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EXTRACORPOREAL ELIMINATION OF TIROFIBAN: AN IN-VITRO INVESTIGATION

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Introduction: The role of platelet glycoprotein IIb/IIIa (GP IIb/IIIa) antagonists in the treatment of acute coronary syndromes is increasingly appreciated. The short acting GP IIb/IIIa antagonist tirofiban has been shown to be beneficial when used in the context of cardiac surgery. Tirofiban has an elimination half-life of approx. 2 hours achieved by renal clearance. Renal failure prolongs the half-life and continues inhibition of platelet aggregation refractory to transfusions of platelets. Extracorporeal elimination is the only option to prevent excessive hemorrhage in this condition. We assessed the extracorporeal elimination of tirofiban by hemofiltration.

Methods: The test circuit simulated CPB conditions. Two hemofilters and one plasmapheresis filter were assessed [table]. Three separate filters of each type were tested serially. The CPB was primed with a total volume of 1000 ml: 450 ml whole human blood, 50 ml donor platelets, 50 ml fresh frozen plasma, 450 ml electrolyte solution and 10,000 IU heparin. Tirofiban was added to a concentration of 200 ng/ml. The flow rate in the dialyzer circuit was adjusted to 1 l/min; 50 ml of electrolyte solution (fresh frozen plasma in the case of the plasmapheresis filter to maintain the oncotic pressure) was given to the CPB. After 1 minute of circulation, 50 ml of filtrate was retrieved from the dialyzer via a filtrate roller pump. After each filtration, the tirofiban blood level was analyzed; the procedure was repeated 16 times. Determination of tirofiban was performed with liquid chromatographic tandem mass spectrometry.

Results: There were no differences regarding volume, composition of the prime or the flow rates in the 16 in-vitro test runs. For arterial filtration pressures and filtration times, see table; for the courses of the tirofiban levels, see figure. As calculated by the subsidence coefficient es in elimination between the filter systems [fig.].

Conclusion: Elimination of tirofiban via hemofiltration follows a sigmoid curve with fast clearance of the high therapeutic concentrations of between 200 and 50ng/ml. These data suggest that ultrafiltration is an effective means for extracorporeal elimination of therapeutic levels of tirofiban. Our results are of particular interest for the management of patients with impaired renal function or a high risk to develop perioperative renal failure who undergo cardiac surgery with administration of tirofiban in the perioperative period.

Table. Filter characteristics and filtration data

Filter system	Type	Material	Pore size [Dalton]	Membrane surface area [m ²]	P _{art} [mmHg]	Time [sec]	B
Hospal Arylane H4	Hemofilter	Polyarylethersulfone	45.000	1.35	225 ± 21	121 ± 9	0.093
MintechHemocor HPH 700	Hemofilter	Polysulfon	65.000	1.45	235 ± 17	125 ± 11	0.085
Asahi Plasmaflow OP	Plasma separator	Polycarbonate	200.000	0.35	182* ± 12	95* ± 7	0.095

B= subsidence coefficient, *significantly decreased compared to other filters

Fig. 1

