

CASE REPORT

Safer and much cheaper circumcision using fibrin glue in severe haemophilia

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Summary. Circumcision is a traditional ceremony for Muslims and Jewish people. In order to reduce the high cost of factor concentrates, we administered locally manufactured heat-treated fibrin glue during operation. Circum-

cision can be performed safely and is much cheaper using fibrin glue plus a small amount of factor concentrates.

Keywords: circumcision, fibrin glue, haemophilia.

Circumcision is a traditional and religious ceremony in Turkey as in other Muslim countries (more than one billion people) and also for Jewish people [1, 2]. It is well known that social and cultural integration of haemophilic boys into society is one of the most important cornerstones of modern haemophilia therapy. In Muslim societies, 'circumcision is the first step to be a man'. Hence, haemophilic boys and their parents may have an inferiority complex because the boys are unable to be circumcised.

Fibrin glue is a topical biological adhesive, the effect of which imitates the final stages of coagulation. Fibrin glue from pooled plasma has been used in Europe for many years for fixation of skin grafts. Usefulness of the sealant as a potent haemostatic agent in the control of bleeding is well documented in the fields of plastic surgery, cardiovascular surgery, neurosurgery, otorhinolaryngology and dental care in patients with either normal or abnormal haemostasis [3–5]. Local use of fibrin glue is a safe and cost-effective tool to treat patients with haemophilia especially for dental extractions and oral surgery [3, 6, 7]. It has also been shown to be useful in circumcision of haemophilic boys [8].

In this report, we evaluated the efficacy and reduction in costs of factor concentrates in circumcision by using fibrin glue in four children.

Case history

Four children with haemophilia (three A, one B) (factor level < 2%) underwent circumcision using fibrin glue and factor substitution. All children were Caucasian, Turkish citizens and Muslims. Their ages were 8, 9, 12 and 17 years. No patient had inhibitors before intervention. Commercial heat-treated fibrin glue (Tisseel-Kit, Immuno AG, Vienna, Austria) was used for all patients.

Circumcision was carried out under general anaesthesia. The prepuce was cut off circumferentially and excised using the Gomco clamp technique. Major bleeding vessels on the shaft were fulgurated or tied. Then 1 mL of a two-component fibrin glue, prepared using thrombin 500 by the water bath method, was applied onto the denuded area through a 22-gauge needle. The skin edges were then approximated with 4/0 interrupted catgut sutures and the incision was covered again with the glue. The wound was covered with a gauze dressing and dampened with tranexamic acid three times a day. The dressing was removed 3 days after the operation.

All of the patients received oral tranexamic acid (50 mg kg⁻¹ day⁻¹; three times daily) for 7 days to delay the clot degradation. For patients with haemophilia A, intermediate-purity concentrates (Nordiate, Novo Nordisk, Denmark; Koate-HP, Bayer, USA; and Factor 8 Y, BPL, UK) were used. In haemophilia B, high-purity factor IX concentrate (Replenine, BPL, UK) was used. A bolus dose of concentrate was injected preoperatively to achieve an factor level activity in plasma of at least 50%. At the end of surgery, the factor level was checked and bolus injections were repeated. The replacement therapy was

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aimed to maintain a factor level of above 50% during the first 4 days postoperatively.

Three other children with severe haemophilia A given only factor substitution without fibrin glue served as a control group. Their ages were 8, 9 and 14 years. They had no inhibitor.

Intermediate-factor concentrates, Koate-HP and Nordiate, were used in these patients together with tranexamic acid for 7 days. We used 8 days of factor substitution after the operation day to achieve and maintain a factor activity level of at least 50% in plasma.

All the children had an uncomplicated course after circumcision. Nobody had a decreased Hb level or required blood transfusion. Wound healing was normal and there was no wound infection or bleeding. Total costs were significantly reduced to \$6300 per patient when using fibrin glue plus 4 days of factor replacement compared with \$13702 per patient in the control group ($P < 0.01$). A haemophilia B patient on high-purity and expensive factor IX concentrate was excluded from cost comparison.

Discussion

Fibrin glue is a solution of concentrated human fibrinogen which is activated by the addition of bovin thrombin and calcium chloride. The resultant clot aids local haemostasis and tissue sealing and is completely absorbed during wound healing without foreign body reaction or extensive fibrosis [3–5]. Fibrin glue is available in Europe and Canada as a haemostatic agent. A licence has not yet been given in the USA [3]. It is recently reported that the risk of viral transmission can be further reduced by using plasma from a single donor (home-made fibrin glue) [6–8] or using current viral inactivity procedures such as the solvent/detergent method [9]. Apart from the viral transmission risk, inhibitor formation is reported after using fibrin glue. Bovine thrombin preparations also contain bovine factor V. Antibodies against factor V or thrombin have been detected and shown to have cross-reactivity with human factor V. The resulting deficiency of factor V can produce a bleeding diathesis [10]. To day, all commercial products undergo one or more virus inactivation procedures, and all include fibrinogen, factor

XIII and thrombin of human origin [3]. We follow up our patients periodically with respect to viral transmission and inhibitor formation.

Formerly, we were not able to use the fibrin glue in circumcision, owing to unavailability in Turkey. Our cost of circumcision has recently been significantly reduced after introduction of this method. It was common for haemophilia patients to be overtreated, because of a fear that they would develop excessive bleeding. Before using fibrin glue, our factor substitution duration was at least 7–8 days, as with any other major procedures. Now, we use only 4 days of factor substitution with fibrin glue. However, Martinowitz has suggested that fibrin glue, meticulous suturing and tranexamic acid are enough to cover the patient with factor concentrate for 2–3 days only (personal communication). We also plan to decrease the substitution duration in future as suggested by Martinowitz. Fibrin glue gave us the opportunity to reduce our treatment, and hence it reduces the cost, perhaps through a 'placebo effect'. Moreover, Martinowitz *et al.* reported that satisfactory local haemostasis with fibrin glue was obtained in some haemophilic patients without factor replacement for circumcision [8]. Even with 4 days of factor replacement, we can save half the cost of circumcision without any bleeding complication. We also plan to use continuous infusion of factor substitution for another means of cost saving.

Although our patient numbers are small, the message is clear. Our experience suggests that fibrin glue significantly reduces the requirement of factor replacement. We believe that circumcision can be performed safely and at reduced cost using fibrin glue at the site of the surgical wound rather than small amounts of factor concentrates. We recommend that fibrin glue should be used in haemophilic boys for circumcision.

Acknowledgment

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Table 1. The cost of blood products for circumcision with or without fibrin glue in severe haemophilia A.*

Group	<i>n</i>	Age (years)	Duration of substitution	Mean weight (kg)	Total cost per case (\$)	Total cost per kg per case (\$)
Factor substitution	3	8, 9, 17	8 days	29.3	13702	472
Factor substitution (+ fibrin glue)	3	8, 9, 14	4 days	28.6	6300 (+ 173)	225

*Total cost only contains factor concentrates and fibrin glue. Hospitalization and operation cost was excluded.

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