SURGERY IN HAEMOPHILIA PATIENTS

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Surgical operations on haemophilia patients are not often necessary and the chances of any particular surgeon encountering a case are small. There is no doubt that surgery is the most exacting test of haemostasis in a haemophiliac and all surgeons and physicians are agreed that the dangers of inflicting major trauma are very great and that operations on haemophiliacs should be avoided whenever possible. It is also generally believed that when operations become inevitable, one can confidently expect excessive haemorrhage during operation and a turbulent postoperative course complicated by persistent oozing and haematoma formation.

In the management of bleeding episodes in haemophiliacs, one recognises two types of bleeding; the apparently spontaneous type of bleeding or bleeding that occurs following minimal trauma. This type, which occurs most commonly in the severe haemophiliac, can be relatively easily controlled by raising the plasma AHG level to between 10-20% of normal. The second type of bleeding is that which occurs following trauma like dental extractions and surgical operations. For these conditions higher AHG levels, usually above 50%, are required before haemorrhage can be controlled. Postoperative bleeding will invariably occur with AHG levels below 50% and this is most severe with levels below 10%.

Up till recently, the only treatment available for haemophilia patients was transfusions of fresh whole blood or plasma. Although the control of bleeding episodes in major centres is becoming less of a problem these days because of the ready availability of human AHG concentrates, the same cannot be said of the situation in Singapore where AHG concentrates are not generally available.

Fresh whole blood is generally not suitable for the control of bleeding. Fresh plasma whilst fairly easily available has a low AHG concentration, and it is generally impossible to achieve an adequate AHG level to maintain safe haemostasis because of the large volumes required. Animal AHG concentrates obtained as procine or bovine concentrates are very potent sources of AHG but are very liable to produce allergic reactions due to sensitization to foreign proteins.

In 1965, Poole in America described a method for the production of high potency concentrates of AHG using a closed bag system. This method with minor modifications has been used in our Laboratory for the production of AHG rich cryoprecipitates, Kwa and Chen 1968.

Over the past year, a number of haemophilia patients with severe haemarthrosis, bleeding gums and large muscular haematoma have been treated with these cryoprecipitates. In all instances the response to the cryoprecipitate transfusions has been dramatic with almost immediate arrest of the haemorrhage. With the experience and confidence gained in the care of these patients we have submitted a number of patients for elective surgery, four of whom are illustrated below:—

Case No. 1

HYC, aged 38 years, was referred for coagulation studies prior to being subjected to an operation for a stone in the left kidney. His past history revealed that eight years previously he had an operation for the removal of a ureteric calculi during which operation he bled excessively. His post operative convalescence was also very turbulent with excessive bleeding requiring many blood transfusions. Investigations carried out showed him to be a mild haemophiliac with an AHG level of about 5%.

In April 1967, he underwent a pyelolithotomy for removal of the renal stone. He was given 30 units of cryoprecipitate pre operatively. This raised his AHG level from 16% to 84% post transfusion. The operation was uneventful and the surgeon reported normal haemostasis. He received no blood transfusions during the operation. 12 hours after the first cryoprecipitate transfusion the AHG level had fallen to 30%. He was given a further transfusion of 30 units of cryoprecipitate which raised the AHG level to 54%. 12 hours later, *i.e.* 24 hours post operative, the AHG level had fallen to 37%. He subsequently received daily transfusion of AHG rich cryoprecipitate ranging from ten to 30 units. Estimations of the AHG levels were carried out before and after each transfusion. His post operative convalescence was uneventful with no bleeding episodes except for slight haematuria

on the sixth post operative day when the AHG level was 30%. This was soon controlled by a transfusion of 20 units of cryoprecipitate. On the eighth post operative day his stitches were removed after a transfusion of 20 units of cryoprecipitate had been given. He was discharged from hospital two weeks after operation.

Fig. 1 shows the plasma AHG levels before and following cryoprecipitate transfusions. It will be seen that on the second, third and fourth post operative days the plasma AHG levels attained were well above 100%, reaching a maximum of 155% on the fourth post operative day. The AHG levels were well maintained throughout the period. Apart from the fifth post operative day, when ten units of cryoprecipitate were given, the pre-transfusion levels of AHG were all within the 40% to 70% range.

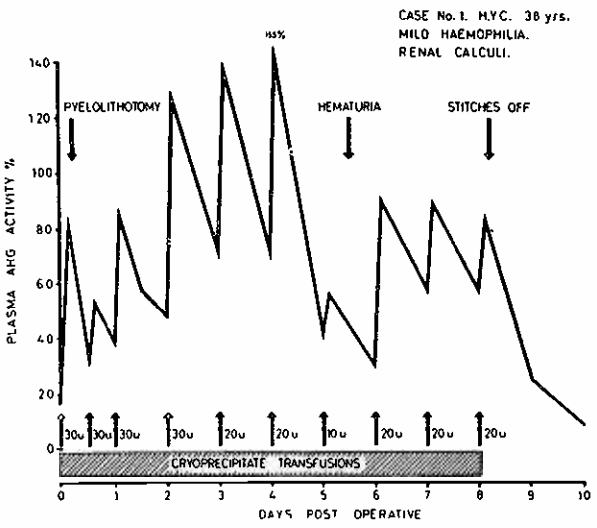

Fig. 1. Showing Pre and Post Transfusion AHG Levels in Case No. 1.

Patient received a total of 230 units of cryoprecipitate during his stay in hospital. No blood transfusions were given.

Case No. 2

YKC aged 23 years is a known severe haemophiliac with an AHG level of less than 1%. He was admitted in April 1967 with a large haematoma of the thigh. He was given transfusions of fresh frozen plasma in volumes ranging from 250ml. to 800ml. The plasma AHG levels after transfusions rose from 0% to the 6% to 22% range. This however was not sufficient to control the haemorrhage and on the fifth day the haematoma showed excessive accumulation of blood with signs of infection.

A surgical incision and drainage of the haematoma was performed. Approximately 500ml.

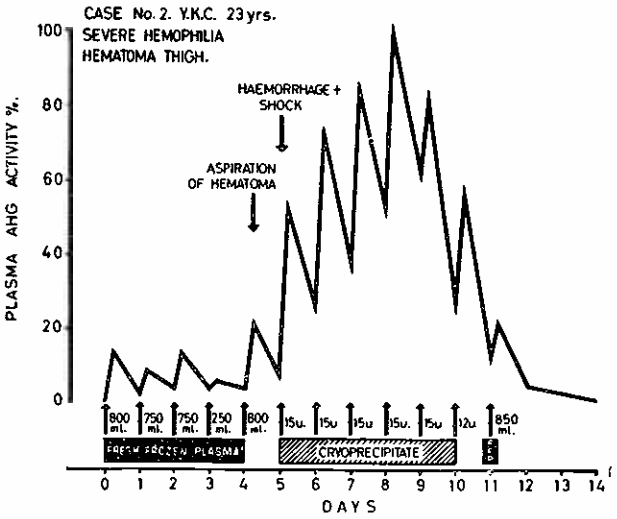

Fig. 2. Showing Pre and Post Transfusion AHG Levels in Case No. 2.

of stale clotted blood was evacuated. 24 hours after the drainage patient bled excessively and went into shock. 15 units of cryoprecipitate were immediately transfused. This resulted in an immediate arrest of the haemorrhage and the circulatory collapse was corrected. He was thereafter given cryoprecipitate transfusions daily in amounts ranging from 12 to 15 units.

Studies of the post transfusion AHG levels, Fig. 2, showed that the cryoprecipitate transfusions were able to raise the plasma AHG activity to values between the 54% to 100% range. The plasma AHG levels estimated 24 hours after the transfusion, *i.e.* just prior to administering the cryoprecipitate, ranged from 26% to 60%. Cryoprecipitate transfusions were discontinued after six days by which time the haematoma had almost completely resolved and the wound was almost completely healed. No further haemorrhage occurred once cryoprecipitate therapy was instituted. A total of 87 units of cryoprecipitate were transfused over six days. He also received six pints of fresh whole blood on the fourth day before institution of cryoprecipitate therapy.

Case No. 3

TKT aged 52 years was referred in July, 1967 for coagulation studies prior to undergoing an excision biopsy for a lump in the breast. His past history revealed excessive bleeding requiring blood transfusions following a dental extraction about 15 years ago. Investigation showed him to be a mild haemophiliac with an AHG level of 8%. A trial transfusion of 600ml. of fresh frozen plasma was able to raise the AHG level from 8% to 22%.

Prior to the operation, 20 units of cryoprecipitate were transfused over a period of 25 minutes. The level of AHG following the initial transfusion was found to be 44%. He was submitted to a simple mastectomy. Haemostasis was well maintained throughout the operation and no excessive bleeding was evident. He was given a transfusion of 20 units of cryoprecipitate on the second day and 10 units daily thereafter. His post operative convalescence was uneventful apart from the development of a small haematoma over the operation site on the third day. This was immediately controlled by the transfusion of 10 units of cryoprecipitate. His stitches were removed on the ninth day after which he was discharged from the hospital.

The response of plasma AHG activity to cryoprecipitate transfusions is shown in Fig. 3 below.

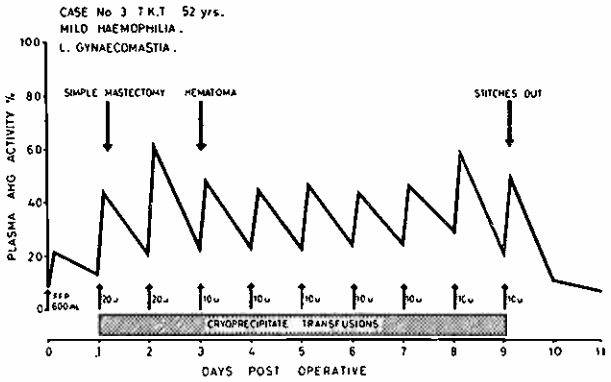

Fig. 3. Showing Pre and Post Transfusion AHG Levels in Case No. 3.

The transfusions were able to raise the AHG levels to above 40%. The lowest levels recorded were 24 hour post transfusion and samples taken prior to administration of the cryoprecipitate showed the levels to range from 20% to 28%.

He received a total of 110 units of cryoprecipitate for his operation. No blood transfusions were given.

Case No. 4

TBS, a 14 years old student, is a known severe haemophiliac with a plasma AHG level of less than 1%. He was admitted in October 1967 for extraction of a carious lower molar. Prior to the extraction, acrylic dental splints were prepared. Patient was given a transfusion of ten units of AHG rich cryoprecipitate just before the extraction. This raised the plasma AHG level from less than 1% to 35%. The dental extraction, which was performed under general anaesthesia, was uneventful with no excessive haemorrhage.

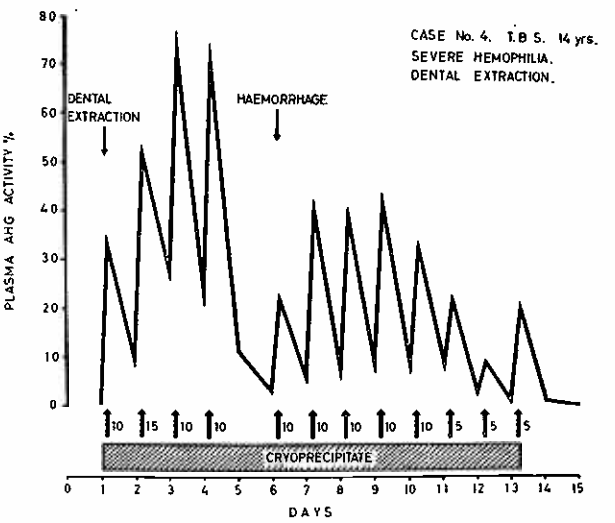

Fig. 4. Showing Pre and Post Transfusion AHG Levels in Case No. 4.

Gel foam soaked in topical thrombin solution was applied to the socket which was then protected with the dental splint. No stitches were applied.

On the first post operative day he was given 15 units of cryoprecipitate followed by ten units every morning over the next two days. No bleeding from the socket occurred during this time. On the fifth post operative day the plasma AHG level was 12%. No transfusions of cryoprecipitate were given that morning. However, that evening he began bleeding from the socket. Estimation of the AHG level on the sixth day showed a level of 2%. Ten units of cryoprecipitate were given. This raised the AHG level to 23% with immediate arrest of the haemorrhage. Thereafter, patient was given ten units of cryoprecipitate daily. This was reduced to five units daily, on the 11th., 12th. and 13th. days.

Patient was discharged from hospital on the 14th. day with a wound that was well healed with no further bleeding.

A total of 110 units of cryoprecipitate had been given over 13 days for the dental extraction. No blood transfusions were given.

DISCUSSION

The approach to surgery in haemophilia is strictly conservative. Experience with factor replacement therapy recently has however, allowed some types of surgery to be performed.

In planning the operation it is essential to have close cc-operation between the surgeon, anaesthetist, haematologist and physician. Preliminary investigations to confirm the type and degree of factor deficiency and to exclude the

presence of circulating anticoagulants are essential. Replacement therapy and blood transfusions must be supported by regular estimations of the plasma AHG levels.

Anaesthesia must be administered with care to avoid injury to the tissues of the upper respiratory tract. It is important for the surgeon to be meticulous about haemostatic technique to prevent post operative bleeding.

The pre-operative AHG levels should be raised to at least 30% of normal for minor operations and above 60% for major surgery. These levels have to be maintained for 10 to 14 days or longer depending upon the rate of healing. It is generally better to administer larger quantities of AHG and to have higher levels in the plasma than to be on the conservative side with risk of complicating post operative bleeding which will be difficult to control and will inevitably lead to delay in the healing.

The effectiveness of AHG rich cryoprecipitates in raising the plasma AHG activity in haemophiliacs to levels safe enough for them to be submitted for surgery without risk of excessive haemorrhage is demonstrated in the four patients described. Similar results have been recorded by other workers, Hattersley 1966, Jung et al 1966, Lien et al 1966, Bennett et al 1967, Brown et al 1967.

Case No. 1 was the first haemophiliac patient to be submitted for elective surgery. As such, relatively larger quantities of cryoprecipitate were administered to the patient. This is shown by the fact that AHG levels on the second, third and fourth postoperative days were well over 120% of normal. When the AHG level fell to less than 50% haematuria resulted. This was soon corrected by further transfusions of cryoprecipitate. Major renal surgery has been performed on severe haemophiliacs in the past all of whom had a turbulent post operative course complicated by prolonged post operative haemorrhage, Vermooten 1950; Mookini and Kelly 1960.

Case No. 2 illustrates the effectiveness of cryoprecipitate as compared to fresh frozen plasma. Although given at the maximum volume the patient could tolerate, fresh frozen plasma could only raise the AHG level to the 20% region. This was insufficient to control the bleeding following surgical drainage of the haematoma, resulting in circulatory collapse. Cryoprecipitate transfusions were then given resulting in almost immediate arrest of the bleeding. Haemostasis was thereafter maintained with daily transfusions of cryoprecipitate.

In case 3, very much smaller quantities of cryoprecipitate were used. This was sufficient to maintain the AHG level between 40-60%, at which levels no excessive bleeding occurred at operation or post operatively.

In case 4, the dental extraction was performed under ideal circumstances with no excessive haemorrhage at all. However, when cryoprecipitate transfusions were not given on the fourth post operative day, the AHG level fell to less than 10% resulting in bleeding from the socket. This led to some delay in healing of the wound necessitating continuation of daily cryoprecipitate transfusions up till the 13th. day.

The main advantage of cryoprecipitate transfusions over fresh whole blood or plasma is that higher AHG levels can be attained in the patient without risk of circulatory overload. As a result, patients can then be submitted for surgery with relatively little risk of haemorrhage.

Because of the small volume of the cryoprecipitate transfusion, infusion time is considerably reduced with corresponding lessened risk of thrombophlebitis.

Many patients with haemarthrosis and other moderately severe bleeding episodes have been successfully treated on an outpatient basis and have been allowed to go home after receiving their cryoprecipitate transfusions.

The cryoprecipitate is made available at little extra cost and does not put any strain on the availability of blood for other patients as the by-products of the process, *i.e.* platelets, red cells and AHG poor plasma can be made available for other patients in the form of specific component therapy.

The surgical management of haemophilia has thus progressed from one of despair and nihilism of a decade ago to one of confidence with the knowledge that should surgery be indicated in a haemophiliac, the surgeon will be presented with a patient that is little different, haemostatically speaking, from any other patient.

SUMMARY

The use of AHG rich cryoprecipitates in the management of four patients undergoing various surgical procedures has been described.

ACKNOWLEDGEMENT

I wish to record my appreciation and thanks to the following surgeons, Mr. Y. Cohen, Mr. W. Fung, Mr. K. T. Chan and Mr. F. M. S. Lee, who were responsible for performing the operations on Case Nos. 1, 2, 3 and 4 respectively.

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