Paediatrica Indonesiana

p-ISSN 0030-9311; e-ISSN 2338-476X; Vol.64, No.3 (2024). p.244-9; DOI: https://doi.org/10.14238/pi64.3.2024.244-9

Original Article

Circumcision in subject with hemophilia: the Yogyakarta Method

Pudjo Hagung Widjajanto[1], Agus Wibowo[2], Ivan Onggo Saputro[2], Nur Budiono[3], Nurul Hadi[4], Agus Tusino[5], David Wijaya Sutowo[1]

Abstract

Background Circumcision is one of the most common surgical procedures in boys in Indonesia. In cases patient with hemophilia (PWH), doctors tend to avoid this procedure due to increased bleeding tendency. In 2007, we developed a protocol for clotting factor concentrate (CFC) administration for circumcision in PWH, namely, the "Yogyakarta Method."

Objective To evaluate the outcomes of the Yogyakarta Method for circumcising PWH.

Methods This descriptive study was based on medical records of PWH who underwent circumcision at Dr. Sardjito Hospital (DSH), Yogyakarta and 3 surrounding hospitals under DSH supervision from 2008-2017 and 2018-2022. Diagnoses of hemophilia were based on clinical findings and factor assays. Subjects with hemophilia A received factor VIII (25 IU/kg/dose) and those with hemophilia B received factor IX (50 IU/kg/dose) before, during and after the procedure. In addition, patients received tranexamic acid (15 mg/kg/dose). Circumcision was performed by a pediatric surgeon or urologist.

Results From 2008-2017, 28 PWH underwent circumcision, 14/28 of whom were in DSH. Twenty-six patients had hemophilia A and 2 had hemophilia B. Their severities were mild (12 subjects), moderate (10 subjects), and severe (6 subjects). Subjects' median age was 10.5 (5-19) years and their median CFC use was 8 (range 7-10) doses in hemophilia A and 4 (range 4-5) doses in hemophilia B patients. Three of 28 PWH had bleeding episodes after the procedure. Following the encouraging results from the initial 2008-2017 study period, most of PWH circumcised in 2018-2022 underwent the procedure in the same 3 district hospitals rather than at DSH (21/28 subjects), and had similar CFC consumption. Only 1 bleeding episode occurred after the procedure during the second study period.

Conclusion The Yogyakarta method is safe and sufficient to control bleeding in circumcision of PWH. This method is also suitable in a district hospital setting. **[Paediatr Indones. 2024;64:244-9; DOI: https://doi.org/10.14238/pi64.3.2024.244-9**].

Keywords: *circumcision; hemophilia; clotting factor concentrates; district hospital*

Circumcision is the most common surgical procedure in the world, as it is an integral part of social and religious culture.[1,2] A 2007 WHO report stated that approximately 30% of males are estimated to be circumcised globally.[3] However, in people known to have bleeding disorders such as hemophilia, this procedure is sometimes avoided because of their risk of excessive bleeding.[4,5] In a prospective study of 580 infants with hemophilia, 53% had a bleeding episode by the age of 1 month. Bleeding post-circumcision accounted for almost half (47.9%) of the bleeding episodes.[6] There have been wide variations in reported frequencies of adverse events following circumcision, but serious adverse events are rare.[7] Although circumcision may pose a challenge in hemophilia patients, it can be safely performed with careful pre-operative planning,

From the Division of Pediatric Hematology & Oncology, Dr. Sardjito Hospital/Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada[1], Indonesian Hemophilia Society, Yogyakarta Chapter[2], Department of Urology, Dr. S. Hardjolukito Air Force Central Hospital[3], Pediatric Department, Dr. Tjitrowardojo District Hospital of Purworejo[4], and Dr. Soedirman District Hospital of Kebumen[5], Central Java, Indonesia.

Corresponding author: Pudjo Hagung Widjajanto. Division of Pediatric Hematology & Oncology, Dr. Sardjito Hospital/Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada Yogyakarta. Jl Kesehatan No. 1 Sekip Sinduadi, Yogyakarta 55284, Central Java. Indonesia. Email: pudjo.hagung.w@ugm.ac.id.

Submitted February 8, 2023. Accepted May 30, 2024.

adequate laboratory support, adequate hemostasis during and after surgery, and optimal post-operative recovery and rehabilitation.[8] In 2007, we started a pilot study on standardized CFC administration during circumcision in PWH called the "Yogyakarta method." No bleeding or other complications were found.[9] Since then, the method has been applied in DSH and other hospitals near Yogyakarta. Here we present the clinical outcomes of 15 years of implementation (2008-2017 and 2018-2022) of this method.

Methods

A descriptive study was performed using medical record data from patients who underwent circumcision from 2008-2017 or 2018-2022 at DSH, which is an official hemophilia treatment center (HTC), or surrounding hospitals, namely, Airforce Central Hospital of Dr. S. Hardjolukito in Yogyakarta, and 2 district hospitals in Purworejo and Kebumen, Central Java. In the latter 3 hospitals, the procedure was performed under the supervision of the HTC at DSH. Patients with incomplete medical records were excluded from our study. The diagnosis of hemophilia was based on bleeding history, family history, symptoms, and laboratory factor assay confirmation.

Informed consent was obtained from parents before the procedure. The CFC use was calculated based on our protocol (**Figure 1**). Hospitalization started one day before circumcision for pre-operative preparation, the day of circumcision was counted as day 1 (D1). Bleeding events were evaluated during the procedure and hospitalization, at outpatient visits at day 7 and 14 after circumcision, or between those days if a patient experienced a bleeding episode. Additional CFC was administered during hospitalization and outpatient visits if any bleeding events occurred.

Patients received 25 IU/kg factor VIII (FVIII) in case of hemophilia A or 50 IU/kg factor IX in hemophilia B, regardless of factor activity level. The first dose was administered 30 minutes before the procedure, the second dose during the procedure, followed by every 12 hours after circumcision in those with hemophilia A, or every 24 hours in those with hemophilia B. Tranexamic acid (15 mg/kg) was started 30 minutes before circumcision, continued during circumcision, then given every 8 hours after the procedure (**Figure 1**). Complete wound healing is defined as wound healing with no dehiscence or sign of infection (**Figure 2**), whereas incomplete wound healing is defined as wound healing with dehiscence or sign of infection. In cases with no bleeding manifestations and healed wounds, the CFC was stopped after 3 days (D3).[9] In cases of bleeding or incomplete wound healing, CFC was continued and other interventions were performed as needed until the bleeding was controlled. Inhibitor measurements were not done due to lack of laboratory facilities. The type of CFC used were plasma-derived concentrates provided by the Indonesian Health Insurance Program. Circumcision procedures were performed by pediatric surgeons or urologists.

Results

During the 2008-2017 study period, a total of 44 PWH underwent circumcision in DSH and 3 other hospitals, 16 of whom were excluded due to incomplete medical records. Of the 28 PWH included, 26/28 had hemophilia A and 2/28 had hemophilia B. Subjects' median age was 10.5 (5-16) years. Twelve out of 28 had mild hemophilia, 10/28 had moderate hemophilia, and 6/28 had severe hemophilia. The procedures were conducted in DSH (14 PWH), Dr. S. Hardjolukito Hospital (9 PWH), Purworejo (3 PWH), and Kebumen (2 PWH).

Median CFC use was 8 (7-10) doses of FVIII in hemophilia A and 4 (4-5) doses of FIX in hemophilia B. Twenty-four PWH showed complete healing without any bleeding post-circumcision (**Figure 2**), while 4 patients experienced bleeding on days 2, 6, 7 and 9 post circumcision, respectively. None of the 4 patients had serious bleeding, bleeding stopped after 1-2 additional doses of CFC. No adverse events of CFC and tranexamic acid or other complications were noted during or after the procedure. No clinical signs of an inhibitor appearance were found during hospitalization and outpatient follow up.

Of the 21 PWH circumcised in 2018-2022, most of the procedures (70%) were conducted in the 3 hospitals outside DSH and showed similar results to that of the previous study period, in terms of CFC use and bleeding episodes during and after circumcision (**Table 1**).

Division of Pediatric Hematology Oncology, Dr. Sardjito Hospital / Faculty of Medicine, Public Health Nursing Universitas Gadjah Mada

Clotting factor administration protocol for circumcision in hemophilia A

Name ..... DOB...../Age ..... y/m #Medical record .....

FVIII activity ..... % Inhibitor data + / - / NA .....

Body weight ..... kg FVIII ..... U/dose, always bolus iv Tranexamic acid (TA) ..... mg/dose, iv

Doctor in charge/surgeon .....

Day	Day 1			Day 2		Day 3		Day 4		Day 5	
Time	-30 min	Circum	+ 12h	+24h	+36h	+48h	+60h	+72h	+84h	+96h	+108h
Date											
Hour											
FVIII 25IU/kg	●	●	●	●	●	●	●	◌	◌	◌	◌
TA 15 mg/kg	●	●	●	●	●	●	●	◌	◌	◌	◌
Vial lot number											
Adverse event											

Circum=circumcision, DOB=date of birth, FVIII=factor VIII, TA=tranexamic acid, y=year, m=month, h=hour, min=minute

Figure 1. The "Yogyakarta method" of CFC administration for circumcision in hemophilia A

Figure 2. Completely healed wound at day 3 post-circumcision.

Table 1. Characteristics of PWH and outcomes

Characteristics	2007-2017 (n=28)	2018-2022 (n=21)
Type of hemophilia		
Hemophilia A	26	18
Hemophilia B	2	3
Severity		
Mild	12	6
Moderate	10	13
Severe	6	2
Median factor activity (range), %	4.5 (0.7-16)	2.3 (0.8-27.1)
Median age (range), years	10.5 (5-19)	11.2 (2.5-29.3)
Median CFC use (range), doses	8 (7-10)* 4.5 (4-5)**	7 (7-9)* 4 (4-5)**
Bleeding episodes, number of PWH	3 Day 2**,4*,7*,9*	1 Day 6**
Other adverse events	0	0
Hospital		
Dr. Sardjito	14	6
Dr. S Hardjolukito	9	6
Purworejo	3	4
Kebumen	2	5

*Hemophilia A; **hemophilia B; bleeding episodes later than 4 days occurred after they left the hospital

Discussion

In Indonesia, circumcision is generally conducted at the elementary school-aged boys, depending on the social and financial state of the family. Boys may have feelings of inferiority if they are not circumcised during elementary school, since they believe that circumcision defines their transformation to adulthood. Therefore, circumcision is sometimes perceived as a form of social pressure, as many boys do not consider themselves to be men until after undergoing this rite.[2]

The age of circumcision varies among countries. Circumcision is usually conducted during the neonatal period in Israel, the USA, Canada, Australia, New Zealand, and in much of the Middle East, Central Asia, and West Africa. Meanwhile, neonatal circumcision is uncommon in East and southern Africa, where the median age at circumcision varies from boyhood to the late teens or twenties.[3] In Indonesia, the most common age for circumcision is between 5 and 12 years.[10] The median of ages of our PWH at circumcision were 10.5 and 11.2 years, in the two study periods, respectively, which is during the elementary education period and similar to that in Indonesian children without hemophilia. Our protocol may offer several benefits for both hospitals and patients. The protocol is required by the hospital to provide enough number of CFC for this procedure, without the protocol the hospital wouldn't provide the CFC. Furthermore, our protocol may increase patient confidence and supports a belief that circumcision is safe when CFC is well prepared. Of our subjects who underwent circumcision at older ages, there were 8/28 PWH between 12-16 years during 2008-2017, as well as 7/21 PWH aged 12-19 years and 1 PWH aged 29 years during 2018-2022. This situation may illustrate the lack of health facilities that provide circumcision for PWH due to obstacles of CFC availability and/or the perception of healthcare providers or families that PWH should avoid surgical procedures because of excessive bleeding risk. The fact that so many subjects were older than 12 years may represent PWH increased trust in the protocol and their continued desire to be circumcised.

We found that CFC use 3-4 days post-circumcision with 7-8 doses of 25 IU/kg CFC in hemophilia A, 4-5 doses of 50 IU/kg in hemophilia B, or approximately 200 IU/kg total, regardless of hemophilia severity, were adequate to control bleeding during and post-circumcision. This result was comparable to that of other studies. When viewed as dose per injection, our doses were similar to that used in a study, which

were 20-25 IU/kg for hemophilia A and 50 IU/kg for hemophilia B.[11] A study in Egypt also used a similar dose per injection (25 IU/kg).[12] Likewise, a study in Senegal used 30 IU/kg per dose.[13] We suggest using a lower dose for moderate or mild hemophilia. There were 3 bleeding episodes in 3 of our PWH that occurred 3-4 days after CFC administration. The episodes were mild and completely resolved after an additional 1-2 doses of CFC. All 3 subjects had severe hemophilia. A trial in Turkey also reported that 5 of their patients had transient, minimal bleeding that responded quickly to factor administration.[14]

Interestingly, half of our PWH underwent the procedure in district hospitals outside DSH/HTC, thus, raising optimism that this procedure can be performed in smaller facilities if they have an adequate supply of CFC available for the circumcision procedure. As such, offering this protocol may be beneficial to the hospitals and for SWH who wish to be circumcised, as the procedure can be done safely and more economically, as patients would have a shorter distance to travel from their residence to the facility. However, supervision from the hematology oncology consultant was needed in this condition to ensure the outcome of circumcision.

Based on results from our initial time period, we reduced CFC administration to 3 days in the protocol and shifted the site of circumcision to district hospitals. This duration of administration is longer than that reported by a previous study, which administered CFC for 1-2 days.[15] However, our duration of administration was shorter compared to other studies in Turkey and Senegal, which reported the CFC administration for 7-18 days and 5-12 days, respectively.[13,14] Our duration of the CFC administration aligns with the WFH recommendation which stated that minor surgery (such as circumcision) should be given CFC replacement for 1-5 days. However, the CFC replacement should be adjusted depending on the clinical course of the procedure and also the outcome such as bleeding and wound healing.[16]

During the 5-year period of 2018-2022 with 21 PWH (18 hemophilia A and 3 hemophilia B), most (72%) underwent the procedure in district hospitals and had similar outcomes in terms of the CFC administration and bleeding episodes. This result may convince physicians and potential patient families that minor surgery in PWH is safe, if performed along with adequate CFC availability. In fact, two additional district hospitals in the surrounding Yogyakarta area in Banyumas and Klaten already successfully performed circumcision for several PWH.

Based on our findings, we suggest that the government allow PWH to undergo circumcision, since this procedure is done only once during their lifetime and should be performed during childhood, when the body weight is still low, thus, requiring only small amounts of the CFC. The strength of our study was the standardized dosing under the supervision of one HTC. The limitation of our study was that data were collected retrospectively.

In conclusion, the Yogyakarta method is safe and sufficient to prevent and control bleeding in circumcision of PWH. To reduce cost and extend circumcision services to PWH the Yogyakarta protocol can be performed in district hospitals with guaranteed availability of clotting factor concentrates.

Conflict of interest

None declared.

Funding acknowledgement

The authors received no specific grants from any funding agency in the public, commercial, or not-for-profit sectors.

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