Title: AMRINONE ASSOCIATED THROMBOCYTOPENIA: DOES IT OCCUR WITH SHORT TERM ADMINISTRATION?

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Thrombocytopenia coupled with alteration of normal platelet function is deleterious in patients undergoing cardiac surgery. Consequently, any pharmacological agents utilized in the peri-operative period must preserve platelet function. Thrombocytopenia and associated platelet dysfunction have been reported with the chronic use of amrinone therapy in patients with congestive heart failure.[1] The use of amrinone in the peri-operative setting has been limited due to concerns over the possibility of thrombocytopenia. Amrinone's ability to provide rapid vasodilatation combined with positive inotropic action provides a therapeutic advantage in selected cardiac patients. However, the effect of short term amrinone therapy on platelet function has not been defined. Therefore, we designed a prospective study to evaluate the effect of amrinone on platelet function in the early postoperative period.

Methods. With a protocol approved by the Human Investigation Committee, 8 patients in the intensive care unit (n=8) who received amrinone immediately following cardiac surgery and cardio-pulmonary bypass (CPB) were evaluated. Amrinone therapy was instituted for the treatment of acute left ventricular dysfunction, with the dose titrated to achieve hemodynamic stability. The mean time for starting therapy was 3.9 ± 0.8 hours following CPB with termination of therapy occurring at 31 ± 0.6 hours post CPB. Patients receiving any additional medications known to interfere with platelet function were excluded from the study. Blood samples for determination of platelet count and function (aggregation studies) were obtained prior to the institution of amrinone therapy (control) and following 1, 6, and 24 hours of continuous infusion. The infusion rate and total amount of amrinone delivered was recorded at each interval. In addition, a template bleeding time was performed at the completion of the amrinone therapy. No medications or parental infusion known to cause thrombocytopenia or to alter platelet function were administered during the study.

To perform aggregation studies, platelet rich plasma was prepared from each 15 cc aliquot of blood. Aggregation studies were performed by exposure to ADP (2 uM) and epinephrine (5 uM). Measurement of aggregation was performed by using a chrono-log (R) Aggregometer (Model #540). Results are expressed as % aggregation as compared to control values for each patient and plotted as a dose response curve. Data are expressed as mean ± standard deviation. Statistical analysis was performed using correlation of coefficients and one way analysis of variance with P 0.05 considered significant.

Results. (Table 1) Platelet counts in all patients were greater than 100,000 during the control period. No significant alteration in the platelet count was observed in response to the administration of amrinone (P = NS). Neither the total dose delivered (mg) nor the rate of infusion (ug/kg/min) resulted in any decrease in the number of available platelets (r = 0.21, r = 0.29, respectively).

Aggregation studies performed with exposure to ADP during the control period revealed a mean aggregation of 48% (Table I). No significant alteration in platelet aggregation was observed in response to the infusion of amrinone during the study period (P = NS). Similarly, aggregation studies with exposure to epinephrine revealed no alteration in platelet function during the 24 hours infusion period (P = NS). In addition, bleeding time was found to be within normal limits in all patients at the completion of amrinone administration (mean 5.1 ± 1.1 min, nl= 6 min).

Discussion. Our data demonstrate that the short term administration of amrinone, at clinically relevant dosages, does not produce thrombocytopenia in the immediate postoperative post cardiopulmonary bypass period. Although the control period showed diminished platelet aggregation, platelet function did not further decline following amrinone infusion. Furthermore, no significant deviations were seen in either ADP or epinephrine aggregation at any point during the study period.

The thrombocytopenia associated with amrinone therapy reported in the medical literature occurs following chronic administration.[1] The thrombocytopenia is postulated to occur as a result of the accelerated peripheral loss of platelets.[2] However, following cardiac surgery when the short term management of acute left ventricular failure is desired, the administration of amrinone for up to 24 hours failed to result in any statistically significant reduction in either platelet count or aggregation. In conclusion, the use of amrinone in patients undergoing cardiac surgery with CPB is not associated with deterioration of platelet function.

TABLE 1
Platelet Counts and Aggregation Studies
During Amrinone Infusion
(mean ± SD)

	Platelet Count	% Aggreg. ADP (5uM)	% Aggreg. Epi (5uM)
Control	124,000 ± 11820	42 ± 2.2	34 ± 2.6
1 hr p Infusion	133,000 ± 12472	46 ± 2.7	35 ± 2.3
6 hr p Infusion	128,000 ± 11916	47 ± 3.1	39 ± 1.7
24 hr p Infusion	143,000 ± 12620	45 ± 2.4	33 ± 2.2

References:
1. Kinney EL, Ballard JO, Carlin B, Zelis R: Amrinone mediated thrombocytopenia. Scand J Hemat 31:376-380, 1983.
2. Ansell J, Tiarks C, McCue J, Parrilla N, Benotti JR: Amrinone-induced thrombocytopenia. Arch Int Med 144:949-952, 1984.