Short Report

Fibrin Glue for the Control of External Bleeding in Haemophilia: a cost effective and novel approach

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Abstract

Objective: To see the efficacy of fibrin glue for external bleeding in haemophilia patients to maintain haemostasis.

Study Design: During last 5 years 68 bleeding episodes were treated in 32 haemophilia patients.

Setting: Haemophilia Care Unit, Ziauddin Medical University Karachi and Bismillah Taqee Blood Diseases Centre, Karachi.

Patients and Method: Sixty eight episodes occurred in 32 patients who had variable degree of severity of disease and presented with minor external post-traumatic bleed. There were 66 males and 2 females whose ages ranged from 6 months to 28 years. Fibrin glue was constituted by mixing fibrinogen (cryoprecipitate) and a 1:50 dilution of commercially available Thrombin calcium (Stago, France) (3). Twenty ml of thawed cryoprecipitate was filled in one syringe while 10 ml diluted thrombin in another syringe. This was poured on the wound.

Results: Out of 68 patients, who received fibrin glue treatment, 41 patients responded well with fibrin glue alone while 23 patients required single dose of factor concentrate. Four patients received multiple dose of factor VIII concentrate along with FFP.

Conclusion: Fibrin glue can be used to control the bleeding in haemophilia patients. It reduces the use of factor concentrate (JPMA 53:310;2003).

Introduction

Haemophilia A and B are X-linked recessive disorders caused by qualitative or quantitative deficiency of factor VIII and factor IX respectively. The most common presentation is haemarthrosis, haematoma and intra-cranial haemorrhage.[1-3] The mainstay of treatment is replacement of the deficient clotting factor. High cost of commercially available factor concentrate prohibits its use in our setting where Cryoprecipitate and Fresh frozen plasma (FFP) is the most common modality available.[1] Transmission of human immunodeficiency virus (HIV), hepatitis B (HBV), hepatitis C (HCV) and other infectious agents is another important risk associated with this treatment. About 5-15% of patient with haemophilia, develop inhibition factors to the deficient clotting factor.[2,3] The concept of application of fibrin glue at the site of bleeding (open wound) in haemophilia patients to attain haemostasis is gaining popularity in the last few years. The idea is to maintain haemostasis quickly and reduce the use and exposure of factor concentrate so that the potential risks of blood products could be minimized. Role of fibrin glue is being evaluated in haemophilia patients requiring surgery and found to be useful. It has been shown to reduce the use of quantity of factor concentrates in such patients.[3,4] Fibrin glue is composed of thrombin and homologous source of fibrinogen which when applied in an orderly manner mimic the final common pathway of normal coagulation, bypassing the defect in the coagulation cascade.[2-5] On this background, we started using home made fibrin glue in our patients who presented with external bleeding who would otherwise have been treated with cryoprecipitate or high purity factor concentrate. We present our experience of using fibrin glue in a small group of patients with congenital bleeding disorder.

Patients, Methods and Results

Since July 1998, 68 patients with moderate to severe congenital bleeding disorders presented with bleeding from external injuries and mouth. They were assessed clinically, and severity of their bleeding disorder was identified from

Table. Patients characteristics.

Patients variables	No. of patients
Total cases	32
Bleeding episodes	68
Bleeding disorders	
Haemophilia A	21
Haemophilia	3
vWD	4
Glanzmman's thrombasthenia	2
actor VII deficiency	1
Hypofibrinogenaemia	1
Episodes of bleeding	
Gum bleeding	18
Bleeding from tongue	3
Bleeding from lips	3
Bleeding from palate	2
Lacerated skin wound	42
Age	6 months - 28 years
Sex	3 female, 29 male

their records. Patients' characteristics are shown in table. Fibrin glue was applied on the bleeding site and pressure applied. Fibrin glue was composed of fibrinogen (cryoprecipitate) and a 1:50 dilution of commercially available Thrombin calcium (Stago, France).[3] Twenty ml of thawed cryoprecipitate was filled in one syringe while 10 ml diluted thrombin in another syringe. After cleaning the wound, cryoprecipitate was poured on the bleeding site. Then diluted thrombin was sprinkled on to it. Inside the wound crater, a white gel of fibrin formed in most cases. Bleeding gums or other shallow bleeding sites required multiple applications of fibrin glue.

Out of 68 episodes of external bleeding, 41 responded to the application of Fibrin glue alone, 23 required a single dose of factor concentrate along with Fibrin glue while 4 patient needed 11 doses of factor concentrate with 18 applications of Fibrin glue. The possible reason behind ineffectiveness may be that the patients were bleeding from tongue, hard palate wound and lower lip.

Comments

This study demonstrated that the use of fibrin glue in external bleeding gave a good local haemostatic response. Under normal circumstances, such an episode usually requires at least 3-4 days treatment of factor replacement to control bleeding. When fibrin glue is used, over 60% bleeding episodes were controlled without factor replacement therapy. This agrees to what has been reported in the literature. In a study reported by Martinowitz et al, the need for factor replacement was eliminated in 90% of patients who underwent tooth extraction.[4] In another study, haemophilic patients undergoing general and orthopaedic surgeries, combination of infusion of missing factor and use of fibrin sealant resulted in less blood loss than patients who did not received Fibrin glue.[2,6] There was a reduction in the use of factor concentrates from 65,000 units to 22,000 units .[2] In economic terms, the expenses were 30% less than would have incurred without the use of fibrin glue. Martinowitz et al reported the use of Fibrin glue with suturing alone without factor replacement for circumcision in haemophilia patients with 80% success rate.[6,7]

Our study is in agreement with others and has shown more than 60% reduction in the use of factor concentrate and therefore the cost of treatment. Haematological treatment options in countries with limited resources are either no treatment or improvisation of modern treatment. Sixty percent reduction in the use of factor concentrate would mean saving thousands of rupees for the treatment centre providing haemophilia care to persons with haemophilia. Another important consideration is reduction in the exposure to plasma-derived treatment products will reduce the risk of transmission of transfusion-transmitted diseases to the recipients.

There are limitations for the use of fibrin glue; that it cannot be used in closed wounds and internal bleeding but its use is worth considering in haemophilia patients undergoing surgery and dental extraction etc. Despite a very good safety profile of commercially available fibrin sealent/glue, there are documented and theoretical risks associated with it e.g., transmission of viral infections, development of inhibitors, anaphylaxis and delay in wound repair.[9-11] Large controlled clinical studies are needed to evaluate the efficacy, safety and cost effectiveness of fibrin glue in external post-traumatic bleeding, mucosal bleeding and in surgical procedures carried out in haemophilia patients.

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