Adaptation of the Vessel Wall Functional Activity in Young Smoker Men in Cold Altitude Climatic Zone

E. Chaduneli, M.D., Ph. D.
National Center of Therapy
3, Chachava Ave
380059, Tbilisi
Georgia

L. Goderdzishvili, M.D.
Central Military Hospital
6, Navtlugi St
380016, Tbilisi
Georgia

Summary

The vessel wall functional activities reserve capacity was performed using venous cuff test in smoker militaries. The test was combined with 10-min. venous occlusion on the arm. The comparative study was conducted in smoker and non-smoker militaries in different climatic and terrestrial condition. Using the series of laboratory tests on haemostasis system depression of the fibrynolisis system in smoker militaries have been detected in its baseline activity as well as in high altitude zone.

Key words: venous occlusion test, fibrinolysis activity, vascular disorders, smoking, climatic condition, and altitude zone.

Introduction:
Clinical experience suggests that many physicians harbor a misconception regarding the pathogenesis of thrombotic disorders, particularly in those individuals with recurrent episodes. Patients are often evaluated for "hypercoagulobility "with a multitude of coagulation and platelet function tests, as if its detection would account for the cause of the thrombosis. This misperception has the potential of obscuring the true cause of the thrombotic problem, and the investigative approach it generates often results in a battery of costly coagulation tests, many of which have little bearing on the underlying problem.
Approaching the path physiology of thrombotic disease on the basis of Virchow's triad, rather than on the basis of the primary or secondary abnormalities of hemostasis , provides a better conceptual foundation on which to base an investigation (1,2).
Virchow postulated that trombosis results from abnormalities of blood vessel, abnormalities of blood flow, or of abnormalities of blood constitution. This simple but broad concept retains its validity today and forms the basis for an understanding of the pro-thrombotic state.
Using Virchow's theory one can implicate any one or a combination of the tree elements in the pathogenesis of thrombosis or the creation of a pro-thrombotic state. However, by necessity a disturbance in any one of the limbs of this triad must activate and proceed through the hemostasis mechanism, the final common pathway to thrombosis.
The fibrinolysis system is considered to play an important role in many physiological and pathological processes (6). However, a great deal of the experimental data has been obtained with methods (e.g. fibrin-plate lysis, whole blood clot lysis time or euglobulin clot lysis time), which are difficult to perform and are uncertain in terms of what they really measure. In view of the rapid progress in our knowledge about the fibrinolytic process and its regulation there is a great demand for more specific methods to assay its individual activation at different condition. Therefore, it is interesting to take in consideration the mosaic

Paper presented at the RTO HFM Symposium on "Blowing Hot and Cold: Protecting Against Climatic Extremes", held in Dresden, Germany, 8-10 October 2001, and published in RTO-MP-076.

character of the haemostasis system, for example, tissue plasminogen activator in arms are several time more than in legs vessel endothelium. Several plasminogen activators contribute to total fibrinolytic system.
For the plasminogen release from the endothelium study the venous occlusion test of the arm is widely used. In previous period (4,7) there was used venous stasis of 20-min duration. However, the ensuing pain experienced by the patients has been the major obstacle for its repetitive use. According to other authors results we accepted 10-min occlusion yielded results which were equally informative as those obtained 20-min while causing loss discomfort for the patients. Therefore, the individuals exhibited their peak activity after 10 min.
The results come from the same researchers who has show that venous cuff test using in small groups is equally informative and important for the vascular wall functional activity evaluation and its individual difference detection (3).
It have been detected that formation of plasmin measured as increased in plasmin-antiplasmin complex is obtained to a much larger extend by venous occlusion than exercise the activator content in the latter samples was somewhat higher. The reason for this is not known, but one can speculate that exercise activates also the coagulation cascade, thus producing fibrin, which may stimulate the plasmin activator.
It have to be note, that vessel's reflex zones with the hemo- and baro-receptors represents the local regular system. Also, muscles and internal organs produce thrombolytic ingredients and fibrinolysis activators. Thus, under the cold temperature or either in the terrestrial elevation, as well as hypoxia, the stress reaction exists as the necessary human adaptation to environment and depends to the duration of the stress.
Humor factors (hypercatecholaminemia, erythremia, milk acid concentration increase, etc) have a same influence on the microcirculation. There have been considered (5) that the major risk factors to the altitude disease (elevation on zone higher than 2000 m.) exhibition are as follows:
quickly elevation, young age, physical load, chronic pulmonary disease, alcohol take.
Concerning the previous data it have been detected that cigarettes can trigger depression of the vessel wall endothelium prostacycline capacity. Smoking not only chronically increases thrombogenic risk, but it also an abrupt short-term risk. Over the long term, smoking damages the protective living inside blood vessel, making them more susceptible to plaque formation. More immediately, smoking causes blood vessel to constrict and stimulates platelets to form clots
Therefore, based on the multifactor prospective studies and angiografic investigations it have been detected that smoking is an independent risk factor of major vascular diseases.

Material and methods:

The vessel wall functional activity and its reserve capacity have been evaluated in smoker militaries with peripheral vessel disorders (vascular acrosyndroms, acrocyanose, Livedo reticularis, Raynod's phenomenon, acrorhigose, acrocholose). The diagnosis was made clinically and due to nitroglycerine-test performance.
Militaries were assigned to the Georgian Army in Tbilisi with the altitude level about 500 m.(I group) - 34 persons in age 18-29 years.
The second group was combined with same personnel, temporary sent on a mission (during 5-7 days) in the region with terrestrial elevation above 2500-3000 m. and average winter temperature –10-25 C.
Only healthy non-smoker militaries (10 men) were used throughout this study as a control group, who were all well informed of the nature of the investigation.
To determine baseline fibrinolytic activity volunteers and patients were resting 30 min.
Venous occlusion was obtained by placing at the upper arm a cuff inflated midway between systolic and diastolic pressure. Prior to and after the stasis for 10 min. a blood sample was occasionally drawn from the same arm. The plasma samples were collected with precaution to prevent any contact activity and care was taken that blood flowed easy to avoid contact phase activator. The blood was centrifuged for 20 min. at 2500 to obtain platelet-poor plasma. The following haemostsis system parameters have been detected: circulated fibrinogen, fibrinogen-B, fibrinolysis activity, antithrombin III activity, kallekrein-kinin frozen test, prothrombin activity.
For the microcirculation capacity evaluation, as well as for the blood vessel organic or functional damage difference, generally accepted nitroglycerine test have been performed. The nitroglycerine test has been done in 25 persons using sublingual nitroglycerine administration in dose 0,5 mg. and accomplished rheovasogram.
Statistical evaluation was done by the paired Student t-test.

Results:

The positive Nitroglycerine test was exhibited in all of the patients.
The mean basic rheovasogram's index in smoker patients with Raynod's syndrom on the left hand was 0,398 ± 0,078, on the right hand 0,386 ± 0,07.
After 2 min. nitroglycerine administration the rheovasogram index was increased to 0,628 ± 0,121 on the left hand and to 0,599 ± 0,121 on the right one.
During the following 3 min the successive increase of the index has been detected – 0,743 ± 0,145 on the right hand and 0,812 ± 0,155 on the left hand. The basic fibrinolytic activity (blood sample taken after 30 min. rest). in the first group's persons has been increased in 23% cases as compared with the control group with the fibrinolysis pronounced increase in 48%. After the venous stasis 71,5% of the patients showed decrease of the fibrinolysis instead 16% in the control group. No change has been detected in 15,5% in the experimental group and in 36% in the control one. (Figure 1,2)

Fig. 1

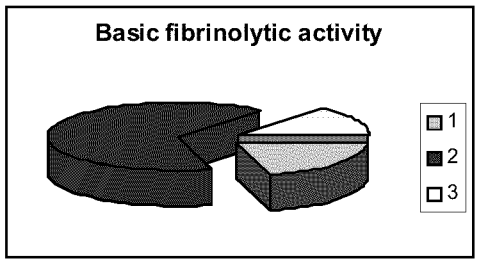
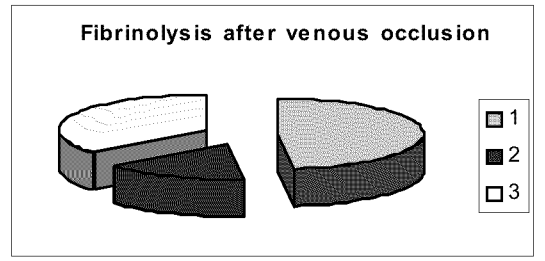


Fig. 2



1- Fibrinolysis increase; 2-fibrinolysis decrease; 3-no change

The mean basic fibrinolys activity was estimated as 23,0 ± 6,07% in the first group and as 17,5 ± 5,93% in the control.
After the venous occlusion all subject of the first group showed decrease of the fibrinolysis activity ranging to 16,86 ± 5,92% and in the control group an increase to 19,5 ± 7,51%.
Concerning to the other haemostasis system parameters (table1) it have to be noted that significantly pronounced alteration have been exhibited in the fibfinogen-B basic concentration in the patient's group: (7,55 ± 0,61 g/l instead 5,51 ± 0,99 g/l in the control), as well as in the antithrombin III level (35,14 ± 3,05% and 43,83 ± 3,41%, accordingly). After the cuff test the difference in fibrinogen-B concentration has been increased to 8,56 ± 0,54 g/l in the first group, so it was significantly higher as among healthy person.
Antithrombin- III's level in the postocclusion period was pronounced increased in the healthy militaries ranging to 43,33 ± 2,97% as comparing to the smokers with antithrombin -III level equal to 34,43 ± 2,69%.
There was also detected kallekrein-kinin's bridge alteration in both groups with the tendency to compensate minimization: 16,71 ± 6,72% prior to and 11,92 ± 3,46 after occlusion in experimental group and 18,57 ± 5,96 and 10,02 ± 2,17 in control.
Thus, the release of the tissue plasminogen and antithrombotic factors in response to venous occlusion differs considerably among healthy and patients with vascular disturbances. No significant difference was found in the prothrombin activity, thrombocytes aggregation, circulate fibrin-monomeres or circulate fibrinogen.
According this data, we choose to implement more informative parameters for the vessel wall functional activity evaluation in the high altitude zone. All samples before and after vascular occlusion were also analyzed in same persons from the control and patients groups.
It have to be note, that only in 7,8% patients with vascular disorders the fibrinolytic activity has been increase, instead 21% in healthy person. The mean basic fibtinolys activity was estimated as 18,01 ± 4,23% in I group and as 21,14 ± 6,43% in the control group. Immediately after venous occlusion the fibrinolytic activity has been decrease to 16,43 ± 5,67% in the experimental group. In the healthy person it was somewhat higher increased to 23,14 ± 6,17%.

Venous occlusion influence on the hemostasis parameters

Table 1

Hemostasis parameters	Prior to venous occlusion		After venous occlusion duration 10 min.		P_{3-4}
	I group n1	Control group n2	I group n3	Control group n4	
Prothrombin activity in %	18.86±0.59	16.67±0.61	18.57±0.46	16.5±0.79	
Thombocytes spontaneous activity in %	7.7±2.24	9.0±2.04	8.0±0.46	8.5±2.19	
Fibrinogen in g/l	3.67±0.32	3.14±0.44	3.99±0.37	3.47±0.39	
lFibronogen-B in g/l	7.55±0.61	5.51±0.099	8.56±0.54	6.07±1.01	<0.05
Fibrin monomers in opt.un.	0.35±0.02	0.31±0.05	0.36±0.03	0.32±0.03	
Fibrinolysis activity in %	23±6.07	17.5±5.93	16.86±5.92	19.5±7.51	
Antothrombin activity in %	35.14±3.06	43.83±3.41	34.43±2.69	43.33±2.95	<0.05
Kallekrein-kinin bridge in %	16.71±6.72	11.92±3.46	18.57±5.96	10.0±2.17	

Conclusion:

The approach to the evaluation of a pro-thrombotic state can be summarized as follows: multiple risk factors for the development of thrombotic disease exist. These factors mediate their pathophysiologic effect through one or number of the elements of Virchow's triad, and the final common pathway leading to clot formation is through the activation of the hemostatic system (2). A primary abnormality of hemostasis should not be expected in every patient with recurrent thrombosis, but when suspected, defects in the inhibitory mechanisms should be sought.

For a long time it has been known that blood fibrinolytic activity is increased during venous stasis and exercise. It has also been reported (6) that this is due to release of the tissue plasminogen activator from the endothelium cells in the vessel, probably because of the ultrafiltration and haemoconcentration as a result of the venous stagnation.

Evidence of sub clinical activation of hemostasis may occur with primary inhibitory deficits, but such activation often suggests a secondary state of hypercoagulobility. It is important to remember that the majority of individuals who develop thrombotic disease probably do so as a result of blood vessel or blood flow abnormalities with no disturbance of the hemostasis system, except only transiently at the time of the clinical event.

Research work has given the possibility to eliminate an increase of the fibrinolysis activity after the 10 min. of the stasis in healthy volunteers, which was significant compared to its basic activity. However, there were pronounced individual difference of the vessel's endothelium responsiveness to hypoxia condition in the smoker militaries with accomplished vascular disorders. For this reason, it is advisable to conduct 10-min. venous occlusion test. If abnormalities are obtained, as a result of the fibrinolysis depression, it remains to be established which prophylaxis provides the normalization of the vascular wall functional activity (physical activity's increase, stop smoking, antioxidants drug therapy, the elevation regimen's optimization, such as elevation on 300m. during the day).

We have many best way to help smoker people quit now and to protect them against thrombogenic disturbances. And may be those better ways plus this way of explanation what's really going in their blood, might be an additional help to the young smokers.

Reference:

1. Acki N. Genetic abnormalities of the fibrinolitic system. Semenars Thrombosis, // Hematol.1984;v.10,n 1, 42-50.
2. Ansell Y.E. Hypercoagulobility: a conceptual and diagnostic approach. //Amer. Heart J.; 1987, Oct., 910,913.
3. Baluda V.,Sokolov E. Cuff test in the hemostasis functional activity assesment. // Hematol. and Transfusiol.; 1987,9,51-53.
4. Bauer Y., Bachman F. Fibrinolysis activity in healthy volunteers before and after 5 and 20 minutes of venous occlusion.// Thrombosis Research; 1984, 34, 153-174.
5. Juhan J-Vague, Valadier J. Deficient T-PA release and elevated PA inhibitors levels in patients with spontaneous and recurrent deep venous thrombosis.// Thromb. and Haemost.; 1987, v. 57, 1, 67-72.
6. McDonnell J, Altitude sickness;// Austr, Fam. Phisician, 1990, 19, 205-208.
7. B. Wiman, G. Mellbring. Plasminogen activity release during venous stasis as determined by a new specific assay. // Clinica. Chimica Acta; 1983,127,279-288.