

RESUMOS DOS ARTIGOS PUBLICADOS NA REVISTA PORTUGUESA DE HEMORREOLOGIA E JOURNAL OF BLOOD RHEOLOGY

1. Some Abnormalities of Red Cell Membranes in Essential Hypertension

Carlota Saldanha, J. Braz-Nogueira, Sandra Marques, Carlos Moreira, J. Nogueira da Costa, J. Martins e Silva

Rev. Port. Hemorreol. 1987, 1(1):3-8.

The (Ca^+ , Mg^{2+}) ATPase activity, the membrane fluidity, the total phospholipid contents and the individual phospholipids, phosphatidylcholine (PC), lysophosphatidylcholine (LPC), phosphatidylethanolamine (PE), phosphatidylinositol (PI) and sphingomyelin (SM) were determined in red blood cell membranes of 54 patients with essential hypertension (31 treated, THP, and 14 untreated, UHP) and compared with 25 apparently healthy and normotensive subjects. The total membrane phospholipids were significantly reduced in both groups ($p < 0.01$ in UHP and $p < 0.001$ in THP). The SM, LPC and PI levels were significantly higher than the control group ($p < 0.002$, $p < 0.005$ and $p < 0.01$, respectively). However, PE was significantly reduced ($p < 0.01$) in the UHP. SM and PE were significantly reduced ($p < 0.001$) and increased ($p < 0.03$), respectively in erythrocyte membrane in THP. A significant increase of Ca^{2+} , Mg^{2+} ATPase ($p < 0.05$ in UHP and $p < 0.001$ in THP) and of fluorescence polarization ($p < 0.001$ for both groups) was observed, when compared with the controls. These results may confirm the existence of localized membrane lesions in red cells of hypertensive subjects. These abnormalities could explain some rheological disturbances that have been associated with primary hypertension.

2. Red Cell Deformability and Other Rheological Abnormalities in Essential Hypertension

J. Nunes, J. Braz-Nogueira, Amália Nunes, J. Nogueira da Costa, J. Martins e Silva

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In 45 essential hypertensive (RHT) patients (31 treated and 14 untreated) and 25 normotensive controls (NC), filterability index (F.I.) plasma viscosity (P.V.), fibrinogen (Fbg) and 2,3-DPG were determined. EHT treated group presented a F.I. (mean: 20.35 ± 12.28) with a small difference ($p < 0.03$) in relation to the normotensive controls (mean: 13.69 ± 2.7) and to the EHT untreated subjects (mean: 12.92 ± 1.69). Between the latter two groups there was no significant difference. P.V. levels showed a marginal difference between treated and normal controls, as well as between treated and non-treated patients. Fibrinogen levels studied in all these groups did not show significant differences. However, there was a slight difference between treated (mean: 419 ± 119 mg/100ml), not treated (mean: 461 ± 86 mg/100ml) and normotensive control (mean: 442 ± 128 mg/100ml) group. In EHT untreated there was a highly significant correlation between systolic blood pressure and P.V. ($r = 0.74$; $p < 0.01$) and Fbg ($r = 0.80$, $p < 0.001$). In all 45 hypertensive patients there was a highly significant correlation between P.V. and Fbg. Concerning 2, 3-DPG, there was no difference between the three groups.

3. Evaluation of the Effects of Starting Haemodialysis on Some Haemorheological Parameters in Patients with End-Stage Renal Failure

José M. V. Barbas, L. Cardoso, C. Saldanha, J. Martins e Silva
Rev. Port. Hemorreol. 1987, 1(1):25-28.

In this study we evaluated some haemorheological parameters in a group of 7 patients, 4 men and 3 women, 28 to 70 years old (mean age 51.8 ± 16.5 years), with end-stage chronic renal failure, a few days before they started chronic haemodialysis and 1 and 3 months afterwards, in order to evaluate any changes produced by haemodialysis treatment. There were no significant differences for the values of erythrocyte aggregation, red cell filterability, erythrocyte acetylcholinesterase or fibrinogen, measured before and 1 and 3 months after the beginning of chronic haemodialysis. The plasma viscosity increased significantly after the beginning of haemodialysis and the same happened with haemoglobin concentration.

4. Haemorheology, Capillary Microscopy and Oxygen Transport in Scleroderma Patients

J.P. Freitas, J. Nunes, L. Cardoso, R. Martins, A.M. da Silva, J. Martins e Silva
Rev. Port. Hemorreol. 1987, 1(1):29-32.

In 10 patients with scleroderma (types I, II and III of Barnett) confirmed by clinical, biological and functional examination, significant alterations on the filterability of whole blood fibrinogen and α_2 -macroglobulin were observed. A vascular areas and megacapillaries were the more frequent alterations in naifold capillary microscopy. A detected right shift of the oxygen dissociation curve expressed by an increased P50, might suggest that rheological phenomena and capillary disorders contribute to the pathogenesis of scleroderma.

5. Blood Rheology and Noenzymatic Protein Glycosylation in Diabetic Patients

C. Saldanha-Proença, J. Martin-Martins, J.P. Freitas, C. Santos Moreira, J. Nunes, P. Souza-Ramalho, J. Martins e Silva
Rev. Port. Hemorreol. 1987, 1(2):67-73.

Metabolic control, plasma viscosity, erythrocyte filterability and retinopathy were assessed in a group of 69 diabetic subjects - both, type I (IDDM-Insulin Dependent Diabetes Mellitus) and type II (NIDDM-Non Insulin Dependent Diabetes Mellitus) - and compared to 20 normal controls. Diabetic patients were in a state of poor metabolic control with gross abnormalities of blood rheology; also vascular disease was highly prevalent. Abnormal blood rheology was not dependent on short or long term metabolic control; only those factors related to plasma viscosity seemed to influence the severity of retinopathy.

6. Haemorheological Changes in Behçet's Disease

Sousa-Ramalho P., Santos M.D., Martins R., Freitas J.P., Cardoso L., Pinto J., Saldanha C., Martins e Silva J.
Rev. Port. Hemorreol. 1987, 1(2):89-94.

Twenty subjects with Behçet's disease (11 male and 9 female) of mean age of 35.4 ± 12.72 years were studied and in 2 cases followed during various relapses. Routine general, clinical and laboratory tests were carried out. Complete ophthalmological investigations were undertaken including biomicroscopy and fluorescein angiography of the retina. Blood viscosity parameters such as haematocrit, haemoglobin, red cell filterability index (Reid et al 1976), plasma viscosity (Leonard 1981) and erythrocyte acetylcholinesterase activity (Kaplan et al 1964) was investigated and compared to a normal control group of 22 subjects, age and sex matched. Abnormal red cell deformability and high plasma viscosity were recorded in some Behçet patients during the active periods of the disease. A significant increase of erythrocyte acetylcholinesterase (AChE) was also recorded in these patients.

7. Some Haemorheological Abnormalities in Glaucoma

P. de Souza-Ramalho, C. Saldanha, R. Martins, D. Santos, L. Cardoso, C. Moreira, J. Martins e Silva

Rev. Port. Hemorreol. 1987, 1(Supl. 1):61-64.

A restrict haemorheological and biochemical profile was evaluated on a heterogeneous group of 22 confirmed glaucoma patients (70♂ and 15♀) with ages between 44 and 80 years old. Patients with diabetes mellitus, hypertension or any other inflammatory pathology were excluded. The results of this preliminary study indicate a significant decrease and increase in patients values respectively of erythrocyte filterability ($p < 0.05$) and erythrocyte aggregation ($p < 0.05$) when compared with normal values. The activity of erythrocyte acetylcholinesterase is significantly increased ($p < 0.001$) in glaucomatous patients. These findings may suggest the interaction of abnormal haemorheological determinants on the mechanism of disease.

8. Haemorheological Factors in Brain Failure

Carlos Garcia, A.L. Cunha Monteiro, H. Beaumont, Carlos Moreira, Carlota Saldanha, J. Martins e Silva, Luís Cardoso

Rev. Port. Hemorreol. 1987, 1(Supl. 1):85-91.

Elderly patients frequently complain of poor memory, insomnia, dizziness, troubled concentration and apathy. Some authors claim that such combination of signs and symptoms should not be considered as an independent entity and that those patients should be classified as suffering from depression, dementia or stroke. In order to contribute to the clarification of this question, some blood haemorheological parameters (haematocrit, plasma viscosity, erythrocyte aggregation and red cell filterability) were determined in three groups of elderly individuals: 26 patients with depression, 15 patients with Alzheimer's disease and 24 apparently healthy controls. Plasma butyrylcholinesterase and erythrocyte acetylcholinesterase activities were also investigated in the three clinical groups. No significant differences were found between the three groups for the laboratory parameters studied.

9. Evolution and Prognostic Value of Plasma Viscosity in Ischaemic Heart Disease

L. Botas, D. Ferreira, L. Cardoso, A.I. Santos, J.P. Guimarães, C. Moreira, J. Monteiro, C. Brites, C. Ribeiro, J. Martins e Silva

Rev. Port. Hemorreol. 1987, 1(Supl. 1):93-108.

For about one year, the great majority of patients hospitalized in Sta. Maria's Hospital "Arsênio Cordeiro" Coronary Care Unit were studied. Twenty-seven had decompensated chronic heart failure (group A), 56 had unstable angina (group B) and 245 had acute myocardial infarction (group C). Definition of these groups followed the usual clinical electrocardiographic and enzymologic criteria. Plasma viscosity and fibrinogen were determined in the acute phase of the illness (1st to 4th days) and in the second week (8th through 10th days) after onset. In groups A and B plasma viscosity presented no significant differences, as compared to the control group, in the 1st day of the illness, as all along the studied period. In group C plasma viscosity was increased when compared to the control group in the 1st day and during all the period of study ($p < 0.001$). Fibrinogen showed no significant differences when compared to the control group, in the first day of illness in group A and B, but in group B fibrinogen was slightly increased in the 2nd and 8th days ($p < 0.05$). Plasma viscosity and fibrinogen were more elevated in group C after the first 48 hours in comparison to the other two groups. There was no difference between groups A and B as regards these two parameters. Plasma viscosity showed no differences in group C patients with or without acute heart failure, but fibrinogen was increased in these patients ($p < 0.001$). Plasma viscosity significantly increased in the first 3 days in patients of group C who died while still hospitalized. In conclusion, plasma viscosity and plasma fibrinogen were more elevated in the first days following a myocardial infarction, and their values may allow a selection of high risk groups, as regards complications during hospitalization. Patients with unstable angina and decompensated heart failure did not present any significant alterations during hospitalization.

10. Blood Rheology Study in Normal Humans After Diuretic Medication

C. Saldanha, L. Cardoso, C. Moreira, T. Quintão, J. Martins e Silva
Rev. Port. Hemorreol. 1988, 2(1):25-29.

Eleven healthy males with ages between 22 and 41 years were treated with two different diuretics (bendroflumethiazide plus spironolactone and hydrochlorothiazide plus amiloride) daily and orally for two weeks each association, with a washout period of thirty days between the two different diuretics. Haematocrit, plasma viscosity, erythrocyte aggregation and red cell deformability, and other biochemical parameters such as erythrocyte acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) were determined before and after the administration of each diuretic. Comparing the results obtained before and after both medications only the values of AChE showed significant difference.

11. Evaluation of Plasma Viscosity – A Comparison of two Methods

Luís Cardoso
Rev. Port. Hemorreol. 1988, 2(2):101-108.

Plasma viscosity was measured with a Harkness' viscometer and by the method of Leonard in eighty six samples of plasma from individuals undergoing haemorheological studies in our laboratory. Harkness' method was performed at 37°C and according to the recommendations of

the “International Committee for Standardization in Haematology”. The values of relative plasma viscosity obtained by Leonard’s method were corrected for water viscosity at 37°C. Statistical analysis of the results showed a good correlation between Harkness’ and Leonard’s methods ($r= 0.90$). A slight (mean: 0.027 ± 0.038) yet statistically significant difference ($p<0.001$) between both methods was observed. The usefulness of Leonard’s method in evaluating plasma viscosity when more accurate methods are not available is considered.

12. Determination of Some Haemorheologic Parameters in Patients with Chronic Renal Failure Being Submitted to Chronic Haemodialysis

J. Barbas, Carlota Saldanha, C. Moreira, L. Cardoso, Ana I. Santos, Teresa Quintão, J. Martins e Silva

Rev. Port. Hemorreol., 1988, 2(2):145-152.

Thirty-nine patients with chronic renal failure on haemodialysis have been investigated for some haemorheological parameters and were compared with 20 controls. Lower haemoglobin concentration ($p<0.001$), packed red cell volume values ($p<0.001$) and erythrocyte filterability ($p<0.001$) as well as higher plasma viscosity ($p<0.01$) and fibrinogen concentration ($p<0.001$) were observed in the patients group. These results may suggest that haemodialysis does not relevantly correct some of the most frequent blood rheologic abnormalities usually observed in human renal failure.

13. Haemorheological and Microcirculatory Changes in Systemic Lupus Erythematosus

Barbas J., Pinto Y., Cardoso L., Moreira C., Saldanha C.

Rev. Port. Hemorreol. 1989, 3(1):57-82

In the ESRD-HD group a decrease in red cell deformability was observed ($p<0.001$), as well as a significant increase in fibrinogen ($p<0.001$) and plasma viscosity ($p<0.001$). No significant differences have been found in red cell aggregation, α_2 -macroglobulin, α_1 -antitrypsin or acetylcholinesterase values. In the lipid profile of red cell membranes, significant elevation of phosphatidylethanolamine ($p<0.001$) and phosphatoylinositol/phosphatidylserine ratio ($p<0.01$) have been observed in ESRD-HD patients, as well as a significant reduction of phosphatidylcholine ($p<0.001$) and sphingomyelin ($p<0.001$). No significant differences have been obtained in cholesterol and total phospholipid contents, or in membrane microviscosity. Analysis of protein profiles in ESRD-HD patients revealed significant elevations of protein bands 2 ($p<0.01$) and 2.1 ($p<0.01$), and a decrease of bands 4.5 + 4.9 ($p<0.001$) and 5 ($p<0.05$). A positive correlation was evident between plasma viscosity and fibrinogen levels ($p<0.001$), and a negative correlation was found between butyrylcholinesterase and total red cell membrane phospholipid content ($p<0.01$). No correlations have been detected between red cell filterability index and such parameters as haematocrit, mean corpuscular volume, mean corpuscular haemoglobin concentration, lipid fluidity, lipid and protein profiles of red cell membrane, parathyroid hormone and enzymatic activity of acetylcholinesterase.

14. Haemorheological and Microcirculatory Changes in Systemic Lupus Erythematosus

Cardoso L.M., Pereira da Silva J.A., Santos A.I., Freitas J.P., Alves de Matos A.C., Moreira C., Viana-Queiroz M., Martins e Silva J.

Rev. Port. Hemorreol. 1989, 3(2):211-216.

Twenty five patients with systemic lupus erythematosus (24 females and 1 male, aged between twelve and fifty eight years) were studied for haemorheological and biochemical parameters (plasma viscosity, erythrocyte filterability and aggregation, α 2-macroglobulin, α 1-antitrypsin, fibrinogen, C-reactive protein, haemoglobin, haematocrit and erythrocyte sedimentation rate) and compared with a group of matched controls. Only 3 patients presented active disease. All patients were submitted to dermatological examination: 71% of the patients showed microhaemorrhages in nailfold capillary microscopy. For haemorheological parameters slight significant differences between patients and controls were observed. Those abnormalities may contribute to the systemic tissue injury and vascular occlusion events frequently presented by SLE patients.

15. Effects of Partial Correction of Anaemia with Recombinant Human Erythropoietin on the Haemorheological Profile of Haemodialysis

Patients

Barbas J.M., Martins-Prata M., Cardoso L., Teixeira Sousa, F., Moreira C., Pinto dos Santos J., Saldanha C., Martins e Silva J.

Rev. Port. Hemorreol. 1989, 3(2):269-276.

Some haemorheological parameters were evaluated in a group of 14 patients with chronic renal failure on maintenance haemodialysis and moderate to severe anaemia, before and 3 months after administration of recombinant human erythropoietin (rHuEPO), and in 20 apparently healthy control subjects. Before rHuEPO the patients exhibited significantly increased plasma viscosity ($p < 0.001$) and fibrinogen levels ($p < 0.001$). Erythrocyte deformability and haematocrit were significantly ($p < 0.001$) reduced. There were no significant differences in erythrocyte aggregation index and alpha-2-macroglobulin levels. Three months of rHuEPO administration produced a significant increase in haemoglobin and haematocrit levels ($p < 0.001$), and no significant variations in the other parameters. Eventual consequences of this increase in haematocrit with persistence of the abnormalities in some haemorheological parameters on cardiovascular morbidity of these patients are discussed.

16. Variability of Some Haemorheological Parameters in Patients with Chronic Renal Failure on Regular Haemodialysis

Barbas J.M., Cardoso L., Pinto Y., Moreira C., Saldanha C., Martins e Silva J.

Rev. Port. Hemorreol. 1990, 4(1):109-118.

Variations of haemorheological parameters from a group of 19 patients with chronic renal failure on regular haemodialysis were analysed in two occasions with 6 months interval. The patients were compared with a group of 20 apparently healthy volunteers. At the first determination (T_0), the patients exhibited significantly higher values of fibrinogen ($p < 0.01$) and significantly lower values of hemoglobin ($p < 0.001$), erythrocyte filterability ($p < 0.001$) and

butyrylcholinesterase ($p < 0.001$) than controls. Meanwhile, significantly lower values of phospholipids of the red cell membrane external leaflet and significantly higher values of internal leaflet phospholipids were observed. Six months later (T6) some variations in the previous results were detected. Values of plasma viscosity ($p < 0.01$), fibrinogen ($p < 0.05$), total phospholipids ($p < 0.01$), cholesterol ($p < 0.01$) and phospholipids of red cell membrane external leaflet were significantly higher than basal results (T0). The results obtained suggest that haemodialysis treatment does not correct red cell filterability, although variation on red cell membrane lipid profile and membrane fluidity exhibited a slight tendency to normal values. Insofar, red cell rigidity may be a potential cause of microvascular disabilities in this pathologic entity. Erythrocyte membrane microviscosity was lower in patients than in controls, although it attained statistical significance ($p < 0.05$) only on the second determination (T6).

17. Blood Rheological Observations in Renal Transplant Patients

Barbas J., Cardoso L., Pinto Y., Saldanha C., Martins e Silva J.
Rev. Port. Hemorreol., 1990, 4(2):207–213.

Chronic renal failure is often associated with major hemorheological alterations. This study was undertaken to evaluate some blood rheological parameters, along with the characterization of protein and composition of red cell membranes, in a group of 16 renal transplant recipients (TxR). The results were compared with those obtained from a group of 18 control subjects. A significant ($p < 0.001$) increase of plasma viscosity (PV) and erythrocyte aggregation (EA) ($p < 0.05$) and a significant decrease in erythrocyte filterability (EF) ($p < 0.001$) were found in the TxR group. A significant ($p < 0.001$) increase in the total phospholipids and a significant ($p < 0.01$) decrease of the cholesterol/phospholipids ratio was observed with the red cell membranes from the TxR group. The fluorescence polarization was significant ($p < 0.001$) higher in TxR patients. Significantly ($p < 0.05$) increased values of protein band 4.2 and significantly ($p < 0.05$) decreased values of band 2.1 and band 1+2 (spectrine) were also detected in the red cell membranes from the patients. No significant correlations were evidenced between the haemorheological parameters and the other variables studied. The persistence of some haemorheological abnormalities after renal transplantation may constitute another risk factor for cardiovascular accidents.

18. Is Blood Viscosity Influenced by Blood Lipids?

Pereira Miguel M.J., Pedro M., Vicente O., Moreira C., Saldanha C., Martins e Silva J.
Rev. Port. Hemorreol., 1991, 5(1):95–100.

Hyperlipoproteinaemia, mainly dependent of increased low density lipoprotein (LDL)-cholesterol level is commonly associated with high risk of arterial disease. This situation may be also related with increased blood viscosity and/or clear abnormalities of its major determinants. Some studies have reported positive correlation between rheological parameters and lipoprotein and lipid fractions, although the results diverge in further observations. In the present study whole-blood viscosity (at 22.5 s^{-1} and 225 s^{-1} shear rate) and red cell aggregation index were correlated with total cholesterol, LDL-cholesterol, high density lipoprotein (HDL)-cholesterol, apolipoprotein A1, apolipoprotein B, and triglycerides levels obtained in blood samples collected from 18 apparently normal adult volunteers of both sexes. Whole blood

viscosity at low and high shear rates, and red cell aggregation were unrelated to any lipid or lipoproteins fractions. These results suggest that blood lipoproteins and the haemorheologic factors here studied are not significantly related variables.

19. Flunarizine as Effector of Red Blood Cell Aggregation

C. Saldanha, C. Moreira, J. Martins e Silva
Rev. Port. Hemorreol., 1991, 5(1):127–136.

The effect of flunarizine on erythrocyte aggregation index (EAI) was observed in blood samples obtained from patients with stroke (ST) and healthy adults (C) sex and age matched. Blood aliquots were incubated with flunarizine (F) at 5×10^{-6} , 1×10^{-5} and 2×10^{-5} M, with flunarizine plus excipient (F+E) at the same active substance concentrations, and with excipient (E) at the same percentage as that existent in (F+E). There was no effect of excipient on erythrocyte aggregation. A significant decrease of red blood cell ability to aggregate in both groups (ST: $p < 0.05$; C: $p < 0.005$) was observed in samples incubated with 2×10^{-5} M flunarizine. The inhibitory action of flunarizine (10^{-5} M) on EAI was also significant in blood aliquots (F+E and E) of the control group ($p < 0.001$). The results obtained at zero time were maintained after 30 minutes of incubation at constant temperature. With exception of the excipient, a significant decrease of osmolality was observed ($p < 0.001$) in the other manipulated blood samples. Diminished erythrocyte aggregation index and plasma osmolality values obtained in presence of flunarizine might also occur with stomatocytic shape induced by the Ca^{2+} antagonist flunarizine.

20. Effect of Buflomedil on Erythrocyte Aggregation Index

C. Saldanha, C. Moreira, J. Martins e Silva
Rev. Port. Hemorreol. 1991, 5(2): 255–260.

In order to evaluate the short-term effect of buflomedil in red cell aggregation, blood samples collected from 10 patients with non-insulin-dependent diabetes were used for “in vitro” studies. The effect of buflomedil on red cell aggregation index was assessed at final concentration of 10, 50 and 100 μM . In these experimental conditions red cell aggregation, as well as plasma osmolality, were decreased by buflomedil, compared with control samples. No variations were observed for pH and plasma viscosity in diabetic or control samples under incubation. The short-term effects induced in red cell aggregation by buflomedil may also contribute to improve the perfusion of microcirculatory deteriorated territories “in vivo”.

21. Alterações Hemorreológicas num Caso de Escleromixedema

C. Malcata, M. Galvão, J. Martins e Silva, J.L. Bernardo, M.L. Ferreira, P. Torres
J Blood Rheology. 1993, 7(2): 111–113.

Scleromixedema is a dermatological disease, included in the chronic mucinous disorders, characterised by infiltrative skin lesions, the absence of thyroid disease and, in many cases, the presence of a peculiar serum monoclonal paraprotein. We present the case of a Scleromixedema patient, with neurological abnormalities suggesting blood hyperviscosity, and altered

hemorheological tests. To decrease blood viscosity, isovolemic hemodilution was performed. A rapid improvement was observed within six hours after this therapy. We consider this technique safe and easy to perform, with benefit in this case. Isovolemic hemodilution must be considered in severe cases, when a rapid correction of hemorheological parameters is desired.