sciences”.

Statistical Analysis

All statistical analyses were completed applying the SSPS version 16.0 (SPSS, Inc., Chicago, IL, USA). For analyzing categorical data, a chi-square test was used. To compare the numeric values, the independent t test was used. In order to detect a linear relationship between frequency of seizure and PVIs, Spearman correlation test was carried out. The values for each group are indicated as the mean±SD. The $p<0.05$ was considered statistically significant.

Results

In this study, 199 epileptic seizure patients, 73 (36.7%) females and 126 (63.3%) males, in total were included. The mean age of patients was 38.69 ± 20.11 years. The clinical and demographic characteristics of patients are reported in Table 1.

Among the 199 recorded ES episodes, 59 attacks (29.6%) were focal seizures and 140 (70.4%) were generalized convulsive seizures. To identify the possible influence of the type of seizure on platelet volume indices (PVIs), we measured the association among these variables. We found that levels of PLT were higher in focal seizure than in generalized convulsive seizures (254.44 ± 80.86 vs. 224.14 ± 76.29 ; $p=0.01$, respectively). There was a statistically significant difference between the type of seizure and MPV (9.51 ± 1.04 fL for focal seizure vs. 9.82 ± 1.10 fL for generalized seizure, $p=0.05$). However, no statistically significant difference was observed with PDW (12.18 ± 2.04 for focal seizure vs. 12.71 ± 2.06 for generalized seizure, $p=0.097$).

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Based on Spearman correlation test, a poor positive statistically significant correlation was observed between the frequency of seizure and PLT ($r: 0.1, p=0.03$) in epileptic seizure.

However, no statistically significant correlation was found between other variables.

Table 1: Characteristics of the patients based on type of seizure.

Variable	Total (199)	Focal onset (59)	Generalized onset (140)	P- value
Age(year)	38.69±20.11	36.20±21.12	39.74±19.66	0.2
Sex, n (%)				
Female	73(36.7)	22(30.1)	51(69.9)	0.9
Male	126(63.3)	37(29.4)	89(70.6)	
Frequency of seizure	2.13±1.06	2.22±0.94	2.09±1.10	0.4
Laboratory parameters				
Platelet count ($\times 10^3/\mu\text{l}$)				
<100	233.12±78.68	254.44±80.86	224.14±76.26	0.01
100-300	2(1%)	0(0%)	2(100%)	
>300	159(79.9%) 38(19.1%)	44(27.7%) 15(39.5%)	115(72.3%) 23(60.5%)	
MPV(fl)				
<7.7	9.73±1.09	9.51±1.04	9.82±1.10	0.05
7.8-11.2	7(3.5%)	2(28.6%)	5(71.4%)	
>11.3	175(87.9%) 17(8.5%)	54(30.9%) 3(17.6%)	121(69.1%) 14(82.4%)	
PDW (%)				
<9	12.56±2.06	12.18±2.04	12.71±2.06	0.09
9-17	5(2.5%)	2(40%)	3(60%)	
>17	187(94%)	56(29.9%)	131(70%)	
PCT (%)				
	0.17±0.05	0.17±0.05	0.17±0.04	0.05

Discussion

In the current study, we achieved novel insights into the role of PVIs in epileptic seizures pathophysiology. We demonstrated that MPV increases in generalize seizure patients. Our findings suggest that increasing the levels of MPV in these patients exacerbates the epileptic seizures, in terms of frequency. In the current study, we did not utilize a group as a control since our intention was to inspect the association between the seizure type (focal versus generalize) as well as seizure frequency and PLT, MPV, PDW, and PCT levels.

Increasing clinical evidence is highly in favor of the role of inflammation in human epilepsy pathophysiology. The results of both clinical and neuropathological studies suggest that inflammation has a pivotal role in seizure

disorders which do not have any infectious or immune-mediated etiology (7). Many clinical surveys have detected increased serum or CSF levels in mediators of inflammation (e.g. cytokines such as Interleukin (IL)-6, Tumor Necrosis Factor (TNF)- α and IL-1 β and the IL-1 receptor antagonist (4). These studies have revealed several critical aspects of the inflammatory process (7, 8): 1. Inflammation is induced by recurrent seizures; 2. Loss of neuronal cells due to seizures is not an essential event for inflammation to occur, though liberation of proinflammatory cytokines can lead to cell loss (9), where these dying cells may prolong inflammation; 3. Brain inflammation following seizure is an enduring process and can remain days after the end of seizures (10); 4. In epilepsy models made by status epilepticus, traumatic brain

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injury or extended febrile seizures, inflammation happens prior to the inception of spontaneous seizures and this may suggest that uncontrolled inflammation may have a role in the development of the epileptic process (11). Endothelial cells of the brain blood barrier (BBB) can also induce inflammatory mediators, suggesting that inflammation could spread from glial cells to the brain microvasculature. Additionally; during the epileptogenesis phase, the release of inflammatory mediators could occur by macrophages and granulocytes from the brain from the blood (11). A major constituent of the inflammatory reaction is platelet indices where the intensity of inflammation is associated with the size of platelet (12). As an indicator of platelet function, The role of MPV has been explored in correlation with various inflammatory disorders, such as cystic fibrosis, Systemic Lupus Erythematosus (SLE), rheumatoid arthritis, FMF, meningitis, Behçet's disease, and febrile seizures (12, 13). According to the scientific documentations, numerous studies have shown the association of low or high MPV indices with acute or chronic inflammatory disorders (14-16). Although the usefulness and validity of PDW in clinic have not been established yet, some scientists insist on using PDW in inflammatory disorders. Herve et al reported that the PDW represents the variability in PLT size, regarding the activity of the number of PLT, the PDW may potentially provide more information than MPV does (17).

MPV values were previously evaluated only in children with FS, while the relationship between the type of seizure and PVIs had not been assessed before. Ozaydin et al postulated that since epilepsy is an inflammatory natured brain disorder and hence MPV drops in inflammatory conditions, MPVs in complex FS should be lower than simple FS (18). The drawback of this research was that in spite of the large sample size, it was a retrospective study. Conversely, Çocuklarda et al found that

with less than 1 hour of seizure in children diagnosed with complex FS, MPVs and PDWs were significantly higher than in simple FS (3). This finding suggested that in the complex FS, during the acute phase of diseased brain activity, more inflammatory changes happen. A previous study investigated the MPVs levels in children with FMF diagnoses, and compared it based on attack and attack-free periods. The results showed that during acute attacks, as the disease severity score increased, the MPV values in children with FMF were escalated (19). In line with this investigation, we observed lower number of PLT count and PCT elevated MPV values in generalized seizure group; so we speculated that for the compensation of the decreased number of platelets, the bone marrow quickly produces thrombocytes. These new thrombocytes are larger in mean size which may be a potential reason for the increase in MPV. Accordingly, due to secreted chemokines, cytokines, and other inflammatory mediators, new produced platelets are larger in size and show more reactivity. MPV was higher in generalized convulsion seizures, therefore; we thought that the increased MPV shows the growing intensity of inflammation process in generalize seizure group.

Conclusion

In conclusion, our survey demonstrated that there were significantly increased levels of MPV in generalized convulsion seizures. These results favorably suggest that the higher the MPV values are, the more intense the inflammation process in GCS is.

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Conflicts of Interest

The Authors declare no conflicts of interest.

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This study was approved by the "Ethics Committee of Shahid Beheshti University of Medical Sciences (Tehran, Iran)"; Registration Code: IR.SBMU.RETECH.REC.1396.416.

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