PEDIATRIC DENTISTRY/Copyright © 1979 by The American Academy of Pedodontics/Vol. 1, No.3/Printed in U.S.A.

CLINICAL reports

Considerations in the dental management of the factor VIII-deficient child with inhibitors

William C. Berlocher, D.D.S.
David L. King, D.D.S., Ph.D.

Abstract

Approximately 10% of hemophilia A patients develop antibodies to factor VIII as a result of replacement therapy. The presence of such an inhibitor poses significant problems in the management of the child dental patient. The dental management for restorative therapy of two children with a factor VIII deficiency and a significant inhibitor level is described. The proposed dental treatment should be examined thoroughly, and all procedures that may stimulate hemorrhage should be modified in such a manner that the risk of initiating bleeding is minimized. An oral premedicant in combination with nitrous oxide-oxygen inhalation may be used in most restorative situations as an alternative to the injection of local anesthesia. Various forms of pulpal therapy should be employed to maintain a healthy periradicular tissue thereby obviating the need for surgical intervention. An effective preventive program will reduce the need for further dental treatment and will simplify any necessary procedures.

Classic hemophilia or hemophilia A is a coagulation disorder which affects about one person in 30,000. It is characterized by a deficiency of the circulating factor VIII, which is also known as antihemophilic factor or antihemophilic globulin. A decrease in factor VIII will impair coagulation function, and the affected person may experience hemorrhagic episodes, the severity of which depends on the magnitude of the factor deficiency.

The activity of the factor VIII molecule may be determined by immunologic assay in which an affected individual's coagulation function is compared to normal plasma. Normal plasma is designated as having 100% activity, and hemophiliacs are categorized as severe, moderate, or mild on a comparative basis. Severe hemophiliacs have a factor VIII activity of less than 1%. Usually, these individuals will experience spontaneous hemorrhages involving the skin, mucosa, muscles, and viscera. Hematuria and hemarthrosis also occur frequently in these patients. Moderate hemophiliacs have factor VIII activity that is 2 to 6% of normal. These individuals will not bleed spontaneously, but they will hemorrhage after light trauma. Mild hemophiliacs have antihemophilic globulin activity that is 6 to 30% of normal. Prolonged bleeding in mild hemophiliacs is usually a consequence of severe trauma or a surgical procedure that stresses the coagulation process.

Hemophilia A follows an inheritance typical of the X-linked recessive pattern. The gene specific for the disease is carried by the female, and the disease is expressed in the male. The female carrier will often have a depressed factor VIII level that averages about 50% of normal. The range of antihemophilic factor in these carriers is highly variable, however, and levels have been found to occur below 30%. Carrier females should, therefore, be screened for coagulation function as a precautionary measure prior to surgical procedures.

Current methods of managing anticipated or accidental hemorrhage include exogenous factor VIII supplementation using fresh frozen plasma, cryoprecipitate, or pooled factor VIII concentrate.

Approximately 10% of hemophilia A patients develop antibodies to factor VIII as a result of replacement therapy.[1] These antibodies or inhibitors will destroy the infused factor. The antibodies are usually the result of repeated replacement therapy needed for the severe cases of hemophilia A. Bleeding in these individuals may be managed sometimes by large doses of factor VIII which will leave an excess of the needed antihemophiliac globulin after the inhibitor has neutralized the major portion of the dose. This manage-

Accepted: March 1979

ment technique is beneficial only in patients who possess mild levels of inhibitors. It has the pejorative effect of raising the inhibitor level, thus compromising effective future replacement therapy.

Hemorrhage may be controlled sometimes with supplementation of activated factor IX. A sufficient amount of this factor will override the factor VIII portion of the intrinsic coagulation pathway and initiate clotting. Blatt[2] has reported on the complications that are inherent with this agent.

Webster[3] lists the following complications which are encountered when rendering dental treatment on hemophiliacs.

1. Postsurgical hemorrhage
2. Posttreatment periodontal bleeding
3. Postinjection hematomas
4. Hemorrhage secondary to inadvertent trauma to oral or perioral soft tissues

The severity of these complications is not increased in the hemophilia A patient with inhibitors, but effective treatment of these complications is made extremely difficult by the presence of inhibitors. If steps are taken to minimize or eliminate potential postoperative problems when formulating a treatment outline and treating the hemophiliac, the necessity for adjunctive therapy is greatly reduced. The purpose of this paper is to describe the dental treatment of two children with severe hemophilia A, both of whom had significant inhibitor levels. The objective of the management plans was to minimize the need for intervention by the hematologist.

Treatment rationale for the hemophiliac with inhibitors

Preliminary measures

Dental management of the classic hemophiliac has made substantial gains in recent years with the advent of factor VIII replacement. Hemophilia A patients without inhibitors may have dental procedures accomplished in combination with appropriate factor therapy. Unfortunately, the hemophiliac with inhibitors cannot benefit from these advances. Most often, factor VIII replacement is not successful, and the risk of raising the antibody titer is significant.

ε-Aminocaproic acid has proven to be especially helpful in the treatment of the hemophilias.[4,5] This drug does not assist in the hemostatic mechanism but blocks the activation of plasminogen to plasmin, thus helping to preserve the clot. ε-Aminocaproic acid is an especially useful drug in treating the hemophiliac with inhibitors. Without the benefit of a sufficient amount of antihemophilic factor, preservation of whatever clot is formed is critical.

Dental treatment of the hemophiliac should never be attempted without consultation with the patient's primary care physician or hematologist. The physician should be contacted prior to the patient's visit to review the patient's medical history and to assess current factor VIII activity. Options in hematologic management should be considered, keeping in mind the type of dental treatment to be rendered. Treatment should not begin unless there is total agreement and understanding between the dentist and the medical specialist.

Dental anesthesia

The administration of local anesthesia in dental operative and surgical procedures is an innocuous and effective method of pain control for most patients. Unfortunately, injection carries the risk of hematoma formation and possible respiratory obstruction in the severe hemophiliac who is unable to benefit by replacement therapy. There have been reported cases of fatal hemorrhage caused by block anesthesia in these patients.[6-8] Infiltration injections should be avoided also although pericemental injections may be used with minimal risk on selected cases where alternative methods of pain control are not feasible.

Conscious sedation techniques have been developed which produce levels of dental analgesia sufficient to accomplish many routine dental procedures. Album[9] has suggested the use of meperidine for premedication of children undergoing dental treatment. The drug is a potent analgesic and produces a well-sedated patient. It has the added benefit of being effective when administered orally. This is especially advantageous when applied to the hemophilia A patient with inhibitors because of the risk of hematoma formation if the drug is given intramuscularly. Intravenous injection of meperidine is also contraindicated because of the potential for increased side effects. Proter[10] states that approximately 5% of children premedicated with oral meperidine experienced nausea and/or emesis. Therefore, it is often combined with an antiemetic to alleviate this possible side effect. A comedicant such as promethazine will provide antiemetic properties as well as potentiating the action of meperidine. This will allow the dentist to decrease the narcotic dose yet still provide the desired sedation.

Simon and Vogelsberg[11] have stated that nitrous oxide-oxygen sedation may be used in children to reduce untoward motions and reactions to dental procedures, to create a semihypnotic state with a fully conscious patient, to increase the child's tolerance for longer dental procedures, and to lower the child's pain reaction threshold. They suggest, for good patient management, that nitrous oxide-oxygen sedation should not be used alone to control pain associated with dental procedures or to replace local anesthesia in normal, healthy children. However, in the hemophiliac patient with inhibitors, where local anesthesia is contraindicated, nitrous oxide-oxygen used in conjunction with a narcotic such as meperidine will often

provide an adequate level of sedation and analgesia. With this approach to pain control, the risk of postoperative complications associated with the injection of local anesthetics is obviated.

Restorative procedures

Planning the oral reconstruction of the classic hemophiliac with inhibitors poses a number of problems that are not encountered in the routine dental patient. Restorative procedures must not be delayed because the patient has hemophilia. Care must be taken to protect the perioral tissues from trauma when the teeth are restored. The rubber dam always should be used to minimize the risk of accidental injury and to insure the best possible physical properties in the restorative material.[12] In order to reduce gingival impingement by the rubber dam clamp, a cotton gauze pad may be placed over the tooth before it is clamped.

Interproximal amalgam restorations and stainless steel crowns may be accomplished with a minimal amount of discomfort to the patient. Some gingival bleeding may be unavoidable during the tooth preparation for these restorations, but if the operator is careful, any bleeding that is encountered will be slight and easily controlled by direct pressure. Meticulous restorative dentistry is critical to the hemophiliac dental patient with inhibitors.

The indirect pulp-capping technique advocated by Massler[13] is ideally suited for the hemophiliac. This technique works particularly well for the patient with inhibitors because the superficial layer of infected dentin may be removed without local anesthesia, and the technique is applicable to both primary and permanent teeth. Endodontic procedures such as pulpotomies and pulpectomies should be considered, when possible, instead of extraction. Several reports attest to the excellent success rate of the formocresol pulpotomy in both vital and nonvital primary teeth.[14,15] This method is applicable to the hemophiliac with inhibitors because the coagulant effect of formocresol is usually sufficient to promote hemostasis.

Prevention

It is obvious that oral reconstruction of the hemophilia A patient with inhibitors is a challenging task. No less important is the obligation to implement adequate preventive measures. Effective preventive dental practices reduce the need for future restorative procedures and, thus, the potential risk of hemorrhage as a result of oral neglect. The parents and child should be instructed in the proper use of the toothbrush, dental floss, and disclosing tablets. Diet counseling is an important component of a total preventive program. If the child does not benefit from an optimum content in the community water supply, a fluoride supplement is indicated. An accelerated program of topical fluoride application should be instituted also.

Case report: case one

The patient was an 11-year-old, 79-pound Mexican-American male who was referred by the South Texas Hemophilia Center for a routine dental evaluation. He was diagnosed at the age of 8 months as having hemophilia A. A current assay showed antihemophilic factor activity of 2.3%. The child had experienced sporadic spontaneous bleeding episodes which had been treated by supplementation of factor VIII. He was currently under treatment for a hemarthrosis of the left knee. The weight and stature of the child were normal for his age. The patient had one female sibling, and a family history revealed a maternal uncle who was a hemophiliac. The patient showed an inhibitor level of 0.6 Bethesda unit.

A thorough dental examination and radiographic survey revealed carious lesions in the four permanent first molars. The patient's oral hygiene was extremely poor with the gingival tissues being mildly erythematous and edematous. Palpation of the perioral soft and hard tissue was unremarkable. A consultation with the child's hematologist was requested, and he recommended that the restorative therapy be accomplished without the injection of local anesthetics or augmentation of factor VIII. Two days before his dental appointment, the patient received a prescription for epsilonaminocaproic acid, 100 mg/kg, to be taken orally every 6 hours. Instructions were given to continue the medication for 7 days after the child's scheduled dental appointment. The patient and his mother then received oral hygiene counseling, and he was placed on a home topical fluoride program.

One hour prior to his restorative appointment, the patient was given a syrup containing meperidine (62.5 mg) and promethazine (32.5 mg). During the operative procedures, additional analgesia was provided using nitrous oxide-oxygen in a 50 to 60% concentration. Carious teeth were isolated with a rubber dam, and amalgam restorations were placed in the four permanent first molars. All the teeth then were cleaned and polished carefully using a fluoridated prophylaxis paste. After completion of the procedures, the child was allowed to breathe 100% oxygen for 5 minutes. After a period of observation to insure the adequacy of hemorrhage control, the patient was released from the dental operatory. Additional oral hygiene instructions were given to the mother at this time.

A 2-week postoperative check showed all restoration to be intact and the gingival tissues to be slightly improved. The alloy restorations were polished, and the child and parents were given hygiene counseling again. The patient was placed on a 6-month recall program, is currently maintaining adequate oral hygiene, and is free of any obvious oral pathology.

Case report: case two

This was a 9-year-old, 69-pound Caucasian male seen at the Santa Rosa Outpatient Pediatric Dental Clinic for a routine dental evaluation. He had been diagnosed at the age of 3 days as having classic hemophilia. A recent assay revealed a factor VIII level of 2% and an inhibitor level of 0.65 Bethesda unit. He had experienced only minimal bleeding problems until age three when the first of many hemarthroses was experienced. At the time of the dental examination, he was receiving therapy for joint involvements of the left knee and right ankle. The child had been on home factor VIII therapy previously, but exogenous factor VIII had not been administered for approximately 6 months due to his inhibitor level. He was the third child of four brothers. His sibilings gave no history of any bleeding problems, but only one had been tested for factor VIII deficiency.

Carious lesions were found in the occlusal surfaces of the four permanent first molars and the distal surface of the mandibular right second primary molar. The periodontal tissues were in excellent condition, and the patient's oral hygiene was adequate. A soft and hard oral tissue examination was unremarkable except for the carious lesions. The patient had been on a home topical fluoride program for approximately 1 year.

The child's hematologist advised against the replacement of factor VIII or the injection of local anesthesia because of the significant inhibitor level. ϵ-Aminocaproic acid (3 g) to be given orally every 6 hours was prescribed beginning 2 days prior to the patient's restorative appointment and continuing postoperatively for 7 days.

The patient was given an oral dose of meperidine (50 mg) and promethazine (25 mg) 1 hour before beginning his dental procedures. The carious teeth were isolated with a rubber dam, taking care to avoid gingival trauma. Occlusal alloy restorations were placed in the first permanent molars, and the mandibular second primary molar was restored with a proximal-occlusal alloy. During tooth preparation, a 50% concentration of nitrous oxide-oxygen was administered. Gingival hemorrhage was encountered during matrix adaptation on the Class II alloy but was controlled with direct pressure. Completion of the restorative procedures was followed by a thorough prophylaxis and topical fluoride application. The child breathed 100% oxygen for 5 minutes to avoid diffusion hypoxia and was observed for 15 minutes postoperatively to assure absence of hemorrhage. During this observation period, the mother was given additional hygiene counseling.

Two weeks postoperatively, the patient's oral hygiene was evaluated and found to be excellent. The restorations were polished at this time, and a 6-month recall examination was scheduled.

References

1. Harker, L. A.: "Disorders of Coagulation," in *Hemostasis Manual*, 2nd ed., Philadelphia: F. A. Davis Company, 1974, p. 32.
2. Blatt, P. M., Lundblad, R. L., Kingdon, H. S., McLean, G., and Roberts, H. R.: "Thrombogenic Materials in Prothrombin Complex Concentrates," *Ann Intern Med*, 81:766–770, 1974.
3. Webster, W. P.: "Dental Aspects of Hemophilia," in *Proceedings of the Institutes of Hemophilia*, ed. Rusalmen, H., New York: National Hemophilia Foundation, 1965, pp. 54–59.
4. Needleman, H. L., Kaban, L. B., and Kery, S. V.: "The Use of Epsilonaminocaproic Acid in the Management of Hemophilia in Dental and Oral Surgery Patients," *JADA*, 93:586–590, 1976.
5. Walsh, P. N., Rizza, C. R., Matthews, J. M., Eipe, J., Kernoff, P. B. A., Coles, M. D., Bloom, A. L., Kaufman, B. M., Beck, R., Hanan, C. M., and Biggs, R.: "Epsilonaminocaproic Acid Therapy for Dental Extractions in Haemophiliacs and Christmas Disease: a Double Blind Control Trial," *Br J Haematol*, 20:463–475, 1971.
6. Archer, W. H., and Zubrow, H. J.: "Hemorrhage Following Regional Anesthesia for Operative Dentistry in a Hemophiliac," *Oral Surg*, 7:464–473, 1954.
7. Leatherdale, R. A. L.: "Anesthesia for Dental Anesthesia in Hemophilia," *Anaesthesia*, 13:27–32, 1958.
8. Parnell, A. G.: "Danger to Haemophiliacs of Local Anesthesia," *Br Dent J*, 116:183, 1964.
9. Album, M. M.: "Premedication for Difficult Children," *J Dent Child*, 22:48–56, 1955.
10. Proter, J. A.: "Meperidine Hydrochloride as a Dental Premedication," *Dent Surv*, 40:53, 1964.
11. Simon, J. F. and Vogelsberg, G. M.: "Use of Nitrous Oxide Inhalation Sedation for Children," in *Behavior Management in Dentistry for Children*, ed. Wright, G., Philadelphia: W. B. Saunders Co., 1975, pp. 178–196.
12. Chiono, O. and Kasper, C.: "Hemophilia," in *Dentistry for the Handicapped Patient*, ed. Nowak, A., St. Louis: The C. V. Mosby Company, 1976, pp. 134–150.
13. Massler, M.: "Preventive Endodontics: Vital Pulp Therapy," *Dent Clin North Am*, 11:663–673, 1967.
14. Proter, J. A.: "Formocresol in Vital and Non-vital Teeth: a Clinical Study," *J Dent Child*, 30:239–242, 1963.
15. Rolling, I., and Thylstrup, A.: "A Three Year Clinical Follow-up Study of Pulpotomized Primary Molars Treated with the Formocresol Technique," *Scand J Dent Res*, 83:47–53, 1975.

Dr. W. C. Berlocher is a senior resident in the Postgraduate Pediatric Dentistry Program at the University of Texas Health Science Center at San Antonio. He received his D.D.S. degree from the University of Texas Dental Branch at Houston. He is a student member of the American Academy of Pedodontics. Requests for reprints should be addressed to Dr. W. C. Berlocher, University of Texas Health Science Center at San Antonio, San Antonio, Texas 78284.

Dr. D. L. King is an associate professor and director of the Postgraduate Pediatric Dentistry Program at the University of Texas Health Science Center at San Antonio. He received his D.D.S. degree and Certificate in Pedodontics from the School of Dentistry, University of Minnesota, and his Ph.D. (anatomy) from the University of Minnesota Graduate School. He is a Fellow of the American Academy of Pedodontics and a Diplomate of the American Board of Pedodontics.