TITLE: HEMODYNAMIC AND VENTILATORY EFFECTS OF URAPIDIL AND NITROGLYCERINE FOLLOWING CORONARY ARTERY BYPASS GRAFTING

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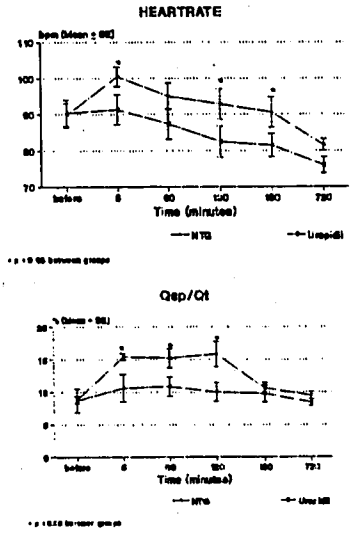
This study was undertaken to determine the influence of urapidil and nitroglycerine (NTG) on hemodynamics, venous admixture and arterial oxygenation following coronary artery bypass grafting (CABG).
Thirty patients who developed arterial hypertension following CABG, despite sedation, were randomly treated with either urapidil (postsynaptic alpha$_1$-adrenoceptor blocker with additional alpha$_2$ adrenoceptor blockade, agonist of 5-HT$_{1a}$ receptors in the brain) (initial bolus of 25 mg, followed by a continuous infusion of 30-90 mg per hour) (n=15) or NTG (administered as a continuous infusion of 1 - 5 µg/kg/min) (n=15). After surgery all patients were mechanically ventilated in the intensive care unit ( $FIO_2$:0,5; PEEP:+5 cm H2O). The $FIO_2$ was kept on these standard values for 30 minutes. After that time $FIO_2$ was adjusted to give normal blood oxygen gas tension ( $FIO_2$ always > 0,3). Duplicate samples of arterial and mixed venous blood were obtained simultaneously before administration of either drug and at each time point. Cardiac index (CI), stroke index (SI), systemic (SVRI) and pulmonary (PVRI) vascular resistance indexes and alveolar-arterial oxygen partial pressure difference ($A\text{-}aDO_2$) were calculated using standard formulae. Statistical analyses were performed using the Friedmann and Wilcoxon test (including Bonferroni correction) for intragroup comparison and the Mann Whitney rank sum test for intergroup comparison. Data acquisition followed over 12 hours. Changes were considered to be significant when $p < 0.05$.
Both drugs significantly decreased arterial pressure. Three patients were withdrawn because hypertension failed to respond to NTG. Significant tachycardia was noted only in the NTG group. TPRI and PVRI decreased significantly in both groups. CI and SI increased significantly only in the urapidil group. $Qs/Qt$ and $A\text{-}aDO_2$ increased significantly in NTG treated patients, whereas no considerable changes were seen in the urapidil group.
It is concluded that urapidil has advantages compared to NTG in the treatment of hypertension following CABG.




## A74

Title: PLATELET RECEPTORS FOR ADHESIVE LIGANDS ARE DECREASED DURING CARDIOPULMONARY BYPASS

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Introduction: Cardiopulmonary bypass (CPB) produces changes in platelet structure and function which contribute to peri-operative bleeding. The platelet glycoprotein (GP) receptors for the adhesive ligands fibrinogen (FBGN) and von Willebrand Factor (vWF) are critical to normal platelet adhesion and aggregation, respectively. Using monoclonal antibodies (MAB) directed against these platelet GP and flow cytometry, we directly measured the GP surface density to assess changes occurring over the course of CPB.
Methods: After institutional approval, 12 patients having elective coronary artery bypass were studied. Serial samples of arterial whole blood were drawn 5 minutes after heparinization, 10 minutes after onset and prior to separation from CPB. The samples were fixed and incubated with a fluorescein (green fluorescent) MAB directed against the invariant non-adhesion structure HLA-ABC on the platelet surface, and a phycoerythrin (red fluorescent) MAB to either the FBGN receptor, GPIIb/IIIa or the vWF receptor, GPIb. The red/green fluorescence intensity ratio of individual platelets was measured to detect changes in the density of immunoreactive GP receptors, while standardizing for platelet size and gross alterations in membrane accessibility. Mean changes in GP density for each time point were pooled and analyzed by ANOVA.
Results: Both GPIb and GPIIb/IIIa showed a decrease in mean density after 10 minutes of CPB, which became significant by the end of bypass (Fig.1, +/- S.D.). At termination of CPB, GPIIb/IIIa showed a 31% decrease, and the GPIb density fell by 47%. Theses changes in GP density affected all platelets uniformly.
Discussion: GPIb mediates the initial adhesion of platelets to the damaged vessel wall. GPIIb/IIIa is critical to subsequent platelet aggregation at the site of vascular injury. This study demonstrates that CPB induces loss of both GPIb (47%) and GPIIb/IIIa (31%) from the platelet surface, unrelated to general membrane changes (including mechanical shearing), as receptor density was calculated relative to an invariant membrane structure, HLA backbone. We hypothesize that loss of these receptors contributes to the functional platelet impairment found clinically. Plasmin generation in vitro has been shown to cause degradation of both GPIb and GPIIb/IIIa; activation of the fibrinolytic system during CPB may result in the loss of surface receptors demonstrated here.
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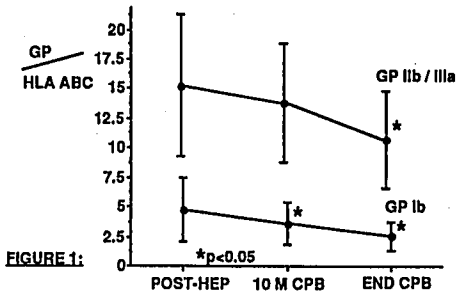


FIGURE 1: