

EFFECT OF ACETIC ACID AND CLOFIBRATE ON PLASMA LIPID IN RATS WITH ATHEROSCLEROSIS

Khalid H. H. Sharaf
Department of Physiology
College of Veterinary Medicine
Mosul University

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الخلاصة

أستخدمت في هذه الدراسة مجموعتين من ذكور الجرذان البالغة البيضاء نموذجاً تجريبياً تراوحت أعمارها بين 3-4 أشهر ، وأوزانها 155-262 غم ، المجموعة الأولى مكونة من خمسة جرذان سليمة هي عينة سيطرة سليمة أما الثانية فمكونة من 20 جرذاً مصاباً بالتصلب العصيدي المحدث ببيروكسيد الهيدروجين والكولستيرول ، قسمت الى أربعة مجاميع متساوية العدد ، المجموعة الأولى عوملت بزيت زهرة الشمس بالتجريب عن طريق الفم واعتبرت عينة سيطرة مصابة بالتصلب العصيدي ، والمجموعة الثانية عوملت بـ 300 ملغم كلوفايبريت/كغم وزن جسم ، (عقار مخفض للدهون البروتينية بالدم) بالتجريب عن طريق الفم واعتبرت عينة قياسية ، اما المجموعة الثالثة والرابعة فجرعت بحامض الخليك 5.23 و 10.45 ملغم /كغم من وزن الجسم على التوالي عن طريق الفم واعتبرت عينات تجريبية. جمعت عينات الدم من وريد منضمة العين باستعمال أنبوبة شعرية محتوية على الهيبارين ، تم تقدير الدهون الكلية والكولستيرول الكلي والدهون البروتينية عالية الكثافة والشحوم البروتينية الواطئة والواطئة جداً بالبلازما ودلائل التعصد والكولستيرول الكلي بالكبد ، كما تم تقدير الحالة التغذوية لمجاميع الجرذان كافة. اظهرت النتائج ان حامض الخليك كان سبباً في زيادة الدهون البروتينية الواطئة الكثافة والواطئة جداً ودلائل التعصد هذا فضلاً عن انخفاض الدهون البروتينية عالية الكثافة بالبلازما بالإضافة الى نقصان وزن الجسم وتدهور الحالة التغذوية وعليه يعتبر حامض الخليك من العوامل التي تزيد من مستوى الدهن بالدم.

ABSTRACT

In this study two major groups of albino adult male rats (3-4 months old and 155-262g weight) were used as experimental model for this study. First group contains five healthy rats used as healthy control group. Second group consisted of twenty rats with atherosclerosis induced by hydrogen peroxide and cholesterol, which was further subdivided into four subgroups with five rats in each. First subgroup was orally treated with sunflower oil alone and considered atherosclerosis control group, the second subgroup was treated with 300mg clofibrate drug/kg rat body weight and considered hypolipidemic standard reference group, third and fourth subgroups were orally treated with 5.23 and 10.45mg acetic acid/kg body weight, respectively. Blood samples were collected from retro-ocular eye vein by using heparinized capillary tubes. Plasma total lipid (TL), total cholesterol (TC), high density lipoprotein-cholesterol (HDL-c) and liver total cholesterol (TC) were determined. Nutritional status of the rats was estimated throughout body weight gain and apparent digestibility. Analysis of variance and Duncan test showed that, the acetic acid caused an increase in plasma TL, TC, very low density lipoprotein-cholesterol and low density lipoprotein-cholesterol (VLDL-c+LDL-c), atherogenic indices, and liver TC values and a decrease in plasma HDL-c. Furthermore, body weight losses and bad nutritional status were recorded. Therefore, acetic acid was regarded as a hyperlipidemic material.

INTRODUCTION

Atherosclerosis is an evision disease caused by blood hyperlipoproteinemia and arterial and cardiac disorders. The major concept in this state is controlling the cholesterol metabolism. Mammalian cells have few LDL risk type receptors. On other hand Infamilial hypercholesterolemia, the receptor is deficient, therefore atherosclerosis is common. In other approach, the blood HDL value which considered to be the protective and useful cholesterol carriers type, is low (1). The atherogenic ratios TC/HDL and LDL/HDL are regarded as the important factors in assessing the risk of fatal heart disease (2). Diet modification for hypercholesterolemic patients is the first line of lowering cholesterol concentration in blood and liver, but it had limited efficacy. Therefore, the patients, who are taking cholesterol lowering drugs for long term, (more than 5 years), unfortunately those drugs may be increased cancer mortality (3).

Clofibrate (Atromid-S), the ethyl ester of chlorophenoxyisobutyric acid, is hydrolyzed and absorbed in gastrointestinal track, resulting anion transported material in plasma bounded to albumin. Clofibrate was used as vehicle for androsterone, it lowers the concentration of plasma

lipid content of diet, eliminated feces weight, feces lipid content, apparent digestibility (dry matter absorption by rats) and dietary lipid absorption percentages between the atherosclerotic rat groups orally treated with acetic acid and clofibrate.

The body weight gains of atherosclerotic rat groups were lower than that weight of healthy control rat group. Those body weight gains of atherosclerotic rats treated with acetic acid were lower than the weight gain of rat group treated with clofibrate. The ingested diet and eliminated feces of atherosclerotic rats treated with acetic acid were lower than that weights of atherosclerotic rats treated with clofibrate and in turn lower than that weights of healthy control rat group. Apparent digestibility of atherosclerotic rat groups treated with acetic acid were lower than that digestibility of rat treated with clofibrate and also in turn, were lower than the digestibility of healthy rat control group. Acetic acid may caused bad digestibility in atherosclerotic rats comparing with healthy rat group. The dietary lipid absorption of atherosclerotic rat groups treated with acetic acid was higher than that absorption of rat treated with clofibrate. Lipid absorption of the atherosclerotic rats was lower than that absorption of healthy rats.

Table (4) showed a significant differences ($p < 0.05$) between plasma TL, TC HDL-c, VLDL-c+LDL-c levels of atherosclerotic rat groups orally treated with clofibrate and acetic acid compared with healthy and atherosclerotic rat control groups. Furthermore, there were significant differences ($p < 0.05$) between atherogenic indices and liver TC level of the atherosclerotic rat groups treated with clofibrate and acetic acid compared with healthy and other atherosclerotic rat groups. The TL, TC, VLDL-c+LDL-c levels, atherogenic indices and liver TC of atherosclerotic rat groups treated with 300mg clofibrate hypolipidemic drug were lower than that of atherosclerotic rat control group. In addition, HDL-c of the clofibrate rat group was higher than that of atherosclerotic control group, while the TL, TC, VLDL-c+LDL-c, atherogenic indices and liver TC of atherosclerotic rats treated with acetic acid were higher and HDL-C level was lower than that values of atherosclerosis rat control group for 15 days experimental period. The TL, TC, VLDL-c+LDL-c, atherogenic indices, and liver TC values of atherosclerotic rats were higher and HDL-C was lower than HDL-c of healthy rat group.

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Table (3): Effect of acetic acid and clofibrate hypolipidemic drug on the nutritional status of healthy and atherosclerosis-induced male adult rats (mean⁽¹⁾ ± S.E.)⁽²⁾

Physiological status of rats	groups	Body weight (g)		Ingested diet (g)		Eliminated feces (g)		Apparent digestibility %	Dietary lipid absorption %
		initial	gain	Weight	Lipid content	Weight	Lipid content		
healthy	Control	A	A	A	B	A	C	A	A
	Control	186.30±10.98	34.98±3.12	174.98±7.53	9.73±0.73	31.68±1.09	2.15±0.21	99.82±1.82	77.90±0.85
Atherosclerosis	Clofibrate 300 mg/kg B.W.	B	C	B	C	C	B	C	C
		167.04±12.06	3.30±0.27	103.44±5.11	6.79±0.47	22.22±1.14	4.54±0.37	78.52±1.21	33.14±0.27
	A	B	A	A	A	A	A	B	B
	246.28±16.62	4.40±2.33	186.78±10.38	12.25±0.68	35.58±3.26	6.89±1.23	80.95±2.01	43.76±1.58	
Acetic acid 5.23 mg/kg B.W.	A	D	C	D	D	C	C	C	B
	198.13 ± 13.08	2.15±0.38	79.64 ± 6.11	5.22 ± 0.71	18.64±2.11	2.87±0.41	76.59±3.72	45.10±2.09	
Acetic acid 10.45 mg/kg B.W.	A	E	D	E	E	B	C	D	B
	204.71 ± 12.92	1.93 ± 0.24	68.42 ± 5.01	4.49 ± 0.62	28.15 ± 2.00	2.38 ± 0.54	58.86 ± 2.20	47.00 ± 1.93	

(1) mean of five rats. (2) Different letters in the same column are significantly different at p < 0.05.

Table (4): Effect of acetic acid and clofibrate hypolipidemic drug on the plasma lipids, lipoproteins, atherogenic indices and liver total cholesterol of healthy and atherosclerosis-induced male adult rats (mean⁽¹⁾ ± S.E.)⁽²⁾

Physiological status of rat	groups	Plasma lipids and lipoproteins												Atherogenic indices				Liver TC mg/100g
		TL mg/dl		TC mg/dl		HDL-C mg/dl		VLDL-C+LDL-C mg/dl		TC/HDL-C		VLDL-C+LDL-C /HDL-C						
		1 day	15 days	1 day	15 days	1 day	15 days	1 day	15 days	1 day	15 days	1 day	15 days					
Healthy	Control	B	C	C	C	A	A	C	C	B	C	C	C	B				
		326.84±	424±	57.06±	80.18±	48.56±	61.58±	8.50±	18.70±	1.18±	1.30±	0.18±	0.30±	4.64±				
Atherosclerosis	Control	A	A	A	A	B	C	A	A	A	A	A	A	A				
		676.28±	724.1±	106.6±	118.1±	36.50±	30.72±	71.18±	77.45±	3.00±	3.52±	2.01±	2.52±	9.64±				
	A	B	B	B	A	B	B	B	A	B	B	B	B	B				
	79.37	84.19	3.15	4.66	3.00	3.42	4.66	5.17	0.17	0.12	0.10	0.32	0.34					
Clofibrate 300mg/kg B.W.	A	A	A	A	B	B	B	B	A	B	B	B	B					
	708.40±	544.9±	91.48±	100.3±	37.80±	47.30±	53.68±	53.08±	2.42±	2.12±	1.42±	1.12±	4.07±					
Acetic acid 5.23mg/kg B.W.	A	A	A	A	B	C	A	A	A	A	A	A	A					
	692.34±	795.1±	108.7±	109.9±	33.98±	30.82±	74.79±	79.12±	3.20±	3.57±	2.20±	2.57±	9.93±					
Acetic acid 10.45mg/kg B.W.	A	A	A	A	B	C	A	A	A	A	A	A	A					
	706.91±	822.1±	112.1±	117.7±	32.04±	29.96±	80.14±	87.80±	3.50±	3.93±	2.50±	2.93±	9.98±					
		B.W.	B.W.	B.W.	B.W.	B.W.	B.W.	B.W.	B.W.	B.W.	B.W.	B.W.	B.W.					
		75.32	89.95	8.79	7.88	3.62	3.92	5.97	4.95	0.22	0.29	0.53	0.57					

(1) mean of five rats. (2) Different letters in the same column are significantly different at p < 0.05.

DISCUSSION

Ordinary diet ingredients were formulated according to American national academy of sciences/nutritional research council (1978) and modified in order to meet the nutritional and physiological requirements of albino rats. While the addition of 1% cholesterol was considered a lipid supplementation of atherosclerosis diet. As recommended by Sharaf and Ali (7) and Kalloo (20).

The body weight gain (BWg) of the healthy rats was higher (34.98) than that of atherosclerotic rat groups (3.30, 4.40, 2.15 and 1.93g respectively). This result seem to agree with the result obtained by Sharaf and Ali (7) in the rats. The BWg of the atherosclerotic rats orally treated with 5.23 and 10.45mg/kg BW was lower (2.15 and 1.93g) than that of atherosclerotic rats (4.40) orally treated with 300mg clofibrate/kg BW. The increasing concentration of acetic acid caused a decreasing in the BWg of the atherosclerotic rats. BWg of the atherosclerotic rats treated with colifbrate was higher (4.40) than that of the atherosclerotic rats control group (3.30). The ingested diet (weight, and lipid content) and eliminated feces (weight and lipid content) were followed the BWg manner. These results were in agreement with the results obtained by Ali (21) in the rats. The apparent digestibility of atherosclerosis rat groups treated with 5.23 and 10.45mg acetic acid/kg BW were lower than that of the atherosclerotic rats treated with clofibrate and atherosclerotic rat control groups, this was due to the lowest diet weight intake comparing with the healthy and atherosclerotic rat groups. The dietary lipid absorption percent of the atherosclerotic rat groups treated with acetic acid was higher than that of clofibrate and atherosclerotic rat control groups, but it is lower than lipid absorption of healthy rats, this may be due to the effect of acid medium of acetic, which hydrolyzed the ester linkage of lipid compounds and in turn increased lipid absorption in the atherosclerosis status.

Treating rats with dietary cholesterol and hydrogen peroxide in drinking water resulting to active free radical roots, which caused the atherosclerosis status, and in turn caused an increasing values of blood lipid profile (TL, TC, VLDL-c, and LDL-c) as well as atherogenic indices (TC/HDL-c, and VLDL-c+LDL-c/HDL-c) in atherosclerotic rats (control, clofibrate and acetic acid treated rat groups). These results agreed with the results obtained by Khudair (22) and Gorinstein *et al.* (23). The atherosclerosis status decreased blood HDL-c value comparing with healthy control rat group, these results agreed with the conclusion reported by Kinosian (2), Khudair (22) and Malinow *et al.* (24) The atherogenic indices of the rat groups treated with 5.23 and 10.45mg acetic acid/kg rat body weight were still higher values (3.57 and 3.93 for TC/HDL-c, 2.57 and 2.93 for VLDL-c+LDL-c/HDL-c respectively for 15days experimental period) than that value (2.52) for

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control atherosclerotic rat group. Atherogenic indices of the atherosclerotic rat groups (control, clofibrate and acetic acid treated rats) were higher values than that value (0.30) for healthy control group, this result agreed and similar to the result postulated by Kinosian (2).

Liver TC values for the rat groups treated with acetic acid were still similar values (9.93 and 9.98) to that value of atherosclerotic control group(9.64), and higher than that (4.07) value of clofibrate rat group, this result agreed with the result obtained by Malinow *et al.* (24) and Tinker *et al.* (25).

From the data of tables (3 and 4), acetic acid may be regarded as hyperlipidemic material, caused a decrease in body weight, nutritional status, and an increase in the lipid profile, atherogenic indices and liver TC.

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