
Heparin Resistance in the Pre-Cardiotomy Patient

Dennis C. Rivard, BS, CCP

Johns Hopkins Hospital
Baltimore, MD

Key words: Heparin, heparin resistance, cardiopulmonary bypass

ABSTRACT

Patients who undergo heart surgery utilizing cardiopulmonary bypass are systematically anticoagulated with heparin. Heparin is also used for anticoagulation in patients with myocardial infarctions. A discrepancy has been observed in reactivity to heparin in the operating room between patients who are on intravenous heparin and those who are not.

A comparison study utilizing 40 patients was performed. Group A consisted of 20 patients who had no heparin therapy history preoperatively. Group B consisted of 20 patients who had been on intravenous heparin therapy for up to four hours prior to their surgery. All patients were coronary artery bypass grafting candidates and were heparinized for cardiopulmonary bypass, utilizing a 3000u/kg protocol with a target activated clotting time (ACT) of 480 seconds. Heparin lot numbers were evenly distributed between the two groups.

Group A demonstrated a mean post heparin bolus ACT of 541 seconds, while group B showed a mean ACT of 358 seconds. The nonheparin therapy patients required a mean additional perioperative heparin dose of 3,800 units to maintain the ACT above 480 seconds. The heparin therapy patients had a mean additional dose of 16,500 units.

Patients who receive IV heparin therapy prior to cardiopulmonary bypass may require additional heparin to adequately anticoagulate them for extracorporeal circulation.

INTRODUCTION

The use of intravenous heparin therapy in acute myocardial infarction patients has demonstrated a statistically significant reduction in negative clinical outcomes.^{1,2,3} Therefore, a greater percentage of cardiac surgical patients who are partially anticoagulated are presented to the operating room for cardiac revascularization. A variability in reactivity to heparin has been observed in patients who are receiving intravenous heparin preoperatively. The purpose of this study was to investigate if any significant differences existed in patients reactivity to heparin perioperatively between the pre-cardiotomy heparin

therapy patient and the nonheparin therapy patient.

MATERIALS AND METHODS

A prospective comparison study sampling 40 patients was performed. Group A was comprised of 20 patients who had no history of intravenous heparin therapy preoperatively. Group B consisted of 20 patients who had been on heparin up to four hours prior to surgery. All patients were adult coronary artery bypass graft candidates and were selected for this study pre-sternotomy. Criteria for group A consisted of:

1. pT < 12 seconds
2. pTT < 40 seconds
3. platelet count > 150,000/mm³
4. bleeding time < 5 minutes.

Criteria for the heparin therapy patients were:

1. platelet count > 150,000/mm³
2. IV heparin therapy > 12 hours.

All patients received beef lung heparin^a and heparin lot numbers were evenly distributed between the two groups. The pre-cardiopulmonary bypass heparin bolus dose was determined utilizing a 3,000u/kg protocol. The target activated clotting time (ACT) was 480 seconds. ACT values were analyzed utilizing an automated technique.^b Additional heparin administration to maintain an ACT of 480 seconds during cardiopulmonary bypass was determined from the classic Bull Dose Response Curve.^{4,5}

RESULTS

The mean cardiopulmonary bypass time for the nonheparin and heparin group were 143 minutes and 130 minutes respectively. This difference was considered not clinically significant for this study. The heparin therapy group was on heparin an average of 72 hours (range 48-288 hours). The average baseline ACT of group A was 158 seconds and 176 seconds for group B (Chart 1). Group A demonstrated a mean post-bolus ACT of 541 seconds after an average of 25,000u sodium heparin. Group B demonstrated a mean post-bolus ACT

Address correspondence to: Dennis C. Rivard, Johns Hopkins Hospital, 618 Blaylock, 600 N. Wolfe St., Baltimore, MD 21205

a. LyphoMed, Melrose Park, IL
b. International Technidyne Corp., Edison, NJ

of 358 seconds after an average of 26,500u heparin administration. Seven out of 20 patients (35%) in the nonheparin group required an average of 3,800u of heparin during extracorporeal circulation. Thirteen out of 20 patients (65%) in the heparin group received an average of 16,500u heparin. The post-bolus ACT of the heparin therapy patient was 30% lower than in the nonheparin therapy group and required an additional 77% more heparin to achieve adequate anticoagulation for extracorporeal circulation.

CONCLUSION

At present, patients who undergo open heart surgery utilizing cardiopulmonary bypass are anticoagulated. This study suggests that not all patients respond to the standard heparin dose previously described. Patients who receive intravenous heparin therapy prior to cardiac surgery may require additional heparin to adequately anticoagulate them for cardiopulmonary bypass. Close monitoring of this population is necessary to determine the adequacy of heparinization in these patients for extracorporeal circulation.

REFERENCES

1. Report of the Working Party on Anticoagulant Therapy in Coronary Thrombosis to the Medical Research Council. Assessment of short-anticoagulant administration after cardiac infarction. *Br Med J* 1969; 1:335-42.
2. Chalmers TC, Matta RJ, Smith H JR.: Evidence favoring the use of anticoagulants in the hospital phase of acute myocardial infarction. *N Engl J Med* 1977; 297:2092-6.

3. Drapkin A, Merskey C.: Anticoagulant therapy after acute myocardial infarction: relation of therapeutic benefit to patient's age, sex, and severity of infarction. *JAMA* 1972; 222:541-4.
4. Bull B, Korpman R, Huse W.: Heparin therapy during extracorporeal circulation. I. Problems inherent in existing heparin protocols. *J Thor Cardvasc Surg* 1975; 69:674-84.
5. Bull B, Huse W, Brauer F.: Heparin therapy during extracorporeal circulation. II. The use of a dose-response curve to individualize heparin and protamine dosage. *J Thor Cardvasc Surg* 1975; 69:685-89.

CHART 1.

Chart of mean patient data.

	Group A	Group B
Baseline ACT (sec)	158	176
Heparin Bolus (units)	25,000	26,500
Post Bolus ACT	541	358
Add. Heparin on Pump	3,800	16,500