MANAGEMENT OF THE HAEMOPHILIC PATIENT IN DENTISTRY AND CERVICOFACIAL SURGERY

Lidia Cureniuc[1], Emilia Pătrășcanu[2]*, Daniela Șulea[3*] ,Emilia Bologa[4] ,Liviu-Vlad Hârtie[5] , Carmen-Gabriela Stelea[3], Maria Paula Comanescu[6], Delia Hînganu[7], Victor-Vlad Costan[3], Cristina Popa[3],Oana Viola Bădulescu[8] ,Otilia Boișteanu[1]

1. ”Sf. Spiridon” Hospital,Iași, Department of Anaesthesiology and Intensive Care
2. “Grigore T. Popa” University of Medicine and Pharmacy, Iași,Faculty of Medicine,Department of Anaesthesiology and Intensive Care.
3. ”Grigore T. Popa” University of Medicine and Pharmacy, Iaşi, Romania, Faculty of Dental Medicine, Department of Oral and Maxillo-Facial Surgery.
4. ”Grigore T. Popa” University of Medicine and Pharmacy, Iași, Romania, Faculty of Dental Medicine, Department of Odontology and Periodontology
5. “Nicolae Oblu” Neurosurgical Hospital, Iasi, Department of Anesthesiology,
6. “Sf. Spiridon” Hospital, Iași,Department of Surgery.
7. ”Grigore T. Popa” University of Medicine and Pharmacy, Iași, Faculty of Medicine, Department of Morphofunctional Sciences I
8. “Grigore T. Popa” University of Medicine and Pharmacy,Iași,Department of Pathophysiology.

*Corresponding author; Emilia Pătrășcanu, e-mail: epatrascanu@gmail.com;
Daniela Șulea, e-mail suleadaniela@gmail.com

All authors have the same contribution as the first author

ABSTRACT

In patients with haemophilia, any oral surgery carries the risk of prolonged and excessive bleeding. Close collaboration between haematologists and oral surgeons is necessary to prevent excessive bleeding. No procedure can be considered minor in a patient with haemophilia because of the serious potential consequences. Successful treatment protocols using systemic treatment, antifibrinolytic agents and local haemostatic measures are described in the current literature.

Key words: haemophilia, factor replacement therapy, dental extraction, local anaesthesia

INTRODUCTION

The lack of factors necessary for the coagulation pathway results in a bleeding disorder known as haemophilia. This disruption of the coagulation cascade leads to excessive bleeding due to inadequate formation of fibrin clots. The insufficiency of clotting factors VIII or IX causes haemophilia A and haemophilia B, which are X-linked inherited disorders.Haemophilia is generally labelled according to clotting factor levels. Severe forms of the disease occur at levels of less than 1% of normal, moderate forms between 1% and 5%, and mild forms between 5% and 40%. (1) Both forms of haemophilia share similar clinical features, such as bleeding that occurs spontaneously or post-traumatically (muscle haematoma; haemophilic arthropathy caused by recurrent bleeding into joints and bleeding into the central nervous system). In the absence of appropriate exogenous clotting factor replacement therapy, these manifestations of the disease can lead to disabling or even fatal sequelae that impact negatively on quality of life (2).

Haemophilic patients can now expect to live close to the average life expectancy thanks to advances in treatment. Life expectancy has increased, and quality of

life has improved with the use of personalised prophylactic therapy.

Most patients undergo elective surgery in a haemophilia treatment centre under the supervision of qualified medical professionals. No procedure can be considered minor because of the serious potential consequences. In order to allow the patient to undergo surgery with the same risks as a person without coagulation disorders, haemophilia treatment during elective surgery aims to correct the factor deficiency both during surgery and in the post-operative period.

Dental extractions are the most common interventional procedure performed and pose a significant risk to people with inherited bleeding disorders if haemostasis is not carefully managed. Bleeding complications in this patient group can range from simple oozing at the extraction site to widespread intraoral haematoma and even life-threatening airway obstruction or haemorrhage.Edoema and bleeding in the neck and oral cavity make emergency intubation challenging(3).

The dentist must contact the haematologist beforehand to explain the dental procedure to be performed, the patient's medical condition, and the type of local post-operative haemostatic measures to be used. A multidisciplinary team is in place, and it is strongly recommended that patients are referred to a haematologist prior to any dental treatment in order to provide a personalised assessment of risks and the need for preventive therapy. (4)

ORAL HEALTH STATUS IN PATIENTS WITH HAEMOPHILIA

The same oral conditions (dental caries and gingivitis/periodontitis) that affect people without congenital bleeding disorders can also affect people with haemophilia. Previous studies show conflicting results regarding the dental, gingival and periodontal status of people with haemophilia compared to the healthy population. They may experience disease-specific barriers to accessing dental care due to their bleeding tendency, which may lead to delays in oral care and severe dental problems, as well as increased reluctance to have regular dental visits and fear of dentists. It is important to emphasise that some dental problems, such as caries or periodontal disease, are cumulative and begin in childhood. In healthy patients, tooth exfoliation does not cause any significant complications during childhood; however, patients with inherited blood disorders are more likely to experience frequent and spontaneous bleeding, which in most cases is the moment of diagnosis. (5)

The most common problem is oral bleeding, which can be spontaneous or triggered by minor trauma such as normal daily tooth brushing. Some have neglected their dental hygiene for fear of causing oral bleeding and have a higher incidence of dental caries. (6) According to the third World Federation of Haemophilia guidelines, patients with inherited bleeding disorders should be educated about the importance of good oral hygiene to prevent dental problems and potential complications. Dental examinations should be performed on a regular basis, starting with the eruption of baby teeth. Plaque should be removed from teeth by brushing twice a day with a medium-textured brush. Where possible, dental floss or interdental brushes should be used. In regions where there is no natural fluoride in the water supply, fluoride toothpaste should be used; fluoride supplements may also be prescribed where appropriate. An orthodontic assessment should be recommended for all patients aged 10-14 to determine whether there are problems associated with overcrowding, which can lead to periodontal disease. The cost to the health service would be significantly

reduced if dental care in this population were improved. (7)

MATERIAL AND METHOD

The study retrospectively reviewed medical histories of patients treated at the Department of Maxillofacial Surgery of the „Sf. Spiridon" Hospital in Iasi, Romania, between 2020 and 2023. Five patients suffering from hemophilia A, aged between 21 and 62, three with severe form (factor VIII < 1%) and two with moderate form (factor VIII=1-5%),who had plan dental extractions. Every patient had a prior diagnosis of the type and severity of the disease All of them had caries destruction, with severe toothaches and changes in the dietary habits.

In all 5 patients, tooth extractions were performed with the supplementation of coagulation factor prior to the surgery in doses and at times established by the national expert protocol and in accordance with the haematologist's recommendation. .Replacement therapy with recombinant factor VIII (rFVIII) and monoclonal therapy (emicizumab) were applied systematically in combination with antifibrinolytic treatment and local haemostatic measures. In all cases injection was administered half-hour before surgery,with a clotting level around 20-30% for unique dental extraction and 40-50% in multiple dental extractions . Tranexamic acid and acid epsilon-aminocaproic where used systematically in all the interventions.

Local anaesthesia was achieved by infiltration of 2% lidocaine with epinephrine in all patients. General anaesthesia it was necessary for one patient because of the lack of cooperation and co-morbidities. All routine and specific dental procedures were performed with extreme caution, and a minimally traumatic surgical technique without mucoperiosteal flap was used for tooth extraction. After avulsion, a curette was used to ensure that no inflammatory tissue remained in the socket, a curettage was performed to remove any granulation tissue, and local haemostatic measures were applied. A gelatine sponge was placed in the extraction socket with haemostatic absorbable sutures. A dressing was applied to the wound so that the patient would compress it when closing the mouth. The patient was instructed to keep the cotton in place for at least one hour after surgery. He was warned against any movement that could dislodge the clot and increase bleeding. Eating or drinking, spitting, rinsing, tooth brushing were all contraindicated for at least 24 hours.

RESULTS AND DISCUSSIONS

A total of 16 dental extractions in 5 patients during 9 interventions were performed. Two patients presented postoperative bleeding among the haemophilia A, severe form subgroup the postoperative evolution was satisfactory, without complications in the moderate form subgroup. The bleeding occurred in the second and third day after tooth extraction. The first bleeding it was with an important hematoma in the floor of the mouth with mild respiratory insufficiency. The decision was to intubate the patient with monitoring in Intensive Care. It was necessary the administration of blood, fresh frozen plasma and by-passing agent (recombinant activated factor VII-rFVIIa). The evolution was favourable, with subsequent extubation of the patient. After this episode, the team raised the suspicion of an acquired coagulation deficiency that needs further diagnostic.

The second case of bleeding was a local hematoma in a patient with severe form of haemophilia, with inhibitors, in treatment with emicizumab.For the second extraction the patient received emicizumab and recombinant activated factor VII(rFVII) with no bleeding events.

Only a careful analysis of risk factors before the procedure will allow a safe surgery without complications. This suggests that even with established treatment methods, it may be challenging to predict postoperative bleeding following oral surgery in patients who have haemophilia. In order to stop these individuals from bleeding excessively, postoperative monitoring is required.
Most dentists find it difficult to treat haemophiliac patients because even minor injuries can have potentially fatal consequences. However, in consultation with a haematologist, some patients can be treated on an outpatient basis, while others require inpatient treatment, depending on the severity of the condition and the procedure to be performed. Prior to any dental procedure in the oral cavity, haemostasis management should be individually planned with the advice of a haematologist. (8)

The World Federation of Haemophilia (WFH) has published guidelines on FVIII/FIX dosing for dental procedures. For patients with moderate and severe haemophilia A and B who require invasive oral procedures, factor replacement therapy is recommended and remains the standard of care. (7)

There are potential risks associated with this therapeutic approach. In addition, factor concentrates are expensive and may lead to the development of antibodies or inhibitors that can dramatically neutralise the already low levels of endogenous clotting factors, leaving the patient prone to spontaneous bleeding and making it difficult to achieve haemostasis. (9) Gene therapy appears to be revolutionising treatment but is still in the early stages of clinical trials and is being carried out on very small samples. (10)

In addition, the WFH guidelines recommend the use of systemic or topical antifibrinolytic agents as adjunctive treatment in pre- and post-operative management to reduce the need for factor replacement therapy. Epsilon-aminocaproic acid and tranexamic acid are examples of antifibrinolytics, which are plasminogen inhibitors that prevent fibrin clots from being broken down by proteolysis. Local haemostatic measures such as wound sutures, topical antifibrinolytics, oxidised cellulose and fibrin sealant should be used as appropriate whenever possible after tooth extraction. (11)

The administration of local anaesthesia is an essential part of dental practice, ensuring that treatment is comfortable and painless. Modern local anaesthetic techniques use very fine needles and cause very little tissue trauma. The World Federation of Haemophilia (WFH) has published the latest guidelines for the dental management of patients with inherited bleeding disorders in 2020, which suggest that local anaesthetic infiltration can be used without the need for factor replacement therapy and that injections can be safely performed by clinicians of any experience level using a standard technique.

However, the WHF suggested that augmentation of factor levels was required prior to an inferior alveolar and posterior superior alveolar nerve block as these techniques carry a risk of intramuscular haematoma and have potential for respiratory insufficiency .(7)

The surgery should be scheduled early in the week to allow for patient observation throughout the day and easier management of any of any post-operative bleeding. In order to prevent hypertensive episodes, which might result in bleeding, blood pressure levels must be optimally controlled. (12)

Patients should be instructed to notify the haematologist/dental surgeon immediately if they experience prolonged bleeding or difficulty breathing, speaking or swallowing after surgery, as these

conditions can be fatal. Those who are not in hospital should go to the nearest emergency centre immediately.

Patients should also be advised to follow a soft diet for at least 3-5 days after surgery and to brush carefully around the wound site to avoid disturbing the clot and wound healing in the socket. (13)

The choice of analgesic should take into account whether or not a particular substance inhibits coagulation and/or impairs platelet aggregation, particularly acetylsalicylic acid but also other non-steroidal anti-inflammatory drugs. In many cases, paracetamol (acetaminophen) is currently used as a first-line treatment for pain following tooth extraction.

CONCLUSIONS

As recommended by multiple authors, more and better designed studies are needed to establish a standardised protocol for the management of haemophilic patients undergoing dental extractions. Currently, there is no consensus on the management of haemophilic patients undergoing invasive dental procedures. Published data are derived from retrospective series describing standard procedures at individual institutions.

References

1. Blanchette VS, Key NS, Ljung LR, et al. Definitions in hemophilia: communication from the SSC of the ISTH. J Thromb Haemost. 2014;12(11):1935–9.
2. Berntorp E, Shapiro AD. Modern haemophilia care. Lancet 2012; 379:1447–56.
3. Stelea, C, et al. Airway management in head and neck cancer surgery. Romanian Journal of Oral Rehabilitation, 2020, 12.4.
4. de Azevedo Kinalski M., Brondani L.P., de Mattos Carpena A.L.M., Dos Santos M.B.F.: Delayed bleeding in a hemophilic patient after sinus floor elevation and multiple implant placements. J Oral Implantol 2021.
5. Salem K, Seyyedkhamesi S, Aminian M. Evaluation of oral and dental health status in hemophilic children and adolescents in the city of Rasht. J Pediatr Res 2018; 5: 182–186.
6. Czajkowska S, Rupa-Matysek J, Gil L, Surdacka A. Assessment of Oral Health and Healthy Habits in Adult Patients with Congenital Hemophilia. Eur J Dent. 2023 Feb;17(1):161-172.
7. Srivastava A, Santagostino E, Dougall A, Kitchen S, Sutherland M, Pipe SW, Carcao M, Mahlangu J, Ragni MV, Windyga J, Llinás A, Goddard NJ, Mohan R, Poonnoose PM, Feldman BM, Lewis SZ, van den Berg HM, Pierce GF; WFH Guidelines for the Management of Hemophilia panelists and co-authors. WFH Guidelines for the Management of Hemophilia, 3rd edition. Haemophilia. 2020 Aug;26 Suppl 6:1-158.
8. Hermans C, Altisent C,Batorova A , et al.Replacement therapy for invasive procedures in patients with haemophilia: literature review. European survey and recommendations.Haemophilia. 2009; 15 (3): 639 – 658.
9. Xi M, Makris M, Marcucci M, Santagostino E, Mannucci PM,Iorio A. Inhibitor development in previously treated hemophiliaA patients: a systematic review, meta-analysis, and meta-regres-sion. J Thromb Haemost 2013; 11:1655–1662.
10. Pasi KJ, Laffan M, Rangarajan S, Robinson TM, Mitchell N, Lester W, Symington E, Madan B, Yang X, Kim B, Pierce GF, Wong WY. Persistence of haemostatic response following gene therapy with valoctocogene roxaparvovec in severe haemophilia A. Haemophilia. 2021 Nov;27(6):947-956.
11. Hewson I,Makhmalbaf P,Street A ,McCarthy P ,Walsh M .Dental surgery with minimal factor support in the inherited bleeding disorder population at the Alfred Hospital.Haemophilia. 2011; 17 (1): e185 - e188

12. Boisteanu, O, et al. Deliberate Hypotension in anesthesia for major maxillofacial surgery.Romanian Journal of Oral Rehabilitation, 2022, 14.4.
13. Stromer W, Pabinger I, Ay C, Crevenna R, Donnerer J, Feistritzer C, Hemberger S, Likar R, Sevelda F, Thom K, Wagner B, Streif W. Pain management in hemophilia: expert recommendations. Wien Klin Wochenschr. 2021 Oct;133(19-20):1042-1056