

ESTIMATION OF EPTIFIBATIDE CLEARANCE BY DIALYSIS USING AN *IN VITRO* SYSTEM. Joanna Q. Hudson<sup>1,2</sup>, Christie A. Green<sup>2</sup>, Elizabeth A. Beach,<sup>1</sup> Lisa K Jennings<sup>2</sup>. University of TN Departments of Clinical Pharmacy and Medicine, Memphis, TN, USA. Eptifibatide (Integrilin) is a glycoprotein IIb-IIIa inhibitor that prevents platelet aggregation and is approved for patients with acute coronary syndromes and those undergoing percutaneous coronary intervention. Due to limited safety data and very limited data on its removal by dialysis, this agent is contraindicated in dialysis patients. The purpose of this study was to determine dialysis clearance (CL<sub>D</sub>) of eptifibatide (E) using an *in vitro* system. Eptifibatide (concentration 2 mg/L) was added to a phosphate buffer solution (pH  $\cong$  7.4) with bovine albumin (concentration 2 g/L) to mimic *in-vivo* conditions. Polyvinyl chloride tubing connected the drug reservoir to the selected dialyzer to provide a closed-loop, fixed-volume system. Three dialyzers were tested: low-flux polyamide blend (Gambro Polyflux 8L, PF8L), polysulfone (Fresenius F-160, PS), high-flux polyamide blend (Gambro Polyflux 210, PF210). *In-vitro* dialysis was performed for 1 h at a dialysate flow rate (DFR) of 500 mL/min, reservoir flow rates (RFRs) of 200 and 400 mL/min, and the minimal ultrafiltration rate (10 mL/h). Each procedure was repeated three times. E CL<sub>D</sub> was calculated as  $CL_D = RFR (C_a - C_v)/C_a$  where C<sub>a</sub> and C<sub>v</sub> are the E concentrations at the inlet and outlet of the dialyzer, respectively, measured at regular time intervals.

Dialyzer	PF8L		PS		PF210	
	200	400	200	400	200	400
CL <sub>D</sub> (mean $\pm$ SD)	122 $\pm$ 18	205 $\pm$ 52	132 $\pm$ 7	127 $\pm$ 59	137 $\pm$ 23	225 $\pm$ 43

E CL<sub>D</sub> was substantial for all dialyzers and flow conditions (range 122-225 mL/min) and was not significantly different among the dialyzers tested ( $p > .05$ ). CL<sub>D</sub> was flow dependent for the PF8L and PF210 dialyzers. The relatively low molecular weight (832 Daltons) and low degree of protein binding (25%) of E are conducive to its transfer across the dialyzers tested as confirmed in this *in vitro* study. The estimated fraction of E removed by dialysis is 65-75%. These data indicate that E is extensively removed by dialysis and provide information that may be used to design E dosing regimens in the dialysis population.