Aprotinin Levels During Pediatric Open Heart Surgery
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Introduction: Aprotinin has had mixed reviews in the literature as to its efficacy in its off label use in pediatric cardiopulmonary bypass (CPB). These differing results may be related to the wide variety of dosages regimens used and the fact that during CPB pediatric patients undergo a wide variety of fluid shifts. The size of CPB circuits, hemofiltration and modified ultrafiltration (MUF) all play part in aprotinin levels. In 1996, D’Errico et al showed aprotinin to be effective in repeat sternotomy patients undergoing CPB (1). Using this same dose regimen we hypothesized that the aprotinin drug levels would stay above the 200 KIU/ml stated necessary to decrease inflammation in adult patients (2,3).

Methods: After Institutional Review Board approval and with informed consent, 20 children, between 5 and 15 kg, undergoing CPB with the use of aprotinin were enrolled in this study. The aprotinin dose was 240mg/m^2 bolus over 20 min and in the pump prime followed by an infusion of 56mg/m^2/hr. Four plasma samples were collected at the following times: the end of the initial bolus of aprotinin, 10 minutes after initiation of CPB, at the end of CPB and 3 minutes after MUF. Samples were also obtained from the bypass prime, and the hemofiltration fluid at the end of bypass and at the end of MUF. These samples were analyzed using an amidolytic substrate assay for aprotinin (Unitest.) (4).

Results: The demographics are as follows: age, 1.3 ± 1.0 yr; weight, 9.4 ± 3.4 kg; BSA 0.44 ± 0.12m^2. There were 8 males and 12 female patient of which half were cyanotic prior to OR. The average level of aprotinin remained above the 200 KIU/ml (Table 1). Aprotinin was removed in the hemofiltrate and MUF fluid as expected with a sieving coefficient of 1.0 (5). Plasma aprotinin levels were significantly different between end of load and 10 mins on CPB, and between 10 min on CPB and the end of CPB (p < 0.001). There were significant positive relationships between duration of CPB, the amount of ultrafiltrate removed and the decrease in aprotinin levels (p<0.05).

Discussion: Using BSA for dosing pediatric patients, the average plasma levels were all greater than 200 KIU/ml. Of interest, aprotinin is removed during hemoconcentration and during MUF. Aprotinin levels also fall in relationship to the length of time and amount of fluid removed during bypass. Thus, one may consider increasing the aprotinin infusion to maintain a more consistent aprotinin level for long case or cases where there is a large amount of hemofiltration taking place.

Refs:
2. Dietrich et al, Anesthesiology, 1990