

Changes in Blood Viscosity and Erythrocyte Indices in Chronic Heroin Abusers

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Whole blood viscosity (WBV) and hematometric indices of erythrocytes as red blood cell count (RBC), mean erythrocyte volume (MCV), hemoglobin (HGB), hematocrit (HCT), mean hemoglobin content of erythrocytes (MCH), HGB/HCT values (MCHC) and red blood cell distribution width (RDW) have been studied in a group of 15 chronic opioid addicts under methadone maintenance therapy with mean age 26.53 ± 7.34 years. WBV elevation and changes in MCV, HGB, HCT, RDW were found in intravenous drug users compared to healthy individuals as well as RBC decreased leading to an increase in MCH and MCHC values. Correlation analysis suggested that the correlation among the RBC, HGB, HCT and WBV was the closest. Heroin macrocytosis (heroin macrocytic anemia) was established, related with the increased RDW in chronic heroin abusers. The results are in accordance with data revealing abnormal effects of alcohol and other drugs on whole blood rheology and hematometric/morphometric characteristics of erythrocytes.

Key words: whole blood viscosity, erythrocyte hematometric indices, chronic heroin abusers, heroin macrocytosis (heroin macrocytic anemia).

Introduction

The current circulating opiate concentrations in the blood and the hematometric indices of the erythrocytes (RBC, HGB, HCT, MCV, MCH, MCHC and RDW) are provided by blood and/or by plasma measurements. Hemorheological parameters and their relationships with the hematometric indices, influencing on blood rheology have not been studied yet despite the importance of the knowledge for better understanding the blood flow, blood cells' and blood vessels' abnormalities, observed in chronic heroin abusers [2, 8, 9]. The aim of the study is to investigate the changes, resulting under the effect of heroin on WBV and erythrocyte hematometric indices in heroin abusers under methadone maintenance therapy.

Materials and Methods

Whole blood heparinized samples from 15 chronic (HIV-seronegative) heroin addicts (3 female and 12 male; mean age 26.53 ± 7.34 years) under methadone maintenance therapy, obtained from the National Center for Addictions in Sofia have been studied. Blood samples were collected with heparinized tubes and rheological measurements were completed within 3 hours after sample preparation. Whole blood viscosity (WBV) was measured using a rotational viscometer Contraves Low Shear 30 (Switzerland) with the standard measuring system MS 1/1 at a steady flow over a shear rate range of 0.0237 s^{-1} to 128.5 s^{-1} at temperature 37°C . The results have been compared with a control group of 19 healthy subjects (9 female and 10 male; mean age 34.84 ± 4.06 years). The hematometric indices of erythrocytes (red blood cell count (RBC), mean erythrocyte volume (MCV), hemoglobin (HGB), hematocrit (HCT), mean hemoglobin content of erythrocytes (MCH), HGB/HCT ratio (MCHC) and red blood cell distribution width (RDW)) were analyzed by automated cell counter. Student's t-test for determining differences in the mean values of the examined parameters at level of significance $p < 0.05$ was used. Relationships between the WBV and the erythrocyte parameters were evaluated using the simple correlation coefficient (r). Statistical analysis was done on MATLAB 6.5.

Results and Discussion

It was found that the mean whole blood viscosity values of the investigated group of heroin abusers were elevated (31.61 at mean shear rate 28.47 s^{-1}) compared to that of healthy persons (21.53) over the whole shear rate range (Table 1). These elevations were statistically significant at higher shear rates range (20.4 s^{-1} , $p = 0.1$; 94.5 s^{-1} , $p = 0.05$). At low shear rates the standard deviations were more than 50% of the mean. No significant difference was found in RBC between the control group and that of heroin abusers, although the red blood cells number of heroin addicts was lower (Fig. 1). It was determined that there are significant differences between HGB ($p < 0.05$), MCV ($p < 0.05$) and RDW ($p < 0.005$) in erythrocytes of normal individuals and heroin addicts: increased values of MCV and RDW in heroin addicts and decreased HGB content in their erythrocytes were obtained (Figs. 2, 3 and 4). HCT was insignificantly decreased in chronic heroin users (43.37 ± 4.04) compared to the control samples (44.37 ± 3.97). The values of MCH and MCHC were increased in heroin addicts (MCH = 51.79 ± 8.57 ; MCHC = 355.84 ± 99.3), although statistically insignificant compared to the controls (MCH = 29 ± 1 ; MCHC = 330 ± 10). Linear correlation analysis shows that WBV in intravenous drug users correlates positively ($p < 0.05$) only with the changes in the hematometric indices of erythrocytes – RBC, HGB and HCT. The simple correlation coefficient (r) in heroin addicts varies between $r = 0.5 - 0.6$ at different shear rates (Fig. 5). RBC of drug users was decreased leading to an increase in MCH and MCHC values (negative relationship – $p < 0.05$).

The elevation of WBV at low as well as at high shear rates suggested that RBC aggregation and rigidity are probably increased, and the latter one is statistically significant. The observed decreased RBC count and blood HGB levels in heroin addicts support our previous and other data [1, 6, 8, 10] for high prevalence of anemia among chronic opioid users.

It is well known fact [4] that a low hemoglobin level is associated with an increase in RDW. We supposed that increased RDW in chronic heroin abusers is in accordance with their low hemoglobin levels. Increased RDW was also reported in cases of nicotine and alcohol abuse [7]. RDW is a coefficient of variation of mean RBC volume and is considered as a biomarker for the nutritional status of patients (vitamin B_{12} , folic acid and iron deficiency [7]). Having in mind that elevated RDW has been obtained only in pathological

Table 1. Whole blood viscosity at different shear rates in healthy individuals and drug abusers

Shear rates (s ⁻¹)	Whole Blood Viscosity (mPa.s)	
	Healthy subjects (n=19)	Drug abusers (n=15)
0.0237	75.11 ± 42.81	113.96 ± 75.68
0.0596	46.22 ± 21.88	72.09 ± 55.02
0.1102	37.56 ± 16.46	61.21 ± 41.77
0.512	22.78 ± 9.27	30.41 ± 14.64
1.285	16.98 ± 7.44	21.76 ± 7.84
5.96	9.73 ± 4.07	11.98 ± 3.23
11.02	7.72 ± 2.02	9.84 ± 2.43
20.04	6.48 ± 1.49	8.28 ± 1.81*
51.2	5.2 ± 0.89	6.53 ± 1.25**
94.5	4.61 ± 0.71	5.83 ± 1.1**
128.5	4.46 ± 0.77	5.83 ± 0.99

Data represent mean value ± SD; * p<0.1, ** p<0.05

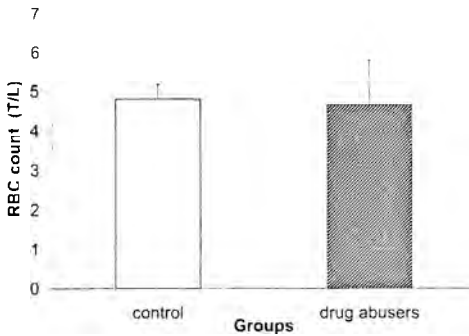


Fig 1. Red blood cell count (RBC) in healthy subjects (n=19) and in chronic heroin addicts (n=15)

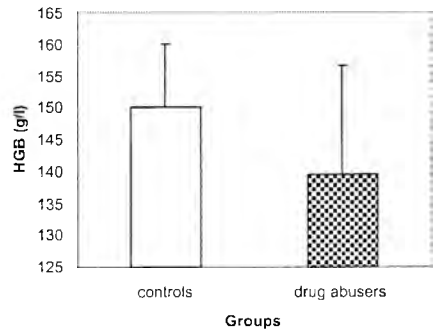


Fig 2. Hemoglobin (HGB) in healthy subjects (n=19) and in chronic heroin addicts (n=15)

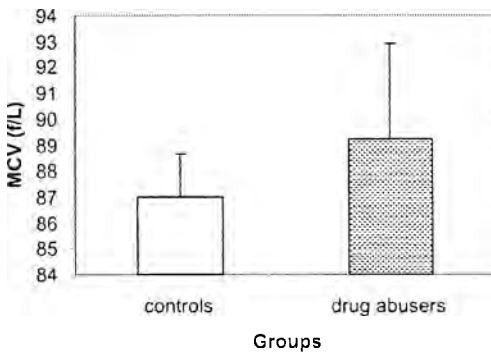


Fig 3. Mean erythrocyte volume (MCV) in healthy individuals (n=19) and in chronic heroin addicts (n=15)

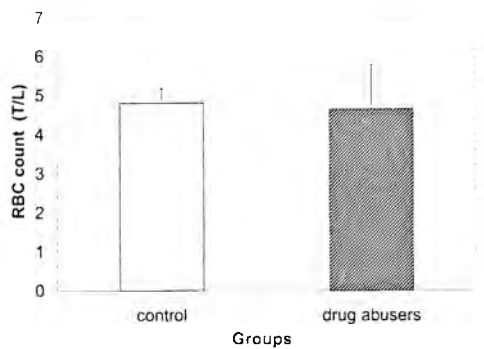


Fig 4. Red blood cell distribution width (RDW) in healthy individuals (n=19) and in chronic heroin addicts (n=15)

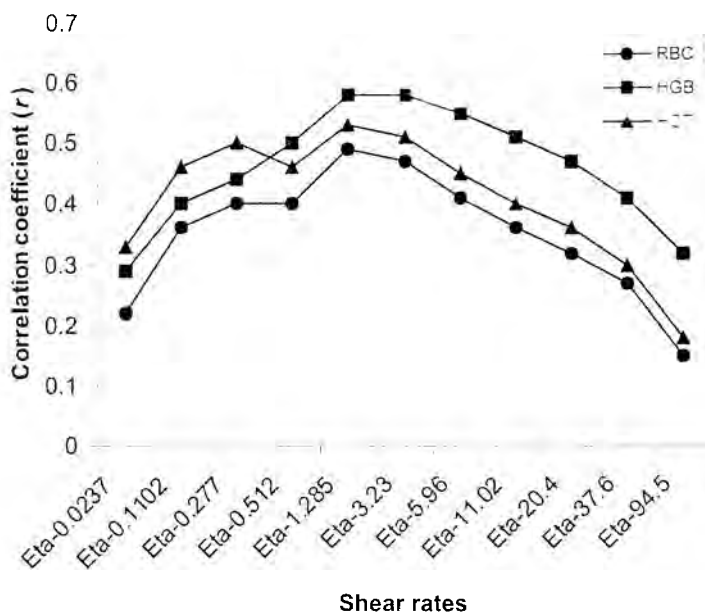


Fig 5. Correlation coefficient (r) between RBC, HGB, HCT and WBV (at different shear rates) in chronic heroin addicts ($n=15$)

states (e.g. in both — micro- and hypochromic anemias — [4]), we suppose that increased RDW as well as lower RBC and HGB levels, could indicate suboptimal nutritional status in heroin abusers. In addition, changes of the erythrocyte membrane properties, enzyme activities and the level of lypoperoxides were also determined among chronic opioid users [2, 9]. The low HCT values in the group of heroin addicts confirm the observed data in mice, experimentally treated with a synthetic analogous to heroin — buprenorphine [1].

We hypothesize that the changes in WBV and in the hematometric indices of erythrocytes (RBC, HGB, HCT, MCV, MCH, MCHC and RDW) of chronic heroin abusers could be associated with heroin-induced negative effects on early bone marrow hematopoiesis (erythropoiesis — [7]). Opioids, shown originally to bind to specific receptors in the brain and on red blood cells as well [8] influenced early bone marrow progenitors affecting their proliferation/differentiation and hematopoietic colony formation [5].

Our data show that elevated MCV of erythrocytes — heroin macrocytosis, is one of the principle red blood cell morphometric abnormalities in heroin addicts. Similar results (increased MCV) were observed in alcohol abusers in state of excessive ethanol consumption and were defined as “alcoholic macrocytosis” [3, 7].

We suggest that further detailed studies will evaluate whether the increased RDW and MCV as well as lower RBC, HGB and HCT levels, observed by us in chronic heroin abusers, result in heroin macrocytosis (heroin macrocytic anemia). On the other hand, RDW and MCV could be simultaneously used as sensitive quantitative indicators in medical diagnostics for establishing the possible origin of heroin macrocytic anemia (as it is pointed out by Romero Artaza et al. [4] for early diagnostics of microcytic and hypochromic anemias). The results obtained could be also of clinical usefulness optimiz-

ing the treatment of some complications associated with chronic drug abuse, such as hypoxemia, major ischemic syndrome, circulatory disturbances, hypertension, cardiac arrhythmia, acute myocardial infarction.

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