Platelet Monoamine Oxidase Activity during Surgical Intervention Under Condition of Hypothermic Perfusion

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 129, No. 4, pp. 393-395, April, 2000
Original article submitted May 13, 1999

Platelet and plasma monoamine oxidase activity was determined at early stages of hypothermic perfusion and circulatory arrest. Monoamine oxidase activity decreased more drastically and restored more slowly against the background of deep (14°C) compared to moderate hypothermia (26-29°C). The decrease in platelet monoamine oxidase activity was accompanied by its increase in the plasma, which attests to mechanical (in tubes) and toxic damage to platelets. The latter is associated with increased partial O_2 pressure in the plasma during hypothermia, which promotes the formation of reactive oxygen species.

Key Words: *extracorporeal circulation; hypothermia; platelets; monoamine oxidase*

Extracorporeal circulation and hypothermia during heart and vascular surgery are associated with damage to platelets, the most vulnerable blood cells [4]. Various factors affect platelets structure and function during extracorporeal circulation, in particular, contact with tubes and gaseous medium, pressure drops, and blood cavitation. The total number of platelets decreases during perfusion with through membrane oxygenators due to adhesion to polymeric surfaces of the perfusion system and the formation of platelet-leukocyte aggregations.

Platelet degradation is predominantly associated with enhanced O_2 solubility in the plasma during hypothermic perfusion, which aggravates toxic effects of O_2 on the platelets.

Platelet degradation during extracorporeal circulation can plays an important role in the development of postperfusion complications, in particular, severe hemostatic disturbances and even sludge syndrome.

In the present study activity of the platelet monoamine oxidase (MAO, EC 1.4.3.4.) was measured at various stages of perfusion.

Inhibitory analysis revealed two types of MAO (A and B) in human and animal tissues [6]. Norepinephrine and serotonin are specific substrates for MAO-A, while benzylamine and biogenic monoamines (2-phenylethylamine and N-methylhistamine) are the substrates for MAO-B.

Inhibitory analysis showed that human platelet MAO belongs to type B MAO (oxidizes benzylamine) [3]. Platelet MAO significantly differs from MAO in the liver, brain, and other organs. Since deep hypothermia damages platelets (this is why deep hypothermic perfusion was refused in the 60s), platelet MAO was chosen as a biochemical marker of their functional state. Simultaneously we studied MAO activity in the plasma, which reflects enzyme release from damaged platelets during perfusion.

MATERIALS AND METHODS

We examined blood from patients (n=26, age 31-56, group 1) undergoing surgical intervention for acquired heart disease with extracorporeal circulation under hypothermic conditions (26-29°C) and patients (n=13, age 33-58, group 2) undrgoing reconstructive surgery on the aorta with extracorporeal circulation under conditions of deep hypothermia (~14°C) and circulatory arrest (~50 min).

MAO-B activity in isolated platelets [2] and plasma was measured as described previously [1] in group

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0007-4888/00/0004-332$25.00

TABLE 1. MAO Activity (nmol/mg protein/ h) in the Blood During Different Stages of Surgical Intervention ($M \pm m$)

Investigated stage	Group 1		Group 2	
	Platelet MAO	Plasma MAO	Platelet MAO	Plasma MAO
Before perfusion	48.825±11.035	0.078±0.009	47.382±10.121	0.075±0.016
Peak of cooling	19.60±6.24	0.120±0.022	24.503±4.018	0.116±0.037
After second perfusion	—	—	4.780±2.532	0.164±0.023
Peak of warming	15.585±4.908	0.170±0.014	2.827±1.259	0.197±0.034
1 hour after perfusion	15.662±4.908	0.142±0.012	12.908±3.170	0.132±0.023
Postoperation day 1	30.745±5.198	0.095±0.018	14.468±4.299	0.127±0.015

Note. All differences with corresponding indices before perfusion are significant.

1: before perfusion (initial), at the peak of cooling and warming, 1 hour after the end of perfusion, and on postoperation day 1; in group 2: the same stages and after repeated perfusion after circulatory arrest. MAO activity was measured in nmol benzylaldehyde/h/mg protein.

The data were processed statistically using Student's t test.

RESULTS

In group 1 patients, platelet MAO activity decreased during cooling (by more than 50%) and further decreased during warming (up to 60%), after termination of perfusion it remained constant for 1 h. On postoperation day 1 platelet MAO activity increased, but did not return to the initial level (Table 1). In parallel with the decrease of platelet MAO activity, plasma MAO activity increased: by 50% during cooling, by more than 100% during warming, and by more than 80% one hour after termination of perfusion; on the next day after surgery platelet MAO activity only slightly exceeded the initial level.

In group 2 patients, platelet MAO activity decreased by almost 50% during cooling, and dropped almost by 90% during second perfusion, during warming platelet MAO activity dropped to 6% of the initial level (Table 1). One hour after perfusion, platelet MAO activity remained reduced by more than 70% and only slightly increased on postoperation day 1. In comparison with group 1 patients, plasma MAO activity in group 2 patients increased to a greater extent during cooling and especially during warming exceeding the initial level by more than 100 and 160%, respectively. On postoperation day 1 plasma MAO activity 70% exceeded the initial level.

These data suggest that perfusion, but not cooling, plays the key role in the decrease of platelet MAO activity, because in both groups the decrease in platelet MAO activity during cooling was similar. However, hypothermic perfusion *per se* can potentiate the toxic effect of O_2 on blood cells. The main cause of the drastic (by more than 100%) decrease in MAO activity in group 2 patients is circulatory arrest, which induced strong and sustained impairment of platelet function.

To evaluate the role of heparin in the decrease of platelet MAO activity, we carried out an *in vitro* experiment: platelets from donor blood were incubated in the presence of low-molecular-weight heparin (about 5100 D). Platelet MAO activity decreased by 11.9%, 13.7%, and 26.3% in the presence of 0.5, 1.0, and 1.5 μM heparin, respectively. Thus, heparin plays a certain, although not the decisive role in the decrease of platelet functional activity during hypothermic perfusion.

Thus, apart from mechanical damage in the perfusion system, platelets are subjected to toxic influence of O_2 caused by increased O_2 solubility in the plasma during hypothermia (400 mm Hg and more). Hyperoxia promotes excessive production reactive oxygen species ($O_2^{\bullet-}$, hydroxylamine, H_2O_2),

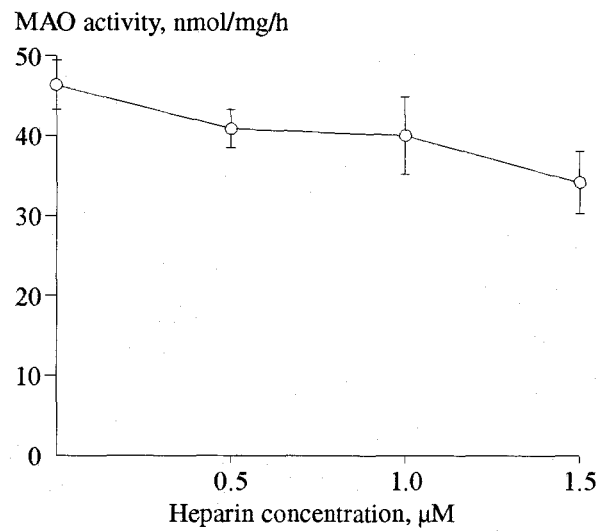

Fig. 1. *In vitro* effect of heparin on platelet monoamine oxidase activity.

which not only damage the cell membranes, but also inhibit MAO [5].

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