The Effect of Arvin on Plasma Lipids of the Rabbit (35255)

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Studies involving perfusion or recirculation of whole blood require effective anticoagulation to prevent blood clotting. The anticoagulant of choice is usually heparin. However, heparin also activates lipoprotein lipase (1) an enzyme catalyzing the breakdown of circulating plasma triglycerides. The resulting increase in plasma free fatty acids affects the intermediary metabolism of fat and carbohydrates (2) and prevents a meaningful interpretation of data concerning the utilization and metabolic transformations of the two nutrients.

Recent reports on Arvin, a new anticoagulant, isolated from the venom of the Malayan pit viper (3–5) and acting by removal of fibrinogen from the circulating blood have suggested that this agent may produce uncoagulable blood without the metabolic changes seen after the use of heparin. The present report describes the effects of Arvin on plasma lipids of normal and hypovolemic rabbits and supports the contention of negligible metabolic effects of this anticoagulant.

Methods. Fourteen adult male New Zealand white rabbits, weighing about 2.5 kg each were used in the study. Ten of the animals received injections into the ear vein of 1 unit/kg of body weight of Arvin dissolved in saline (1 unit/ml) (Lot No. T-135, potency 67 units/ml); the remaining 4 rabbits received physiological saline. Venous blood samples were obtained from the other ear immediately before the treatment and 2, 7, and 24 hr after the injection. The 2-hr. interval for the first bleeding was selected because of the reports that it takes well over 1 hr to develop full anticoagulant activity after Arvin (5). After centrifugation in a refrigerated centrifuge, the plasma was removed and analyzed for free fatty acids (FFA) (6), triglycerides (7), and total cholesterol (8). The extent of coagulation inhibition was measured with the capillary tube version of clot retraction method, as described by Reid *et al.* (9).

Three months later, 5 of the rabbits were used to study the effect of Arvin and heparin on the FFA and blood glucose levels during a hypovolemic shock. Three of the rabbits received 1 unit of Arvin/kg of body weight, while the other 2 animals received 5 mg of heparin/kg of body weight intravenously. Ten min after administration of heparin and 2 hr after administration of the Arvin, the animals were bled until ⅓ of their blood volume was removed. It was assumed that blood volume of the rabbits amounts to 6% of the total body weight (10). Blood samples obtained from the contralateral ear immediately before the bleeding and at the end of the bleeding period were analyzed for FFA and blood glucose (11).

Results. Administration of 1 unit of Arvin/kg of body weight led to a marked inhibition of the coagulation process. Blood samples taken 2 and 7 hr after the treatment did not show any signs of clotting, even after 24 hr of standing at room temperature. Samples taken 24 hr after the treatment began to clot in 2 to 7 hr. The blood from the control animals clotted within 10 min.

The effect of treatment on the plasma FFA and triglycerides is shown in Fig. 1. The FFA levels showed a slight increase from the initial level of 332 ± 41 to 419 ± 50 μEq/liter (mean ± standard error of the mean) 2 hr after Arvin administration; this difference was not significant ($p>0.05$). By the end of the 24-hr experimental period the average FFA level of the experimental group declined to 355 ± 46 μEq/liter. The changes in the control animals were even less pronounced and the levels ranged from 274 ±

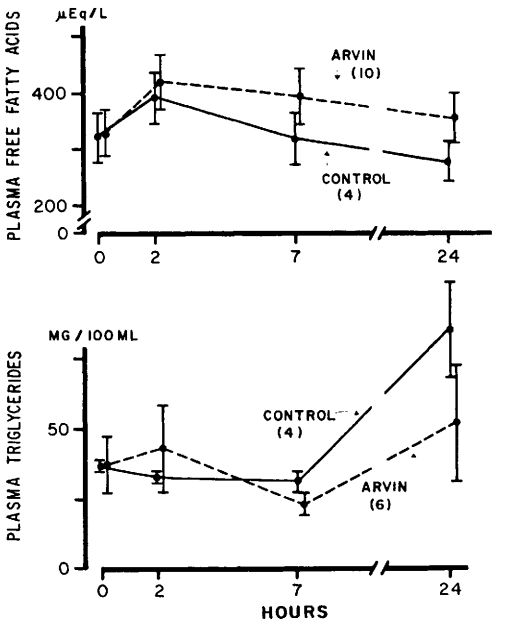

FIG. 1. The effect of Arvin on plasma free fatty acids and triglycerides of rabbits. All animals received 1 unit of Arvin/kg of body weight, intravenously. The vertical lines represent the standard error of the mean; number of animals is shown in parentheses.

34 μEq/liter, seen at the end of the experiment, to 390 ± 43 μEq/liter observed 2 hr after injection of saline. Again, this difference was not significant ($p>0.05$). In a similar way, the plasma triglyceride levels in both the experimental and control groups did not show any significant variation during the first 7 hr following the treatment; however, in both groups there was an increase in values at the end of the study. Plasma total cholesterol levels in the Arvin group ranged from 27 ± 3 mg, observed 7 hr after treatment with Arvin, to 44 ± 3 mg/100 ml, reached after 24 hr; while in the control group the range was from 22 ± 30, also seen 7 hr after Arvin administration, to the pretreatment value of 31 ± 4 mg/100 ml. At none of the time points, was the difference between the Arvin and control groups significant.

The data on plasma FFA and blood glucose changes (Table I) indicate that the loss of blood volume was associated with a rise of blood glucose levels in both the heparin and Arvin groups, while the FFA levels increased only in the animals treated with heparin.

Discussion. The data in the present study indicates that Arvin, unlike heparin, can inhibit blood coagulation without any profound changes in blood lipid levels. An example of the possible differences in metabolic response of animals treated either with heparin or with Arvin is the finding that hypovolemic rabbits receiving Arvin failed to show a rise in plasma FFA, while the animals given heparin demonstrated a marked increase in their FFA levels, reflecting the activation of lipoprotein lipase. Neither of the anticoagulants prevented the rise of blood glucose levels. Hypovolemia usually leads to release of endogenous catecholamines (12), which in turn promote the breakdown of liver glycogen and increases in blood glucose (13). Catecholamines also activate a hormone-sensitive tissue lipolytic system (14); however, the effect of this activation on plasma FFA was probably prevented by the reported vasoconstrictive action of catecholamines on the vasculature of the adipose tissue (15, 16).

TABLE I. Effect of Heparin and Arvin on Plasma FFA and Blood Glucose During Hypovolemia.[a]

		Plasma FFA (μEq/liter)	Blood glucose (mg/100 ml)
Heparin (2)	Control	188	136
	Hypovolemia	1010	377
Arvin (3)	Control	312 ± 45[b]	131 ± 8
	Hypovolemia	344 ± 27	270 ± 3

[a] The number of animals in parentheses. Hypovolemia produced by removing ⅓ of the total blood volume.

[b] Mean ± standard error.

The results of this investigation suggest that the use of Arvin as anticoagulant might affect the intermediate metabolism to a lesser degree than heparin and may permit valid measurements of changes in the various lipid classes.

Summary. Arvin administered intravenously in a dose of 1 unit/kg of body weight to rabbits prevented blood coagulation without any marked effects on plasma free fatty acids, triglycerides, or total cholesterol. Hypovolemic animals pretreated with Arvin showed an increase in blood glucose without any apparent changes in plasma free fatty acids; in hypovolemic rabbits pretreated with heparin, both the blood glucose and plasma free fatty acids were elevated.

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