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Review

Clinical Utility of Red Cell Distribution Width in Alcoholic and Non-alcoholic Liver Cirrhosis

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A B S T R A C T

Red blood cell distribution width (RDW) is a measure of the variation of red blood cell width that is reported as a part of standard complete blood count. Red blood cell distribution width results are often used together with mean corpuscular volume (MCV) results to figure out mixed anemia. The aim of our study was to compare the values of RDW in alcoholic and non-alcoholic liver cirrhosis and to determine if RDW follows the severity of disease according to Child-Pugh score. We retrospectively analyzed 241 patients (176 men and 65 women) with liver cirrhosis and anemia, defined as a hemoglobin value <130 g/L in men and <120 g/L in women, which were hospitalized in our Division in a period between 2006 and 2008. Patients were divided in two groups; in first were patients with alcoholic liver cirrhosis, and in second with non-alcoholic cirrhosis. Severity of disease was determined according to Child-Pugh score. Red blood cells distribution width Normal reference range is 11–15%. Alcoholic liver cirrhosis had 204 patients (85%) while non-alcoholic cirrhosis had 37 patients (15%). In group of alcoholic cirrhosis the average RDW was 16.8%. In relation to severity of disease the average RDW for Child-Pugh A was 16.80%, for Child-Pugh B was 16.92%, for Child-Pugh C was 17.10%. In the group of non-alcoholic cirrhosis the average RDW was 16.73% and in relation to severity of disease for Child-Pugh A was 16.25%, for Child-Pugh B 17.01% and for Child-Pugh C was 16.87%. We didn't find statistically significant difference of RDW between alcoholic and non alcoholic cirrhosis ($p>0.05$) and we didn't proved any statistically significant increase of RDW in relation to severity of disease in group of alcoholic cirrhosis ($p=0.915$) nor in group of patients with non-alcoholic cirrhosis ($p=0.697$). Our study showed that RDW had not any clinical value in differentiation of anemia neither in alcoholic and non-alcoholic liver cirrhosis nor in severity of liver disease.

Key words: *red blood cells distribution width, alcocholic cirrhosis, non alcocholic cirrhosis, severity of disease*

Introduction

Anemia is a frequent complication in patients with cirrhosis and it occurs in 40–70% of patients with this disease[1]. It is defined as the value of hemoglobin or hematocrite below the lower limit of normal values. RDW (red cell distribution width) is a standard laboratory parameter of the red blood count (RBC). It represents a measure of RBC volume variation and distribution in the given blood sample. In healthy people the RBC volume variation is minimal, but in many types of anemia a difference in the volume (or size) of individual red blood cells can be observed. The differences measured are expressed with RDW. Conditions that lead to greater size difference of the individual erithrocytes will be reflected in increased values of RDW[2]. The usefulness of RDW was studied in many pathological conditions such as the inflammatory bowel disease[3], myocardial infarction, heart failure, and renal failure[4,5]. Additionally, RDW has been also studied in pregnancy[6] and in the colorectal cancer[7]. The role of this simple parameter hasn't been evaluated in the liver cirrhosis. In this study we evaluated a possible difference of RDW values between the groups of patients with alcocholic and non alcocholic liver cirrhosis and determined a possible correlation between RDW and the severity of liver cirrhosis.

Patients and Methods

Beginning from January 2006 until December 2008 we surveyed a retrospective data analysis on 241 patients suffering cirrhosis of the liver (176 male: 65 women). We divided the patients into two groups. The first group

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comprised of 204 patients with liver cirrhosis of alcoholic etiology and in the second there were 37 patients with other non-alcoholic etiology. In the group of non-alcoholic cirrhosis, hepatitis B was found in 12 patients and hepatitis C in 25 patients. Severity of the disease was determined by Child-Pugh score. We defined anemia according to hemoglobin values below 130 g/L in men and 120 g/L in women[8]. We measured RDW using the automatic analyzer (Bayer Technicon H-3 RTC, Bayer Diagnostics GmbH, Munich, Germany). Normal range is 11–15%. In this study we used Medcalc 9th Edition. All values are expressed as their means ± SD. Statistical significance of continuous variables between the groups was analyzed with one-way analysis of variance (ANOVA) and proportions were evaluated using test for proportions. The value of $p<0.05$ was considered statistically significant.

Results

Alcoholic etiology was found in 204 patients (85%) and non-alcoholic etiology of liver cirrhosis was found in 37 patients (15%). Mean RDW value was 16.8% in patients with alcoholic cirrhosis and 16.7% in the group with non-alcoholic etiology. Table 1 shows demographic characteristics and the severity distribution according to Child-Pugh score. There was no significant age difference between alcoholic and non-alcoholic liver cirrhosis. The majority of patients with alcoholic liver cirrhosis were men (three times more than women, $p=0.63$). We didn't find the difference between two groups in occurrence of esophageal varrices ($p=0.396$) and hepatic encephalopathy ($p=0.684$). According to Child-Pugh score the majority of patients were most severe and there was no statistical difference in any of severity categories (A, B or C) considering the same score. In Table 2 we analyzed laboratory findings of mentioned groups. Patients with alcoholic etiology of liver cirrhosis had significantly lower values of RBC and longer prothrombin time (PT) then non-alcoholic group. Table 3 represents laboratory findings after we stratified patients into three severity groups according to Child-Pugh score, but regardless to etiology of liver disease. As the disease was classified to be more severe according to Child Pugh score, RBC values gradually dropped ($p<0.001$) and MCV were significantly higher ($p<0.001$). Even though, the average mean value of RDW in patients with liver cirrhosis is higher than in healthy population, mean RDW value in the population of patients with alcoholic cirrhosis is not statistically different compared to patients with non-alcoholic etiology ($p=0.883$). We didn't find any significant difference of the mean RDW values in relation to the severity of illness according to Child-Pugh score, or between two groups of patients regarding their etiology (alcoholic cirrhosis $p= 0.915$, non-alcoholic liver cirrhosis $p=0.697$).

TABLE 1
CHARACTERISTICS OF PATIENTS WITH LIVER CIRRHOSIS

	Liver cirrhosis (n = 241)	Alcoholic liver cirrhosis(n=204)	Non-alcoholic liver cirrhosis(n=37)	p-value
Age (in years)	62.50 ±11.11	62.49±10.26	62.57±15.43	p=0.967
Gender (M:F)	176:65 (73%:27%)	155:49 (76%:24%)	21:16 (57%:43%)	p=0.063
Child-Pugh score				
A	45 (18.67%)	34 (16.67%)	11 (29.73%)	p=0.100
B	77 (31.20%)	65 (31.95%)	12 (32.43%)	p=0.894
C	119 (49.57%)	105 (49.37%)	14 (37.84%)	p=0.266
Oesophageal Varrices	46.44%	45.02%	54.05%	p=0.396
Encephalopaty	16.02%	17.02%	9.52%	p=0.684

TABLE 2
LABORATORY FINDINGS IN PATIENTS WITH LIVER CIRRHOSIS

	Liver cirrhosis	Alcoholic liver cirrhosis	Non-alcoholic liver cirrhosis	p-value
RBC (10^{12})	3.13±0.76	3.27±0.74	3.57±0.82	p=0.028
Hemoglobin (g/L)	102.23±25.12	101.82±24.23	107.15±28.24	p=0.132
MCV(fL)	91.9±10.8	92.4±10.8	88.7±10.2	p=0.052
RDW(%)	16.8±0.2	16.8±3.2	16.7±2.2	p=0.889
Platelets(10^9)	131.66±98.10	131.60±100.45	132.03±85.45	p=0.981
Albumine(g/L)	37.36±10.05	37.21±9.66	38.22±12.33	p=0.705
PT	0.56±0.18	0.54±0.16	0.69±0.23	p=0.001
Bilirubin (μmol/L)	112.02±133.23	121.98±140.12	v 58±66.64	p=0.054

TABLE 3
LABORATORY FINDINGS IN PATIENTS AFTER STRATIFICATION ACCORDING TO CHILD-PUGH SCORE

	Child-Pugh Score			
	A	B	C	p-value
RBC (10^{12})	3.76±0.76	3.26±0.73	3.19±0.72	p<0.001
Hemoglobin (g/L)	108±26.7	99.8±25.0	101.3±23.2	p=0.178
MCV (fL)	85.97±10.69	91.43±10.18	94.35±10.40	p<0.001
RDW (%)	16.64±3.77	16.47±2.49	17.07±3.16	p=0.382
Platelets (10^9)	135.06±93.38	139.87±96.42	118.75±78.52	p=0.225
Albumine (g/L)	40.86±9.27	38.31±9.12	35.50±10.70	p=0.112
PT	0.71±0.18	0.62±0.16	0.47±0.15	p<0.001
Bilirubin (μmol/L)	60.15±88.60	72.00±79.15	158.76±159.96	p=0.001

Discussion and Conclusion

Anemia is a common complication in patients with liver cirrhosis. There are many mechanisms that could simultaneously, in different degree, affect the development of anemia in cirrhotic liver. Etiology of macrocytic anemia include nutritional deficiency, deficiency of vitamin B12 and folic acid[9]. Furthermore, in 11 to 55% of patients with liver cirrhosis hypersplenism occurs leading to hemolytic anemia. Hemolysis of red blood cells contributes to structural abnormalities of erythrocyte membrane and lipid metabolism disorders of the liver. In patients with alcoholic cirrhosis acetataldehid, metabolite of alcohol, depression affects erythropoiesis in the bone marrow[10,11,12]. Continuous blood »steal« of the splanchnic blood system decreases the renal blood flow and increases reapsorption of the fluid leading to hypervolemia and decrease in RBC and hematocrite[12,13]. Microcyte anemia's is caused by iron deficit or due to the reduced protein liver production that includes ferritine and transferrine. Additional causes of microcyte anemia are acute or chronic gastrointestinal hemorrhage[14,15]. Patients with alcoholic etiology of liver disease showed significantly lower values of RBC and longer PT. They also showed lower values of hemoglobin and higher values of MCV than non-alcoholic group. This observation could be explained by the larger number of more severe patients placed in the group of patients with alcoholic etiology of liver cirrhosis, although we didn't find a true significant difference between two groups (49.37%: 37.84, p>0.005). Higher mean MCV value in alcoholic cirrhosis is also related with the alcohol consumption. In order to properly evaluate this thesis we should have made another paired t-test analysis of MCV values before and after cessation of alcohol consumption. With the progression to a more severe Child-Pugh score we can notice a greater raise in mean MCV value. This could be explained by several mechanisms, but mainly by hypersplenism induced hemolytic anemia and disorders of lipid metabolism. Significant longer PT and higher bilirubin levels can be explained by the mere fact that PT and bilirubin are constituents of Child-Pugh score. Thus, there is an already established »good« correlation between this two variables and abovementioned score. Red distribution width in our patients did not prove useful in distinguishing alcoholic from non-alcoholic cirrhosis. Possible reasons might be in the fact that causes of anemia and subsequent changes in RDW in cirrhotic liver are, regardless of etiology, different and many. In healthy people anemia is usually adequately compensated by increased erythropoesis and reticulocyte production that leads to transient increase in RDW value. In patient with cirrhotic liver, the degree of reticulocytosis is additionally orchestrated by inhibition of colony stimulating factors (CSF) in the bone marrow. As a result, a different level of reticulocyte activation and subsequently varying degree of RDW values occurs[14,15]. RBC status and RDW itself are in direct dependence between compensatory mechanisms of erythropoiesis and reticulocyte production on one side, and its inhibition in cirrhotic patients, with known and unknown mechanisms. We didn't demonstrate a statistically significant difference of the mean RDW values with the respect to the degree of severity according to Child-Pugh score. The possible reason is that Child-Pugh score represents a sum of five variables, by which we indirectly determine a one-year and five-year mortality of cirrhotic patients. Instead of using Child-Pugh score, better results would be yielded if we have tried to directly correlate the impact of RDW as an independent predictor on disease outcome, especially mortality and incidence of certain complications of the liver disease.

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KLINIČKA KORIST ŠIRINE DISTRIBUCIJE ERITROCITA U BOLESNIKA S ALKOHOLNOM I NEALKOHOLNOM CIROZOM JETRE

S A Ž E T A K

Širina distribucije eritrocita (engl. red cell distribution width, RDW) je mjera koja pokazuje stupanj odstupanja volumena eritrocita i predstavlja standardni parametar kompletne crvene krvne slike. RDW se često koristi u kombinaciji s mjerom volumena prosječnog eritrocita (engl.mean corpuscular volume, MCV) kako bi se utvrdio uzrok anemije različtite etiologije. Cilj naše studije je bio usporediti vrijednosti RDW u bolesnika s alkoholnom i nealkoholnom cirozom jetre te utvrditi da li vrijednosti RDW-a prate stupanj težine bolesti prema Child-Pugh bodovnom sustavu. Retrospektivno smo analizirali 241 pacijenta (176 muškraca i 65 žena) s cirozom jetre i anemijom, koju smo definirali kao vrijednost hemoglobina <130 g/L za muškarce, odnosno <120 g/L za žene, a koji su bili hospitalizirani tijekom perioda od 2006–2008. na našem odjelu. Pacijente smo podijelili u dvije grupe, na one sa alkoholnom i nealkoholnom etiologiji bolesti. Težinu bolesti smo odredili prema Child-Pugh bodovnom sustavu. Normalna referentna vrijednost RDW-a je 11–15%. Alkoholnu cirozu je imalo 204 pacijenata, a nealkoholnu 37 pacijenata. U grupi alkoholnih ciroza prosječni RDW je bio 17%. U odnosu na težinu bolesti, prosječan RDW za Child-Pugh A je bio 16,80%, Child-Pugh B 16,92%, Child-Pugh C 17,10%. U grupi nealkoholne ciroze prosječni RDW je bio 16,73%, a u odnosu na težinu bolesti je bio za Child-Pugh A 16,25%, Child-Pugh B 17,01%, Child-Pugh C 16,87%. U našoj studiji nismo dokazali statistički značajnu razliku u vrijednostima RDW – a kod alkoholne i nealkoholne ciroze ($p>0,05$) i nismo pronašli statistički značajnu promjenu RDW-a u odnosu na težinu bolesti u grupi bolesnika s alkoholnom cirozom ($p=0,915$) i u grupi bolesnika s nealkoholnom cirozom ($p=0,697$). U našoj studiji pokazali smo da RDW nije koristan parametar za razlikovanje alkoholne od nealkoholne ciroze jetre te ne korelira sa stupnjem težine bolesti.