EFFECT OF ACETYLSALICYLIC ACID ON DEVELOPMENT OF INFARCT-LIKE MYOCARDIAL NECROSES INDUCED IN RATS BY A SINGLE INJECTION OF ISOPROTERENOL

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The development of infarct-like foci of necrosis and the primary development of lesions of the myocardial cells through the direct action of isoproterenol and manifested during the first hour are considerably reduced in animals receiving acetylsalicylic acid. This suggests that acetylsalicylic acid not only prevents platelet aggregation but also increases the resistance of the myocardial cells to the harmful action of catecholamines.

KEY WORDS: Isoproterenol; acetylsalicylic acid; infarct-like necroses.

Recent investigations have shown that propylactic administration of aspirin substantially weakens the development of myocardial necrosis induced in animals by the action of catecholamines [5, 6] and also reduces the size of the zone of ischemic necrosis arising after ligature of the coronary artery [8]. These findings agree with clinical observations of the effectiveness of aspirin in the prevention and treatment of myocardial infarction [11, 12]. However, it is not yet clear whether this action of aspirin is associated purely with its antithrombotic effect [7, 9] or with certain other properties through which the resistance of the myocardial cells to the harmful factor is increased.

The solution to this problem must also shed light on the current question of the role of the disturbance of the microcirculation in the development of infarct-like necrotic changes in the myocardium.

EXPERIMENTAL METHOD

Experiments were carried out on 68 male Wistar rats weighing 200-230 g. Half of the animals received a suspension of aspirin (acetylsalicylic acid) in olive oil via gastric tube daily for 4 days in a dose of 200 mg/kg body weight. The control group received olive oil without aspirin by gastric tube. All the animals then received, at the same time, a single subcutaneous injection of 1% isoproterenol (isopropylnoradrenalin sulfate) in a sublethal dose of 80 mg/kg. The rats were decapitated 30 min, 1 h, and 24 h after injection of the isoproterenol. Fixation of the material and staining of the histological sections were carried out by the standard methods used in the writers' laboratory [4], and the sections were studied in ordinary and polarized light. The degree of damage to the rat myocardium after injection of isoproterenol was determined from encoded data, by three workers separately, using a five-point scale. The results were compared with the aid of Wilcoxon's (White's) nonparametric criterion [3].

EXPERIMENTAL RESULTS

When the myocardium of animals killed 30 min and 1 h after injection of isoproterenol was investigated, changes in muscle cells were found only by polarization microscopy: intracellular myocytolysis, contractural injuries, and primary cloudy swelling of the myofibrils were observed [4]. To assess the degree of injury to the myocardium, only irreversible changes in the muscle cells leading to coagulation

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TABLE 1. Degree of Damage to Myocardium in Rats at Various Times after Injection of Isoproterenol

Time	Treatment	Number of animals	Degree of damage						Mean number of points	α
			0	1	2	3	4	5		
30 min	Isoproterenol	6	—	2	1	3	—	—	2,16	
	Aspirin + isoproterenol	6	3	3	—	—	—	—	0,5	<0,02
1 h	Isoproterenol	10	—	2	—	1	7	—	3,3	
	Aspirin + isoproterenol	10	4	5	1	—	—	—	0,6	<0,002
24 h	Isoproterenol	18	—	—	—	2	2	14	4,66	
	Aspirin + isoproterenol	18	—	—	2	9	6	1	3,33	<0,001

Legend: 0) absence of injuries; 1) irreversible injuries of single cells; 2) irreversible injuries of several separate cells without formation of foci; 3) formation of single foci consisting of several damaged cells; 4) many foci of injury; 5) confluent infarct-like zones of injury. α) level of significance determined with Wilcoxon's (White's) criterion.

Fig. 1. Contractures and primary cloudy swelling of myofibrils in a group of muscle cells from the left ventricle of a rat 1 h after injection of isoproterenol. PAS–hematoxylin, photographed in polarized light, 800 ×.

necrosis – contractures of the II-III degree and primary cloudy swelling of the myofibrils – were taken into account. Damaged muscle cells were arranged singly or in foci consisting of several cells.

As Table 1 shows, in a high proportion of the animals (7 of 16) receiving acetylsalicylic acid before isoproterenol, no severe damage whatsoever took place to the muscle cells during the first hour, and in the other animals the changes were limited to solitary myocytes, whereas in all the animals not receiving acetylsalicylic acid, injection of isoproterenol induced severe damage to the myocardial cells; in most (in 11 of 16) of these animals, foci consisting of several damaged cells appeared (Fig. 1).

In all the rats typical coagulation necroses of myocardial cells appeared 24 h after injection of isoproterenol (Fig. 2). In most animals not receiving acetylsalicylic acid, the separate foci of injury in the middle and lower thirds of the ventricles and ventricular septum merged to form extensive infarct-like zones (Fig. 3). Among the animals receiving aspirin, this picture was observed only in the myocardium of one rat and in the remainder injury to the myocardium was slight and was characterized by scattered, tiny necrotic foci.

Fig. 2

Fig. 3

Fig. 2. Focus of coagulation necrosis of muscle cells from myocardium of the left ventricle of a rat 24 h after injection of isoproterenol: infiltration of monocytes into dying cells. Colloidal iron–PAS–hematoxylin, photographed in monochromatic light, λ = 546 nm, 800 ×.

Fig. 3. Section through heart of rat killed 24 h after injection of isoproterenol: infarct-like zone of myocardial necrosis (boundaries indicated by arrows). Colloidal iron – PAS–hematoxylin, 8 ×.

The results show that acetylsalicylic acid effectively prevents the formation of confluent foci of injury to the myocardium induced by isoproterenol. Acetylsalicylic acid is known to provent platelet aggregation and to inhibit prostaglandin formation [7]. This harmonizes with the view that confluent infarct-like foci of necrosis of muscle cells are formed as a result of disturbances of the microcirculation which, in turn, are caused by aggregation of platelets.

Damage to individual myocardial cells observed at the beginning of the process, immediately after administration of catecholamines, is attributable to the direct action of these substances on myocyte metabolism [1, 2, 4, 10]. Since in the present experiments a significant decrease in the severity of myocardial damage was observed in the earliest stages of the observation, it can be postulated that acetylsalicylic acid not only prevents aggregation of platelets, but also increases the resistance of myocardial cells to the direct harmful action of catecholamines.

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