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Research Article

Oral Health plays a role on Oral Fibrinolytic Activity

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Abstract

Background: In spite of the high incidence of gingivitis and periodontal disease in the hemophiliac population, few are known about the influence of oral health condition as risk factor for bleeding after dental extraction in this patient population. The aim of this report is to use a group of patients under oral anticoagulation as a model of acquired bleeding disorder to show the importance of local fibrinolytic activity in the oral cavity, and propose, based on these data, a safe approach for dental extraction and other dental procedures in hemophilia patients.

Patients and methods: Twelve patients were submitted to twenty dental extractions. Previous studies have demonstrated the role of the periodontal microbiota in binding and fibrinogen degradation, which might have a role on oral fibrinlysis. Oral health was measured using Gingival Index and Plaque Index which are based on recording the level of gingival inflammation due the presence of soft debris and/or mineralized deposits on the indexed teeth, respectively. Samples of non-stimulated saliva were collected before and after extraction. Samples of peripheral blood and alveolar blood were collected for fibrinolytic activity analysis, using the Fibrin Plate Method. The results showed a higher fibrinolytic activity on the alveolar blood samples when compared with the peripheral blood ($p=0.006$) samples. This activity also showed a positive correlation with the oral health indexes (Gingival Index and Plaque Index $p<0.05$). Salivary fibrinolytic activity showed a significant increase after the tooth extraction. Oral fibrinolytic activity was increased after tooth extraction and it was not related to oral health indexes.

Conclusion: The fibrinolytic activity presented on the site of extraction was correlated with the level of gingival inflammation demonstrated by the oral health index of the extracted tooth. The fibrinolytic activity in the surgical site can represent a risk factor for secondary or late bleeding after dental extraction in patient with inherited bleeding disorder.

INTRODUCTION

Oral bleeding is a frequently reported symptom of adults and pediatrics patients with inherited or acquired bleeding disorders [1-5]. Gingival bleeding is also known to be a leading symptom of plaque-induced gingivitis and untreated periodontal disease. Importantly, gingival bleeding in patients with inherited bleeding disorders may be triggered by gingival inflammation, but it is not an original symptom of such diseases [6]. Chronic gingivitis to some degree affects over 90% of the population. If treated, the prognosis is good, but otherwise, it may progress to periodontitis and tooth mobility and loss. Clinically, marginal gingivitis is painless but may manifest with bleeding from the gingival crevice, particularly when brushing the teeth [7]. On the other hand, periodontal disease is a common and highly prevalent oral chronic disease seen in humans [8-10]. It can be considered as a major public health problem, causing tooth loss, disability, masticatory dysfunction and poor nutritional status. Periodontitis follows the development of a pathogenic microbial biofilm at and below the gingival margin. In susceptible patients, this triggers an exaggerated and dysfunctional inflammatory immune response, which destroys the bone surrounding the teeth, causing tooth loss [8-11]. Despite their high prevalence and evident impact on general health, periodontal diseases are commonly regarded as "silent diseases" since patients often live with no or few oral symptoms (i.e. bleeding, swelling and tooth mobility without sense of pain) [11].

Hemophilia an inherited bleeding disorder characterized by a lifelong defect in clotting mechanism. It is characterized as hemophilia A and B, based on the quantitative and/or functional deficiency of factor VIII or factor IX respectively. Hemophilia is classified as mild (>5%), moderate (1-5%) and severe (<1%) base on the residual coagulant activity of the deficient clotting factor in the plasma. Regardless the type and severity of hemophilia, oral hemorrhagic episodes are common in this patient population

[12], mainly due to traumatic injuries, eruption and exfoliation of teeth and poor oral hygiene [13]. Few studies concerning oral health in hemophilia population have been published. Despite the controversial results, poor oral hygiene among adult and pediatric hemophilia population has been reported and it was correlated with consumption of sugars, difficulty in accessing dental care and other socioeconomic factors [1,2,5,14,15].

In spite of the high incidence of gingivitis and periodontal disease in the hemophiliac population, few are known about the influence of oral health condition as risk factor for bleeding after dental extraction in this patient population.

The aim of this report is to use a group of patients under oral anticoagulation as a model of acquired bleeding disorder to show the importance of local fibrinolytic activity in the oral cavity, and propose, based on these data, a safe approach for dental extraction and other dental procedures in hemophilia patients.

MATERIALS AND METHODS

In order to have a homogeneous population with bleeding tendency that could mimic oral cavity conditions observed in the population with hemophilia, with respect to prolonged bleeding during dental procedures, patients under definitive use of VKA (warfarin) for at least 6 months and for more than 2 years, presenting indication for tooth extraction were invited to participate in the study. The medical evaluation and dental procedures were performed at the Hematology outpatient clinic and at the Dental outpatient clinic of the Hematology and Hemotherapy Center, University of Campinas (Hemocentro UNICAMP), Brazil. Patients or their legal representatives provided a written informed consent before entering in the study. The study received Review Board of the Medical School, University of Campinas approval (Protocol number 286/2007).

Oral health examination

Oral health conditions were evaluated after patient's enrollment in the study, using routine dental instruments and panoramic radiography. Oral health status was measured by using the Decayed, Missing and Filled Teeth Index (DMFT) [16], Gingival index (GI) [17], and Plaque index (PI) [18]. The measurement of the state of oral hygiene by Plaque Index is based on recording both soft debris and mineralized deposits on 6 selected teeth. Each of the four surfaces of the teeth (buccal, lingual, mesial and distal) is given a score from 0-3. The scores from the four areas of the tooth are added and divided by four in order to give the plaque index for the tooth (0= no plaque, 3= abundance of soft matter within the gingival pocket and/or on the tooth and gingival margin). The PI was scored for all surfaces of the 6 selected teeth and for all surfaces of the tooth to be extracted.

The Gingival Index was created for the assessment of the gingival condition and records qualitative changes in the gingiva. It scores the marginal and interproximal tissues separately on the basis of 0 (normal gingiva) to 3 (severe inflammation, marked redness and edema, ulceration with tendency to spontaneous bleeding) score. The bleeding is assessed by probing gently along the wall of soft tissue of the gingival sulcus. The scores of the four areas of the tooth can be summed and divided by four to give the GI for the tooth. The Gingival Index was scored for all surfaces of the 6 selected teeth and for all surfaces of the tooth to be extracted.

Peripheral blood collection

Peripheral blood samples were taken before each procedure of dental extraction in order to determine the prothrombin time (PT) and the international normalized ratio (INR) and the for the fibrinolysis assay. For the fibrinolyisis assay, blood samples were centrifuged for 15 minutes at 3000 rpm in a refrigerated (4^0C) centrifuge. The platelet-poor plasma obtained from the blood centrifugation was stored at -80°C until the fibrinolytic activity assay was performed.

Unstimulated Saliva collection

Non-stimulated salivary samples were collected immediately before and after 30 minutes of the tooth extraction, according Davies et al., (1979) [19]. Briefly, patients were asked to spit the saliva on a previously weighted universal container, every each 30 seconds, for 5 minutes.

Dental extractions and alveolar blood collection

Dental extraction was performed using a non-traumatic technique, according to standard dental protocols. In order to avoid salivary contact with to alveolar blood, cotton rolls were used to isolate the surgical field and saliva aspiration was performed during dental extraction. After the dental extraction, the blood originated by the extraction (alveolar blood) was collected using a micropippete (Finnipipette 200 µL – International Microbio, USA) and added into a 3.8% sodium citrate tube. Occlusive suture was performed in order to prevent bleedings.

All patients had received regular orientation regarding oral hygiene, food intake and local care. Patients were also oriented to return for dental follow-up after 7 days of the procedure or anytime if bleeding occurs. The criteria for secondary bleeding were: 1- excessive bleeding immediately after the first hour of dental extraction; 2- bleeding which required local intervention or the use of any systemic intervention for bleeding control, anytime after the dental extraction. If one of these 2 criteria happened, the procedure was considered failure.

LABORATORY STUDY

Preparation of the salivary samples for fibrinolysis assay

The salivary fibrinolytic activity was measured accordantly with Majerus et al., (1996) [20]. Briefly, salivary samples were centrifuged at 2000 rpm for 20 minutes and the supernatant fraction was separated from the cellular pellet (precipitated fraction). The precipitated fraction was reconstituted to initial volume with phosphate buffered saline solution (PBS, pH=7.2). Both samples were stored at 4°C until the salivary assays were performed.

Fibrinogen plaque preparation

The fibrin plaque was prepared accordantly with the protocol used at the Hemostasis Laboratory, Hemocentro. Plasma was obtained from the Blood Bank of Hemocentro. After defrosted,

20% polyethylene glycol was added to the plasma and the mixture was centrifugated at 3000rpm, at 4C for 15 minutes. The supernatant was discharged and the precipitated fraction was reconstituted adding PBS (1/20, pH=6.0), at the proportion of 1/5 of the original volume of plasma. The final concentration of fibrinogen was 804mg/dL. Aliquots of fibrinogen were storage at -20ºC until the assay was performed.

Preparation of the fibrin plaque for the salivary fibrinolysis assays

The salivary fibrinolytic activity was measured using the fibrin plate method [21,22]. Fibrin plates were prepared by the addition of 4.8mL of phosphate buffer saline solution (pH=7.2), 1.2mL of human fibrinogen (804dg/ml) and 0.2mL of bovine thrombin (BC Thrombin Reagent, Dade Behring, Germany) in a Petri Plaque. Each petri plaque was previously divided into 4 identical regions, assigned as: 1- saliva pre-procedure, supernatant fraction; 2 – saliva pre-procedure –precipitated fraction; 3- saliva post-procedure, supernatant fraction; 4 – saliva post-procedure, precipitated fraction. 4.8mL of PBS (pH7.2) and 1.2mL of fibrinogen were added into a petri plaque among with 200 µL of bovine thrombin (Dade Behring, USA). The fibrin net formation occurred after 30 minutes. 30µL of each salivary sample were equally added in each one of the 4 petri plate divisions. The petri plaque was than storage at 37C for 18 hours. After this period, the lysis area was measured taking in account the 2 major diameters of the lysed area and results were expressed in mm^2 (Figure 1).

Euglobulin fraction of alveolar and peripheral blood

The study of euglobulin fractions was performed accordantly with Kowalski et al., (1959). The isolation of the euglobulin fraction has the objective to eliminate the plasminogen inhibitors influence of the fibrinolytic study. Plasma samples of the peripheral and alveolar blood were added into a tube containing 1.8mL of distilled water and 150 of 0.25% of acetic acid and storage for 30 minutes at 4°C. After this period, the tubes were centrifuged for 15 minutes at 2500rpm at 4°C. The supernatant was discharged and the precipitated (euglobulin fraction) were stored at -80°C until the fibrinolysis assay was performed.

Blood fibrinolysis – method of analysis.

The evaluation of the blood and salivary fibrinolysis was done according with modified technique published by Astrup (1956a,b)[23, 24]. Each petri plate was divided into 4 equal parts (Figure 1), as previously described and identified accordantly with each sample (plasma from alveolar or peripheral blood) and time of collection performed (pre or post dental extraction). 4,8mL of PBS 1/20 (pH=6.0) and 1.2mL of fibrinogen and 200 µL of thrombin were added into a plastic petri plate. After the fibrin net formation, 30µL of plasma blood (alveolar or peripheral blood) were added in the central area of each quarter of the petri plate. The petri plate was than storage at 37C for 18 hours. The fibrinolytic activity was measured as a product of two perpendicular diameters of the lysis zone and expressed in square millimeters (mm^2).

STATISTICAL ANALYSIS.

Comparison of fibrinolytic activity of alveolar blood, peripheral blood and salivary fractions were done using the Mann-Whitney test. Correlations between the oral fibrinolytic activity, oral health conditions and salivary flow rate were done using the Spearman's rank correlation (R. Foundation for Statistical Computing, Vienna, Austria, 2008). A p level < 0.05 was considered statistically significant. The graphics were generated by the Graph Prism program (Graph Pad Sofware, USA).

RESULTS

Twenty dental extractions were performed in twelve patients under definitive anticoagulation. Extractions were done without warfarin (Marevan®, Farmoquímica, S.A., Brazil) withdraw. From those 12 patients, there were 9 (75%) female and 3 (25%) male patients and the median age was 51 (27-71) years old. The indications for AVK use were: 3/12 (25%) were under prophylaxis of venous thrombo embolism recurrence, 2/12 (41.7%) were under treatment for atrial fibrillation; 5/12(41.7%) had mitral valve prosthesis; 1/12(8.4%) presented antiphospholipid syndrome and 1/12 (8.4%) had ischemic stroke. Dental extractions were performed due to the presence of severe decay without indication of root canal treatment, severe periodontal disease (periodontal probe≥4mm) or presence of dental roots. The INR mean at the day of the dental extraction was 2.45 (range 1.5-3.2). No bleeding was observed after all dental extractions. In general, the results of the oral health indexes showed a mean of GI of 1.93 (0.14 – 3.0), showing the presence of moderate inflammation (gingivitis) in gun surrounded the 6 evaluated index teeth. The mean of PI was 1.76 (0.14-3.0) showing a moderate presence of dental plaque on the 6 evaluated index teeth.The PI mean and GI mean of the extracted teeth was 1.95 (0 – 3) and 2.15 (0 – 3), indicating a moderate amount of plaque and moderate gingival inflammation in the extracted teeth, respectively.

Salivary flow rate

The mean of salivary flow rate pre-procedure was 0.44mL/

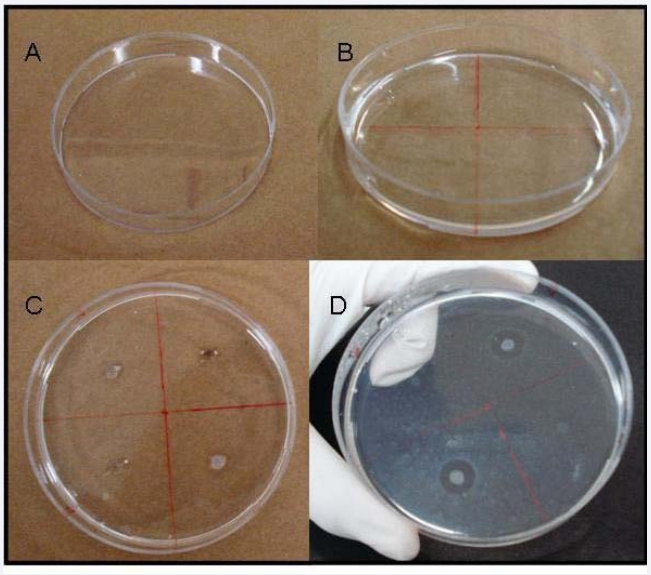

Figure 1 Fibrinolysis evaluation by the Fibrin Plate Method
A: Plaque; B: Fibrin clot formed in the plaque; C: Samples added on the fibrin plate; D: Lyses area measured.

min (0.04-0.74mL/mm) and the salivary flow rate post procedure was 1.06mL/min (0.17mL/min-2.68mL/min). The results showed an increase of salivary flow rate post-procedure of dental extraction of 0.62mL/min ($p<0.005$) but it was not correlated with the increase of salivary fibrinolytic activity ($p>0.005$).

Salivary fibrinolytic activity

The fibrinolytic activity of the salivary supernatant fraction pre-procedure showed a mean of 81mm^2(20mm^2-156mm^2) and the post-procedure salivary fibrinolytic activity mean was 131,15mm^2 (36mm^2-306mm^2) ($p<0.005$). The fibrinolytic activity of the salivary precipitated fraction pre-procedure was 75.8mm^2(9mm^2-176mm^2) and the post-procedure salivary fibrinolytic activity mean was 124.25mm^2(49mm^2-300m^2) ($p<0.005$), (Figure 1 and 2). No statistical differences were observed between the mean of salivary fibrinolytic activity of both pre and post-dental extraction supernatant and precipitated fraction ($p>0.005$) (Figure 2)

Oral health index and salivary fibrinolyitic Activity

In general, no statistical significance was observed between the correlation of the mean of IP and IG indexes with the supernatant and precipitated fractions of saliva pre and post-procedure of dental extraction ($p>0.005$).

Fibrinolyitic activity of the peripheral and alveolar blood

The mean of the fibrinolytic activity of the peripheral blood was 55.8mm^2(25mm^2-165mm^2). The mean of the alveolar blood fibrinolyitic activity was 115.2mm^2(20mm^2-300mm^2), showing an increased fibrinolytic activity of the alveolar blood when compared with the peripheral blood ($p<0.005$).

Oral health index and alveolar blood fibrinolytic activity

There was a statistical significant correlation between the oral health index of the extracted tooth with the alveolar blood fibrinolytic activity for both Plaque Index ($p= 0.002$) and Gingival Index ($p= 0.003$) (Table 1).

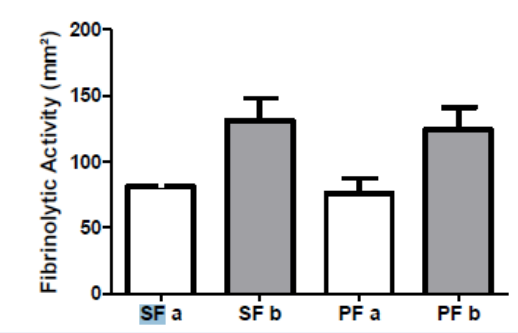

Figure 2 Salivary fibrinolytic Activity Pre and Post-Dental Extraction: SFa=salivary supernatant fraction pre-dental extraction; SFb=salivary supernatant fraction post-dental extraction; PFa= precipited salivary fraction pre-dental extraction, PFb= precipited salivary fraction post-dental extraction.

DISCUSSION

The results of the present study demonstrated an increased fibrinolytic activity in the alveolar blood collected after dental extraction, compared with salivary and peripheral blood fibrinolytic activity. The increase of fibrinolytic activity in the alveolar blood was correlated with oral health index of the extracted tooth at the day of extraction (Plaque Index ($p= 0.002$) and Gingival Index ($p= 0.003$) respectively). The interaction between inflammation and coagulation has been correlated with fibrinolytic system [25]. In fibrinolytic autographs of gingival epithelium is was shown that uPA and tPA were immunologically identified in the gingival sulcus [26]. The association of periodontal microbiota with fibrinogen degradation was previously demonstrated [25,27]. Studies have shown that a strain of Bacteroides an organism implicated in the etiology of several forms of periodontitis, bind and degrade fibrinogen. Interaction with fibrinogen may mediate colonization and establishment of these organisms in the periodontal microbiota [28-30]. Inflammation at the sites with periodontitis associated with more diverse subgingival microbiota and bacterial composition can have a role on the fibrynolitic activity, mostly at the site of dental extraction [30]. Difficulties in regular and appropriated dental brushing [31], mostly on the tooth to be extracted, might explain the wide range of oral health index founded in all sites evaluated, mostly in the tooth to be extracted.

There are few published papers focusing in the oral fibrinolyisis as a risk factor for secondary bleeding after oral surgery in patients with bleeding disorders. Late in 1991, Sindet-Pedersen [32] published a paper addressing the implication of oral fibrinolyisis on bleeding in an experimental and clinical study. According with the author, oral surgery induces changes of fibrinolysis in the oral environment. Initially the fibrinolytic activity of saliva is reduced; due to the presence of inhibitors of fibinolysis originating from the blood and the wound exudate. When bleeding and exudation cease, the fibrinolytic activity of the saliva will increase. Plasminogen and plasminogen activator (t-PA) are present in the oral environment under physiological conditions. Plasminogen is secreted in the saliva and the sources of t-PA include oral epithelial cells and gingival crevicular fluid. The presence of plasminogen and t-PA in the oral environment implies that when fibrin is present, fibrinolysis is triggered. This finding was confirmed by a study showing an increased presence of interleukin 1β, metalloproteinases 3, t-PA in the crevicular fluid of patients with periodontitis [33,34]. In this study, despite an increased salivary fibrinolytic activity post dental extraction has been observed in both supernatant and precipitated salivary fractions, it was not statistically significant when compared with the fibrinolytic activities of both salivary fractions pre-dental extraction. In this case, the increase in the salivary fibrinolytic activity post-dental extraction could be explained by the alveolar blood mixture into the saliva during its collection.

The antithrombin IIII and alpha 2-plasmin inhibitor were measured in blood and gingival tissue of naturally occurring gingivitis rats (ODUS/Odu). The authors demonstrated a decrease in blood coagulabitiy and systemic enhancement of fibrinolytic activity due to increase antithrombin III in gingival tissue and it was associated with the bleeding tendency and inflammatory

Table 1: Oral health Indexes, Salivary and Alveolar Blood Fibrinolytic Activity.

OHI	SFb	PFb	SFa	PFa	Alveolar Blood
GI					
0 – 1	98.4	75.4	115.2	83	61.2
1 – 2	66.6	71.8	109	141	105.6
2 – 3	80.8	85.6	77	436	151.4
P value	*0.17*	*0.23*	*0.29*	*0.25*	***0.003***
PI					
0 – 1	109	61.7	180	83	59.2
1 – 2	63.7	76.8	105	135	115.3
2 – 3	83.8	92.8	148.5	129.4	149.6
P value	*0.26*	*0.12*	*0.33*	*0.19*	***0.002***

OHI= Oral Hygiene Indexes; SFb – salivary supernatant fraction pre-dental extraction ; PFb – salivary precipitated fraction pre-dental extracion; SFa – salivary supernatant fraction after dental extraction; PFa – salivary precipitated fraction post-dental extraction; GI – Gingival Index; PI – Plaque Index. *Spearman's rank correlation*

response in the gingiva on the studied ODUS/Odu animals [35]. In the present study, the fibrinolytic activity of the peripheral blood was diminished when compared with the alveolar blood. In fact, blood samples used for the fibrinolysis assays were taken at the moment of blood collection for TPA measurement, i.e., pre-dental extraction. For ethical reasons, no peripheral blood samples were taken after the dental extraction.

There are many published papers addressing the importance of local measures in order to avoid secondary or late bleeding after dental extraction in patients with acquired or inherited bleeding disorders [36-40]. The use of topical antifibrinolytic mouthwash previously periodontal treatment and irrigation of the alveolar bone along with obliterate suture has been recommended as local management preventing bleeding tooth extraction in patient with bleeding disorders [41]. The results of this study reinforce the value of local use of antifribrinolytic agents in order to diminish alveolar blood fibrinolytic activity after tooth extraction.

In conclusion, the results of this study showed and increased fibrinolytic activity of the alveolar blood after tooth extraction. The increased fibrinolytic activity was correlated with the level of gingival inflammation demonstrated by the oral health indexes of the extracted tooth. The fibrinolytic activity in this case, may play a role on the secondary bleeding episodes, despite the protocol of clotting factor replacement therapy used, in cases of patients with inherited bleeding disorders. Oral health conditions should be taking in consideration on the planning for dental extraction in pediatric and adults patients with inherited and acquired bleeding disorder.

REFERENCES

1. Mielnik-Błaszczak M. Evaluation of dentition status and oral hygiene in Polish children and adolescents with congenital haemorrhagic diatheses. Int J Paediatr Dent. 1999; 9: 99-103.
2. Azhar S, Yazdanie N, Muhammad N. Periodontal status and IOTN interventions among young hemophiliacs. Haemophilia. 2006; 12: 401-404.
3. Alpkilic Baskirt E, Ak G, Zulfikar B. Oral and general health-related quality of life among young patients with haemophilia. Haemophilia. 2009; 15: 193-198.
4. Kabil N, ElAlfy MS, Metwalli N. Evaluation of the oral health situation of a group of Egyptian haemophilic children and their re-evaluation following an oral hygiene and diet education programme. Haemophilia. 2007; 13: 287-292.
5. Rodrigues LV, Moreira Mdos S, de Oliveira CR, de Medeiros JJ, Lima Ede A Neto, Valença AM. Tooth loss and associated factors in patients with coagulopathies in the State of Paraíba, Brazil. Rev Bras Hematol Hemoter. 2013; 35: 319-324.
6. Weickert L, Krekeler S, Nickles K, Eickholz P, Seifried E, Miesbach W. Gingival bleeding and mild type 1 von Willebrand disease. Blood Coagul Fibrinolysis. 2017; 28: 19-23.
7. Coventry J, Griffiths G, Scully C, Tonetti M. ABC of oral health: periodontal disease. BMJ. 2000; 321: 36-39.
8. Chapple IL. Time to take periodontitis seriously. BMJ. 2014; 348: g2645.
9. Chapple IL, Busby M, Clover H, Matthews R. Periodontal disease and systemic disease. J R Soc Med. 2014; 107: 94..
10. Chapple IL, Wilson NH. Manifesto for a paradigm shift: periodontal health for a better life. Br Dent J. 2014; 216: 159-62.
11. Buset SL, Walter C, Friedmann A, Weiger R, Borgnakke WS, Zitzmann NU. Are periodontal diseases really silent? A systematic review of their effect on quality of life. J Clin Periodontol. 2016; 43: 333-344.
12. Sonbol H, Pelargidou M, Lucas VS, Gelbier MJ, Mason C, Roberts GJ. Dental health indices and caries-related microflora in children with severe haemophilia. Haemophilia. 2001; 7: 468-474.
13. Gaddam KR, Nuvvula S, Nirmala S, Kamatham R. Oral health status among 6- to 12-year-old haemophilic children--an educational intervention study. Haemophilia. 2014; 20: e338-341.
14. Zaliuniene R, Peciuliene V, Brukiene V, Aleksejuniene J. Hemophilia and oral health. Stomatologija. 2014; 16: 127-131.
15. Zaliuniene R, Aleksejuniene J, Peciuliene V, Brukiene V. Dental health and disease in patients with haemophilia--a case-control study. Haemophilia. 2014; 20: e194-8.
16. Organization WHO. Assessement Forms. In: Oral Health Surveys Basic Methods. 1997: 21-50.
17. Loe H, Silness J. Periodontal disease in pregnancy. I. Prevalence and severity. Acta odontol scand. 1963; 21: 533-551.

18. Silness J, Loe H. Periodontal Disease In Pregnancy. Ii. Correlation between Oral Hygiene and Periodontal Condtion. Acta Odontol Scand. 1964; 22: 121-135.

19. Davies AJ, Strachan CJ, Hurlow RA, Stuart J. Fibrinolytic activity of tissue surfaces during surgery. J Clin Pathol. 1979; 32: 822-825.

20. Majerus P, Dalcette B, Hermans M, Pourtois M, Capel P. Variations in fibrinolytic activity of human whole saliva. Eur J Oral Sci. 1996; 104: 341-345.

21. Haze C, Garfunkel AA, Eldor A, Kadouri A. Inhibition of tissue plasminogen activators and urokinase by human saliva. Oral Surg Oral Med Oral Pathol. 1994; 77: 356-361.

22. Virtanen OJ, Sirén V, Multanen J, Färkkilä M, Leivo I, Vaheri A, et al. Plasminogen activators and their inhibitors in human saliva and salivary gland tissue. Eur J Oral Sci. 2006; 114: 22-26.

23. Astrup T. The biological significance of fibrinolysis. Lancet. 1956; 271: 565-568.

24. Astrup T. Fibrinolysis in the organism. Blood. 1956; 11: 781-806.

25. Peetermans M, Vanassch T, Roger HL. Bacterial pathogens activate plasminogen to breach tissue barriers and escape from innate immunity. Crit Rev Microbiol. 2016; 42: 866-882.

26. Barlow Y, Willoughby J. Pathophysiology of soft tissue repair. Br Med Bull. 1992; 48: 698-711.

27. Barlow Y, Southam JC. Plasminogen activators in normal and malignant oral epithelium in vivo and in vitro. Arch Oral Biol. 1992; 37: 749-756.

28. Lantz MS, Rowland RW, Switalski LM, Höök M. Interactions of Bacteroides gingivalis with fibrinogen. Infect Immun. 1986; 54: 654-658.

29. Lantz MS, Allen RD, Duck LW, Swistalski LM, Hook M. Porphyromonas gingivalis surface components bind and degrade connective tissue proteins. J Periodontal Res. 1991; 26: 283-285.

30. Camelo-Castillo A, Novoa L, Balsa-Castro C , Blanco J Mira A Tomás I. Relationship between periodontitis-associated subgingival microbiota and clinical inflammation by 16S pyrosequencing. J Clin Periodontol. 2015; 42: 1074-1082.

31. Evangelista LM, Lima CC, Idalino RC, Lima MD, Moura LF. Oral health in children and adolescents with haemophilia. Haemophilia. 2015; 21: 778-783.

32. Sindet-Pedersen S. Haemostasis in oral surgery--the possible pathogenetic implications of oral fibrinolysis on bleeding. Experimental and clinical studies of the haemostatic balance in the oral cavity, with particular reference to patients with acquired and congenital defects of the coagulation system. Dan Med Bull. 1991; 38: 427-443.

33. Sindet-Pedersen S, Gram J, Jespersen J. The possible role of oral epithelial cells in tissue-type plasminogen activator-related fibrinolysis in human saliva. J Dent Res. 1990; 69: 1283-1286.

34. Toyman U, Tüter G, Kurtis B, Kivrak E, Bozkurt S, Yucel AA et al. Evaluation of gingival crevicular fluid levels of tissue plasminogen activator, plasminogen activator inhibitor 2, matrix metalloproteinase-3 and interleukin 1-beta in patients with different periodontal diseases. J Periodontal Res. 2015; 50: 44-51.

35. Sagawa T, Shinohara M. Coagulation and fibrinolytic activity in rats with naturally occurring gingivitis. J Osaka Dent Univ. 1999; 33: 35-41.

36. Kämmerer PW, Frerich B, Liese J, Schiegnitz E, Al-Nawas B. Oral surgery during therapy with anticoagulants-a systematic review. Clin Oral Investig. 2015; 19: 171-180.

37. van Galen KP, Eveline TE , Evelien P, Mauser-Bunschoten , Robert JJ van ES , Roger EGS. Antifibrinolytic therapy for preventing oral bleeding in patients with haemophilia or Von Willebrand disease undergoing minor oral surgery or dental extractions. Cochrane Database Syst Rev. 2015: CD011385.

38. Di Capua M, Coppola A, Nardo A, Cimino E, Di Minno MN, Tufano A, et al. Management of bleeding in acquired haemophilia A with recombinant activated factor VII: does one size fit all? A report of four cases. Blood Transfus. 2015; 13: 328-332.

39. Coppola A, Windyga J, Tufano A, Yeung C, Di Minno MN. Treatment for preventing bleeding in people with haemophilia or other congenital bleeding disorders undergoing surgery. Cochrane Database Syst Rev. 2015: CD009961.

40. Correa ME, Annicchino-Bizzacchi JM, Jorge J Jr, Paes de Almeida O, Ozelo MC, Aranha FJ, et al. Clinical impact of oral health indexes in dental extraction of hemophilic patients. J Oral Maxillofac Surg. 2006; 64: 785-788.

41. 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: 49-53.

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