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Study of Blood Hematocrit and Platelet Aggregation in RVO

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Abstract

Retinal vein occlusion (RVO) is the second commonest cause of reduced vision due to retinal vascular disease after diabetic retinopathy. Multiple factors, both systemic and ocular, are apparently involved in the production of this retinal vascular accident.As venous stasis and blood hypercoagulability have been considered as the risk factors in retinal vein occlusion.So a case control study was undertaken to determine the levels of blood hematocrit and platelet aggregation in retinal vein occlusion. Total 60 patients of the study were divided into group A (30 patients of fundoscopically diagnosed RVO) and Group B (30 age and sex matched controls). The levels of blood hematocrit and platelet aggregation were measured.The results obtained in these patients were compared to those of controls.Data analysis was performed using Graph Pad Instat software, Version 3.05.A significantly increase in levels of blood hematocrit ($p<0.05$)and platelet aggregation($p<0.05$) was found in group A compared to group B . The study concluded that elevated level of blood hematocrit thereby increasing the hyperviscosity and increase in the platelet aggregation may contribute to the pathogenesis and progression of RVO. Thus interventions for RVO that reduce the platelet aggregation and hematocrit will reduce the viscosity of the blood and prevent the progression and complications of RVO.

Keywords: RVO, Hematocrit, platelet aggregation, hyperviscosity.

Introduction

Retinal vein occlusion (RVO) is the second commonest cause of reduced vision due to retinal vascular disease after diabetic retinopathy. [1] It was first described almost more than 100 years ago, and has been an area of interest for many investigators. RVO presents mainly in older individuals, over 50% of cases occurring in persons older than 65 years.[2]

Patients with RVO present with painless, decreased vision, complete loss of vision, or a blind spot in their visual field.

The pathogenesis is multifactorial and still unclear. The classic risk factos related to RVO are diabetes mellitus, hypertension, hyperlipidemia, systemic vascular diseases, hyperviscosity, increased erythrocyte sedimentation, certain medications, smoking, drinking etc.Open-angle glaucoma or other conditions inducing increased intraocular pressure are established local predisposing factors.

However, the condition may be due to either one or a combination of systemic changes known as Virchow's triad:

a) Hemodynamic changes (venous stasis),

b) Degenerative changes of the vessel wall and

c) Blood hypercoagulability.[3]

The retinal venous circulation is characterized by low flow and high vascular resistance, it is particularly affected by blood viscosity.[4] The main determinants of blood viscosity are hematocrit and plasma fibrinogen.[5]The greater the number of red cellsper unit volume, the larger the aggregates of red cells. Fibrinogen is the linking molecule in the red cell aggregates[6]. Blood viscosity increases exponentially as the hematocrit increases.[7] Blood viscosity is an important determinant of blood flow and may be a contributory factor in the production of a number of vascular diseases of the eye. Stagnation of blood flow caused by increased blood viscosity may predispose to thrombosis in the genesis of RVO and may worsen ischemia once RVO has occurred.[8,9]

Thrombosis and thrombolysis are involved in every RVO. Thrombosis may develop due to endothelial injury, abnormal fibrinolysis, procoagulant activation and platelet abnormalities.[10,11]Platelets have an important role in the initiation of atherosclerotic lesions and subsequent complications which contributes to degenerative changes of vessel wall.[12]Abnormal platelet aggregability and *in vivo* platelet function has been reported, suggesting that platelet aggregation might be an important sequel to endothelial swelling, thus leading to the occlusion.[13]Thus considering the role of hemodynamic changes and blood hypercoagulability in RVO, to know the effective risk, present study was undertaken to determine levels of blood hematocrit and platelet aggregation in RVO.

Material and Methods

This study was conducted as a case control study. The study protocol was approved by the Ethical Committee of the Institute. Informed written consent was obtained from all the study subjects enrolled in the study.

The total number of study subjects included was 60. All the subjects included were above 20 years of age. Detailed clinical history and relevant clinical examination data and written consent were obtained from all subjects after explaining the study procedure. The 60 subjects were divided into twogroups.

Group A: Consists of 30 FFA diagnosed patients of Retinal Vein Occlusion.

Group B: 30 age and sex matched healthy controls without Retinal vein Occlusion.

Inclusion criteria

a) Age- cases of RVO between 20 to 80 years diagnosed on routine fundus evaluation,
b) Sex- Both male and female,
c) Patients willing to give consent

Exclusion criteria

a) Patients on Lipid lowering drugs,anticoagulants,
b) Anemic patients,Smokers,
c) Women taking oral contraceptive pills,
d) Patients of Ocular trauma,
e) Patients with CRAO diagnosed on fundus examination,
f) Patients not giving consent.

Collection of Blood Samples:

Study details were explained to the subjects. Informed written consent was taken. Clinical examination was done as per the proforma and blood samples were collected. 12 ml of venous sample was withdrawn from the anti-cubital vein of each participant after taking all aseptic precautions using sterile needles and syringes. 2ml of sample was added to a bulb containing EDTA.K_2H_2O 1.5-2.2mg/ml for estimation of hematocrit. The blood hematocrit was measured on the Erma PCE -210 Automated Cell Counter. 9ml of blood was added in plastic centrifuge tubes by syringes already flushed with tri-sodium citrate (3.8% sol) Platelet aggregation time was measured using colorimetric method as given by O'Brien J.R.[14] All the calculations

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were done using Microsoft Office Excel 2010 and statistical analysis was done using the Graph Pad Instat software, Version 3.05. All statistical data was analysed by Student's unpaired, two tailed t-test. P-value less than 0.05 ($P < 0.05$) was considered to be statistically significant (S). P value of less than 0.001 ($P < 0.001$) was considered to be statistically highly significant (HS). P-value more than 0.05 ($P > 0.05$) was considered to be statistically non-significant (NS).

Results

In this study, there was a significant increase in the Blood hematocrit levels in group A as compared to that of group B ($p<0.05$)(Table 1). There was also a significant increase in Platelet aggregation (%)in group A as compared to group B($p<0.05$)(Table 2).

Table 1: Comparison of Blood hematocrit levels in all groups.

Parameter	Group A (n=30) (mean ± SD)	Group B (n=30) (mean ± SD)	P value
Blood hematocrit (%)	55.36±11.05	47.90±10.56	<0.05(S)

S (P < 0.05) = significant.

Table 2: Comparison of mean Platelet aggregation levels in all groups.

Parameter	Group A (n=30) (mean ± SD)	Group B (n=30) (mean ± SD)	P value
Platelet aggregation (%)	27.90 ±11.57	21.33 ± 7.71	<0.05(S)

S (P < 0.05) = significant

Discussion

Retinal vein occlusion (RVO) is the most common retinal vascular disease after diabetic retinopathy.[1] Due to its multifactorial nature, diagnosis and management of this condition remains a challenge. However from Virchow's triad hemodynamic changes and blood hypercoagulability are two main contributors of the condition.[3] Blood viscosity is an important determinant of blood flow and may be a contributory factor in the production of a number of vascular diseases of the eye. One of the main determinants of blood viscosity is hematocrit.[5] Increase in blood hematocrit which is one of the major determinant of blood viscosity leads to increased blood viscosity which causes stagnation of blood and may favour venous occlusion. Apart from this increased platelet activation and aggregation may again be a contributing factor to the venous thrombus formation thus leading to RVO. Considering these above facts blood haematocrit (contributing to hemodynamic changes) and platelet aggregation(contributing to blood hypercoagulability) were evaluated in Fundus Fluorescein Angiography (FFA) diagnosed cases of retinal vein occlusion and the results were compared with the controls. It was observed that the levels of blood hematocrit ($p<0.05$) and platelet aggregation ($p<0.05$) were significantly altered in retinal vein occlusion patients.

In this study the mean blood hematocrit levels were significantly higher in group A than group B ($p<0.05$)(Table 1). These findings coincide well with some previous study [4,15-19]. However few studies found no significant increase in blood hematocrit in RVO in their study.[20,21]

Viscosity is the resistance to flow of a fluid caused by friction between adjacent layers of the fluid. Increased blood viscosity has been associated with arterial and venous thrombosis elsewhere in the body.[5] The retinal venous circulation is characterized by low flow and high vascular resistance, and is particularly affected by blood viscosity.[4] Increased blood viscosity might play a role in retinal venous occlusion as increased blood viscosity leads to a decreased rate of retinal blood flow and stagnation of blood flow may predispose to thrombosis in the genesis of RVO and may worsen ischemia once RVO has occurred.[8,9] As clotting begins, the molecular

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interactions of the proteins and cellular components of the blood change, and the viscosity dramatically increases.

In this study platelet aggregation levels were significantly elevated in group A (27.900 ± 11.57%) as compared to group B (21.33 ± 7.71%) (P <0.05) (Table-2) .These findings coincide well with some previous studies.[11,22]

Thrombosis and thrombolysis are involved in every RVO. Thrombosis may develop due to endothelial injury, abnormal fibrinolysis, procoagulant activation and platelet abnormalities.[10,11]Atherosclerosis causes thickening of the arteriolar wall of the retinal arteries. The thickened artery compresses the vein within a common adventitial sheath inducing turbulence, endothelial damage and thrombosis of retinal vein.[23]This exposes type I and III collagen fibrils to the lumen where they bind to platelet receptors and stimulate thrombus formation. Atherosclerosis and vascular endothelial dysfunction lead to platelet activation and consequently to local thrombosis and inflammation.[24] Platelet activation and aggregation can also occur on the surface of intact endothelium. Platelet aggregation may be an important cause of endothelial swelling thus leading to the occlusion. Thus thrombosis may be favored by increased platelet activation. Hence platelets may be involved in retinal vein occlusion and its complications. Increased platelet aggregability may also be involved in impending central vein occlusion.[25]

If increased viscosity is a factor promoting ischemia, then reducing viscosity to low normal levels for several months after the onset of venous occlusion might prevent retinal ischemia and neovascularization, as well as its complications of neovascular glaucoma or vitreous hemorrhage and its sequelae.

It will also prevent the recurrence of RVO in the same eye or in the opposite eye. In addition, as increased hematocrit and increased platelet aggregation are associated with vascular disease; these findings in patients with RVO may potentially contribute to an increased risk of cardiovascular disease and stroke. Thus attempts at lowering the levels of these parameters will prevent the occurrence of cardiovascular disease and stroke. Also the visual outcome can be predicted from the rheologic findings. Measurement of these parameters also gives a guide to the management of RVO, like if hematocrit is raised in RVO by haemodilution the blood flow can be improved and the retinal vein occlusion treated. In Patients of RVO with raised platelet aggregation anti-platelet aggregating agents may be considered as a guide for treatment. Also in patients with impending RVO or at risk of RVO by assessment of these parameters and by further lowering the levels of these parameters the risk of development of RVO can be reduced. Thus assessment of these parameters in patients of RVO may give us a guide to the diagnosis, monitoring progression and management of RVO.

Conclusions

From the present study it can be concluded that elevated levels of blood hematocrit as well as platelet aggregation may contribute to the pathogenesis of RVO.Thus assessment of these parameters in the patients of RVO may give us a guide to the diagnosis, monitoring progression and management of RVO.

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Abbreviations

% - Percentage

>- More than

± - plus or minus

≥ - Greater than or equal to

↑ - Increase

↓ - Decrease

ADP – adenosine diphosphate

BRVO – branch retinal vein occlusion

CRVO- central retinal vein occlusion

DM – diabetes mellitus

EDTA – ethylenediaminetetraacetic acid

FFA-Fundus Fluorescein Angiography

Hct - hematocrit

mg/dl – miligram per deciliter

µg/dl – microgram per deciliter

mmol/L – milimole per litre

ng/ml – nanogram per milliliter

Opd- outpatient department

PAF – platelet activating factor

PAT III – platelet aggregation test III

PPP – platelet poor plasma

PRP – platelet rich plasma

PV – plasma viscosity

RBC – red blood cell

RCA – red cell aggregation

r.p.m. – revolutions per minute

TpA – tissue plasminogen activator

TXA_2 – Thromboxane A_2

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