Title: HEPARIN ACTIVITY DURING PEDIATRIC OPEN-HEART SURGERY

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Introduction. Although heparin activity in adults[1] during cardiopulmonary bypass has been described, there has been no such study of small children. Consequently, pediatric dosages of heparin and protamine are extrapolated from data obtained from adults. The possibility that this may not be valid because of differences in pump prime and plasma volumes and rates of change in core temperature between adults and small children prompted this study.

Methods. We studied plasma heparin activity of 13 randomly selected pediatric patients [age: 2.5 ± 2 years (mean ± SD); mass: 12.1 ± 6.2 kg] undergoing open-heart surgery (approved by the Human Experimentation Committee of the University of Florida). Heparin levels were measured by comparing thrombin times of patient plasma samples to thrombin times of plasma samples containing known heparin concentrations[1] (accuracy ± 0.15 units/ml). All patients received an intravenous loading dose of 300 units heparin/kg before bypass started. The perfusion pump prime contained between 2250 and 2500 units of heparin for nine cases (Group I) and between 3375 and 5000 units for four cases (Group II). This produced heparin concentrations between 1.9 and 3.1 units/ml prime in Group I and between 4.5 and 7.4 units/ml prime in Group II. The paired and unpaired t-statistic was used to evaluate the significance of group and concentration differences with $P<0.01$ reported as significant unless otherwise designated and with $P>0.05$ considered insignificant. Values are expressed as means ± standard deviation unless otherwise designated.

Results. The pattern of heparin activity was consistent within each group of patients. After the initial loading dose, plasma heparin levels peaked at 5.23 ± 0.90 units/ml in Group I and 3.56 ± 1.1 units/ml in Group II. After the initial peak, these levels decreased significantly within ten minutes to 3.99 ± 1.0 units/ml for Group I and 2.61 ± 0.57 units/ml for Group II. This represents a 25% decrease from peak levels of both groups. The differences between Group I and Group II were not significant ($P\geq0.06$) because of variability within each group. After bypass began, differences between Groups I and II became significant. Group I levels began to decrease immediately after bypass began and decreased approximately 40% within 15 minutes to 2.41 ± 0.52 units/ml. In contrast, Group II levels increased 80% over pre-bypass levels to 4.71 ± 0.7 units/ml and then decreased ($P<0.02$) to 3.44 ± 0.21 units/ml at the end of the same 15 minute period. Thereafter, Group II levels remained 1.17 ± .17 units/ml higher than Group I levels. The heparin levels within both groups underwent only a small insignificant net decrease (<0.3 units/ml) during the remainder of the period of heparinization (57 ± 27 min). However, there was a small transient but significant 0.64 ± 0.34 unit/ml increase and decrease in heparin levels of both groups in the middle of the bypass period. This event coincided with the addition of heparinized blood to the bypass pump in three cases, but no definite cause could be found in the other ten cases.

Discussion. The pattern of heparin activity in small children is different than that reported in adults.[1] During bypass, children had heparin levels 30% higher than adults previously studied. The role of heparin in the pump prime is central to this difference. Our patients received pump prime volumes (500-1500 ml) which were between 110 and 1150% of their own plasma volume. It would be expected that, when bypass began, heparin levels would move in the direction of pump prime heparin concentrations. This is exactly what happened! When bypass began, heparin levels increased 80% in Group II and remained higher than pre-bypass levels for the duration of the case. Group I patients resembled adults inasmuch as they received pump prime with heparin concentrations lower than that of their own plasma. Their levels fell 40% when bypass began and remained lower than Group II levels. Regardless of pump prime, both groups maintained levels which would be expected to produce clotting times in the efficacious (400 to 600 sec) range.[1,2] There was no significant net heparin decay in either group during hypothermia or normothermia, although the duration of hypothermia (<30 min) was inadequate to study decay. The transient upward fluctuation in heparin levels during mid-bypass corresponded to the administration of exogenous heparinized blood for three patients and to the period of rewarming for seven patients. Possibly, the fluctuations may represent entry into the plasma of heparin sequestered extravascularly. Such sequestration is consistent with the observation that initial plasma heparin levels were only 50% of the predicted.

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References:
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