Review Article

JRAD Journal of Research and Advancement in Dentistry

J Res Adv Dent 2021;11:2:72-76.

Dental management of Thalassemic patients undergoing pediatric bone marrow transplantation: Analysis of literature

Vaishali Selkari[1*] Ashish Saxena[2] Ajay Parihar[3] Neha Verma[4]

[1]PG Student, Department of Pedodontics and Preventive Dentistry, Government Dental College, Indore, Madhya Pradesh, India.
[2]Professor and Head, Department of Pedodontics and Preventive Dentistry, Government Dental College, Indore, Madhya Pradesh, India.
[3]Professor and Head Department of Oral Medicine and Radiology, Government Dental College, Indore, Madhya Pradesh, India.
[4]Assistant Professor, Department of Prosthodontics, Government Dental College, Indore, Madhya Pradesh, India.

ABSTRACT

Background: Dental treatment of children suffering from thalassemia should be planned on the basis of pre-requisite of general anaesthesia, immunosuppressant drugs of child and blood transfusion protocol in consideration. The oral manifestation of such patients may be due to drug they are taking or may be due to the disease. Dental treatment planning for a patient undergoing bone marrow transplantation before, during and after is very important and a thorough knowledge is required for this. It is discussed in this paper that dental treatment in children going to hematopoietic stem cell transplantation suffering from thalassemia need to follow certain protocols, continuous observation of their cellular count and the importance of pediatric dentist in a multidisciplinary team is required for the well-being of patient. Oral infections, ulceration, bleeding are the most common oral manifestations in preconditioning phase and Immune-suppressed status of these patients makes it necessary to identify and remove the sources of infection from oral cavity. It is also important to motivate the patient about the importance of oral health care before and after the treatment to reduce potential oral cavity complications.

Keywords: Thalassemia, hematopoietic stem cell transplantation, immunosuppression.

INTRODUCTION

Thalassemia, the most common hereditary hemoglobinopathy in the world was originated in Mediterranean, middle eastern and Asian countries.[1] Among all the types of thalassemia, β thalassemia major is more dangerous and severe. Patients with thalassemia are usually anemic and require regular blood transfusions which causes excess iron in an individual's bloodstream. This excess iron gets deposited in organs, causes several heart problems. Patient may develop splenomegaly due to which they have to go for removal of spleen, consequently, they are left more prone to catching infections. Expansion of bone marrow occurs as a result of compensated erythroid hyperplasia for ineffective erythropoiesis. [2,3]

The facial features of thalassemic patients resembles mongoloid features due to prominence of the cheeks, protrusion of the maxillary anterior teeth, depression of the bridge of the nose which gives rise to the characteristic rodent or chipmunk facies. Anemic pallor, sore or burning tongue is seen due to anemia and folate deficiency. It has been observed that in these patients' rate of dental decay is higher as compared to those who do not have the disease due to painful swelling of salivary glands and a dry mouth which leads to reduced salivary defense. Therefore, if they do not pay attention to their dental care at initial stage, there is a higher risk of dental decay leading to abscess and infections.[2,3] Management of Thalassemia includes continuous blood transfusions as a temporary remission and permanent cure is by hematopoietic

Received: Oct. 12, 2020: **Accepted**: Nov. 21, 2020
*Correspondence Dr. Vaishali Selkari.
Department of Pedodontics and Preventive Dentistry, Government Dental College, Indore, Madhya Pradesh, India.
Email: Not Disclosed

pISSN 2278-0076
eISSN 2321-9270

stem cell transplantation (HSCT) or bone marrow transplantation.

For thalassemia, Allogeneic hematopoietic stem cell transplantation is used. It is a complex and potentially curative procedure that involves the infusion of healthy hematopoietic cells, following a preconditioning therapy. The rationale of allogeneic transplantation is the complete replacement of the patient's totipotent stem cells compartment with healthy hematopoietic progenitor cells obtained from the donor. Conditioning therapy or pre-transplant preparation, a crucial step in the transplantation, is required for eradication of hematopoietic system and suppression of immune system by administration of bisulfan (14 –16 mg/kg) and cyclophosphamide (200 mg/kg), respectively.[1,4]

Graft rejection and the graft versus-host disease (GVHD) are the two main complications of hematopoietic stem cell transplantation (HSCT).[5] Immune-suppressed status among these patients makes them more susceptible to infection, resulting in an increased risk of infectious complications including the development of severe septicemia that may be life- threatening.

Oral cavity is an important port of entry for systemic infections in patients undergoing bone marrow transplantation. In preconditioning phase, the most common oral manifestations are oral infections, ulceration, bleeding, and temporomandibular joint dysfunction. To prevent these infectious complications or to reduce morbidity, comprehensive oral care for identifying and treating all sources of potential infections before transplantation has been incorporated in the treatment regimen of these patients. [5,6]

Dental Considerations

By decreasing the number of micro-organisms through optimal oral care, the patients may decrease their chance of a life-threatening systemic infections.[7] Ideally, before conditioning, all the potential sources of infection, pain should be eliminated because first few weeks after the transplant the patient will have a low immunity. However, it is not always achievable due to urgency of transplantation, patient's general health and remission status and complexity of oral diseases.[8]

Objectives of dental care before bone marrow transplant is to identify and remove the existing sources of infection in the oral cavity, plan the timing of treatment by communicating with patient's physician and to educate the patient and parents about the importance of oral care before, during and after treatment.

At the time of first visit, an orthopantomogram(opg) of maxilla and mandible should be done and if required additional intra-oral x-rays can be done.[8] Oral hygiene instructions have to be delivered both to the patients and their caregivers. It is recommended that at this stage, toothbrushing be done twice daily, with a soft brush and with nonabrasive fluoridated toothpaste. Alcohol-free chlorhexidine mouth rinses are advised. The patients should remember to make at least an hour break between the application of antibacterial rinses and tooth brushing or use of locally acting antifungal suspensions. Flossing once daily, scaling and application of topical fluoridation is advised. [7,8,9]

It has been observed that before and after chemotherapy, the oral bacterial flora changes and there is an increase of oral colonization with potentially pathogenic microorganisms especially Enterococcus faecalis and Candida spp. Among autologous and allogeneic hematopoietic stem cell transplantation (HSCT) patients root canal infections can be associated with a substantial increase in morbidity, and with significant impairment of the patient's quality of life. Therefore, periapical lesions should be treated because they are a risk factor for acquisition of viridians bacteremia after transplant. According to American Academy of Pediatric Dentistry, endodontic treatment should be performed at least 1 week before chemotherapy begins, so that there is enough time to evaluate periapical infection resolution. In asymptomatic tooth, treatment can be delayed. [4,5,10,11]

Assessment of periodontal and oral hygiene status should be performed in patients undergoing hematopoietic stem cell transplantation (HSCT), because prolonged neutropenia may be associated with oral complications. The patient should undergo scaling and root planning, to check for periodontal disease and related bacterial infection. It has also been suggested that bleeding caused by scaling and root planning can cause bacteremia.[12,13]

We should always try to eliminate potential sources of traumatic injury to the mucous membrane. like orthodontic appliances, ill-fitting prostheses, deficient/rough restorations and fractured and/or chapped teeth. Orthodontic devices that do not irritate soft tissue can be maintained if the patient maintains a good oral hygiene status. Orthodontic treatment that was discontinued, can be restarted after 2 years of health from completing the therapy.

It is preferable to complete all dental treatments at least 2 weeks before the initiation of the conditioning. But if there is not enough time to complete all the procedures, it is recommended to concentrate primarily on active infections. Root tips, non-restorable teeth, mobile teeth should be extracted. In order to ensure hemostasis after extraction, suturing is recommended instead of intra-alveolar dressings. The administration of aspirin should be avoided as it increases the risk of bleeding and antibiotics should be prescribed only after consultation with the patient's physician. [7,8,9]

Antibiotic coverage must be performed for invasive procedures such as extraction and periodontal causal treatment that can cause significant bleeding and spread of bacteria in the blood. Therefore, it should be planned with a multidisciplinary approach, and patients should be treated with 2g amoxicillin orally 1h before treatment. US National Cancer Institute, 2011, recommends antimicrobial prophylaxis when the neutrophil count is less than 2,000 cells/mm3 of blood, or in patients with increased susceptibility to endocarditis. Intravenous antibiotics should be administered to high-risk patients when there is an odontogenic infectious outbreak.[5,14,15]

For invasive dental procedures, a platelet count of at least 60,000 cells/mm^3 is acceptable as per US National Cancer Institute. When spontaneous bleeding is observed, the dentist should perform oral hygiene motivation procedures. If these measures are not sufficient, then platelet transfusion can be considered. Vasoconstrictor agents (adrenaline), clot-forming agents (topical thrombin and/or hemostatic collagen agents) and tissue protectants: cyanoacrylate can be used to control the bleeding as these products help in sealing the bleeding sites and protect organized clots.[15,16]

Epsilon-Aminocaproic acid (EACA) may be useful in patients with unstable clots. When EACA or tranexamic acid is used,a noticeable reduction in post-operative bleeding is seen following dental extraction. Tranexamic acid as a topical hemostatic agent is considered effective in reducing the incidence of post-operative bleeding in patients receiving oral anticoagulants, 500 mg tranexamic acid/5 ml saline solution mouthwash minimizes gingival bleeding.[16,17,18]

Noninvasive procedures like clinical examination, radiographs, oral hygiene instruction, simple restorations, atraumatic restorative treatment-ART, supragingival scaling and prophylaxis may be performed at any stage of the disease or chemotherapy and these procedures do not require additional care.[5]

DISCUSSION

Every year, more than 50,000 children are born with thalassemia worldwide. In India, the prevalence of β-thalassemia is 3-4% with an estimate that around 10,000-12,000 children are born every year.[3]

Allogenic hematopoietic stem cell transplantation was initiated in early 1980s to replace the defective gene in patients. It has been well established for several decades as the only therapy for patients with thalassemia major. Over the last decade, outcomes have improved enormously, even in high-risk patients due to better risk stratification, more effective targeted dose adjustment of bisulfan during conditioning and continually improving supportive care.[19]

Definitive dental treatment and preventive measures are needed before the bone marrow transplant as oral health of most patients undergoing such treatment is not satisfactory and infectious complications may occur after the transplant. Only 40% of the patients undergo dental examination at the pre-transplant stage, according to Barker. Various authors differ in their opinions regarding elimination of potential foci of infection before conditioning regime. Some are in favor of radical cure and recommend removal of all existing and potential foci of infection, so that risk of local and systemic complications associated with immunosuppression will be lower. Some authors

are in favor of minimally invasive treatment before bone marrow transplantation.[6,8]

Bacteria or viruses are responsible for approximately 55% of post-transplantation infections and 15% - 30% infections are caused by fungi. Conditioning regime before transplantation causes damage to body barriers leading to severe neutropenia and ultimately increases the risk of bacterial infections. The patient needs to be supported with RBC and platelets transfusion, as they rapidly fall after preparative conditioning.[7,20]

Patients have impaired immune functions during the first 6 months post-transplantation, which may be fully restored by one year and even more delayed, if there are any complications like graft versus host disease. Therefore, dental treatment should be done before transplant because patient may not be able to experience any dental procedure for upto 1 year after the transplant.[7,9,20]

Thalassemic patients often suffer from oral ailments that are a consequence of basic illness or therapy. The patient must be made aware of all the adverse effects of the therapy before conditioning regime which affect oral cavity, methods of their prevention and treatment should also be instructed. Oral hygiene instructions should be delivered to the patients and their caregivers and they should be motivated to begin proper oral hygiene several weeks before transplantation, as it may reduce potential oral cavity complications before and after transplantation.[7,8,20]

CONFLICTS OF INTEREST

The authors declare they have no potential conflict of interests regarding this article.

REFERENCES

1. Lucarelli G, Isgro A, Sodani P, Gaziev J. Hematopoietic Stem Cell Transplantation in Thalassemia and Sickle Cell Anemia. Cold Spring Harb Perspect Med 2012;2:a011825

2. Aggarwal R, Prakash A, Aggarwal M. Thalassemia: An overview. J Sci Soc 2014;41:3-6.

3. Helmi N ,Bashir M , Shireen A , Ahmed IM. Thalassemia review: features, dental considerations and management. 2017, Vol: 9, Iss: 3, 4003-4008,

4. Bollero P, PassarelliP.C, D'addona A, Pasquantonio G, Mancini M , Condo R, Cerroni L. Oral management of adult patients undergoing hematopoietic stem cell transplantation. European Review for Medical and Pharmacological Sciences. 2018; 22: 876-887

5. Zimmermann C et al. Dental Treatment in Patients with Leukemia. Journal of Oncology. 2015

6. Melkos AB, Massenkeil G, Arnold R, Reichart PA. Dental treatment prior to stem cell transplantation and its influence on the post transplantation outcome.Clin Oral Investig. 2003 Jun;7(2):113-5

7. Marcio A. da Fons. Pediatric bone marrow transplantation: oral complications and recommendations for care.. Pediatric Dentistry 1998; 20:Z

8. Bogusławska-Kapała A ,Hałaburda K , Rusyan E, Gołąbek H, Strużycka I. Oral health of adult patients undergoing hematopoietic cell transplantation. Pre-transplant assessment and care. Ann Hematol 2017

9. Rakocz M et al. Dental management of the child undergoing bone marrow transplantation. JADA 1982 Vol. 104, April

10. Graber CJ, De Almeida Kn, Atkinson JC, Javaheri D, Fukuda Cd, Gill Vj, Barrett Aj, Bennett Je. Dental health and viridans streptococcal bacteremia in allogeneic hematopoietic stem cell transplant recipients. Bone Marrow Transplant 2001; 27: 537542.

11. Haverman tm et al. Oral complications in hematopoietic stem cell recipients: the role of inflammation. Mediators Inflamm 2014; 2014: 378281

12. Horliana AC et al. Dissemination of periodontal pathogens in the bloodstream after periodontal procedures: a systematic review. PLoS One 2014; 9: e98271.

13. Daly CG, Mitchell dh, Highfield Je, Grossberg de, Stewart d. Bacteremia due to periodontal probing: a clinical and microbiological investigation. J Periodontol 2001; 72: 210-214.

14. Nih. National Cancer Institute (US). Oral complications of chemotherapy and head/neck radiation for health professionals. NIH, 2016.

15. Little Jw, Falace Da, Miller CS, Rhodus N. Dental management of the medically compromised patient. Elsevier 2012; 23: 403-406.

16. Watterson C, Beacher N. Preventing perioperative bleeding in patients with inherited bleeding disorders. Evid Based Dent 2017; 18: 28-29.

17. Costa Fw, Rodrigues Rr, Sousa Lh, Carvalho Fs, Chaves Fn, Fernandes Cp, Pereira Km, Soares Ec. Local hemostatic measures in anticoagulated patients undergoing oral surgery: a systematized literature review. Acta Cir Bras 2013; 28: 78-83.

18. Elad S, Garfunkel Aa, Or R, Michaeli E, Shapira My, Galili D. Time limitations and the challenge of providing infection-preventing dental care to hematopoietic stem-cell transplantation patients. Support Care Cancer 2003; 11: 674-677

19. Srivastava A , Shaji R. Cure for thalassemia major – from allogeneic hematopoietic stem cell transplantation to gene therapy. Haematologica 2017 Volume 102(2):214-223

20. Braga-Diniz JM, Santa-Rosa CC, Martins RC, Silva MES, Vieira LQ, Ribeiro Sobrinho AP. The need for endodontic treatment and systemic characteristics of hematopoietic stem cell transplantation patients. Braz. Oral Res. 2017;31:e50