J. Maxillofac. Oral Surg. (Apr–June 2019) 18(2):197–202
https://doi.org/10.1007/s12663-018-1117-0

CLINICAL PAPER

Management of Odontogenic Fascial Space Infection in Hemophilia Patients: A Proposed Protocol

Md. Kalim Ansari[1] · Ghulam sarwar Hashmi[1] · Syed Saeed Ahmed[1] · Sajjad Abdur Rahman[1] · Tabishur Rahman[1]

Received: 19 February 2018 / Accepted: 30 April 2018 / Published online: 9 May 2018

Abstract
Purpose The purpose of this study was to suggest a protocol for the management of odontogenic space infections in patients with hemophilia which is often incompletely addressed by clinicians because of the fear of excessive bleeding leading to prolonged morbidity.
Methods and Results Six diagnosed cases of hemophilia (four cases of hemophilia A and two cases of hemophilia B) with odontogenic fascial space infection were included in the study. Apart from routine investigations, assessments were also done to identify inhibitors to factor VIII/IX. Factor VIII/IX was replaced along with infusion of factor eight inhibitor bypass activity (FEIBA) one hour before incision and drainage. All the cases were treated by incision and drainage along with removal of foci under local anesthesia. The postoperative outcome was uneventful in all cases except one in which postoperative bleeding was noted from the extraction site on the third day which was again managed following the designed protocol.
Conclusion Maintaining good oral hygiene and seeking early dental care are of prime importance in patients with hemophilia to avoid invasive procedures. However, if odontogenic infection develops in these patients, performing timely incision and drainage using our protocol will minimize the complications and give successful outcome.

Keywords Hemophilia · Factor VIII and IX · Gelatin sponge · Fascial space infection · Third molar extraction

✉ Md. Kalim Ansari
drmdkalimansari@gmail.com

[1] Department of Oral and Maxillofacial Surgery, Aligarh Muslim University, Aligarh, Uttar Pradesh 202002, India

Introduction

Hemophilia is an X-linked congenital disorder characterized by prolonged bleeding (due to defect in factor VIII/IX), many times in association with little or no trauma, in which proper treatment may save lives or prevent permanent sequelae. Approximately two-thirds of the cases have clear, sex-linked recessive patterns of inheritance, and the rest are assumed to be of spontaneous mutations. This genetic pattern results in men being affected and women being carriers. Hemophilia is classified according to the clinical severity as follows: mild (6–50% of normal factor VIII/IX activity), moderate (1–5% of factor VIII/IX activity) and severe (< 1% of factor VIII/IX activity). In mild cases of hemophilia, severe bleeding occurs with major trauma or surgery and spontaneous bleeding is rare. In moderate class of hemophilia, there are episodes of occasional spontaneous bleeding and prolonged bleeding with minor trauma or surgery. Severe cases of hemophilia are usually associated with spontaneous bleeding into joints or muscles, predominantly in the absence of identifiable hemostatic challenge [1].

Clinicians must be familiar with the associated complications so that proper and expeditious treatment can be rendered when needed. One such complication requiring special mention is the development of inhibitors (antibody) directed against either factor VIII or IX following treatment to replenish the missing factor. The antibody attaches to the factor VIII or IX and neutralizes or inhibits its ability to stop bleeding, rendering the treatment of hemophiliacs as a major challenge. Such patients may require concentrates known as "bypassing therapies" to enable hemostasis to be achieved.

When treating patients with bleeding disorders such as hemophilia, the clinician must pay special attention to

treatment planning, location, and setting of the treatment. The patient's hematologist or medical service provider must be consulted prior to and during the treatment period, as the condition often requires a multidisciplinary involvement.

Guidelines are available for performing surgical as well as dental management in hemophilia patients [2–4]. However, the available literature is sparse which is specific to the management of odontogenic fascial space infection in hemophilia patients. Some clinicians recommend extraction of offending tooth/teeth without incision and drainage in order to avoid bleeding as a complication [5]. This approach may further complicate the case, causing progression of disease to involve the other spaces if incision and drainage is not performed timely.

The usual protocol for the management of odontogenic space infection is incision and drainage, removal of the focus/foci and antibiotics prescription along with supportive measures. However, when treating patients with bleeding disorders such as hemophilia, the clinicians must proceed in a logical way to successfully manage such cases.

Our center is a tertiary care center with facility of comprehensive hemophilia treatment. These patients are given factor replacement without any cost, and hence we often get such patients with odontogenic fascial space infection due to poor oral health. The purpose of this article is to devise a protocol for the management of odontogenic fascial space infection in hemophilia patients on the basis of our experience.

Method

A total of six diagnosed cases of hemophilia (four cases of hemophilia A and two cases of hemophilia B) between 2015 and August 2017 with odontogenic fascial space infection with age between 30 and 45 years (mean age 37.8 years) who attended the OPD of Department of Oral and Maxillofacial Surgery at our institute with a chief complaint of pain and swelling were included in the study.

History, clinical examination and various other investigations like X-ray, preoperative factor level, complete blood count, PT and PTT were advised. Since all the patients were known cases of hemophilia with the history of previous factor VIII/IX transfusion, assessments were also done to identify inhibitors to factor VIII/IX. The results of investigation are tabulated (Table 1).

After making the final diagnosis and assessment of the investigations, consultations were made with the hematologist and the physician of the patient concerned. Written

Table 1 Summary of the preoperative biographical, clinical and laboratory data of patients in this study

No. of pt.	Age	Hemophilia type	Type of infection	± of inhibitor	PTT (s)	Preoperative factor level (%)	CBC (%)	Tooth involved	Post-op complications (if any)
1	30	A	Left buccal space	+(4 BU)	38.50	0.80	$N = 84$	8	Bleeding from socket, 3rd post-op day
2	38	A	Ludwig angina	–	50.40	18	$N = 86$	6	No
3	45	B	Rt. submandibular and submasseteric space	–	48.20	8.6	$N = 84$	7	No
4	36	A	Rt. submandibular and buccal space	–	58.30	7	$N = 88$	8	No
5	42	A	Left masticator space	+(3 BU)	42.30	0.90	$N = 84$	7, 8	No
6	36	B	Rt. buccal and infraorbital space	–	46.60	10	$N = 78$	8	No

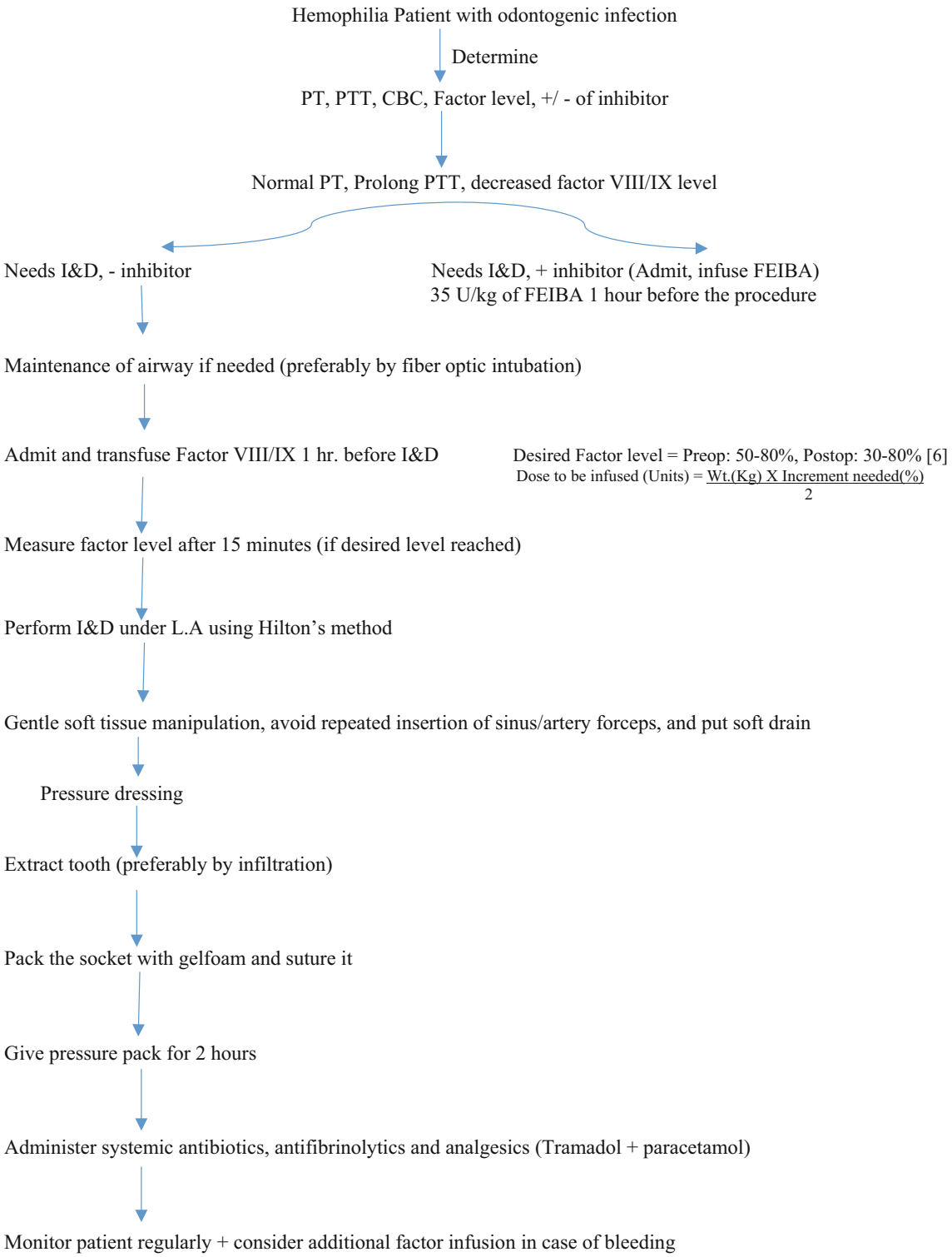

Fig. 1 Designed protocol for management

consents were obtained from all the patients, and patients were treated following the protocol outlined in Fig. 1.

Postoperatively, patients were admitted and observed for any complication for a period of 5–7 days. Because of the nature of this report and the small numbers of patients, no statistical methods were used to analyze the results.

Designed Protocol for Management

This protocol has been developed by the authors for treating hemophilic patients requiring incision and drainage (I&D) for managing odontogenic space infection. Patients should be assessed preoperatively for prothrombin time (PT), partial thromboplastin time (PTT), complete blood count (CBC), factor level and presence or absence of the inhibitor. Hemophilic patients would generally have normal PT, prolonged PTT and decreased factor level VIII/IX. Treatment for all hemophilic patients should be carried out under admission in a hospital setting, and if needed, airway should be secured by fiber optic intubation. The presence of inhibitor in hemophilic patients would necessitate the infusion of factor VIII inhibitor bypass activity (FEIBA) 1 h before initiating incision and drainage. Subsequent treatment modality would be similar to managing patients without the presence of inhibitor. The treatment steps would include transfusion of the factor 1 h before the procedure.

The desired preoperative factor level to prevent complication of bleeding should be 50–80%, while postoperative factor level should range from 30 to 80%. The factor level was measured 15 min after factor replacement, and if desired level was achieved, I&D was done using Hilton's method. Care was exercised in soft tissue manipulation as well as in avoiding repeated insertion of sinus/artery forceps. Once all the pus was drained, the wound was irrigated, a soft drain inserted and a pressure dressing given. The teeth were extracted under local anesthesia in the same appointment. Gelfoam was placed in the extraction socket for additional hemostasis and sutured. Pressure pack was placed for 2 h at the site of extraction. Systemic antibiotics, fluids, antifibrinolytics (tranexamic acid) and analgesics (tramadol + paracetamol) were prescribed. The patient was monitored regularly for any complication, and in case of postoperative bleeding, additional factor was infused. Query ID="Q6" Text="To maintain consistency, we have followed passive voice in the paragraph 'The desired preoperative factor…additional factor was infused.' Please approve."

Results

Out of six cases, four were of hemophilia A and two were of hemophilia B. Mean age of patients was 37.8 years. Two of hemophilia A cases had severe form, while two had mild form. The cases of hemophilia B had milder form. The two severe hemophilia A patients were positive for the presence of inhibitor (a low-titer-inhibitor-positive hemophilia A patient with the inhibitor level of 3 and 4 Bethesda units, respectively) and had bilateral knee joint deformity. In all the cases, mandibular molars were the source of infection. Preoperatively, only one patient reported with difficulty in breathing and was kept under observation, and after incision and drainage, the symptoms subsided.

All the cases were treated by incision and drainage along with removal of foci under local anesthesia after achieving adequate factor level. The postoperative outcome was uneventful in all cases except one in which postoperative bleeding was noted from the extraction site on the third day which was again managed following the designed protocol.

The result of the study indicates that the success rate of odontogenic infection management in hemophilia patients using the above designed protocol is impressive. Only one patient of severe hemophilia A required additional postoperative infusion of FEIBA and factor VIII to stop the postoperative bleeding. If the designed protocol is followed properly, intraoperative and postoperative bleeding complication is hardly observed.

Discussion

Hemophilia is a clotting disorder caused by deficiency in blood coagulation factors. A general examination of the patient might indicate a tendency to bleed, bleeding wounds, evident hematomas or swollen joints. Since hemophilia is X-linked, men typically express the disease, whereas women tend to be asymptomatic carriers. It has been suggested that patients with hemophilia B have lower bleeding frequencies and better long-term outcomes [6].

Odontogenic fascial space infections are commonly encountered in clinical practice and the most important therapeutic modality for pyogenic orofacial infections is surgical drainage and the need for extraction of the involved teeth, which is the primary source of infection [7].

There is evidence to suggest that patients with hemophilia delay dental treatment due to the fear of bleeding from procedure, necessitating more complex treatment when they finally present [8]. Due to neglected oral health care and seeking dental treatment late, patients with hemophilia usually report to their clinician with various fascial space infections.

Guidelines are available for dental and surgical management of hemophilia patients [2–4]. The literature is scarce when it comes to the management of odontogenic fascial space infection in patients with hemophilia. Some clinicians preferred conservative management in the form of removal of focus/foci only [5]. Those who have performed incision and drainage have not discussed the details and alteration needed in doing I&D in such patients [9].

We are of the opinion that a consensus should be reached regarding management of such condition in hemophilia patients and hence we suggest a protocol to successfully manage these patients without complications.

In this study, we have treated six cases of hemophilia patients with different fascial space infections using our protocol as outlined in Fig. 1 with excellent results.

Management of odontogenic infection in hemophilia patients should be done using the combination of systemic and local therapies to counter the bleeding episode. Systemic therapy includes increasing factor levels and inhibiting fibrinolysis. We transfused factor VIII/IX (depending on the need) preoperatively in each patient 1 h before the procedure and measured it after 15 min to assess the desired level. After gaining the adequate factor level, I&D was done. However, certain modifications like avoiding repeated insertions of artery forceps, gentle soft tissue manipulations and using soft rubber drain like gloves should be used in such patients. Local measures to control hemorrhage typically should be done using one of the three forms: antifibrinolytics, topical thrombin/fibrin glue and hemostatic pads coupled with basic hemostatic principles of primary wound closure, pressure and careful tissue management during intraoral procedures.

In the present study, out of six cases of hemophilia, two were of severe form of hemophilia A (factor level $< 1\%$) and two patients were found positive for the presence of inhibitor.

A potential complication of factor replacement therapy is the development of antibodies/inhibitors to factor VIII/IX. Inhibitors usually develop early in a person's treatment [10]. Antibodies to both factor VIII and IX have been found in 8–20% of the patients with severe hemophilia A and in 2.5–16% of those with severe hemophilia B [11, 12].

Some hemophiliacs who develop inhibitors develop them in low concentrations only. Those with the inhibitor concentration greater than 10 BU is referred to as "high responders" [13, 14]. The inhibitor levels in the present cases were 4 and 3 BU, which shows that patients were "low responders" of inhibitors. Patients with inhibitors cannot easily be given factor VIII or IX concentrates, and their treatment is a major challenge [15, 16]. They may require concentrates known as "bypassing therapies" to enable hemostasis to be achieved [17]. One such bypassing agent is FEIBA. FEIBA is an activated prothrombin complex concentrate prepared from normal human plasma which contains a property that appears to bypass factor VIII in hemostasis. Two of our cases required FEIBA due to the presence of the inhibitor. In one patient, postoperative bleeding was observed from the extraction site which was managed by infusing additional factor.

In hemophiliacs presenting with fascial space infections, the main reason behind the avoidance of surgical intervention is the fear of uncontrolled bleeding. The reasons could be low factor VIII or IX levels or development of antibodies to these factors when they are administered for restoring the factor levels to acceptable values.

The World Federation of Hemophilia (WFH) suggests administration of FEIBA in patients with the presence of inhibitors.

We confirmed the presence of an inhibitor and quantified the titer preoperatively and prophylactically administered FEIBA to those patients apart from the replenishment of factor VIII or IX in all the patients.

As our center is a tertiary care center and well equipped in emergency management, incision and drainage and extraction of the tooth were done simultaneously to expedite the recovery of the space infection.

Keeping in mind that the mainstay therapy for odontogenic fascial space infection is prompt surgical drainage and removal of the source of infection, even in cases of cellulitis, our stepwise protocol will help the clinician in managing odontogenic infection in hemophiliac patients without complications. However, more studies with larger samples are needed to exactly assess its effectiveness.

Conclusions

Maintaining good oral hygiene and seeking early dental care are of prime importance in patients with hemophilia to avoid invasive procedures. However, if odontogenic infection develops in these patients, performing timely incision and drainage using a protocol will minimize the complications and give successful outcome.

Compliance with Ethical Standards

Conflict of interest The authors declared that they have no conflict of interest.

Informed Consent Informed consents were obtained from all the patients.

References

1. Patton LL (2003) Bleeding and clotting disorders. In: Burket's oral medicine: diagnosis and treatment. 10th edn. BC Decker, Hamilton, pp 454–477
2. Rickard K (1995) Guidelines for therapy and optimal dosages of coagulation factors for treatment of bleeding and surgery in haemophilia. Haemophilia 1(Suppl.l):8–13
3. Stubbs M, Lloyd J (2001) A protocol for the dental management of von Willebrand's disease, haemophilia A and haemophilia B. Aust Dent J 46(1):37–40
4. Lloyd J et al (2000) Guidelines on therapeutic products to treat haemophilia and other hereditary coagulation disorders in Australia. Melbourne, Medical Advisory Panel for HFA (AHCDO)

5. Sudheesh KM et al (2016) 'Antihemophilic factor is not the only answer for all factor VIII deficiencies'. Case report of odontogenic infection in a patient with hemophilia A, complicated by factor VIII inhibitors, and managed by transfusion of antihemophilic factor and factor VIII inhibitor bypass activity. Indian J Dent 7(3):149–152
6. Franchini M (2014) Current management of hemophilia B: recommendations, complications and emerging issues. Expert Rev Hematol 7(5):573–581
7. Bahl R, Sandhu S, Singh K, Sahai N, Gupta M (2014) Odontogenic infections: microbiology and management. Contemp Clin Dent 5(3):307–311
8. Rafique S, Fiske J, Palmer G, Daly B (2013) Special care dentistry, 1: dental management of patients with inherited bleeding disorders. Dent Update 40(8):613–616
9. Farrkh A, Garrison E, Closmann JJ (2016) Dental surgical management of the patient with hemophilia. Gen Dent 64(4):14–17
10. Nilsson IM (1994) Hemophilia. Pharmacia Plasma Products, Stockholm
11. Shapiro SS, Huntin M (1975) Acquired inhibitors to the blood coagulation factors. Sem Thromb Hemost 1:336
12. Sultan Y (1992) The French Hemophilia Study Group. Prevalence of inhibitors in a population of 3435 hemophilia patients in France. Thromb Haemost 67:600–602
13. Kasper CK (1989) Treatment of factor VIII inhibitors. Prog Hemost Thromb 9:57–86
14. Lusher JM (1987) Factor VIII inhibitors. Etiology, characterization, natural history, and management. Ann N Y Acad Sci 509:89–102
15. Nilsson IM, Hedner U, Björlin G (1973) Suppression of factor IX antibody in hemophilia B by factor IX and cyclophosphamide. Ann Intern Med 78:91–95
16. Nilsson IM, Hedner U (1976) Immunosuppressive treatment in haemophiliacs with inhibitors to factor VIII and factor IX. Scand J Haematol 16:369–382
17. Brewer A (2008) Dental management of patients with inhibitors to factor VIII or factor IX. World Federation of Haemophilia, Montréal **(treatment of haemophilia monograph, no 45)**