Levels of soluble fibrin monomer complexes in the course of myocardial infarction

A. Nowak, B. Lipiński, and J. Drzewiecki

From the Third Medical Clinic Silesian School of Medicine, Katowice,
and the Department of Biochemistry Postgraduate Medical School, Warsaw, Poland

Plasma fibrinogen concentration, euglobulin clot lysis time, and soluble fibrin monomer complexes in whole blood samples with protamine sulphate were determined in healthy subjects as well as in patients with atherosclerosis, coronary insufficiency, or myocardial infarction. Fibrinogen content and soluble fibrin monomer complex levels were higher while fibrinolytic activity was lower in patients with atherosclerosis, coronary insufficiency, and myocardial infarction than in the healthy subjects. The blood soluble fibrin monomer complex level was significantly raised in patients with myocardial infarction as compared with patients with coronary insufficiency. These parameters, studied during the first three weeks in cases of myocardial infarction, showed a gradual increase of soluble fibrin monomer complex levels in poor risk patients while there was a conspicuous decrease in good risk patients. The determination of soluble fibrin monomer complexes in the whole blood can be useful for prognosis in myocardial infarction as well as for its differentiation from attacks of coronary insufficiency.

A decreased fibrinolytic activity and raised fibrinogen level in myocardial infarction have been reported by several authors (Chakrabarti, Hocking, and Fearnley, 1969; Ogston, 1962; Protasova, 1969; Sikka *et al.*, 1968; Szczeklik *et al.*, 1958).

Recently Lipiński and Jęlaszewicz (1969) have put forward a hypothesis that an inhibition of fibrinolysis accompanied by an increase of soluble fibrin monomer complexes in blood are responsible for a hypercoagulable state.

The aim of the present work was to study the dynamics of changes in these monomer complexes and fibrinogen level in blood as well as fibrinolytic activity in patients with myocardial infarction in comparison to groups of healthy subjects, atherosclerotic patients, and those with coronary artery disease.

Material and methods

The study was carried out on inpatients. Group A comprised 40 healthy subjects (mean age 30 years); group B consisted of 23 patients with atherosclerosis (mean age 60 years); group C of 16 patients with coronary insufficiency (mean age 49 years); and group D of 14 patients with myocardial infarction (mean age 53 years).

Fasting blood samples were drawn from antecubital veins in the morning.

In the patients with myocardial infarction, blood was collected at intervals of one to three days for three weeks after the onset of infarction. This group was divided into two subgroups according to the following criteria:

a) 'Poor risk' group comprised patients with circulatory insufficiency, persistent and frequent coronary pain attacks, and or cardiac arrhythmias during the whole period of observation. Two out of 5 patients in this group died in the third week after the onset of infarction.

b) 'Good risk' group comprised patients showing no such symptoms as described above. None of 9 patients of this group died.

The level of soluble fibrin monomer complexes in blood was determined by the method described by Lipiński, Kotelba-Witkowska, and Zajdel (1970). The method consists in the addition of 0.1 ml 1 per cent protamine sulphate (Biomed, Poland) in saline to 1 ml oxalated blood. After 5 minutes of incubation at 25°C the mixture was transferred into a nonheparinized microhaematocrit tube, sealed, and centrifuged for 2 minutes at 12,000 rpm. The level of soluble fibrin monomer complexes was expressed as a percentage of white precipitate formed over a layer of the red cells with respect to the total volume of the sample.

Fibrinolytic activity was determined by recording the euglobulin clot lysis time as described by Kowalski, Kopec, and Niewiarowski (1959). Fibrinogen was determined by the method of Quick (1951).

TABLE 1 Blood levels of soluble fibrin monomer complexes, fibrinogen, and fibrinolysis in 4 groups of subjects

	Patient group	No. of patients	$\bar{X}$	SD	Group test	t	P
Soluble fibrin monomer complex (%)	A	40	1.9	± 1.41	A:B	6.28	<0.001
	B	23	2.9	± 0.79	A:C	7.13	<0.001
	C	16	3.0	± 0.71	A:D	9.88	<0.001
	D	14	4.4	± 1.44	C:D	3.45	<0.01
Euglobulin fibrinolysis (min)	A	33	163	± 57	A:B	1.85	>0.05
	B	20	195	± 78	A:C	1.58	>0.05
	C	16	191	± 68	A:D	4.33	<0.001
	D	14	291	± 154	C:D	2.47	<0.02
Fibrinogen (mg/100 ml)	A	38	310	± 110	A:B	3.01	<0.01
	B	23	420	± 170	A:C	1.17	>0.05
	C	16	350	± 130	A:D	4.59	<0.001
	D	14	500	± 170	C:D	2.95	<0.01

A – Healthy subjects; B – Atherosclerosis; C – Coronary insufficiency; D – Myocardial infarction. The results represent the mean values of determinations made during the first 3 days after the onset of infarction.

Results

The results of the determination of the monomer complex level and fibrinogen content in the blood, as well as the fibrinolytic activity are presented in Table 1.

It is evident from Table 1 that the level in the patients with myocardial infarction, atherosclerosis, and coronary insufficiency, is significantly higher than in the healthy subjects. Moreover, the content in blood of patients with myocardial infarction was significantly higher than in those with coronary insufficiency.

Conspicuous inhibition of fibrinolysis was observed in patients with myocardial infarction in comparison with healthy subjects and patients with coronary insufficiency.

The fibrinogen level was significantly raised in patients with myocardial infarction compared with healthy subjects, patients with atherosclerosis, and those with coronary insufficiency. The behaviour of soluble fibrin

monomer complexes, fibrinogen level, and fibrinolysis time in 3 consecutive weeks after the onset of infarction is illustrated in Table 2. These results indicate that in patients with a good prognosis ('good risk' group) an obvious decrease in the monomer complexes gradually occurs, while in the patients with a bad prognosis ('poor risk') their blood levels significantly increase in the third week of observation ($P < 0.001$).

The difference between the blood soluble fibrin monomer complex level in both groups of patients in the third week is highly significant ($P < 0.01$), whereas in the first week it is insignificant.

No significant alteration in behaviour of fibrinogen level and fibrinolysis was observed in both groups of patients in the consecutive weeks after the onset of the infarction.

The dynamic changes in the level of soluble fibrin monomer complexes, fibrinogen content, and fibrinolysis in one patient with a

TABLE 2 Behaviour of soluble fibrin monomer complexes, fibrinogen, and fibrinolysis in myocardial infarction patients in consecutive weeks after onset of infarction

	Weeks after onset of infarction	Patients with myocardial infarction			
		'Good risk' (9 persons – 55 determinations)		'Poor risk' (5 persons – 40 determinations)	
		$\bar{X}$	SD	$\bar{X}$	SD
Soluble fibrin monomer complexes (%)	1st	3.9	± 1	4.7	± 1
	2nd	3.6	± 0.9	4.5	± 1.9
	3rd	2.7	± 0.23	6.1	± 1.1
Euglobulin fibrinolysis (min)	1st	240	± 104	430	± 270
	2nd	260	± 153	280	± 43
	3rd	240	± 67	340	± 140
Fibrinogen (mg/100 ml)	1st	450	± 160	570	± 40
	2nd	440	± 70	470	± 70
	3rd	450	± 150	500	± 180

good prognosis and one with a bad prognosis are shown in the Figure.

It is evident from this Figure that in the patient with a mild course of myocardial infarction the level was initially increased but returned to normal values on the seventh day of observation and remained constant during the whole period of observation. Corresponding changes were found in the fibrinogen level and fibrinolytic activity in blood. In the subject with 'poor risk', suffering from recurrent coronary attacks and cardiac arrhythmia, the level fluctuated considerably till the eighth day, and then considerably exceeded the normal value till the end of observation. This patient survived. Raised fibrinogen concentration and inhibition of fibrinolysis were observed in the patient only during the first week after the onset of infarction.

Discussion

The results of our study concerning fibrinogen and fibrinolysis in myocardial infarction agree with the results reported by other

authors (Szczeklik *et al.*, 1958; Ogston, 1962; Chakrabarti *et al.*, 1968; Sikka *et al.*, 1968; Moschos *et al.*, 1969; Protasova, 1969).

It was previously reported by Lipiński and Worowski (1968) that the soluble fibrin monomer complex content in the plasma of patients with myocardial infarction was considerably increased. These results were obtained by a single determination in a small group of patients using a different method from that applied in the present work. The results of the present study indicate that an increase of the level in circulating blood occurs in all the clinical forms of atherosclerosis. The highest level was observed in patients with myocardial infarction: this phenomenon was steady. During the first week after the onset of infarction the blood level of soluble fibrin monomer complexes was above the normal values in 85 per cent of the subjects. It is worth noting that in healthy subjects the content in blood is constant (Lipiński *et al.*, 1970).

It is interesting to discover whether the process of myocardial infarction is accompanied by a hypercoagulable state. At present we cannot say whether the increased level of soluble fibrin monomer complexes is a cause or a result of myocardial infarction. Persisting high levels in the blood and their increase together with continuing clinical symptoms suggest the existence of a hypercoagulable state. It is possible that such hypercoagulability is the result of a disturbance in the dynamic equilibrium between blood clotting and fibrinolysis (Astrup, 1959; Copley, 1957; Duguid, 1949).

This possibility is corroborated by the fact that the fibrinolytic activity of blood is lower in patients with myocardial infarction and coronary insufficiency.

The question arises, what is the role of increased level of soluble fibrin monomer complexes in myocardial infarction?

It is known from the studies *in vitro* that these complexes can be paracoagulated (non enzymatic precipitation) by a number of physicochemical agents. These include basic proteins such as protamine sulphate and other basic tissue proteins, lysozyme and platelet factor 4 (Stewart and Niewiarowski, 1969; Kopeć, Węgrzynowicz, and Latallo, 1970).

The paracoagulated precipitates of the soluble fibrin monomer complexes show by electron microscopy a characteristic periodicity typical of fibrin (Horn, Hawiger, and Collins, 1969).

Theoretically the paracoagulation reaction of soluble fibrin monomer complexes may occur in circulating blood. This is particularly

FIG. Changes in the level of soluble fibrin monomer complexes (SFMC) and fibrinogen as well as fibrinolytic activity in the course of myocardial infarction in two patients.

likely when the blood level is increased as was observed in hypercoagulable states (Lipiński and Jelaszewicz, 1969; Lipiński *et al.*, 1967), and in myocardial infarction as well. The increased content of these monomer complexes represents a potential substrate for the paracoagulation induced with basic protein which may be released from blood cells (platelets, leucocytes) or tissue cells into the blood stream. This may result in local precipitation of amorphous masses of parafibrin. It can be speculated that the increased content of these soluble monomer complexes in patients with a bad prognosis ('poor risk' group) may contribute to the postinfarction symptoms. Because of its simplicity and rapidity, the test for these complexes may be of diagnostic and prognostic value in myocardial infarction and may provide important information even at the bedside.

The behaviour of these soluble fibrin monomer complex levels in blood has practical importance in the differentiation of attacks of coronary insufficiency and infarction.

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Requests for reprints to Dr. Andrzej Nowak, 3rd Medical Clinic, Silesian School of Medicine, Katowice, ul. Francuska 20, Poland.