

Circumcision in children with bleeding diathesis

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Summary

Aim: Circumcision is one of the most commonly performed procedures in children, however there are few reports which describe circumcision in patients with bleeding disorders (BD). The aim of this study is to present our experience in circumcision of children with BD.

Material and Method: We retrospectively searched the patient records of 18 children (3-14 years old) who were followed up at Cerrahpaşa Medical Faculty Pediatric Hematology Clinic for BD and who were circumcised at Cerrahpaşa Medical Faculty Pediatric Surgery Clinic between 2000 and 2010. Management strategies, complications and outcomes were reviewed.

Results: Seven children had a BD related to the first phase of hemostasis; 3 children had Glanzman thrombasthenia, 2 had Bernard-Soulier syndrome and 2 had chronic immune thrombocytopenic purpura. Other 11 children were followed up for a BD related to the 2nd phase of hemostasis; 3 had von-Willebrand disease (vWD), 1 had factor V deficiency, 1 had haemophilia B and 6 children had haemophilia A. No patient with inherited platelet disorder and/or thrombocytopenia required platelet replacement. Circumcision was performed with fibrinolytics and fibrin glue in these patients and there was no bleeding. In children with haemophilia (without inhibitors) and vWD, 2-3 doses of factor replacement therapy (15-25/kg/d) which was started before surgery were given until after 24-48 hours of circumcision. Fibrinolytics and fibrin glue were also used in these patients and bleeding was not observed in any patient. In 2 hemophilia A patients with low responding inhibitors, by-pass agents were used for 12 and 18 days respectively. Bleeding was controlled with sequential use of rFVIIa and aPCC.

Conclusions: Children with a BD can be safely circumcised in a center with experience. In circumcision of children with BD, antifibrinolytics and local hemostatic agents are helpful in decreasing factor doses in haemophiliacs and offer the possibility to omit platelet transfusion in patients with platelet disorders. (*Turk Arch Ped 2011; 46: 304-8*)

Key words: Circumcision, bleeding diathesis, haemophilia

Introduction

Circumcision is one of the most commonly performed surgical interventions in children (1). Studies have shown that circumcision decreases the frequency of urinary tract infection (UTI), sexually transmitted diseases, penile cancer and phimosis (2-9). Boys have been circumcised for thousands years because of cultural and religious beliefs in some populations including mainly our country (10). The rate of known risks of circumcision in normal children ranges between 0.2% and 0.6%, but vital threat occurs in children with bleeding disorders. Despite known risks, families of the children with bleeding disorders want their children to be circumcised. For most patients and families this procedure is the most important step in being a member of the population and almost a social

obligation for boys (11). In children with bleeding disorders, appropriate measures should be taken before circumcision as with other surgical interventions. Since few publications about circumcision in these children are present, clinical experiences of centers are important.

The aim of this study was to share our experiences about circumcision in children with bleeding disorders and discuss the efficiency and safety of circumcision and the frequency of complications in these children.

Material and Method

In this study, the medical records of the patients with bleeding disorders who were followed up in Cerrahpaşa Medical Faculty Division of Pediatric Hematology and

circumcised in the Department of Pediatric Surgery and Urology in the same center were evaluated retrospectively. Circumcision was performed between 2000 and 2010 in 18 boys (3-11 years of age) followed up because of bleeding disorder. Medical indication was not present in any of the patients and the procedure was performed with the request of the family.

Hemostasis is generally examined in three phases. First phase diseases are vascular and platelet disorders, second phase diseases are related to deficiency of coagulation factors, third phase diseases are related with dissolving of the clot. In seven of the subjects, the problem was related to the first phase of hemostasis : three subjects had Glanzmann thrombasthenia, two subjects had Bernard-Soulier syndrome and two subjects had chronic immune thrombocytopenic purpura (ITP). The other 11 subjects were being followed up for conditions related to the second phase of hemostasis: three subjects had von Willebrand disease (vWH), one subject had factor V deficiency, one subject had hemophilia B and six subjects had hemophilia A (two of them with inhibitors). 2 of the 6 hemophilia patients had inhibitors. Z-plasty was performed on the short circumcision skin developed as a complication of circumcision in a hemophylic subject with high inhibitor followed up in another center.

Results

The first phase of hemostasis

Platelet counts in the two patients with Bernard-Soulier syndrome were 23 000/mm³ and 63 000/mm³. In the patients who were followed up with a diagnosis of chronic ITP, platelet count was <50 000/m³ and splenectomy was not performed. Thrombocyte suspension was not given to any of the patients with platelet count disorder and/or platelet dysfunction. The procedure was performed without problems only using antifibrinolytics and local fibrin glue and no bleeding was observed.

The second phase of hemostasis

The factor level was <1% in the patient followed up for factor V deficiency. Fresh frozen plasma (FFP) was given to the patient before circumcision for once. 12 hours before the

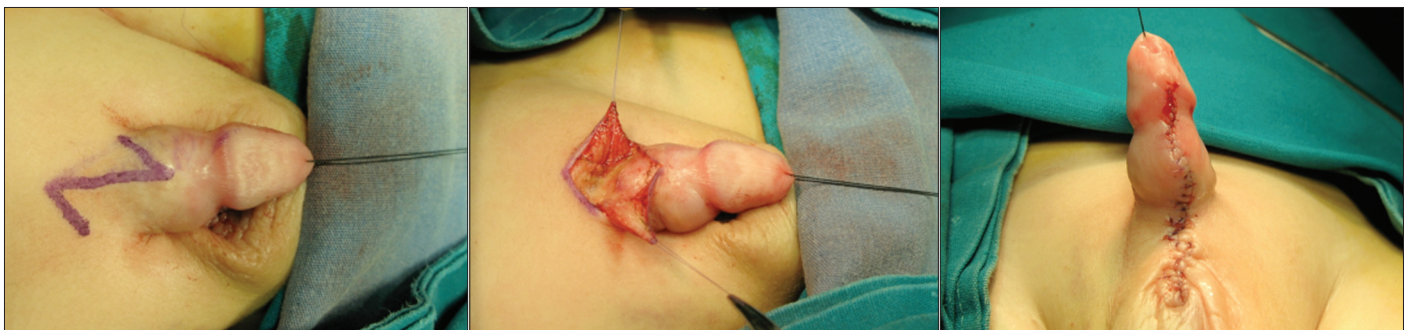
procedure tranexamic acid (25 mg/kg/dose PO/IV in 2-3 doses, the highest dose: 500 mg) was started and continued for three days. Fibrin glue was used during circumcision. In patients with type 1 (n:2) and type 2 (n:1) vWH, factor (25U/kg) was given for once before the circumcision, tranexamic acid was continued for five days and fibrin glue was used. Factor level of the patients with hemophilia B was 2%. Factor (30U/kg) was administered 2 days before circumcision and one day after circumcision and again tranexamic acid was continued for five days and fibrin glue was used. No bleeding was observed in any of the patients.

In two hemophilia A cases in whom inhibitor was found, the level of inhibitor was found to be low (<5 BU). Bypass agents including activated prothrombin complex (aPCC) (100U/kg, every 12 hours) and recombinant activated FVII (rFVIIa, every three hours) (90-120 mcg/kg) were given in an alternate way in high doses. Hemostasis was disrupted during removal of compression bandage and dressing after the operation, though emphasized and sequential treatment was continued for 12 and 18 days (14.4 g rFVIIa and 76 000 U FEIBA were used in the first patient and 6 g rFVIIa and 25 500 U FEIBA were used in the second patient). A second suturing was required to provide hemostasis in both patients.

Other than these patients, an eight year-old boy was investigated because of unstoppable bleeding and was diagnosed as hemophilia A in another center. Factor VIII level of the patients was found to be <1% and also a high level of inhibitor was found (>30 BU). The patient was referred to our hospital for prepuce plasty and rotation flap procedure because of problematic circumcision performed in an external center. In our center, the level of inhibitor was found to be very high (594 BU). The patient was given bypass agent (RFVII) and tranexamic acid for five days and Z-plasty was performed without any problem (Picture 1).

Discussion

Circumcision has known benefits as well as risks arising from being a surgical procedure. However, this risk is rather low in healthy children with no bleeding disorder. In children with bleeding disorder, circumcision is a procedure which can even constitute a vital threat, if not performed under appropriate conditions and with appropriate measures as with other



Picture 1. Z-plasty in the subject with hemophilia A with inhibitor

surgical procedures. In the retrospective study performed by Rodriguez et al. (11), the results of 48 patients who were circumcised between 2000 and 2007 in USA Mayo Clinic were evaluated. While bleeding was observed after circumcision in 3 of 21 patients who were known to have bleeding disorder, bleeding occurred in 8 of 27 patients who were not known to have bleeding disorder during circumcision. The frequency of bleeding was found to be 23% in all patients with bleeding disorder. In only three of these patients, circumcision was performed because of medical indications (phimosis). In all the other patients, the reason for circumcision was familial request similar to our study. In our country, circumcision has traditional, religious and cultural properties. In children with bleeding disorders, the most important discussion about circumcision is its necessity. However, families and patients request circumcision because of psychosocial pressure, although they know the risks and costs. In a study performed by Kavaklı et al. (12), 105 hemophilic patients and their families were questioned and 94% of them requested circumcision. In this study, circumcision was an obligation for children in view of 100% of the mothers and 76% of the fathers. Only one family did not request circumcision because of the risk of bleeding and 72% stated that it was a traditional or religious obligation. Only 48% thought that it had medical benefit. 80% of the patients considered circumcision as the first step to manhood. In the study performed by Rodrigues et al. (11), 13 patients were asked about the reasons for circumcision. 9 of the patients stated that not being circumcised rendered themselves different from their friends and peers and 11 patients stated that this was a social tradition. Only 2 families did not request circumcision because of the risk of bleeding. This study shows that tradition and faith are important in terms of circumcision practices also in Western populations. Consequently, families and patients request circumcision. Modern hemophilia treatment includes integrating patients with hemophilia socially and culturally into society. In all chronic patients, the importance of not only physical, but also psychological and social health is emphasized.

In children with bleeding disorders, the second important subject of discussion is the property of the procedure. Most

studies about circumcision and especially circumcision in hemophilic patients and patients with other bleeding disorders have been performed in our country. In the study performed by Karaman et al. (13), circumcision of hemophilic patients with a specially designed device (diathermic knife which works with battery and electric) under local anesthesia using economical dose factor was named as "Istanbul Protocol". Tranexamic acid was started 12 hours before the procedure, intravenous tranexamic acid was given during the operation and continued for 7-10 days after the procedure in all patients. Bolus factor concentrate was administered one hour before the operation to obtain a level of factor in plasma as 40%. Following local anesthesia circumcision was performed with a diathermic knife and factor administration was continued after circumcision (Table 1). This protocol was included in the World Hemophilia Federation's booklet of circumcision in hemophilic patients in 2010.

Kavaklı K et al. (14-18) from Turkey introduced "İzmir Protocol" to the world. In İzmir Protocol, circumcision is performed under general anesthesia in inhibitor negative patients, fibrin glue is used during the operation, factor support is given for two days with a target level of 50-100% and tranexamic acid is used (Table 2). If bleeding is observed in the patient with this treatment, it is recommended to administer extra two doses of FVIII. If bleeding persists, it is recommended to apply a second fibrin glue and/or to continue tranexamic acid up to 10 days.

Fibrin glue was first used by Martinowitz et al (19). It was used in 10 patients with severe hemophilia aged between 8 days and 21 years. Bleeding was observed in three of these patients, although factor support was given to only two of them. Fibrin glues contain fibrinogen, thrombin plasminogen and FXII. The reason that they are not used in some centers is that they are obtained from plasma and carry a risk of viral contamination. Recombinant thrombin which does not include plasma is a new hemostatic substance (RECOTHROM, Zymogenetics, USA), but it has not been brought to our country yet.

Ankaferd is a herbal hemostatic agent invented in Turkey (20). Ankaferd is a mixture of the herbs including Thymus

Table 1. "Istanbul Circumcision Protocol" in hemophilic children

• Intravenous injection of 20U/kg factor (in severe hemophilics 25U/kg) 2-4 hours before the operation
• 10 mg/kg tranexamic acid during the operation (or 0.3 µg/kg desmopressin infusion)
• Half of the first dose of factor is given intravenously 8-16 hours after the operation
• On the 2 nd and 3 rd day (and in severe cases on the 4 th day), 15 U/kg in mild cases, 25U/kg in moderate hemophilia and 40 U/kg in severe hemophilia (and one dose of desmopressin infusion in mild cases)
• In severe cases, 20-40 U/kg between the 5 th and 8 th days, 10-20 U/kg between the 9 th and 12 th days and afterwards 10 U/kg factor every other day (a total of 1-4 times)
• In moderate cases, 20 U/kg between the 4 th and 7 th days, 10 U/kg factor injection and one dose of desmopressin between the 8 th and 10 th days and afterwards 10 U/kg every other day (a total of 1-2 times)
• In mild cases, 15 U/kg factor between the 4 th and 10 th days, one dose of desmopressin between the 8 th and 10 th days and afterwards 10 U/kg factor every other day (a total of 1-2 times)

Table 2. "İzmir Circumcision Protocol" in hemophilic children

• Circumcision is performed under general anesthesia.
• The patient stays in the hospital for 3 days.
• During the operation fibrin glue (Beriplast-P/ Behring or Tissel-Kit/ Baxter) is sprayed on the area of cut by the surgeon before and after suture application.
• Factor support is started one hour before the operation and the patient is operated after FVIII level is measured.
• Factor support is calculated with a target factor level of 50-100%.
• Bolus factor support is continued for 2 days with intervals of 12 hours.
• The last dose is given while removing the dressing.
• Oral tranexamic acid is started one day before the operation (15 mg/kg/dose-three doses a day) and completed in 7-10 days.
• A sedative (melleril) is administered in children older than 12 years of age in terms of the risk of penile erection.
• The patient is discharged after three days.
• No administration of factor is needed at home.

vulgaris, Glycyrrhiza glabra, Vitis vinifera, Alpinia officinarum and Urtica dioica. It has different forms including spray, tampon and fluid. Ankaferd Blood Stopper® products were approved by the Turkish Republic Ministry of Health Drug and Pharmacy General Directorate in May 2007 for use in control of "external" bleedings. There are increasing number of studies about use of Ankaferd in circumcision in patients with hemorrhagic diathesis (21-23).

We formed our circumcision protocol which we use in our center by imitating İzmir protocol. In contrast to İzmir Protocol, we used lower doses of factor, but we did not observe bleeding. We attributed our success to use of fibrin glue and tranexamic acid. Our two patients in whom bleeding was observed were hemophilia patients with inhibitors. It is rather difficult to control bleeding in hemophilia patients with inhibitor and vital bleedings can not be stopped. There are few studies about circumcision experience in hemophilia patients with inhibitor. In the surgical experience of Balkan et al.(20) in hemophilic patients with inhibitor, circumcision was reported in one patient. The bleeding in this patients could only be controlled on the 15th day after using intensive by-pass agent and 2 units of erythrocyte suspension had to be transfused because of bleeding. Ankaferd (blood stopper) was used in one patient (20-24). In a study by Zülfikar et al (25) where the authors shared their 11-year experience of hemophilic patients with inhibitor, bleeding could be controlled with difficulty in two patients who were circumcised.

There are few publications about surgery in patients with Glanzmann's thrombasthenia in the literature and most of them are case reports (26,27). Antifibrinolytics, thrombocyte suspension, fibrin glue and rFVIIa can be used during local operations, but patients given thrombocytes carry the risks of development of alloantibody and refractory platelets (28). In our center, we let thrombocyte suspension be prepared for each patient considering that thrombocyte suspension could be needed to control bleedings during circumcision in patients with Glanzmann's thrombasthenia and monitored bleeding personally by attending the operation. It was planned to give thrombocyte without delay in case of a bleeding possibility, but

thrombocyte suspension was not needed, since bleeding was not observed due to use of fibrin glue and tranexamic acid.

Conclusively, circumcision can be safely performed in patients with bleeding disorders, if appropriate measures are taken and necessary drugs are provided excluding the hemophilic patients with inhibitor. We do not recommend circumcision in patients with inhibitor, since bleeding control is difficult. In our two patients, circumcision was performed on request of the families, although the bleeding risk was explained to the families in detail. Our recommendation about circumcision in patients with bleeding disorders:

- Circumcision can be performed in patients with bleeding disorders after discussing the risks with the families.
- With necessary replacement and antifibrinolytic and fibrin glue the procedure can be performed without any problem.
- The doses stated in the protocols can be changed by closely monitoring the patient.
- It should be kept in mind that circumcision is risky in patients with inhibitor even if the families request circumcision.

Conflict of interest: None declared.

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