TITLE: TOTAL CORONARY RESISTANCE AND VESSEL SEGMENT RESISTANCES DURING ADENOSINE INDUCED HYPOTENSION

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Introduction: Potent coronary vasodilators are thought to act primarily on the small arteriolar resistance vessels. In a recent study diameters of differently sized coronary arterial vessel segments increased during adenosine infusion, yet to different extents[1]. However, the effect of this differential dilatation on segmental resistances and the relation to total coronary vascular resistance were not discussed. The aim of the present study, therefore, was to investigate changes of total and segmental coronary resistances during maximal coronary vasodilation by adenosine.

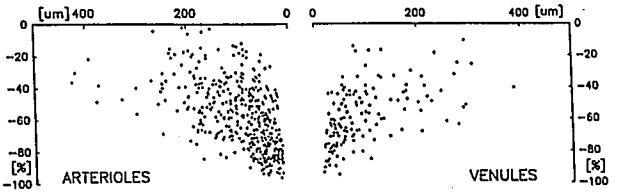
Methods: Investigations were performed in 19 mongrel dogs during general anesthesia. Catheters were placed for hemodynamic monitoring. A left sided thoracotomy was performed and part of the myocardium immobilized by a heart holder. Epicardial coronary microvessel diameters were measured by intravital fluorescence-video-microscopy. Regional myocardial blood flow was determined by radioactive microsphere method.

Data were obtained during a control period, where only a narcotic was applied and during coronary dilatation by continuous infusion of adenosine in a rate that reduced mean arterial pressure to 60 mm Hg.

Percent changes in vessel segment resistances (R_{Seg}) were calculated from vessel diameters during control (D_c) and during adenosine (D_a) by the law of Hagen-Poiseulle, assuming that vessel length and blood viscosity remained constant:

$$R_{Seg} = (D_c^{-4} \cdot D_a^{-4} - 1) \cdot 100$$

Results: Mean arterial pressure was reduced from 85±2 to 59±1 mm Hg by 21±2 mg adenosine per min and kg. Systemic and coronary vascular dilatation were indicated by 37% and 253% increases in cardiac output and left ventricular blood flow, respectively. Total coronary vascular resistance decreased from 71±6 to 13±1 mmHg•min•g/ml. Coronary arterial and venous microvessels were grouped accordng to diameters during control: I. 20-40 µm,II. 40-60 µm, III. 60-100 µm, IV. 100-150 µm, V. 150-200 µm and VI. >200 µm. Adenosine infusion increased diameters in all arterial and venous vessel segments, significantly more pronounced in the smaller vessels. Percent changes in vessel segment resistances are given in the scatter plot, including 465 arterial and 145 venous vessels. The 82 % decrease of total coronary resistance (TR) is indicated by the horizontal bar.



Conclusion: The observation that segmental resistance in arterial vessels larger than 100 µmdecreased considerably less than total resistance is in accordance with previous data[2] in that these vessels contribute only little to total resistance. Then, however, the decrease of resistance in the main resistance vessels should at least slightly exceed the decrease of total coronary resistance. In the present study this is true for only the smaller part of the vessels between 20 and 60 µm. We therefore conclude that the main site of regulation of coronary blood flow is even distal to the smallest arterioles (20 µm)visualized in the present study. Also, resistance decreased in all segments during adenosine induced dilatation, but a redistribution of resistance occurred, in that the relative fraction of total resistance increased in the larger arterioles.

[1]Habazettl et al. Anesthesiology 71:A482,1989
[2]Chilian et al. Am J Physiol 251:H779-H789,1986

TITLE: EFFECT OF LEUKOPENIA ON PULMONARY HYPERTENSION FOLLOWING HEPARIN-PROTAMINE IN PIGS

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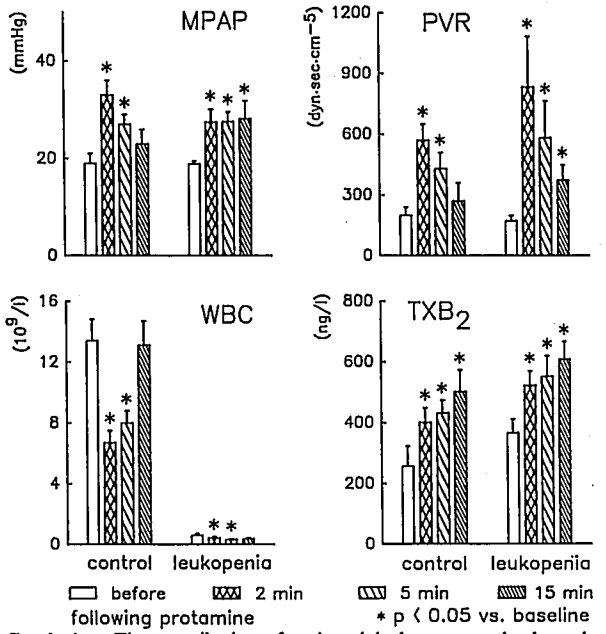
Introduction: Heparin (HEP) reversal by protamine (PROT) is regularly associated with a transient decrease of leukocyte counts in humans[1] and in animals[2,3]. Also, activated leukocytes have been suggested to play a major role in a mediator sequence which finally results in thromboxane A_2 release and pulmonary hypertension[3]. We, therefore, investigated if activated leukocytes play a causal role in pulmonary hypertension following HEP-PROT.

Methods: 8 pigs were equipped with a central venous catheter and given 30 mg cyclophosphamide per kg and day. Leukocyte counts were monitored daily. Experiments were performed on day 6 or 7, with leukocyte counts between 0.4 and 0.9 times 10^9 cells/l with 1-2 % of polymorphonuclear leukocytes. During general anesthesia and after catheterization, baseline recordings of hemodynamics were obtained and blood samples withdrawn. 250 IE/kg HEP were injected and measurements repeated after 10 min. 100 mg PROT were then infused over two min and recordings were obtained after two, five and 15 min. Thromboxane B_2 plasma concentrations were measured by RIA. Results are compared to a control group (n=8), where HEP and PROT were given according to the same protocol, but without any pretreatment. Differences within groups were evaluated by Friedman ranked analysis of variance, differences between the groups by U-Test.

Results: At baseline leukocyte and platelet counts were significantly lower in neutropenic than in control animals. Mean pulmonary artery pressure (MPAP), pulmonary vascular resistance (PVR), white blood cell counts (WBC) and TXB_2 plasma concentrations (TXB_2) are shown in the figure. Reactions to protamine infusion were not statistically different between the groups.



Conclusion: The contribution of activated leukocytes to the hemodynamic effects after HEP-PROT appears to be negligible. Also, leukocytes are not a major source of the TXA_2, released during the HEP-PROT reaction.

[1] Hobbhahn et al. Anesthesiology 69:A118,1988. [2] Conzen et al. Anesth Analg 68:35-31,1989. [3] Morel et al. Circ Res 62:905-915,1988