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TITLE: EFFECT OF EXOGENOUS EPINEPHRINE ON ALANINE TURNOVER AND UREA PRODUCTION RATE IN VOLUNTEERS

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Introduction: The clinical use of the catecholamine epinephrine (EPI) is primarily related to its hemodynamic effects. But beside the hemodynamic action of EPI there are clear metabolic effects both on carbohydrate and amino acid metabolism. We investigated the effect of EPI infusion on the turnover rate of alanine and the production rate of urea using stable isotope technique on healthy volunteers.

Methods: After approval by the ethic committee of the university and informed consent 8 volunteers were studied. They were asked to eat normal hospital diet and to refrain from alcohol three days prior to the study. After an overnight fast a forearm intravenous cannula was inserted at each arm, one for infusion and one for blood sampling. The sampling site was heated by a pad in order to arterialize the venous blood. The study lasted for 480 min. At t=0 min a prime dose of 7 mg/kg BW of $^{15}N_2$-Urea was injected followed by a constant infusion of 0.0117 mg/kg*min. At t=150 min a prime dose of 0.62 mg/kg BW of ^{15}N-Alanine was injected followed by a constant infusion of 0.007 mg/kg*min. The isotopes were purchased from CIL, Cambridge, MA. Prior to the beginning of the study, at 220, 230, 240 min blood samples were drawn to determine isotopic enrichment of $^{15}N_2$-Urea and ^{15}N-Alanine. At t=241 min an infusion of epinephrine 0.1 µg/kg*min was started and further blood samples to determine the isotopic enrichment were drawn at t=300, 310, 320, 380, 390, 400, and at t=460, 470, 480 min. Isotopic enrichment of urea and alanine was determined by gas chromatography/mass spectrometry (HP 5890, HP 5971) in SIM-Mode using TBDMS-derivative for urea and NAP-derivative of alanine. Values are shown as means±SEM. Paired t-test was performed and the Bonferroni correction was applied for multiple testing (p=0.05: significant level).

Results: The alanine flux increased significantly from a basal value of 0.33±0.01 mg/kg*min to 0.56±0.01 mg/kg*min at 320 min and further to 0.59±0.05 mg/kg*min at 400 min (p<0.05). The urea production rate (UPR) decreased significantly from its basal value of 0.29±0.01 mg/kg*min to 0.26±0.04 mg/kg*min at 480 min (p<0.05). See figure 1.

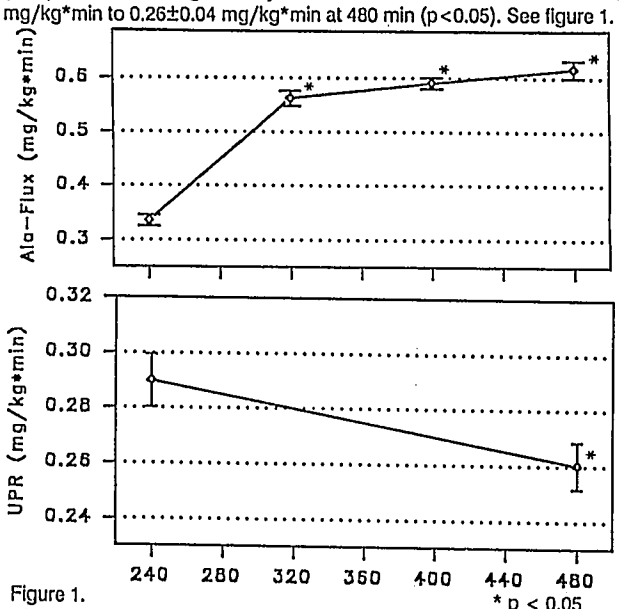

Figure 1.

Discussion: Although alanine turnover was significantly increased during acute administration of EPI, this was not associated with enhancement of protein catabolism as could be shown in urea production rate. This surprising finding needs further validation in catabolic intensive care patients during acute as well as chronic administration of EPI.

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PREVENTION OF POST-BYPASS BLEEDING WITH CYKLOKAPRON AND AMICAR.

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Introduction: Patients undergoing cardio-pulmonary bypass (CPB) are at risk of postoperative bleeding, which contributes to morbidity, mortality and reoperation (3-5%). Platelet dysfunction, fibrinolysis, release of the plasminogen activator and activation of the complement system, are thought responsible. Fibrinolysis has been estimated to cause at least 12 to 25% of post CPB bleeding1.

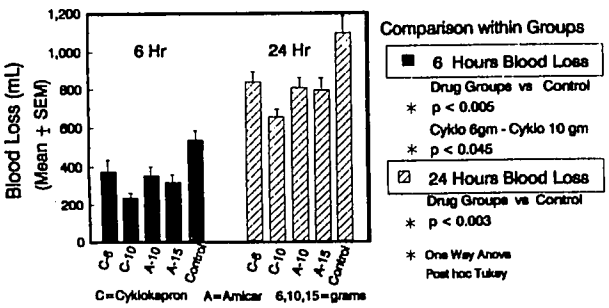
In our institution two antifibrinolytic agents have been used in the pre-bypass period to prevent fibrinolysis: Amicar (epsilon-aminocaproic acid) or a new agent Cyklokapron (Tranexamic acid) as intravenous infusion over 2 hours prior to CPB. Cyklokapron is ten times more potent, binds more strongly and is less expensive than Amicar. Experience with Cyklokapron after CPB is limited2.

Methods: We collected retrospectively, data on 391 patients undergoing CABG (coronary artery bypass grafting) surgery with CPB. Patients were divided into 5 groups. 65 patients received Amicar (10gm), 60 Amicar (15gm), 100 Cyklokapron (6gm), 75 Cyklokapron (10 gm) and 91 were not pretreated. Demographics did not differ. Patients were anesthetized with high dose Fentanyl, Pavulon and Valium. The initial dose of Heparin was 300 U/kg and ACT was maintained above 400 sec. Heparin was reversed with Protamine Sulfate (1mg per 100 U of Heparin).

Mediastinal and pleural drains were employed to collect blood which was autotransfused up to 6 hours post-operatively. We collected and analyzed the following data: postoperative blood loss over 6 and 24 hours; amount of blood and blood products transfused in first 48 hours, hemostatic parameters: Platelets, Prothrombin Time, Partial Thromboplastin Time and Hematocrit.

Statistical analysis was done using analysis of variance (Anova, two-way Anova), analysis of covariance and post hoc Tukey tests for comparison of means (Systat, Systat Inc.)

Results: Postoperative blood loss in groups is presented in Table



Both Cyklokapron and Amicar reduced post-CPB bleeding in the first 24 hours. 10 gm of Cyklokapron was more effective then 6 gm in the first 6 hours , but was not significantly different at 24 hours.

Significantly less red blood cells (p<0.001) were used for the Cyklokapron (10gm) group (mean=0.6U) vs control (mean=1.6U). Conclusions: Antifibrinolytic agents significantly reduces post CPB blood loss and blood products requirement.

References:

1. Am J Hemat 23:223-229, 1986.

2. J Thorac Cardiovasc Surg 99:70-4, 1990.