Effect of smoking marihuana and of a high-nicotine cigarette on angina pectoris

The purpose of this study was to determine the effect of smoking marihuana and of high-nicotine cigarettes on exercise-induced angina pectoris. Smoking 1 marihuana cigarette increased the resting product of systolic blood pressure times heart rate 54%, increased the venous carboxyhemoglobin level, and decreased the exercise time until angina 50% in 10 patients with angina pectoris. Smoking 1 high-nicotine cigarette increased the resting product of systolic blood pressure times heart rate 36%, increased the venous carboxyhemoglobin level, and decreased the exercise time until angina 23%. Smoking either marihuana or high-nicotine cigarettes decreases exercise performance until angina by increasing myocardial oxygen demand and by decreasing myocardial oxygen delivery. Smoking 1 marihuana cigarette decreased the exercise time until angina more than smoking 1 high-nicotine cigarette ($p < 0.001$).

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Patients with angina pectoris due to coronary artery disease experience a decrease in exercise performance until the onset of angina after smoking high-nicotine,[3] low-nicotine,[6] non-nicotine,[4] marihuana,[2] and placebo marihuana cigarettes.[2] Smoking 1 high-nicotine cigarette[3] decreases exercise performance until angina more than smoking 1 low-nicotine[6] or 1 non-nicotine cigarette.[5] Smoking 1 marihuana cigarette decreases exercise performance until angina more than smoking 1 placebo marihuana cigarette.[2] The reports do not indicate whether or not smoking marihuana decreases exercise performance until angina more than smoking high-nicotine cigarettes. To determine this, we investigated the effects of smoking 1 marihuana cigarette and of smoking 1 high-nicotine cigarette on exercise-induced angina pectoris in 10 patients with angina and angiographic documentation of severe coronary artery disease. Our data are reported here.

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Materials and methods

The subjects were 10 men, mean age, 49.6 (± 5.8) yr, with classic stable exertional angina pectoris and angiographic evidence of severe coronary artery disease (> 75% narrowing of the lumen of at least 1 major coronary vessel). All 10 smoked at least 20 high-nicotine cigarettes daily. Four patients had smoked 2 marihuana cigarettes during a previous study.[2] Otherwise, none had smoked marihuana previously.

Table I. *Mean resting heart rate, systolic and diastolic blood pressures, product of systolic blood pressure times heart rate, and venous carboxyhemoglobin in the control periods and before and after smoking marihuana and high-nicotine cigarettes ± 1 SD*

	Control	*Before smoking marihuana*	*After smoking marihuana*	*p value*
Heart rate (bpm)	73.3 ± 5.5	72.8 ± 4.5	103.4 ±5.9	*
Systolic blood pressure (mm Hg)	119.8 ±6.0	119.4 ±5.6	129.8 ±6.5	*
Diastolic blood pressure (mm Hg)	79.6 ±4.7	79.4 ±4.5	86.2 ±4.8	*
Systolic blood pressure × heart rate	8,780 ± 769	8,692 ± 678	13,411 ± 967	*
Venous carboxy-hemoglobin (%)	2.19 ± 0.50		3.20 ± 0.43	*

*$p < 0.001$.

The 10 patients were familiarized with the equipment and the procedures and practiced exercising upright on a Collins constant-load bicycle ergometer before the study began. The study was performed on 4 consecutive mornings. The 10 men did not smoke from 10 to 12 hr prior to the study. They were observed carefully on each study morning to make sure that they smoked only as part of the study protocol.

On 4 successive study mornings, at 7:30 or 8:00 A.M., with the subject in the fasting state, venous blood was drawn and analyzed for carboxyhemoglobin and hemoglobin levels with an Instrumentation Laboratory, Inc. 182 Co-Oximeter. A Holter electrocardiocorder, model 350G, was then attached to the subject.

After this, Leads V_6, V_5, V_4, aV_F, II, and I were recorded in that order, with an electrocardiograph and with the patient supine. An electrocardiogram was then recorded with a modified Lead V_5 with the patient sitting upright on the bicycle ergometer. The resting heart rate was recorded from this electrocardiogram. The resting blood pressure was measured with a mercury sphygmomanometer, with the patient sitting upright on the bicycle ergometer.

Each subject then exercised upright on the bicycle ergometer with a progressive workload[9] until the onset of angina; time was recorded with a stopwatch. The workload used was 25 watts for 180 sec and then 50 watts. Blood pressure and heart rate at the onset of angina were recorded with the patient continuing to exercise until these values were obtained. An electrocardiogram was recorded with a modified Lead V_5 at the onset of angina with the subject in the upright position. Leads V_6, V_5, V_4, aV_F, II, and I were recorded in that order with an electrocardiograph, the patient supine immediately after angina and 1, 2, 3, 4, 5, and 6 min after exercise-induced angina.

One hour after completion of the exercise, Leads V_6, V_5, V_4, aV_F, II, and I were recorded with an electrocardiograph with the patient supine. After this, resting heart rate and blood pressure were obtained as described above with the patient sitting upright on the bicycle ergometer. In a randomized study, each patient smoked on 2 mornings 1 marihuana cigarette and on 2 mornings 1 high-nicotine cigarette containing 1.8 mg of nicotine while sitting on the bicycle ergometer. Neither the investigators nor the patients knew which cigarette would be smoked. However, the aroma of marihuana smoking prevented a double-blind study.

The subjects inhaled 10 puffs of smoke from the marihuana cigarette (approximately ¾ of the cigarette), which contained 18.9 mg of delta-9-tetrahydrocannabinol and 10 puffs of smoke from the high-nicotine cigarette (approx-

Control	*Before smoking high-nicotine cigarette*	*After smoking high-nicotine cigarette*	*p value*
74.0 ± 3.8	73.8 ± 5.0	89.4 ± 5.4	*
120.1 ± 5.6	120.6 ± 6.2	135.3 ± 7.7	*
79.6 ± 4.8	79.7 ± 5.2	88.6 ± 6.5	*
8,887 ± 692	8,907 ± 846	12,105 ± 1,114	*
2.17 ± 0.40		3.05 ± 0.42	*

imately 4/5 of the cigarette). The patient smoked the cigarette at his own pace. Patients 1, 4, 5, 6, and 10 smoked 1 marihuana cigarette on mornings 1 and 4 of the study and 1 high-nicotine standard nonfilter cigarette on mornings 2 and 3 of the study. Patients 2, 3, 7, 8, and 9 smoked 1 marihuana cigarette on mornings 2 and 3 of the study and 1 high-nicotine standard nonfilter cigarette on mornings 1 and 4 of the study.

After the cigarette was smoked, the blood pressure and heart rate were measured as described above. Venous blood was then drawn and analyzed for carboxyhemoglobin and hemoglobin levels. After this, the patient exercised upright on the bicycle ergometer until the onset of angina. Exercise until the onset of angina was timed with a stopwatch, and the blood pressure and heart rate at the onset of angina were measured as described above. The exercise-electrocardiogram protocol described above was then repeated. The data were statistically analyzed using the t test for correlated means.

Results

Table I indicates the mean resting heart rate, systolic and diastolic blood pressures, product of systolic blood pressure times heart rate, and venous carboxyhemoglobin levels (± 1 SD) in the control periods and before and after smoking 1 marihuana and 1 high-nicotine cigarette. Table I also shows the p values after smoking marihuana compared to the control period and compared to before smoking marihuana and the p values after smoking 1 high-nicotine cigarette compared to the control period and compared to before smoking 1 high-nicotine cigarette. All hemoglobin values were within normal limits and showed no significant change.

The increase in mean resting heart rate after smoking marihuana was greater than the increase in mean resting heart rate after smoking 1 high-nicotine cigarette ($t = 11.75$; $p < 0.001$). The increase in mean resting systolic blood pressure after smoking 1 high-nicotine cigarette was greater than the increase in mean resting systolic blood pressure after smoking marihuana ($t = 2.95$; $p < 0.001$). The increase in mean resting diastolic blood pressure after smoking 1 high-nicotine cigarette was greater than the increase in mean resting diastolic blood pressure after smoking marihuana ($t = 2.18$; $p < 0.05$). The increase in mean resting product of systolic blood pressure times heart rate after smoking marihuana was greater than the increase in mean resting product of systolic blood pressure times heart rate after smoking 1 high-nicotine cigarette ($t = 7.24$; $p < 0.001$). The increase in venous carboxyhemoglobin level after smoking marihuana was greater than the increase in venous carboxyhemoglobin level after smoking 1 high-nicotine cigarette ($t = 2.39$; $p < 0.05$).

Table II shows the exercise performance until the onset of angina for each patient in the control periods and after smoking 1 marihuana and 1 high-nicotine cigarette. There was a decrease in exercise time until angina of 50% after smoking 1 marihuana cigarette ($t = 24.77$; $p < 0.001$). There was a decrease in exercise time until angina of 23% after smoking 1 high-nicotine cigarette ($t = 12.85$; $p < 0.001$). The decrease in exercise time until angina was greater after smoking marihuana than after smoking 1 high-nicotine cigarette ($t = 15.19$; $p < 0.001$).

Table III indicates the mean maximal amount of ischemic S-T segment depression after ex-

Table II. *Exercise time until angina in the control periods and after smoking marihuana and high-nicotine cigarettes ± 1 SD*

Patient	*Control (sec)*	*After smoking marihuana (sec)*	*Change from control (%)*	*Control (sec)*	*After smoking high-marihuana cigarette (sec)*	*Change from control (%)*
1	251	108	57	248	164	34
	217	106	51	209	148	29
2	185	74	60	161	127	21
	178	96	46	167	149	11
3	249	134	46	247	200	19
	305	143	53	289	214	26
4	184	83	55	190	123	35
	162	60	63	165	129	22
5	268	113	58	266	192	28
	299	170	43	283	246	13
6	265	162	39	254	211	17
	286	160	44	323	252	22
7	280	149	47	301	212	30
	242	106	56	233	156	33
8	182	93	49	190	145	24
	214	98	54	227	176	22
9	263	136	48	216	177	18
	241	132	45	228	181	21
10	282	140	50	284	239	16
	314	218	31	330	264	20
Mean	243.4	124.1	50	240.6	185.3	23
± 1 SD	±46.6	±37.7		±51.3	±43.5	

ercise-induced angina, and the mean heart rate, systolic blood pressure, diastolic blood pressure, and product of systolic blood pressure times heart rate at the onset of angina pectoris (± 1 standard deviation) in the control periods and after smoking marihuana and high-nicotine cigarettes. Table III also shows the p values after smoking marihuana compared to the control period and the p values after smoking high-nicotine cigarettes compared to the control period.

The decrease in systolic blood pressure, heart rate, and product of systolic blood pressure times heart rate at the onset of angina did not differ significantly after smoking one marihuana cigarette to that after smoking 1 high-nicotine cigarette.

Ischemic S-T segment depression was not observed in the electrocardiographic recordings during the smoking of marihuana or high-nicotine cigarettes in any of our subjects. No significant difference in the amount of maximal ischemic S-T segment depression (using Leads V_6, V_5, V_4, aV_F, II, or I in which maximal ischemic S-T segment depression was observed) after exercise-induced angina was observed between the control periods, after smoking marihuana, and after smoking high-nicotine cigarettes.

Discussion

The product of systolic blood pressure times heart rate correlates with myocardial oxygen consumption and may be used as an indirect

Table III. *Mean maximal ischemic S-T segment depression at angina, heart rate, systolic and diastolic blood pressures, and product of systolic blood pressure times heart rate at onset of angina in the control periods and after smoking marihuana and high-nicotine cigarettes ± 1 SD*

	Control	*After smoking marihuana*	*p value*	*Control*	*After smoking high-nicotine cigarette*	*p value*
S-T segment depression (mm)	1.28 ± 0.30	1.35 ± 0.29	*	1.30 ± 0.30	1.33 ± 0.34	*
Heart rate (bpm)	133.9 ± 7.9	130.2 ± 7.8	†	133.8 ± 8.1	130.9 ± 7.6	†
Systolic blood pressure (mm Hg)	155.1 ± 8.5	153.0 ± 8.4	†	155.0 ± 7.9	153.4 ± 7.8	†
Diastolic blood pressure (mm Hg)	80.1 ± 4.4	80.3 ± 4.6	*	80.0 ± 4.7	80.6 ± 6.2	*
Systolic blood pressure times heart rate	20,807 ± 2,144	19,960 ± 2,110	†	20,775 ± 2,092	20,114 ± 1,990	†

*p not significant.
†$p < 0.001$.

index of myocardial oxygen consumption in evaluating angina pectoris.[1, 7, 8] By causing an increase in product of systolic blood pressure times heart rate, smoking either marihuana or a high-nicotine cigarette caused an increase in myocardial oxygen demand in our subjects with angina pectoris who were unable to increase their coronary blood flow adequately while exercising. Myocardial oxygen demand exceeded myocardial oxygen supply sooner, inducing angina earlier while exercising after smoking either marihuana or a high-nicotine cigarette than in the nonsmoking control state.

Since smoking 1 marihuana cigarette induced a greater increase in resting product of systolic blood pressure times heart rate (54%) than smoking 1 high-nicotine cigarette (36%), smoking 1 marihuana cigarette caused a greater increase in myocardial oxygen consumption than smoking 1 high-nicotine cigarette. It is not surprising, therefore, that smoking 1 marihuana cigarette also caused a greater decrease in exercise time until the onset of angina pectoris than smoking 1 high-nicotine cigarette.

A similar small but significant decrease in product of systolic blood pressure times heart rate at exercise-induced angina occurred after smoking either 1 marihuana cigarette or 1 high-nicotine cigarette. By causing an increase in carboxyhemoglobin level, smoking either 1 marihuana cigarette or 1 high-nicotine cigarette also interfered with myocardial oxygen delivery.

No significant difference between the amount of maximal ischemic S-T segment depression after exercise-induced angina after smoking marihuana or high-nicotine cigarettes was observed. However, compared to the control periods, ischemic S-T segment depression at the onset of exercise-induced angina occurred earliest and after least exercise after smoking 1 marihuana cigarette and earlier and after less exertion after smoking 1 high-nicotine cigarette.

In summary, smoking either 1 marihuana cigarette or 1 high-nicotine cigarette decreases exercise performance until the onset of angina pectoris. This decrease in exercise performance until the onset of angina pectoris is greater after smoking 1 marihuana cigarette than after smoking 1 high-nicotine cigarette.

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