The Assessment of Hemostatic Function in Patients Who Have Undergone Cardiopulmonary Bypass

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The introduction of the cardiopulmonary bypass circulation for patients undergoing cardiac procedures has been associated with excessive hemorrhage and an increased need for blood and blood components on a national level. This is hardly surprising when one reflects upon the physiologic alterations that are induced by cardiopulmonary bypass. The patient's blood is deliberately anticoagulated with heparin. Blood is taken out of its natural environment, exposed to unfamiliar surfaces and chewed up by oxygenators and suction pumps, all of which are known to induce cellular damage and protein changes. In addition, since the cardiac space is physiologically under negative pressure, the making of multiple incisions in the central pumping organ contributes an increased challenge to the normal hemostatic mechanism. There are also some non-operative factors which can predispose to abnormal bleeding. If for some reason or other a patient should have a diminished bone marrow or liver reserve, this would give rise to an inability to manu-
facture the increased quantities of platelets and coagulation proteins imposed by the severity of the hemostatic challenge. All in all, it is truly remarkable that the instigation of cardiopulmonary bypass does not invariably result in abnormal hemorrhage. Nevertheless, excessive bleeding does occur and it is estimated some five to ten per cent of patients have to be taken back to the operating room because of hemorrhage and/or tamponade. In less than half of the patients is persistent bleeding from a suture line or a true 'pumper' ever found. It is more frequent for the cardiac surgeon to be confronted by untidy, generalized oozing which is both frustrating and difficult to control.

In order to gain more insight into the assessment of hemostatic function after cardiopulmonary bypass, a prospective study was undertaken in our Institute. The purpose of this study was to define what could be regarded as normal blood loss after bypass and to correlate, if possible, excessive blood loss with any abnormal coagulation studies. It was felt that if such a correlation existed, then these patients could be treated medically, thus preventing the need for further surgery. In addition, it was hoped that blood component therapy, when indicated, would be more astutely applied.

PATIENTS AND METHODS

A total of 774 consecutive patients undergoing aortocoronary bypass surgery were studied. Prior to surgery each patient's hemostatic function was evaluated clinically and by laboratory means. The laboratory tests included an examination of the peripheral blood smear, clot retraction, bleeding time according to Ivy, the prothrombin time (PT) using thromboplastin and control plasma (Dade), the partial thromboplastin time (PTT) using kaolin/cephalin and control reagents (Hyland), platelet count, platelet aggregation to ADP, collagen, ristocetin, thrombin, epinephrine and serotonin (Bio/Data), fibrinogen (Dade), tri-F-titer (TFT) and fibrin(ogen) split products (FSP) as measured by both tanned red cell hemagglutination inhibition (TRCHI) and by staphylococcal clumping.

The pump prime consisted of 2 liters of Ringers-lactate solution to which 6,000 units of heparin were added. No blood was added to this prime. The bypass circulation was maintained by a Sarns roller pump using polyvinyl chloride tubing and a Harvey bubble oxygenator. Systemic heparinization was achieved with a dose of 300 units/Kg with a further 50 units/Kg given for every thirty minutes on bypass. During bypass heparin levels were monitored by actual heparin assay at thirty-minute intervals. At the termination of bypass, neutralization was attained with protamine sulfate with a dose equivalent from one to two times the total dose of heparin given.

With the exception of the bleeding time, the same laboratory studies were repeated immediately on the completion of surgery and again as indicated by abnormal hemorrhage and/or abnormal values.

All blood samples for laboratory testing were collected either by clean venipuncture stick or from indwelling lines after discarding the first 20 ml. For coagulation studies other than clot retraction, FSP and platelet counts, blood was drawn into plastic tubes containing the correct amount of 3.2% sodium citrate anticoagulant. All testing was performed within 30 minutes of blood collection.

Blood loss, as estimated by the volume of chest tube drainage, was measured at hourly intervals after operation, until no more occurred and chest tubes were removed.
RESULTS

The mean blood loss observed per patient for the first eight hours was 452 ml. The mean total blood loss, until the chest tubes were removed, was 657 ml. Based on these observations, normal blood loss was arbitrarily defined as up to 600 ml for the first eight hours after surgery.

The postoperative hematologic parameters of the patients were in accordance with previous reports. It was observed that after surgery there is a lowering in the hematocrit, platelet count and fibrinogen with an increase in the PT, PTT and FSP. Postoperatively the platelet count shows a wide spread with a mean of 133,000/ul. The PT is generally elevated with a normal distribution ranging from 13 to 20 seconds. The PTT surprisingly is not as prolonged as the prothrombin time, and ranges from 30 to 45 seconds (mean 40.3 sec). Fibrin(ogen) split products in the postoperative period were mildly elevated, with a mean of 6.8 ug/ml, as measured by the TRCHI technique. The staphylocooccal clumping test gave slightly higher values than the TRCHI test. The postoperative mean fibrinogen level is 226 mg/dl, and ranges from 100 to 475 mg/dl. In the TFT the saline row is, on average, shorter than the Amicar (EACA) row, which in turn is also slightly shorter than the Polybrene/EACA row, the normal value of the TFT being 1:64 or higher in each row. All platelet function studies as measured by aggregometry were invariably abnormal.

DISCUSSION

Excessive postoperative bleeding is recognized as one of the most troublesome complications of cardiac surgery using an extracorporeal circulation. In this series the vast majority of coagulopathies were dealt with medically, and surgical reexploration was carried out only in those patients who continued to bleed in the face of normal hemostatic parameters. The reexploration rate for persistent hemorrhage of 0.6% (5 out of 774 patients) is much lower than previous reports and refutes the view that most hemorrhage is mechanical in nature.

Since excessive hemorrhage invariably occurred within the first eight hours after surgery, it was elected to analyze the laboratory data for the patients who bled less and more than 600 ml during this period of time. A simple statistical analysis of the postoperative hematologic data in bleeders and non-bleeders was performed. In this study 21% of the patients who had undergone aortocoronary bypass surgery bled more than 600 ml in the first eight-hour postoperative period (range 600–2500 ml). The majority of these patients could be predicted by a PTT greater than 45 seconds (p = 2 × 10^-19), a PT greater than 19 seconds (p = 6 × 10^-6), a saline titer 1:32 or less (p = 5 × 10^-4), an EACA titer 1:32 or less (p = 0.02), a Polybrene/EACA titer of 1:32 or less (p = 0.05), and a fibrinogen of 200 mg/dl or less (p = 2 × 10^-15). Platelet counts and FSP were of little prognostic value. A platelet count of less than 40,000/ul doubled the probability of bleeding, but these results were not statistically significant (p = 0.47).

Platelet aggregation studies were performed on all these patients and, with the exception of thrombin aggregation, were invariably found to be impaired in the immediate postoperative period. Presumably this also is due to the presence of heparin-protamine complexes, since platelets appear to be of little significance in any hemorrhagic tendency in the postoperative period.7,8
The prediction of excessive hemorrhage in the postcardiopulmonary bypass patient is an aspect of clinical medicine in which laboratory tests are chosen and interpreted in the light of the clinical findings. It is concluded that postoperative coagulation screening is well worth the effort. The battery of tests found most valuable included the PT, PTT, TFT and fibrinogen level. Fibrin(ogen) split product assays were of no value and platelet counts and aggregation studies were not helpful.

In this study twenty-one per cent of patients that come off bypass have coagulation abnormalities sufficiently severe to give rise to excess blood loss. These patients are best detected by the simple laboratory tests mentioned and treated medically with fresh frozen plasma, cryoprecipitate or protamine sulfate accordingly. In contrast, if a patient bleeds excessively, then the decision to reoperate is facilitated by the findings of normal clotting studies. In this series, five patients fell into this category and required reexploration. In each of these a definitive bleeding point requiring surgery was found.

SUMMARY

The present study (a) defines excessive bleeding in patients who undergo cardiopulmonary bypass, (b) evaluates the use of coagulation testing, to predict those patients that will bleed excessively in the postoperative period.

Pre- and postoperative hemostatic evaluation of 774 consecutive patients undergoing aortocoronary bypass surgery was carried out. Cardiopulmonary bypass consisted of a bloodless prime and a Harvey bubble oxygenator. In the postoperative period excessive hemorrhage was defined as that exceeding 600 ml chest tube drainage in the first eight hours. One hundred and sixty-three patients (21%) were noted to be in this category. Excessive bleeding postoperatively was best predicted by a PTT greater than 45 seconds, a PT greater than 19 seconds, a fibrinogen level less than 200 mg/dl and a TFT equal to or less than 1:32. These laboratory findings occur singly or in combination. The assessment of platelet, numbers or function, and fibrin(ogen) split products were of no prognostic value. Using these criteria, the reexploration rate for excessive hemorrhage and/or tamponade was 0.6 per cent (5 out of 774 patients).

No preoperative laboratory test of hemostatic function was useful in predicting coagulopathies resulting from cardiopulmonary bypass.

REFERENCES