A STUDY OF THE EFFECTS OF VENOUS OCCLUSION ON HAEMOSTATIC VARIABLE IN MALES AND FEMALES

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Summary : The response of the coagulation-fibrinolysis system to venous occlusion was studied in 20 healthy subjects of both sexes. All of them showed increased fibrinolytic activity, the increase being greater in females. Fibrinogen content also increased in both sexes. The other parameters of coagulation studied showed varied responses.

Key words : venous occlusion, prothrombin time, fibrinolytic activity, clotting time, platelet count, fibrinogen content, platelet adhesiveness, leucocyte count

INTRODUCTION

There is a dynamic equilibrium between blood coagulation and fibrinolysis and disturbance of this has relevance in the aetiology of thrombus formation and/or atherosclerosis. Such a disequilibrium has been reported as resulting from venous occlusion (5, 6, 11, 16, 19, 21), exercise (2, 3, 7, 10), adrenaline infusion or release (2, 10, 12), mental stress (4), and sex hormones (1).

Activators of the fibrinolytic system (plasminogen activators) have been shown to exist in the endothelium of blood vessels (1, 15) and the blood levels increase due to the release from these sites after a variety of stimuli viz. venous occlusion, exercise, mental stress etc. An alternative fibrinolytic pathway, the fibrinolytic proteases, are also demonstrated in leucocyte granules (17). Both these can degrade fibrinogen and fibrin. These activators maintain the spontaneous fibrinolytic activity of blood and help remove fibrin deposits and thereby counteract thrombosis (15).

The present study was undertaken to confirm the disequilibrium in the fibrinolysis–coagulation system in response to venous occlusion, by the measurement of the fibrinolytic activity of blood and the fibrinogen content and other parameters of coagulation.

MATERIAL AND METHODS

Fibrinolytic activity, fibrinogen estimation, whole blood clotting time, prothrombin time, platelet count, platelet adhesiveness and leucocyte count were estimated in 20 healthy subjects (both sexes - 10 each) in the age group of 17 to 23 years.

All subjects were asked to report in the morning at 9 A.M. fasting and were advised not to smoke prior to investigations. They were made to relax before withdrawing blood. Blood pressure was recorded in recumbent posture. Samples of blood were taken from right anticubital vein after 10 min further rest in recumbent posture.

After the initial sample was taken, the sphygnomanometer cuff around the right upper arm was inflated to a level midway between systolic and diastolic pressure and this pressure was maintained for 5 min. The second blood sample was obtained just before the cuff was deflated ("Occluded level"). Five minutes after release of the cuff a third sample was collected ("Post–occlusion level").

Six *ml* of venous blood was withdrawn. One *ml* of blood was used for whole clotting time by Lee and White method (12) measured in duplicate and the average being taken. 2.4 *ml* was taken in a plastic tube which contained 0.6 *ml* of 3.8% of sodium citrate for platelet adhesiveness, prothrombin time and fibringen estimation. Platelet adhesiveness was measured by Wright's method (22), Prothrombin time by Quick's one stage (18) and fibrinogen estimation by Biuret method (10). Remaining blood was used for fibrinolytic activity by Fearnley's method (7), total leucocyte count and platelet count. Prothrombin time and fibrinolytic activity was also measured in duplicate, average being taken.

For the purposes of calculation clotlysis time has been converted to units of fibrinolytic activity using the reciprocal of the square of the lysis time x 10^6 while fibrinogen has been converted to g/L from *mg/100 cc* (19).

RESULTS AND DISCUSSION

Haemostasis in general and coagulation in particular are usually associated with injured blood vessels. Haemostasis also undergoes changes in response to a variety of

physiological and pathological conditions not related to bleeding or thrombosis like venous occlusion (5,6,11,16,19,21), exercise (2,3,7,10), adrenaline (2,10,12), mental stress (4) and sex hormones (1). It is clear that the fibrinolytic system is activated at the same time that coagulation is initiated.

The results have been summarized in Tables I and II. Fig. 1 shows the comparison between males and females of the hemostatic variables before and after venous occlusion.

The results of the present study showed that the fibrinolytic response to venous occlusion increased in all the 20 subjects (both male and female). This was in agreement with the findings of Sharper *et al.* (19). However, the response was greater in females,

TABLE I : Effect of venous occlusion on fibrinolytic activity and some blood parameters in males.

Parameters	*R.L.*	*O.L.*	*r*	*t*	*R.L.*	*P.O.L.*	*r*	*t*
Fibrinolytic activity in Units±S.D.	15.52 ±4.918	27.73 ±16.82	0.94	7.83 P<0.01	15.52 ±4.918	20.94 ±5.34	0.73	9.074 P<0.05
Fibrinogen content g/L±S.D.	1.68 ±0.33	2.196 ±0.50	0.78	3.58 P<0.05	1.68 ±0.33	1.797 ±0.69	0.92	6.902 P<0.01
Clotting Time Sec±S.D	294.5 ±58.7	236.5 ±56.6	0.77	4.98 P<0.05	294.5 ±58.75	263.0 ±76.7	0.79	0.58 P>0.05
Prothrombin Time Sec.±S.D.	22.9 ±6.26	25.1 ±6.90	0.62	6.86 P<0.01	22.9 ±6.26	28.1 ±5.85	0.77	5.94 P<0.01
Platelet adhesiveness %	33.98	41.07	0.41	+4.51 P>0.01	33.98	40.45	0.75	3.5 P>0.05
Platelet count Lac. mm³±S.D.	2.50 ±1.45	7.43 ±7.61	—0.73	+5.33 P>0.01	2.50 ±1.45	2.85 ±1.7	1.83	0.85 P<0.05
Leucocyte count XIO3/mm³±S.D.	6.795 ±3.77	8.395 ±4.569	0.91	+5.88 P>0.01	6 795 ±3.77	7.803 ±3.415	0.59	0.94 P<0.05

R.L. — Resting level
O.L. — Occluded level
P.O.L. — Post occlusion level

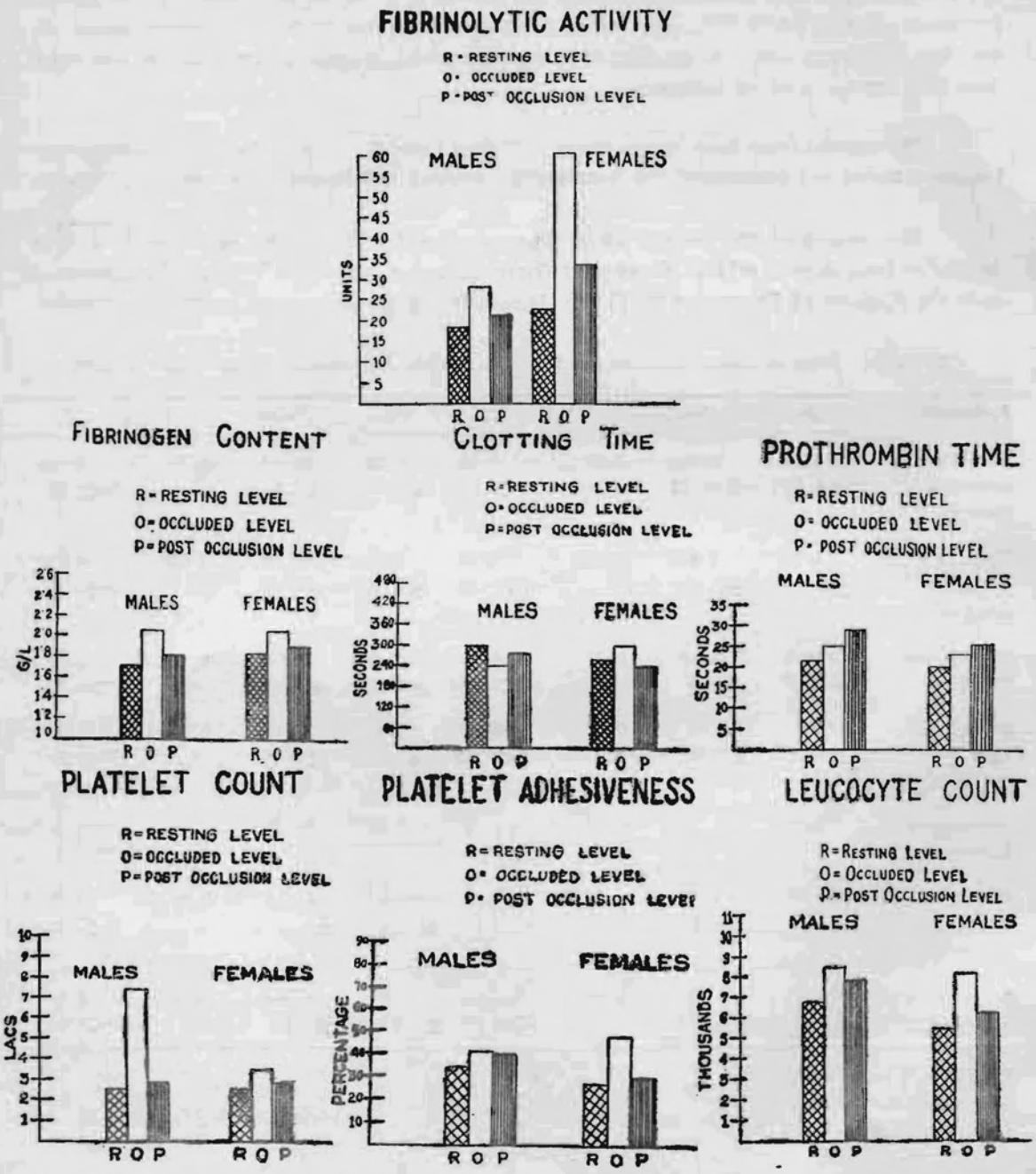

Fig. 1 : The effect of venous occlusion on certain haemostatic variables in males and females.

TABLE II : Effect of venous occlusion on fibrinolytic activity and some blood parameters in females.

Parameters	*R.L.*	*O.L.*	*r*	*t*	*R.L.*	*P.O.L.*	*r*	*t*
Fibrinolytic activity in Units±S.D.	22.44 ±10.8	60.18 ±154.98	0.896	3.38 P<0 05	22.44 ±10.8	33.24 ±17.22	0.885	3.72 P<.0.5
Fibrinogen content in g/L±S.D.	1.855 ±.504	2.135 ±.509	0.508	4.71 P<0.05	1.855 ±0.504	1.915 ±.354	0.606 ±.354	3.25 P>0.05
Clotting time Sec.±S.D.	251.8 188.25	296.5 ±99.7	0.1	3.98 P<0.05	251.8 ±188.25	237.5 ±64.73	0.06	2.38 P<0.05
Prothrombin time in Sec.±S.D.	20.57 ±3.2	23.87 ±3.6	0.27	4.58 P<0.05	20.57 ±3.2	25.63 ±7.72	—1.05	3.35 P<0.05
Platelet adhesiveness in %±S.D.	26.87	47.63	0.36	1.46 P<0.05	26.87	29.35	0.52	0.31 P>0.05
Platelet count in Lac/mm³±S.D.	2.53 ±.9446	3.59 ±1.8	0.83	+1.94 P<0.05	2.53 ±.9446	2.33 ±.9279	0.85	1.32 P>0.05
Leucocyte count X10³/mm³±S.D.	5.47 ±1.6	9.10 ±2.8	—0.02	+3.48 P>0.01	5.47 ±1.6	6.21 ±1.32	0.78	2.77 P<0.05

R.L. — Resting level
O.L. — Occluded level
P.O.L. — Post occlusion level

a findings that cannot be explained though a similar observation was made in females in response to exercise (3). The increased fibrinolytic activity may be mediated via the adrenergic mechanism (2), because there may be an endogenous release of catecholamines caused by pain associated with the occlusion (10). The catecholamines in turn increase plasminogen activator levels by causing release from vascular endothelium.

A rise in fibrinogen content of blood observed in both sexes was difficult to explain, since the increased activator levels in the blood (with subsequent formation of plasmin), digests fibrinogen.

In males, the whole blood clotting times was reduced after occlusion which was probably due to a rapid increase in plasma levels of factor VIII (6,12). On the other hand, the increase in the whole blood clotting times after occlusion in females was probably due to the digestion of substrates (fibrinogen, prothrombin factor V and VIII and fibrin)

by plasmin (13). However, why different mechanisms should operate in the two sexes in response to the same stimulus, needs to be elucidated.

The prothrombin time increased in both sexes and this could be explained on the basis of digestion of prothrombin by increased levels of plasminogen activator liberated from vascular endothelium (13).

The leucocyte count showed a rise in both sexes. Here again the mechanism of rise is difficult to explain. However, the increase would facilitate fibrinolysis through the alternating fibrinolytic system in the leucocytes (17).

Males showed a marked rise in platelet count which could be attributed to an increase in plasmin levels which in turn induces release of platelets (13, 20). Again the absence of a marked increase in females is inexplicable.

The increased platelet adhesiveness observed in both sexes could be due to the action of plasmin formed, on platelet aggregation (13).

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