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POSTER SESSION: DIABETES

HEMATOCRIT IN TYPE 1 DIABETICS

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ABSTRACT

Reduced hematocrit (H) in diabetic patients with vascular complications has been found in several studies, but this fact remains uncompletely understood. In 159 type 1 diabetics we measured packed cell volume (PCV) during a complete check-up of diabetic complications. On the whole sample, PCV was lower in the 98 patients exhibiting detectable complications (40.511 % $\pm$ 0.483 vs $\pm$ 42.211 $\pm$ 0.541, $p < 0.03$) when compared to the 61 others. However when studying separately men and women, the most significant result was found in men with macroangiopathy, who had a lowered PCV (38.4 $\pm$ 0.358 vs 44.33 $\pm$ 0.667 $p < 0.01$), while in women this difference did not reach the significance. Neuropathy, retinopathy or microalbuminuria alone were not associated with significantly reduced PCV. The lowest values were found in subjects with overt nephropathy, who must be considered separately since moderate anemia could result from chronic renal failure. In this study, H lowering seems to be multifactorial and is mainly found in macroangiopathy. Possible explanations for this finding are discussed.

INTRODUCTION

A lowered venous hematocrit has been found in diabetic patients by several investigators (1, 2). A low significance ($p < 0.05$) negative correlation between hematocrit and rigidity index of red cell was also reported by Hanss and coworkers (3) in 311 diabetics, indicating that an impairment in erythrocyte deformability was associated with a reduction in hematocrit. These authors concluded that this correlation was not easy to explain. However, a recent report by Rubinstein and coworkers (4) suggested an attrative hypothesis : they found that blood viscosity in diabetic

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patients with retinopathy was normal if measured at real hematocrit, although it was increased when hematocrit was corrected. Thus, hematocrit seemed to be decreased in order to compensable rheologic abnormalities and to maintain blood viscosity in a physiological range. Rubinstein suggested that this fact could support the theory of Dintenfass (2) concerning the modulation of hematocrit by regulatory mechanisms involving putative viscoreceptors.

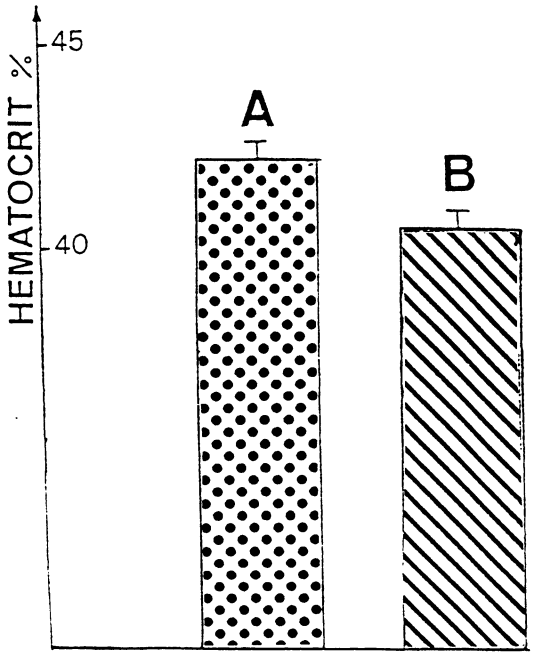

FIG. 1 -- Patients with no detectable complication (A) have a higher hematocrit ($p < 0.003$) than patients with diabetic complications (B).

In this work, we aimed to study the relationships between venous hematocrit and diabetic complications in 169 type I diabetics, in order to detect which were the clinical situations associated with a lowered hematocrit.

PATIENTS AND METHODS

1. Patients.

This study was carried out on 169 hospitalized patients (80 females, 79 males, age : 11 - 74 yr, duration of disease : 1 - 47 yr). All were insulin dependent, treated by two or three dily insulin injections. They underwent a standardized check-up for the detection of diabetic complications. Ophtalmologic examination included fundoscopy and fluorescence angiography. The patients had detailed peripheral nerve electrophysiological measurements carried out using standard techniques. Motor nerve conduction velocity was measured orthodromically in both median and peroneal nerves.

2. In vitro measurements.

Hematocrit was measured by microcentrifugation. Microalbuminuria was assayed by immunonephelometry (Behring laser nephelomoter). Glycosylated hemoglobin was measured by the kit «fast hemoglobins» from Eurobio.

3. Statistics.

Classical comparisons were performed by the nonparametric test of Mann-Whitney for unpaired data. Correlations were determined by least square fitting. Significance was defined as $p < 0.05$. The correspondence factor analysis was performed on Bull-Corail microcomputer with a software developped by Jean-Louis Jacquemin (Université des Sciences et Techniques du Languedoc, Montpellier).

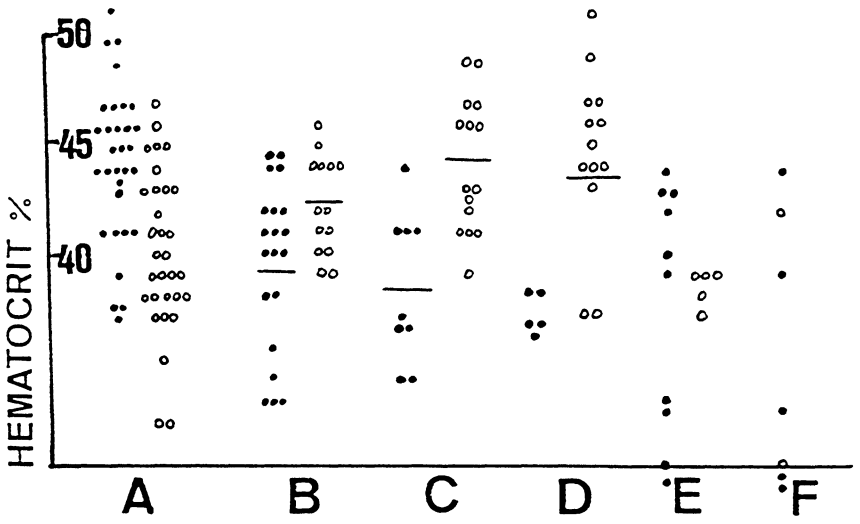

FIG. 2 – Scattergrams of hematocrit in the patients of the study (● = males , o = females). A : without complications. B : retinopathy only ; C : neuropathy only ; D : microalbuminuria only : E : macroangiopathy ; F . overt nephropathy.

RESULTS

1. Statistical comparisons.

On the whole, the 98 patients (49 females, 49 males) with diabetic complications had a lower PCV than the 61 patients (31 females, 30 males) without complications (fig. 1). The scattergrams of hematocrits (fig. 2) in different subgroups of patients show that the lowest values are found in patients with macroangiopathy and overt nephropathy. This reduction is found to be significant in macroangiopathy ($p < 0.01$), but a low significance reduction also exists in patients with retinopathy (21 females, 14 males), whose PCV is 40.36 $\pm$ 0.66 ($p < 0.05$ when compared to the 61 patients without complications). When looking for this difference separately in males and females, no significant result was obtained for retinopathy, whereas in patients with macroangiopathy (fig. 3) the difference remained significant in males ($p < 0.01$). In addition, patients with neuropathy only or with microalbuminuria only showed no tendency to have a lower hematocrit. A relationship between glycemic equilibrium (as evaluated by glycosylated hemoglobin HbA1) and hematocrit was investigated. In the 61 noncomplicated patients these two parameters were not correlated ($r = 0.0007$, n.s.). Hematocrit of the 34 patients of this sbugroup who had 10% or more of HbA1 was 42.43 $\pm$ 0.09 whereas it was 42.67 $\pm$ 0.05 in the 27 others. The difference was not significant. Similary, in the 98 patients with diabetic complications, no correlation between HbA1 and hematocrit can be found ($r = 0.02$; n.s.).

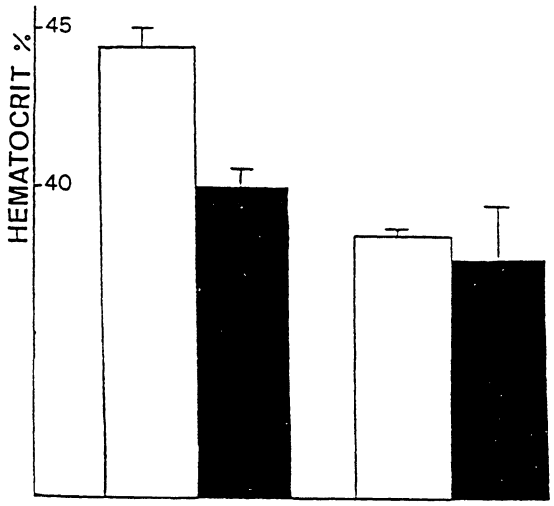

FIG. 3 -- Comparison of patients without macroangiopathy (left) and patients with microangiopathy (right). White columns represent males and black ones represent females.

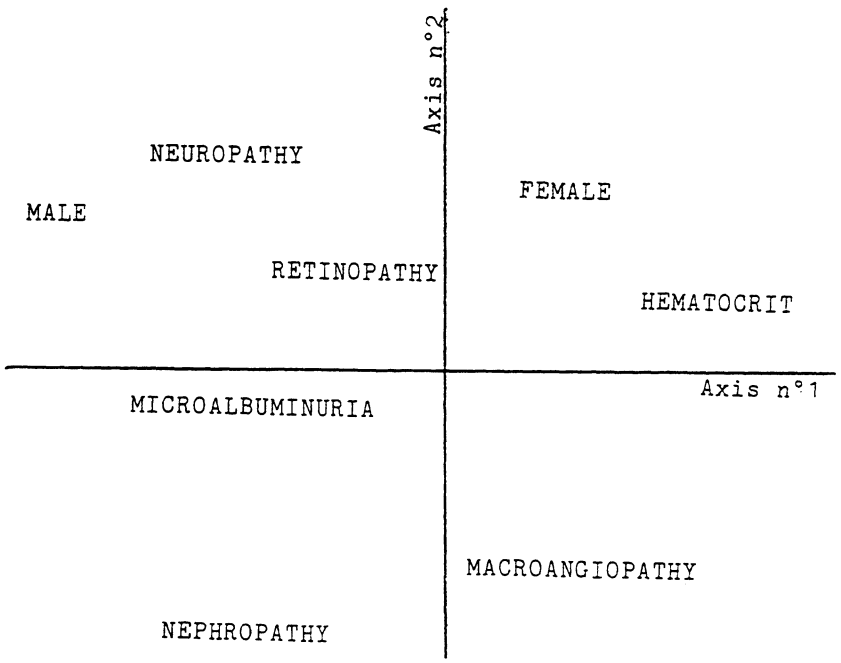

FIG. 4 -- Correspondence factor analysis plotting the relationship between the various items as determined in the 169 diabetics of the study.

2. Correspondence factor analysis.

As shown on fig. 4, the diagram of the correspondence factor analysis provides a synthetic representation of the preceding data. Axis Nol illustrates the negative relationship between hematocrit (on the right) and diabetic complications (on the left). Axis Nol opposites also males and females. Axis No2 separates the different varieties of complications : macroangiopathy and nephropathy, which are associated with a lowered hematocrit, and neuropathy and microalbuminuria, which are not. Surprisingly, retinopathy is found very close from the latter ones, yet it is also found in association with a reduced hematocrit.

DISCUSSION

Data presented above confirm that diabetics with degenerative complications have a lower hematocrit than those without such complications. To our knowledge, Skovborg (1) was the first author to report that hematocrit is higher in normals (46:5%) than in diabetics (45:9%) notwithstanding higher blood viscosity in the latter. Further studies by Dintenfass (2,5) confirmed these results. In 1981, we reported also similar data (6) as a secondary finding in a preliminary work on red cell filterability in diabetes. The study we present here aimed at clarifying these early reports, by investigating the clinical situations in which hematocrit is reduced. As indicated above, we observe that the reduction in hematocrit is mainly associated with vascular complications, whereas patients with functional microangiopathy (as detected by an excessive microalbuminuria) or neuropathy only do not exhibit significant reductions of hematocrit. Furthermore, diabetic nephropathy, which leads into chronic renal failure, is known to be a possible cause of anemia and can play a role in the statistical results observed on nonselected diabetics. Obviously, patients with nephropathy should be excluded from the statistical study of hematocrit in diabetics. In this study, these subjects are presented only in the multivariate analysis, a statistical procedure in which the diversity of patients is not likely to induce bias.

Therefore, many diabetics show decreased hematocrit. Vascular complications seem to be the clinical situation which is most frequently associated to this pattern of rheological behavior. Microangiopathy, as detected by retinopathy, as well as macroangiopathy (including coronary heart disease and peripheral obliterative arterial disease), might result in blood rheologic abnormalities associated with accelerated red cell destruction (3). However, the viscoreceptor theory of Dintenfass provides an attractive explanation : diabetes as well as its vascular complications can be a situation responsible for increased rigidity of the red cells. As any increase in the rigidity of red cells leads to decrease in tissue perfusion (the amplification mechanism being provided by the «inversion phenomenon» at capillary level) a slightly decreased hematocrit might be a feature of an autoregulatory mechanism preserving integrity of tissue perfusion (2). Data consistent with this theory have been published recently by Rubinstein (4). Furthermore, it appears that such an «autoregulatory viscosity mechanism» does not operate always as in some patients one can observe a significantly increased viscosity of whole blood and significantly increased hematocrit (2).

Current studies by C. Le Dévéhat (Le Dévéhat, personal communication, November 1987) are in agreement with these conceptions. This investigator found that the mean hematocrit of diabetic subjects without complications and almost perfectly controlled by portable pump was 42.38%, whereas it was 41.82% in poorly controlled noncomplicated patients. Diabetics with angiopathy without trophic abnormalities had 40.16% and diabetics with angiopathy associated with trophic disorders had a value of 38.66%. This study confirms that patients with angiopathy have lower hematocrit, and suggests that, even without vascular complications, poor diabetic equilibrium results also by itself in a reduction of hematocrit. Normal hematocrit is only found in subjects in whom intensive treatment by pump induces a state of «near-normoglycemia». In our study, no conclusive data can be given concerning the influence of bad glycemic control by itself on hematocrit levels when no diabetic complications can be detected. For instance, no correlation between HbA1 and hematocrit can be found, and packed cell volume is not significantly different between the two subgroups of noncomplicated patients who have HbA1 values higher or lower than 10%. What is clear from the present study is that an amplification of the «hematocrit lowering effect» of diabetes is observed when the patients suffer angiopathy.

Finally, we believe that the negative correlation reported by Hanss (3) between red cell rigidity and hematocrit is of pathophysiological relevance. Rheologic abnormalities of red cells induced by diabetic angiopathy (and possibility also poor glucose control) may be responsible for a reduction in hematocrit by several ways : (a) by a viscoregulatory mechanism, for correcting apparent blood viscosity, as suggested by Rubinstein (4) , (b) by «fragilizing» those rheologically abnormal red cells, which can be more rapidly destroyed in the spleen ; (c) by other unknown mechanisms. For instance, we suggest as a working hypothesis that increased red cell rigidity, by inducing compensatory shifts in capillary circulation according to the theory of blood maldistribution of A. Ehrly (7), may modify the plasma/erythrocytes ratio in venous blood. However, this theory remains totally speculative.

In conclusion, increasing evidence exists that hematocrit is reduced in many diabetics, mainly when they suffer vascular complications. Although the mechanism remains unclear, this rheologic behavior can result in a correction of blood viscosity, preventing its increase to some extent. However, abnormalities in renal function are a possible additional cause of hematocrit reduction. We believe that this aspect of hemorheology of diabetes, which has not been extensively studied, will require further investigations.

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