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CLINICAL EVALUATION OF THE EFFECT OF TRANEXAMIC ACID MOUTH WASH ON ORAL HEALTH STATUS OF HEMOPHILIC CHILDREN

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ABSTRACT

Objectives: The present study evaluates the clinical effect of tranexamic acid mouth wash on oral health status of hemophilic children. **Subjects and methods:** Twenty patients with Hemophilia A or B complain from gingivitis were included in the study aged between 5 and 15 years. Control treatment group obtained intravenous factor replacement therapy. Experimental treatment group was instructed to use tranexamic acid mouth wash (TAMW). **Results:** Spontaneous Bleeding, the median and range of the bleeding episodes was 1(0-8) for control treatment regime CTR and 1(0-12) for experimental treatment regime ETR with no statistically significant difference between both Sides (p= 0.757). Tooth Brushing Bleeding, the median and range of the bleeding episodes was 2(0-13) for CTR and 4(0-16) for ETR with statistically significant difference between both Sides (p= 0.018). **Conclusion:** Tranexamic acid mouth wash was found to be an effective alternative to factor replacement therapy (FRT) in controlling gingival hemorrhage for people with hemophilia undergoing dental scaling. The usage of tranexamic acid wash can help hemophilic children to maintain oral health status by using tooth brushing regularly without fear of gingival bleeding.

KEYWORDS: Tranexamic acid mouth wash, hemophilic children, OHI, ultra-sonic scaling, gingival bleeding

INTRODUCTION

Hemophilia, is the most common severe hereditary hemorrhagic disorder. Both haemophilia A and B are characterized by prolonged and profuse bleeding following mild trauma or, on occasion, even spontaneously. They are caused by factor VIII and factor IX protein deficiencies or malfunction, respectively [(1)]. In Egypt (2020), the identified people with hemophilia were 6,847 where hemophilia A was 5,084 while hemophilia B 1,149 [(2)]. According to the plasma levels of F VIII or F IX activity, haemophilia is classified as "mild," "moderate," or "severe." Patients with "severe" haemophilia commonly undergo periods of spontaneous bleeding into their muscles and weight-bearing joints, whereas those with "moderate" haemophilia bleed more frequently after minor trauma and very seldom after surgery or tooth extractions. Dental treatment is usually not provided to those with congenital bleeding problems [(3, 4)].

Patients with bleeding issues must prioritize their periodontal health. Patients with coagulopathies

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may ignore their oral health because they are afraid of bleeding when they clean and floss their teeth, which worsens gingivitis, periodontitis, and caries. Due to the abundance of expanded capillaries near to the surface of the weaker parts of the gingiva, patients may have episodes of spontaneous bleeding while eating, cleaning their teeth, or if they have periodontal disease[5]. An anti-fibrinolytic agent called tranexamic acid competitively inhibits the activation of plasminogen to plasmin. It helps to stabilize clots and is beneficial as a supplement to treatment for some kinds of hemophilic bleeding [8]. Treatment of mucosal and superficial soft tissue haemorrhage with tranexamic acid is beneficial (e.g., oral bleeding, epistaxis, and menorrhagia) [9, 10]. tranexamic acid can be used to control bleeding after extraction in the form of mouth wash or tablets [11]. The present study evaluates the clinical effect of tranexamic acid mouth wash on oral health status of hemophilic children

SUBJECTS AND METHODS

Study design

Interventional, cross over, clinical trial study.

Study setting: This clinical study was conducted on children aged between 5 and 15years. The involved children were selected from hemophilic children who are frequently visit the Egyptian Society of Hemophilia-dental clinic in Cairo.

Ethical consideration: The Institutional Ethical Committee, Faculty of Dental Medicine, Al-Azhar University, Boys, Cairo, granted ethical permission. (559/2604/04/10/2020; EC Ref No. The haemophilia society granted permission.

Patient consent: Before starting this study, all selected children and his/her parent's or caregiver were informed about all the procedures used in this clinical study. Then, each parent's/caregiver was signed an informed consent having details about the whole clinical procedure.

Inclusion criteria: Hemophilic children A or B complain from gingivitis due to heavy plaque accumulation or calculus. Aged (5-15 years). Co-operative \ educated patients. No history of allergy to tranexamic acid.

Exclusion criteria: Receiving ongoing prophylactic factor replacement therapy during study. Disturbances of color vision due to several incidents of ophthalmic aberrations have been reported after using tranexamic acid. Presence of other systemic disease.

Sample size justifications: From 100 enrolled patients, 20 patients were included in the study.

Preoperative assessment

History of the patients:

Complete medical and dental history was taken for all study participants and all data were collected and recorded at diagnostic sheet.

Clinical examination:

Tooth examination: The selected children were examined by using a mouth mirror and dental explorer under appropriate light condition to detect dental caries, tooth mobility, restorations and any other teeth malposition.

Periodontal and gingival examination: Oral examination was done with children sitting under appropriate light condition by the researcher and by using color coded periodontal probe, mouth mirror and dental explorer to determine the appropriate treatment for each participant according to Oral Hygiene Index (OHI).

Oral Hygiene Index (OHI):

The oral hygiene index (OHI), developed by John C. Greene and Vermillion in 1960, and was used to assess oral hygiene. It included the calculus index (CI) and the debris index (DI) (CI). OHI evaluates the quantity of calculus and plaque on the mouth's teeth. The OHI value, which expresses the individual's oral hygiene state, is calculated by

adding the debris and calculus values. The OHI is an information system that gathers, evaluates, and quantifies clinical data on the state of oral health at the present time, necessary interventions, and treatment outcomes—whether positive or negative—that may be attributed to therapy and behavioural choices. The OHI provides, for the first time, quantification of periodontal state and changes in status over time, therefore satisfying the demand for a quantitative method of evaluating periodontitis risk. For all parties involved, this knowledge is extremely potent. It gives patients a better grasp of their oral health situation and the suggested actions. When the scales for good (0.1 - 1.2), fair (1.3 - 3.0), and bad oral hygiene are used (3.1 - 6.0). Only teeth that have fully erupted were scored. The researcher examined the children's mouths while they were seated, using a periodontal probe with a color-coded tip and the proper lighting conditions. Following that, simple teeth brushing method was shown and oral hygiene education was given [12, 13].

Treatment protocol

Treatment protocol had been explained for all children and their care givers. Each participant was fitted a cannula at the therapeutic unit of the hemophilia center by the nurse to be obtained intravenous infusion of 0.9% normal saline as a placebo, for experimental treatment regimen or intravenous infusion of factor replacement therapy for control treatment regimen in a syringe blinded with an opaque obscuring sleeve. Each participant, immediately before treatment was instructed to use tranexamic acid mouth wash (TAMW) for experimental treatment regime to control gingival bleeding or placebo mouth wash (PLMW) for control treatment regime to achieve the blind study.

For Experimental Treatment Regimen (ETR):

Half an hour before treatment, all hemophilic child patients received intravenous infusion of 0.9% normal saline placebo factor replacement therapy (PL FRT) in a syringe blinded with an opaque obscuring sleeve. Before treatment we recorded (OHI) for each participant who was selected for (ETR). After half an hour according to Periodontal and gingival examination, we started the appropriate treatment for each participant on the selected side either right or left according to the result of coin toss. After treatment, for home use each participant was provided with freshly prepared one conceded bottle 160 ml 5 % Tranexamic Acid Mouth Wash (TAMW) and instructed to use 5 ml per time (TAMW) for 8 days, 4 times per day by holding the solution in the mouth for 2 min then to expectorate. The subject was instructed to visually assess for gingival bleeding four times each day, once after each of the three main meals and once before bed. All participants or their carers received a log book that only contained information on gingival bleeding, tooth brushing, and mouthwash use on the treated side. Then they were informed to return books to the researcher during the second session. Once again we recorded (OHI) for each participant after two weeks.

For Control Treatment Regimen (CTR):

Two weeks' interval, the same set of participants who finished the (ETR) we exchanged the side of treatment, then they received intravenous transfusion of required (FRT) according to the type of hemophilia A or B (I.e. F VIII) for patients with hemophilia A and F IX for patients with hemophilia B) rather than saline as the (ETR) to raise factor concentration around 20-25% (depending on the type of bleeding disorder). Then we recorded (OHI) for the other side as same as (ETR).

After treatment of the remaining side of the mouth each participant was provided with one conceded bottle 160 ml placebo mouth wash (PLMW) for post-operative use. Instructions for inspection for bleeding, tooth brushing, mouthwash use and data recording were the same as for the ETR. Then they were informed to return books to the researcher during the second session. Once again, we recorded the (OHI) after two weeks as same as ETR.

Washing period: Its two weeks after the first treatment protocol to separate the two experimental periods.

Treatment

For each side upper and lower have been treated including scaling and polishing.

- Heavy plaque accumulation and stains removed by low speed contra angle hand piece and nylon brush.
- Supra gingival calculus have been removed by ultra-sonic device (Cristofoli) and ultra-sonic tip G1.

∑ Sub gingival calculus have been removed ultra-sonic device (Cristofoli) and ultra-sonic tip P1.

Mouth wash use:

- **For experimental treatment regimen:** all participants was provided with freshly prepared one conceded bottle 160 ml 5 % Tranexamic Acid Mouth Wash (TAMW) and instructed to use 5 ml per time (TAMW) for 8 days, 4 times per day by holding the solution in the mouth for 2 min then to expectorate.
- **Composition of 5% tranexamic acid mouth wash (TAMW)**

Tranexamic acid mouth rinse was compounded either using crushed powder of commercial tablets or diluting intravenous solution (ampoule) with distilled water.

- **Preparation of mint-flavored (TAMW)100mg ampoule/ ml for 160 ml:**

1. Tranexamic acid 8000mg.
2. Peppermint and mint extract 0.75 ml.
3. Aspartame 58.5 mg.
4. Purified water 160 ml.

- **For control treatment regimen:** all participants used placebo mouth wash (PLMW) as same as experimental treatment regimen.

Data Management and statistical analysis: The Statistical Package for Social Sciences (SPSS) version was used for data management and statistical analysis. 24. Wilcoxon tests were used to compare the two sides and over time. Differences for categorical variables were examined using the Macnemar test. Using the Bonferroni procedure for multiple testing, the p value was adjusted. P-values are always two-sided. P-values less than 0.05 were regarded as significant.

RESULTS

Oral Hygiene Index (OHI)

Pre-scaling, there was no statistically significant difference between the two sides (p=0.655) in the median and range of the OHI scores for CTR and ETR, respectively, which were 3 (2-6) and 4(2-6). After two weeks, there was no statistically significant difference between the CTR and ETR sides in terms of the median and range of the OHI scores, which were both 1(0-1) (p=0.564). Statistically, there was no difference in the median OHI score across time in any individual Side (p 0.001). Table 1 displays the median and range values of the OHI scores for both Sides.

TABLE (1) Median and range of OHI score at different time points in the tested Sides by Wilcoxon test.

Sides-groups / Time	Side A(CTR)			Side B(ETR)			
	Median	**Min.**	**Max.**	**Median**	**Min.**	**Max**	**P value 1**
OHI- pre- scaling	3	2	6	4	2	6	0.655
OHI- after 2 weeks	1	0	1	1	0	1	0.564
P value 2		**<0.001**			**<0.001**		

P≤0.05 is statically significant; P1: for comparison between 2 Sides. P2: for comparison over time in each Side separately, min: Minimum, max: Maximum.

Frequency of bleeding episodes.

Spontaneous Bleeding, the median and range of the bleeding episodes was 1(0-8) for CTR and 1(0-12) for ETR with no statistically significant difference between both Sides (p= 0.757). **Tooth Brushing Bleeding,** the median and range of the bleeding episodes was 2(0-13) for CTR and 4(0-16) for ETR with statistically significant difference between both Sides (p= 0.018).

TABLE (2) Frequency of bleeding episodes

		CTR	ETR	P value
Spontaneous Bleeding	None	6(30.0)	6(30.0)	1.000
	Once or more	14(70.0)	14(70.0)	
Tooth Brushing Bleeding	None	6(30.0)	4(20.0)	0.625
	Once or more	14(70.0)	16(80.0)	

DISCUSSION

One in 5,000 male newborns have haemophilia, a genetic blood clotting condition [14]. Hemophilia comes in two different forms: haemophilia A, which is defined by a clotting disorder (F VIII), and haemophilia B, which is characterised by a clotting disorder (F IX). About 85% of all haemophilia cases are haemophilia A, making it the more prevalent kind [15]. With recommendations to increase preventative measures and educational initiatives, it has been noted how crucial it is to preserve dental and periodontal health in people with hereditary bleeding problems. Obtaining primary care might be difficult for those who have haemophilia. [16, 17]

In the current study, spontaneous bleeding was seen in 6 patients for both ETR and CTR, although there was no statistically significant difference between the two Sides (p=1.000). DDAVP was examined by De la Fuente et al. [18] as a possible therapy for mild to moderate haemophilia A patients who have spontaneous bleeding episodes, including epistaxis. In 9 of 14 patients with mild haemophilia A, clinical improvement, including the end of bleeding, occurred.

In the current study, there was a statistically significant difference between the two sides (p=0.018) in the number of patients who experienced NO bleeding when brushing their teeth: 6 patients for CTR (FRT) and 4 patients for ETR (TAMW). For haemophiliacs trying to limit gingival bleeding, TAMW was just as successful as FRT. Nuvvula et al [19].'s evaluation of freshly made TA mouthwash as an alternative to factor replacement treatment (FRT) in limiting gingival bleeding in haemophiliacs during dental scaling concurs with our findings. They came to the conclusion that TA mouthwash was an excellent substitute for FRT in reducing gingival bleeding in haemophiliacs during dental scaling since 7 patients reported no bleeding in either the ETR or CTR.

The median number of bleeding events in the current study on spontaneous bleeding was 1 for CTR and 1 for ETR, with no statistically significant difference between the two sides (p = 1.000). Therefore, TA mouthwash was discovered to be a successful substitute for FRT in reducing gingival bleeding in haemophiliacs during dental scaling. In agreement with our findings, Lee et al. [20] compared the efficiency of factor replacement treatment (FRT) before dental scaling in haemophiliacs to that of tranexamic acid mouthwash (TAMW) in preventing gingival bleeding following dental scaling. Using TAMW after dental scaling was just as successful in reducing gingival bleeding in haemophiliacs as using FRT beforehand. As a result, this research encourages haemophiliacs to utilise TAMW throughout their scaling procedures.

After analysis of data provided from telephone structure interview, we founded that the taste of TA mouth wash for hemophiliacs during their scaling procedures was accepted by nearly all children (90 %). TA is readily soluble in water [21]. Due to the taste was masked by natural peppermint [22]. The combination was supplemented with TANTUM Verde mouthwash. Patients reportedly found ETR

to be cost-effective and simple to use. All of the study participants said they would feel comfortable utilizing the TAMW routine alone after dental scaling in the future, without FRT. Where 100% of participants said they would feel secure getting dental scaling as long as they simply used tranexamic acid mouthwash to stop gingival bleeding thereafter.

CONCLUSION

With benefits including no chance of developing antibodies and blood product contamination, using tranexamic acid mouthwash was proven to be an efficient substitute for FRT in preventing gingival bleeding for persons with haemophilia undergoing dental scaling. The usage of tranexamic acid wash can help hemophilic children to maintain oral health status by using tooth brushing regularly without fear of gingival bleeding.

REFERENCES

1. SCHRAMM, Wolfgang. The history of haemophilia–a short review. Thrombosis research, 2014, 134: S4-S9.
2. World Health Organization. 2019. Definition of regional groupings.https://www.who.int/healthinfo/global_burden_disease/defiition_regions/en/. Accessed on March 10, 2019.
3. Gouw S, van der Bom J, Ljung R, et al. Factor VIII products and inhibitor development in severe hemophilia A. N Engl J Med. 2013;368(3):231 -39.
4. Calvez T, Chambost H, Claeyssens-Donadel S, et al. Recombinant factor VIII products and inhibitor development in previously untreated boys with severe hemophilia A. Blood. 2014; 124(23):3398-408.
5. Sonbol H, Pelargidou M, Lucas S, et al. Dental health indices and caries related microflra in children with severe haemophilia. Haemophilia 2001; 7:468–74.
6. Patton L. Bleeding and clotting. In Greenberg MS, Glick M, editors. Burket's Oral Medicine Diagnosis and Treatment. 10th ed. Hamilton: BC Decker; 2003. P.454–78.
7. Kalsi H, Nanayakkara L, Pasi K, et al. Access to primary dental care for patients with inherited bleeding disorders. Haemophilia.2012; 18(4):510-15.
8. Leissinger C, Carcao M, Gill C, et al. Desmopressin (DDAVP) in the management of patients with congenital bleeding disorders. Haemophilia.2014; 20(2):158-67.
9. Coetzee M. The use of topical crushed tranexamic acid tablets to control bleeding after dental surgery and from skin ulcers in haemophilia.Haemophilia.2007; 13(4): 443-44.
10. 10. Frachon X, Pommereuil M, Berthier A, et al. Management options for dental extraction in hemophiliacs: a study of 55 extractions (2000-2002). Oral Surg Oral Med Oral Pathol Oral Radiol Endod.2005; 99(3):270-75.
11. Sindet-Pedersen S. Distribution of tranexamic acid to plasma and saliva after oral administration and mouth rinsing: a pharmacokinetic study. J Clin Pharmacol 1987; 27: 1005– 08.
12. Greene, J. C., & Vermillion, J. R. (1960). The oral hygiene index: a method for classifying oral hygiene status. J Am Dent Assoc. 61(2), 172-179.
13. Greene, J. C. (1967). The oral hygiene index—development and uses. The Journal of Periodontology, 38(6P2), 625-635.
14. Berntorp E, Shapiro A. Modern haemophilia care. The Lancet. 2012 Apr 14; 379(9824):1447-56.
15. Bowen D. Haemophilia A and haemophilia B: molecular insights. Molecular Pathology. 2002 Apr; 55(2):127.
16. Baskirt EA, Albayrak H, Ak G, Erdcm AP, Sepet E, Zulfikar B. Dental and periodontal health in children with hemophilia. J Coagul Disord 2009; 1:7-10.
17. Salem K, Eshghi P. Dental health and oral health-related quality of life in children with congenital bleeding disorders. Haemophilia 2013; 19:65-70.
18. De la Fuente B, Kasper CK, Rickles FR, Hoyer LW. Response of patients with mild and moderate hemophilia A and Willebrand's disease to treatment with desmopresin. Ann Intern Med 1985; 103:6-14.
19. Nuvvula S, Gaddam KR, Kamatham R. Efficacy of tranexamic acid mouthwash as an alternative for factor replacement in gingival bleeding during dental scaling in cases of hemophilia: A randomized clinical trial. Contemp Clin Dent. 2014; 5(1):49-53.
20. Lee AP, Boyle CA, Savidge GF, Fiske J. Effectiveness in controlling hemorrhage after dental scaling in people with hemophilia by using tranexamic acid mouthwash. British dental journal. 2005 Jan; 198(1):33-8.
21. Windholz M, editor. The Merck index. 10th ed. Rahway, NJ: Merck & Co.; 1983. p. 1368-9.
22. Donnelly R. F. (2018). Stability of Tranexamic Acid Mouth Rinse. International journal of pharmaceutical compounding, 22(5), 412-16.