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Moderate beer consumption and the blood coagulation in patients with coronary artery disease

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Abstract. Gorinstein S, Zemser M, Lichman I, Berebi A, Kleipfish A, Libman I, Trakhtenberg S, and Caspi A (Hebrew University of Jerusalem; Kaplan Hospital, Rehovot; Israel). Moderate beer consumption and the blood coagulation in patients with coronary artery disease. *J Intern Med* 1997; **241:** 47–51.

Objectives. To evaluate the influence of a short period of moderate beer consumption on the status of the thrombolitic activity in patients with coronary artery disease (CAD).

Subjects and design. From 28 patients with two- or three-vessel CAD 22 were randomly assigned to an experimental group (EG) and six to control group (CG). Before and after completion of the study every one of the 28 patients was examined and a wide range of laboratory tests was performed.

Setting. A University Hospital in Israel.

Intervention. Of the EG, 22 patients consumed 330 mL of beer day^{-1} (20 g of alcohol) for the 30-day period in addition to the usual antiatherosclerotic diet. Patients of the CG did not consume alcohol beverages.

Main outcome measures. Fibrinogen, prothrombin time (PT), coagulant activity of Factor VII (F VIIc) and Factor VII antigen (F VIIag), and plasminogen activator inhibitor (PAI) levels were studied.

Results. After the investigation a statistically significant decrease was found in F VIIc ($P < 0.01$) and F VIIag ($P < 0.001$) and to a lesser extent a decrease in the value of PAI. Fibrinogen and PT remained unchanged in the EG also.

Conclusions. Even a short period of moderate beer consumption results in a decrease in thrombogenic activity. The only sensitive tests were F VIIc and F VIIag. The decrease in thrombogenic activity may be the main cause of decreased mortality in patients with CAD who consume moderate quantities of alcoholic beverages.

Keywords: fibrinogen, prothrombin time, Factor VII, plasminogen activator inhibitor, blood coagulation, coronary artery disease, alcohol consumption.

Introduction

Coronary artery disease (CAD) is the main cause of morbidity and mortality in Western industrialized countries. There are epidemiological studies which indicate that consumption of moderate quantities of alcohol reduce the morbidity and mortality from CAD [1–7].

Many authors who investigated the role of alcohol consumption (including beer and wine) in preventing CAD found increases in the high density lipoproteins (HDL) and antioxidants and decreases in the low-density lipoproteins (LDL) [2, 5, 8–11]. Reduction in the risk of CAD can be related to the prevention of clotting or thrombosis. It was found that alcohol decreases both platelet aggregation and the circulating fibrinogen level [1].

It is generally agreed that in fatal acute transmural myocardial infarction more than 90% of patients have associated coronary thrombosis – the basis of intravenous thrombolytic therapy which revolutionized the treatment of these patients [12–22]. Therefore it is impossible to expect a significant decrease in mortality from CAD without a decrease in the thrombogenic activity. The use of prothrombin time (PT) and the measurement of

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fibrinogen levels was widely recommended in the evaluation of the status of blood coagulation [23, 24]. But recently some authors have used additional tests [25–29]. This work reports on the influence of short-term moderate beer consumption on blood coagulation in patients with CAD through PT and fibrinogen measurements, and additional tests such as Factor VII and plasminogen activator inhibitor (PAI) levels.

Materials and methods

Type of beer used

The Maccabee beer which was used in these experiments was prepared using a standard industrial technological process with 70% malt, 17.5% sorghum and 12.5% sugar. The analysis was done by conventional analytical methods acceptable in the beer industry.

Clinical data

We examined 69 male patients between the ages of 51 and 73 years. All of them presented with well-documented CAD and from them 28 patients were chosen who met the following criteria: (1) the patients had undergone coronary angiography which revealed two- or three-vessel CAD and in consequence had undergone coronary bypass surgery. The clinical manifestations of CAD had appeared at least 2 years before surgery but the patients had been stabilized with anginal syndrome following surgery; (2) the patients consumed alcoholic beverages only occasionally not more frequently than once in 2–3 months and no more than 20 g of alcohol day^{-1}; (3) these patients were not taking drugs which influenced the status of the anticoagulant system. The 28 patients who met the criteria were divided randomly between the experimental group (22 patients) and the control group (six patients).

All patients in both the experimental and control groups consumed the usual Israeli diet rich in vegetables and fruits and with limited quantities of fats as recommended for patients with CAD. The daily consumption was about 1500 kcal.

Before and after completion of the investigation every patient was examined. Their systolic and diastolic blood pressure (BP), heart rate and weight were recorded and a wide range of laboratory tests including measurement of lipids, glucose, proteins, urea, uric acid, creatinine, liver function and others were carried out.

Measurement of Factor VII and PAI levels were performed as follows: (a) the coagulant activity of Factor VII (F VIIc) was determined by the extent of correction obtained in the prothrombin time when patients' plasma was added to substrate plasma severely deficient in Factor VII (Sigma, USA); (b) the quantitative determination of the Factor VII antigen (F VIIag) was carried out by the enzyme-linked immunosorbent assay – Elisa (Asserachrom Ag, Stago, France); (c) the quantitative determination of PAI was carried out by the synthetic chromogenic substrate method (Stachrom PAI, Stago, France).

For 30 consecutive days all of the 22 patients in the experimental group consumed 330 mL of Maccabee beer (about 20 g of alcohol) every day. The six patients in the control group did not consume alcoholic beverages during the 30-day period of our investigation.

In order to verify the statistical significance of various parameters the standard Student–Fisher test was used.

Results

The content of Maccabee beer is shown in Table 1. The data were within an acceptable range of commercial beer.

Clinical and laboratory data are summarized in Table 2. According to the results presented in Table 2 the heart rate, the systolic and diastolic blood pressure and the weight of the patients were not statistically significantly different after the 30-day investigation as compared to their values before the study.

The results which characterize the status of the haemostatic factors are shown in Table 2 and Figs 1 and 2. There are no statistically significant changes in the level of fibrinogen and PT. The fibrinogen levels (mmol L^{-1}) in the blood before the study began ranged from 10.98–17.32 and on completion of the investigation ranged from 10.35–17.52. The PT (%) for the patients before and after the investigation was 83–100 and 86–100, respectively (Table 2).

Table 1 Analytical indices of Maccabee beer[a]

Components	Amount
Proteins (mg mL^{-1})	
Total	5.2 ± 0.09
Albumin	2.4 ± 0.02
Globulin	0.7 ± 0.006
Other proteins	2.1 ± 0.02
Carbohydrates (% on dry substance)	
Total sugars	20.5 ± 0.47
Reducing sugars	14.8 ± 0.32
Sugars (% on dry substance)	
Glucose	0.9 ± 0.04
Maltose	38.5 ± 0.53
Maltotriose	30.5 ± 0.37
Dextrins	30.1 ± 0.29
Amines (mg L^{-1})	
Tyramine	6.52 ± 0.03
Histamine	4.98 ± 0.04
Fats as glycerol (mg mL^{-1})	0.068 ± 0.005
Antioxidants (mg L^{-1})	
Total phenolics	345.4 ± 3.8
Phenolic acids	
p-coumaric	52.4 ± 0.76
Protocatechuic	184.3 ± 3.4
Flavonoids	
Epicatechin	132.0 ± 2.5
Quercetin	1.8 ± 0.03
Reductans (mM)	
Sulfites	0.054 ± 0.001
Alcohol (% volume)	5.1 ± 0.03
Calories (cal L^{-1})	24.5 ± 0.04

[a] All results show mean values of triplicates ± standard deviation.

The change of F VIIc (Fig. 1) was statistically significant ($t = 2.61$, $P < 0.01$). In 15 of the 22 patients investigated, a decrease in the level of the F VIIc was found; there was not a single case showing an increase.

The decrease of F VIIag was statistically significant after the investigation ($t = 3.85$, $P < 0.001$). In 20 out of the 22 patients investigated a decrease in the level of F VIIag was found; there was not a single case showing an increase.

The decrease of PAI after the investigation was not significant ($t = 1.59$, $P > 0.05$) and in 13 of the 22 patients investigated the PAI level remained unchanged (Fig. 2).

There were no statistically significant changes in the clinical and laboratory data of the control group after 30 days of observation.

Table 2 Some clinical and laboratory data

	Control group				Experimental group				
	Before		After		Before		After		
	Range	M ± m	Range	M ± m	Range	M ± m	Range	M ± m	*P*
Heart rate min^{-1}	48–79	62.7 ± 2.05	49–80	62.9 ± 1.32	51–80	63.8 ± 1.75	47–79	64.1	ns
Systolic BP (mmHg)	112–172	146.8 ± 3.4	110–170	145.9 ± 2.8	109–168	145.2 ± 2.6	110–166	144.2 ± 2.9	ns
Diastolic BP (mmHg)	70–92	84.1 ± 1.25	72–96	83.6 ± 1.18	69–90	85.4 ± 0.87	71–96	84.7 ± 1.32	ns
Weight (kg)	57–90	72.5 ± 1.8	58–90	72.8 ± 1.6	56–93	75.9 ± 1.8	56–94	76.3 ± 2.0	ns
Fibrinogen (mmol L^{-1})	11.01–17.29	11.5 ± 0.65	11.0–17.28	11.51 ± 0.64	10.98–17.32	11.47 ± 0.34	10.35–17.52	11.46 ± 0.4	ns
Prothrombin time (%)	82–100	97.1 ± 1.81	83–100	97.0 ± 1.79	83–100	97.2 ± 0.96	86–100	97.0 ± 0.89	ns

NS, not significant.

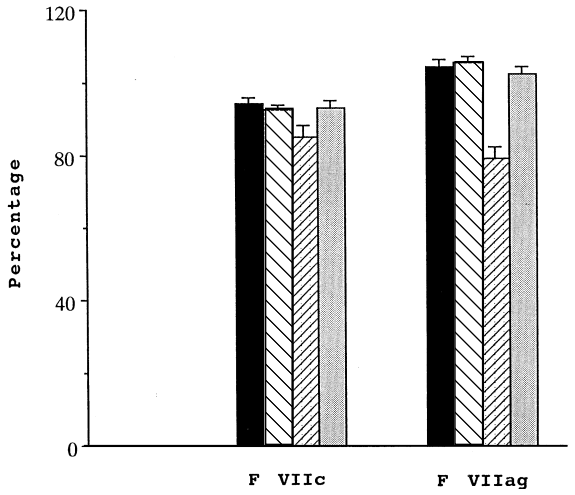

Fig. 1 Factor VIIc and VIIag levels in the control and tested groups before (▨ and ■, respectively) and after experiment (▨ and ▨, respectively). Mean ± standard deviation (vertical lines). Only changes in tested group were significant ($P < 0.01$ and $P < 0.001$, respectively).

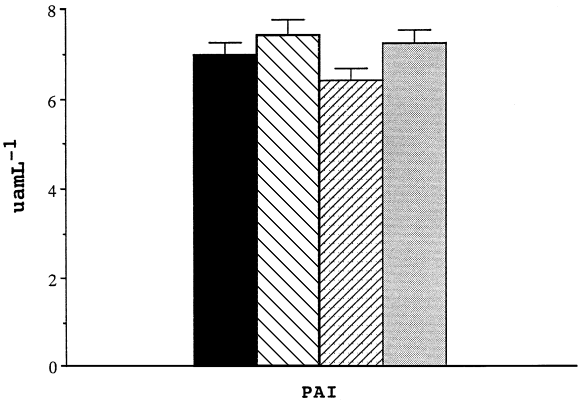

Fig. 2 Plasminogen activator inhibitor (PAI) levels in the control and tested groups before (▨ and ■, respectively) and after the experiment (▨ and ▨, respectively). Mean ± standard deviation (vertical lines). Changes in the tested group were significant ($P < 0.05$).

Discussion

The major risk factors of CAD are high levels of LDL in blood, hypertension, smoking and others. Less is known about indicators of blood coagulation which related to this disease [30–32]. Thus a high level of F VIIc is associated with an increased risk of dying from CAD [30, 33]. Some authors have found a high PAI activity in patients with CAD [34–36].

Many epidemiological studies show that moderate alcohol consumption leads to a decrease in the morbidity and mortality from CAD [1–7].

It is well known that one of the major complications of CAD is myocardial infarction (MI) – the main cause of death from this disease. But the major reason for MI is the closing of the coronary arteries by a thrombus [12, 13, 15]. Therefore if we take into consideration the fact that patients who consume moderate levels of beer, show a decrease in mortality from CAD, this leads to the conclusion that there have been positive changes in the status of blood coagulation.

We did not find statistically significant changes in the levels of fibrinogen and PT after the investigation, but we did find statistically significant changes in F VIIc and F VIIag and to a lesser extent in PAI levels: in all of these tests we noted a decrease in their value, which indicates a decrease in the thrombogenic activity. The decrease in Factor VIIag levels was slightly more than the corresponding activity and no apparent explanation was found. Therefore we examined an additional group of 11 patients and obtained the same data.

The results of this investigation leads to the following conclusions: (a) a moderate beer consumption does not influence the clinical status of patients with CAD; (b) most basic laboratory tests remained unchanged; (c) even a short-term period of moderate beer consumption results in a decrease in thrombogenic activity; (d) among the tests which we used to determine the status of blood coagulation the only F VIIc and F VIIag showed any change; (e) lowering the thrombogenic activity in patients with CAD as a result of moderate beer consumption may be the main cause of the decreased mortality from this disease.

References

1 Renaud S, De Lorgeril M. Wine, alcohol, platelets and the French paradox for coronary heart disease. *Lancet* 1992; **339:** 1523–6.
2 Friedman LA, Kimball AW. Coronary heart disease and alcohol consumption in Framingham. *Am J Epidemiol* 1986; **124:** 481–9.
3 Moor RD, Pearson TA. Moderate alcohol consumption coronary disease. *Medicine* 1986; **65:** 246–67.
4 Marmor M, Brunner E. Alcohol and cardiovascular disease: the status of the U shape curve. *Brit Med J* 1991; **303:** 565–8.
5 Klatsky AL, Armstrong MA, Friedman GD. Alcohol and mortality. *Ann Intern Med* 1992; **117:** 646–54.
6 Jackson R, Scragg R, Beaglehole R. Alcohol consumption and risk of coronary artery disease. *Brit Med J* 1991; **303:** 211–6.
7 Yano K, Rhoads GG, Kagan A. Coffee, alcohol and risk of coronary artery disease among Japanese men living in Hawaii. *New Engl J Med* 1977; **297:** 405–9.

8 Langer RD, Criqui MH, Reed DM. Lipoproteins and blood pressure as biological pathways for effect of moderate alcohol consumption on coronary artery disease. *Circulation* 1992; **85:** 910–5.
9 Suh I, Shaten BJ, Cutler JA, Kuller LH. Alcohol use and mortality from coronary artery disease: the role of high-density lipo-protein cholesterol. *Ann Intern Med* 1992; **116:** 881–7.
10 Frankel EN, Kanner J, German JB, Parks E, Kinsella JE. Inhibition of oxidation of human low density lipoprotein by phenolic substances in red wine. *Lancet* 1993; **341:** 454–7.
11 Rankin SM, Whalley CV, Hoult JR, Jessup W, Wilkins GM, Collard J, *et al*. The modification of LDL by the flavonoids myricetin and gossypatin. *Biochem Pharmacol* 1993; **45:** 67–75.
12 Buja LM, Willerson JT. The role of coronary artery lesions in ischemic heart disease. *Hum Pathol* 1987; **18:** 451–61.
13 De Wood MA, Spores J, Notske R, Mouser LT, Burroughs R, Golden MS, *et al*. Prevalence of total coronary occlusion during the early hours of transmural myocardial infarction. *New Engl J Med* 1980; **303:** 897–902.
14 Rapaport E. Thrombolitic agents in acute myocardial infarction. *New Engl J Med* 1989; **320:** 861–4.
15 Brosins FC III, Roberts WS. Significance of coronary arterial thrombus in transmural acute myocardial infarction. A study of 54 necropsy patients. *Circulation* 1981; **63:** 810–6.
16 GISSI. Effectiveness of intravenous thrombolytic treatment of acute myocardial infarction. *Lancet* 1986; **i:** 97–401.
17 GISSI. Long-term effects of intravenous thrombolysis in acute myocardial infarction. *Lancet* 1987; **ii:** 71–4.
18 ISIS-2. Collaborative Group. Randomized trial of intravenous streptokinase, oral aspirin, both or neither among 17187 cases of suspected acute myocardial infarction. *Lancet* 1988; **ii:** 349–60.
19 Anglo-Scandinavian study of early thrombolysis (ASSET). Trial of tissue plasminogen activator for mortality reduction in acute myocardial infarction. *Lancet* 1988; **ii:** 525–30.
20 GISSI-2. A factorial randomized trial of alteplase versus streptokinase and heparin versus no heparin among 12490 patients with acute myocardial infarction. *Lancet* 1990; **336:** 65–71.
21 ISG. In-hospital mortality and clinical course of 20891 patients with suspected acute myocardial infarction randomized between alteplase and streptokinase with or without heparin. *Lancet* 1990; **336:** 71–5.
22 ISIS-3. A randomized comparison of streptokinase versus tissue plasminogen activator versus antistreplase and of aspirin plus heparin alone among 41299 cases of suspected acute myocardial infarction. *Lancet* 1992; **339:** 753–70.
23 Lee AJ, Lowe GDO, Woodward M. Fibrinogen in relation to personal history of prevalent hypertension, diabetes, stroke, intermittent claudication, coronary heart disease and family history. The Scottish Heart Health Study. *Br Heart J* 1993; **69:** 338–42.
24 Ernst E, Resch KL. Fibrinogen as a cardiovascular risk factor: A meta analysis and review of the literature. *Ann Intern Med* 1993; **118:** 956–63.
25 Williams WG. Kinetics of plasma coagulation factors. In: MC Graw RP, Lerner M, eds. *Hematology*, 3rd edn. McGraw-Hill: 1983; 1222–65.
26 Ogston D, Bennett B. Blood coagulation mechanism. In: Poller J, ed. *Blood Coagulation*. Churchill Livingstone, New York: 1991; 1–15.
27 Juhan-Vague I, Collen D. On the role of coagulation and fibrinolysis in atherosclerosis. *Ann Epidemiol* 1992; **2**(4): 427–38.
28 Sharrett AR. The atherosclerosis risk in communities (ARIC) study. Introduction and objectives of the haemostasis components. *Ann Epidemiol* 1992; **2**(4): 467–9.
29 Folsom AR, Conlan MG, Davis CE, Wu KK. Relation between haemostasis variables and cardiovascular risk factors in middle aged adults. Atherosclerosis risk in communities (ARIC) study investigations. *Ann Epidemiol* 1992; **2**(4): 481–94.
30 Meade TW, North WR, Chakrabarti RR, Stirling Y, Haines AP, Thompson SG, *et al*. Haemostatic function and cardiovascular death: early results of a prospective study. *Lancet* 1980; **i:** 1050–4.
31 Meade TW. Factor VII and ischemic heart disease: epidemiological evidence. *Haemostasis* 1983; **13:** 178–85.
32 Meade TW, Mellows S, Brozovic M, Miller GJ, Chakrabarti RR, North WR, *et al*. Haemostatic function and ischemic heart disease: principal results of the Northwick Park Heart Study. *Lancet* 1986; **ii:** 533–7.
33 Miller GJ, Martin JC, Webster J, Wilkes H, Miller NE, Wilkinson WH, *et al*. Association between dietary fat intake and plasma factor VII coagulant activity – a predictor of cardiovascular mortality. *Atherosclerosis* 1986; **60:** 269–77.
34 Hamsten A, De Faire U, Walldius G, Dahlen G, Szamosi A, Landon C, *et al*. Plasminogen activator inhibitor in plasma: risk factor for recurrent myocardial infarction. *Lancet* 1987; **ii:** 3–9.
35 Korninger C, Jager R, Huber K, Lechner K. Levels of plasminogen activator inhibitor in patients with angina pectoris. *Klin Wochenschr* 1988; **66**(Suppl. XII): 59–61.
36 Olofsson BO, Dahlen G, Nilsson TK. Evidence of increased levels of plasminogen activator inhibitor and tissue plasminogen activator in plasma of patients with angiographically verified coronary artery disease. *Eur Heart J* 1989; **10:** 77–82.

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