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A Protocol for Managing Orthodontic Complications in Patients with Thalassemia and Haemoglobin Disorder; Article Review

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Abstract

Background: Hemoglobinopathies are known as haemoglobin production disorders. Familial disorders caused by thalassemia or sickle cell anaemia are autosomal recessive disorders affecting haemoglobin production and structure. Objectives: This article review aimed to clarify protocols for managing orthodontic complications in patients with thalassemia and haemoglobin disorder. The article explains how to deal with common dental and orthodontic issues that patients with these conditions may experience. It provides guidance on diagnosing and treating these issues to ensure the best possible outcomes for these patients. Conclusion: Hemoglobinopathies can cause dental diseases, which can be particularly concerning for children with this condition. While specialists are responsible for treating dental diseases, prevention is the best approach. Physicians with adequate knowledge of the diseases can address this issue safely and effectively. Paying attention to this matter is essential to ensure the best possible patient outcomes.

Key words: oral health, splenectomy, caries risk, beta thalassemia**.**

Introduction

Thalassemia, or in general, hemoglobinopathies, are genetic disorders that cause an abnormality in the structure of one of the globin chains in the haemoglobin molecule. Since they constitute the most common genetic diseases worldwide, they take an essential place among childhood chronic diseases. Although most abnormal haemoglobins are harmless, some of them have O2 imbalances. These imbalances can negatively affect the patient's treatment process; intercalarily, disorders in oral and dental health can increase the symptoms of an existing genetic disorder. Orthodontists should have the necessary knowledge. With the guidance of Medical Doctors, they can safely apply appropriate treatments to patients and relieve their discomfort.

Hemoglobinopathies are known as haemoglobin production disorders. Familial disorders caused by thalassemia or sickle cell anaemia are autosomal recessive disorders affecting haemoglobin production and structure. These diseases constitute the most common genetic diseases in the world (1). The newborn is usually born with fetal haemoglobin (HbF). During infancy, fetal haemoglobin is replaced by adult haemoglobin (HbA). Adults have some amount of HbA2. These haemoglobin types are distinguished by differences in the sequence of their peptide chains. As a result of DNA mutations, each amino acid chain has a unique amino acid sequence. Qualitative defects in haemoglobin cause the formation of 'haemoglobin variants'. Quantitative disorders in the production of globins cause thalassemia (2). Although most abnormal haemoglobins are harmless, some of them have O2 imbalances.

Some abnormal types of haemoglobin cause anaemia, such as sickle cell anaemia and thalassemia (3). Anaemia is the haemoglobin level being below the age and gender normals. Haemoglobin levels below 11.0g/dl until adolescence, 11.5g/dl in adult women and 13.5g/dl in men are called anaemia. The effect of anaemia is that the blood carries less oxygen (2). Anaemia is ubiquitous, but it is a symptom of a disease rather than a disease. Lifelong transfusion and iron chelation for chronic thalassemia and transfusion and hydroxyurea (a drug used to treat leukaemia) for sickle cell anaemia significantly improve the effects of the disease. Still, side effects caused by treatment can lead to tissue destruction. Allogeneic stem cell transplantation is the only treatment for these patients and should be performed at an early age before the disease progresses and treatment-related complications occur (1).

Hemoglobinopathies usually occur in non-Caucasian people. Sickle cell disorders are most commonly observed in African-Caribbean, Mediterranean, Middle Eastern, Indian, Bangladeshi, and Pakistani people. Thalassemias and glucose-6 phosphate dehydrogenase deficiency are generally observed in Mediterranean people, Vietnamese, Cambodians, Lakhsians, and Chinese (3). According to the World Health Organization (WHO), the density of patients with anaemia and anaemia carriers in Iraq reaches up to 35% in some regions (4). For orthodontic treatment, the medical history must be reviewed in detail, and the patient's haematologist must be consulted. Due to spleen problems, prophylactic antibiotic use and vascular access should be considered. The first goal is to protect yourself from diseases that can be developed with orthodontic treatment in such patients. Therefore, patient and caregiver education should be done in the early periods with close follow-up (1).

The aim of this article is to ensure that orthodontists have the necessary equipment when working with patients with anaemia and that doctors do not ignore the oral health problems of patients with thalassaemia.

Anemias

The oxygen required for the tissues of aerobic metabolism is met by the presence of mature erythrocytes (red blood cells) in the bloodstream. The red blood cell is easily recognized thanks to its unique structure. It has no nucleus, and its lifespan is between 100 and 120 days. At rest, it has the shape of a concave disk, 8μm in diameter, 2μm thick, and 90fL in volume. This shape is perfect for its function and allows it to move easily through the microvascular system. Irregularities in shape and function cause anaemia to occur (5).

Sickle Cell Anemia

Sickle cell anaemia is an autosomal recessive hereditary disease. It occurs as a result of the substitution of a single amino acid in the haemoglobin chain (6,7). Valine and glutamic acid in the β chain of haemoglobin. It is displaced due to a defect in the chromosome. This leads to the formation of damaged erythrocytes. This haemoglobin, formed due to abnormal β chains, is

called haemoglobin S (1). When HbS encounters low-concentration oxygen, it precipitates into long crystals within red blood cells. These crystals elongate the cell, causing haemoglobin to take on a sickle shape instead of the concave disc appearance of normal haemoglobin. Hemoglobin depressions also

It also damages the cell membrane, so cells become extremely fragile. This condition causes severe anaemia and results in patients going into crisis (8,9). Crises occur, especially during inflammation, because integrins on the erythrocyte surface adhere to higher levels of vascular endothelial adhesion molecules under the influence of TNF and other post-inflammatory cytokines. With this adhesion, microcirculation in vascular tissues is blocked (3). Many conditions, such as acidosis, hypoxia, hypothermia, hypotension, stress, hypovolemia, dehydration, fever and inflammation, can occur.

The agent may cause a sickle cell crisis. For an individual to be sick, he must be homozygous (HbSS). If only one of the chromosome pairs is affected (HbSA), the patient is a carrier. African, African-Caribbean, southwestern Asian and Mediterranean peoples may carry up to 40% rates. The rate of sickle cell disease in East Africa is 2%. Sickle cell anaemia is commonly seen in areas with malaria disease, and carriers are less affected by malaria disease (10,11).

The first complaint in children with the disease is bone and joint pain that cannot be associated with any other disease. When these painful periods become frequent, patients become addicted to painkillers. Organ damage begins in early childhood. With the loss of spleen functions, splenic infarction occurs in the first ten years of life. Another target structure is the kidney medulla. The collecting ability of the renal medulla is lost and the patient may experience periods where blood cells are observed in the urine. Patients with sickle cell anaemia are at risk of death due to a central nervous system clot or sepsis (bacteria or toxins entering the blood). They are prone to streptococcus pneumonia, Hemophilus and salmonella infection due to spleen infection and repeated bone marrow inflammation. The classic symptoms encountered in the clinic are intravascular sickling, closure of small vessels, and recurrent painful crises resulting from tissue infarction. Bone marrow, kidney, spleen, lung and brain are the organs at risk of infarction. In young children, dactylitis may develop in the hands and feet due to bone marrow necrosis. Older children complain of joint and bone pain and abdominal pain due to splenic infarction. As a result of loss of spleen functions, the risk of death due to pneumococcal sepsis is observed in children. The risk of damage to vital organs such as the lungs, heart and brain increases as the child grows. In patients who do not receive treatment, heart attack or major cardiopulmonary damage may occur due to vascular narrowing. The risk of heart attack increases by 10% each year in untreated patients. This situation can be reduced below 1% thanks to transfusion therapy. Patients with homozygous sickle cell disease between the ages of 2 and 16 need to be followed up with transcranial Doppler every six months. The tests used in diagnosing the disease are as follows: whole blood, environmental smear, sickle cell solubility test, HPLC and isoelectric focusing tests. The tests used during diagnosis in Iraq are: Prenatal diagnosis in the womb can be listed as Hb electrophoresis in an acid-alkali environment, HPLC and PCR (13).

The most common symptom of sickle cell anaemia is sickle cell crisis. The first intervention during a crisis is administering analgesia because patients are likely to be in pain. For severe pain, morphine is given by subcutaneous injection or intravenously. Fluid replacement therapy is applied. The patient is oxygenated. It is imperative to initiate cefatoxamine (50 mg/kg TDS) or ceftriaxone (50 mg/kg od) in patients exhibiting fever above 38 degrees. Furthermore, blood transfusion must be administered to patients with haemoglobin levels below 6g/dl (12).

Thalassemia

Thalassemia is a hereditary disorder with autosomal dominant inheritance. A decrease in haemoglobin A synthesis occurs due to the low synthesis of one of the alpha or beta globin chains (2). Thalassemias are called by different names depending on the name of the damaged globin chain and the clinical severity of the disease. In beta thalassemias, which are common in the Mediterranean region, damage is observed in the beta-globin chain, and in alpha thalassemias, the alpha chain is damaged. Thalassemia major is a severe thalassemia that requires constant transfusion and carries a high risk of morbidity and mortality. Thalassemia intermedia is a less severe type of thalassemia (14,16). Alpha thalassemia and haemoglobin E disease are common in the Southeast Asian population.

Globin, the protein of the haemoglobin molecule, consists of two α and two non-alpha chains. Alpha globin chains. It consists of two nearby genes (α1 and α2) located on the chromosome. Non-alpha globin chains β, γ and δ. A group of genes encodes it on the 16th chromosome. As a result of the combination of these globin chains, three types of haemoglobin are formed: haemoglobin F (α2 γ2), hemoglobinA (α2 β2) and hemoglobinA2 (α2 δ2). An error in the alpha-globin chain results in the forming of 4 beta-globin chains, resulting in the formation of haemoglobin H. This type of anaemia is characterized by haemoglobins that migrate rapidly during electrophoresis, the presence of the beta-4 subgroup. It leads to an unstable state in which the transporter fails to function and causes accelerated erythrocyte sedimentation and blood destruction. Such signs of instability and sedimentation are not observed in the early period, but ineffective erythropoiesis and clinical symptoms appear later. Usually, silent thalassemia carriers are the parents of the patients. Patients with this condition have haemoglobin disorders that are so subtle that they do not show clinical symptoms (17).

The most common patients in the population are β thalassemia carriers. Insignificant or mild anaemia is observed in carriers. Patients with severe anaemia have serious problems in the production of the β chain. Clinical symptoms' severity varies depending on thalassemia's severity (1).

The fact that there are different treatment options for thalassemia treatments is related to which response will be obtained to which type of treatment and the appearance of collateral effects while fighting the treatment. As a result of iron overload associated with continuous blood transfusion, multiple organ damage may be observed in patients due to the accumulation of this element in the organs. These patients need treatment to prevent organ damage. Severe beta-thalassemia patients are a patient group that should be given special attention in dental treatments because these patients have cardiac problems. Pericarditis, congestive heart failure and arrhythmias may be present. Iron deposition due to repeated transfusion causes painful inflammation in the salivary glands of patients and, accordingly, normal or decreased salivary flow. Excessive storage of iron is the main cause of mortality and morbidity. It is treated with a drug called desferrioxamine, which causes iron turnover. The issues that raise doubts about the treatment are viral transmission and multiple endocrine disorders caused by transfusion.

Additionally, progressive liver fibrosis and cardiac diseases may occur due to iron deposition. Thalassemia intermedia patients face leg ulcers, pulmonary arterial hypertension, extramedullary hematopoiesis and thrombotic disorders. Beta thalassemia major causes an increase in the bone marrow volume due to increased erythrocyte production. This causes patients to experience extramedullary hematopoiesis, especially in the spleen and liver. The orofacial effects of thalassemia are severe and diverse. Increased erythroid force as a result of ineffective erythropoiesis expands the bone. Significant malocclusions occur as a result of severe maxillary advancement, resulting in closed bite and open bite in the anterior region. In these patients, the

lower jaw is usually further back than it should be. This is because the dense structure of the lower jaw does not allow expansion. This malocclusion can be corrected by surgical methods such as maxillary osteotomy and tooth extraction. Orbital hypertelorism is another finding. This condition is described as “cooly face” and “chipmunk face”. If blood transfusion is given from birth, the patient does not show any or very few of these symptoms. In radiology, there is a brush-like appearance in the cranial vault, depending on the timing and effectiveness of the transfusion. There are rarefaction areas in the alveolar bone as a result of the thinning of the cortical part. Obliterated paranasal sinuses are classic X-ray findings. Bilateral hypoplasia of the maxillary sinus affects 10% of patients. Although less frequently, hypoplasia may also occur in the sphenoidal and frontal sinuses. The pale color of the mucosa is associated with the severity of anaemia (17).

If the patient has had a splenectomy, they are more prone to periodontic diseases and dental caries. Treatment of thalassemia patients is directed according to the classification;

Thalassemia minor

Most thalassemia patients are minor thalassemia patient’s carriers due to alpha or beta gene mutation. Microcytosis and hypochromia are observed in patients with alpha thalassemia in which two genes are mutated, in patients with heterozygous beta thalassemia, in patients with regional deletions in the δ and β genes, and in patients with high amounts of fetal haemoglobin. Usually, these patients experience little or no haematological disturbance. This situation is called the 'silent carrier' state (5).

Thalassemia intermedia

These patients have more severe anaemia and marked microcytosis and hypochromia. They not only complain of symptoms secondary to anaemia but also of disorders related to hepatosplenomegaly and skeletal disorders secondary to bone marrow damage. Patients have mild homozygous β thalassemia, the combined forms of α and β thalassemia, or one of the Thalassemias containing high amounts of haemoglobin F (5).

Thalassemia major

Patients with Thalassemia major, also known as Cooly's Thalassemia, have severe thalassemia. It can be life-threatening in the first two years of life. In order for patients to survive, they need constant blood transfusions to keep their anaemia and erythropoiesis under control. Otherwise, they either die in childhood or these children develop disorders that lead to significant skeletal changes, growth retardation and sexual development disorders. In β thalassemia major anaemia, there is a high level of iron (SI) in the serum, total iron adhesion capacity saturation (TIBC) and a tendency to iron accumulation in tissues are observed. Most patients are homozygous for the beta-globin gene mutation; some are double heterozygous for beta thalassemia minor. In some patients, abnormal haemoglobin, such as haemoglobin E, is present (5).

Routine complete blood count (CBC) and peripheral blood smear provide the first clues to the presence of thalassemia. In patients with thalassemia minor, microcytosis is observed, and hypochromia is observed with little or no anaemia. Because microcytosis is regular, red blood cell distribution depth (RDW) does not increase. The peripheral blood smear is microcytic and hypochromic but shows a small amount of anisocytosis, poikilocytosis, or polychromasia. Many red cells are bullseye-shaped. This shows that when intracellular haemoglobin decreases, the cell membrane does not decrease at the same rate, and the excess cell membrane accumulates in the center of the cell, creating a bullseye appearance. There is a more dramatic picture in patients with thalassemia intermedia and thalassemia major. Their anaemia is more severe, and microcytosis and hypochromia are more pronounced. Anisocytosis and poikilocytosis are more

common. RDW increased in the peripheral film. Polychromasia and bullseye appearance are more evident. Once laboratory tests prove thalassemia, treatment is started for the patient. The main treatment for beta-thalassemia is blood transfusion, folic acid and iron cycling agents (desferrioxamine or deferiprone), and ascorbic acid. Hydrocarbamine is used, but its side effects cause significant discomfort. If there is hypersplenism that will cause blood destruction, splenectomy may be considered (2).

Iron Deficiency Anemia

Iron is necessary for the synthesis of haemoglobin, respiratory cytochromes and myeloperoxidase. It plays a vital role in many metabolic reactions. In its deficiency, there is a decrease in exercise capacity. Developmental and behavioral disorders are observed in childhood. Iron, which enters the synthesis of dietary haemoglobin, is found only in animal tissues. This iron, which we get through diet, plays a role in hemoglobin synthesis and is called 'heme iron'. The iron in plant foods is non-heme iron and is absorbed in small amounts. Foods containing vitamin C increase the absorption of non-heme iron. Citric acid, sugar, amino acids, iron, white meat, dark meat, fish and orange juice increase iron absorption from the digestive mucosa. For vegetarians, fibrous foods, grains, lentils, beans and some dried fruits are very good for iron. Iron deficiency is the leading cause of microcytic anaemia. In the early stages, iron is not found in the bone marrow and iron deficiency is not observed until all stores are exhausted.

The most well-known indicator of iron deficiency is decreased serum ferritin levels, but these tests are not always available. Additionally, serum ferritin levels rise like acute-phase proteins during the inflammatory reaction. The best treatment for iron deficiency is the oral use of an iron salt such as ferrous sulfate, 200 mg three times a day. If ferrous sulfate cannot be tolerated, ferrous gluconate can be given at a daily dose of 250 mg.

Vitamin B12 (cobalamin) Deficiency

The body needs vitamin B12 in amino acid synthesis and degradation and DNA/RNA synthesis. Vitamin B12 is mainly found in meat and liver in the diet. Vitamin B12 is stored in the liver. Deficiency usually occurs due to the deficiency of an intrinsic factor or due to intestinal disease or resection. Rarely is vitamin B12 deficiency observed due to a vegetarian diet or medications. Failure to absorb vitamin B12 causes pernicious anaemia. Macrocytic anaemia develops due to the suppression of blood cells. Vitamin B12 deficiency develops very slowly; it takes up to 3 years for the liver stores to be depleted. Positional sense disappears in the early period. These early symptoms disappear with treatment. If left untreated, neurological disorders progress, and subacute combined degeneration of the spinal cord and even paraplegia may occur. The diagnosis of B12 deficiency is made by low B12 in the serum with the development of autoantibodies against gastric parietal cells. Treatment of pernicious anaemia is 1mg hydroxycobalamin five times at 3-day intervals. Thus, lung stores are filled, and treatment continues at 3-month intervals.

Folate (Folic acid) deficiency

Folic acid is necessary in the synthesis and degradation of amino acids and DNA/RNA synthesis in the body. Folic acid plays an important role in the production of new cells, especially in the synthesis of blood, skin and mucosal cells. Folic acid is found in fresh fibrous plants and other vegetables, especially spinach, kale, Brussels sprouts and asparagus. Folic acid is absorbed from the small intestine. It is not stored in the body. Folate deficiency causes anaemia in adults, and if it develops during pregnancy, it may cause neural tube defects or cleft lip and palate in the fetus. If diagnosed, treatment is folic acid at a daily dose of 5mg. Treatment usually takes about four months.

Aplastic Anemia

Aplastic anaemia is characterized by pancytopenia with dysfunctional bone marrow. It is a rare disease that causes leukopenia, thrombocytopenia and persistent anaemia. Chemicals such as benzene, some drugs, radiation, hepatitis virus and graft versus host disease are among the significant causes, but the disease is usually idiopathic. Clinical symptoms are generally the same as in anaemia (normochromatic, normocytic and macrocytic). Patients have an abnormal predisposition to bleeding and infections (2). In treatment, the causative agent must first be eliminated. However, even if the cause is eliminated, the damage to the bone marrow may be irreversible. To control infections

Isolation and antibiotic treatment are necessary for managing the condition. Among the available treatments are bone marrow organ transplantation and androgenic steroid therapy. Blood transfusion may also be an option, but it carries the risk of iron accumulation or inflammation. Unfortunately, the prognosis for this condition is poor, with 50% of patients dying within six months due to infection or hemorrhaging. Isolation and antibiotic use are required. Bone marrow organ transplantation and androgenic steroid use are among the treatments. A blood transfusion may be administered, but iron accumulation or There is a risk of inflammation. The prognosis is poor, and 50% of patients die within six months due to infection or hemorrhage (20).

Fanconi Anemia

Fanconi anaemia is an autosomal recessive syndrome. Fanconi anaemia is a rare genetic disorder that is inherited in an autosomal recessive manner. In very rare cases, it can also be inherited in an X-linked recessive manner. The typical age at which individuals with this disorder develop hematologic problems is seven years old, while 90% of cases result in bone marrow destruction by the age of 40. The first hematologic disorder usually observed is macrocytosis, followed by thrombocytopenia, leading to progressive pancytopenia and severe aplastic anaemia. Patients with Fanconi anaemia are at a higher risk of developing myelodysplastic syndrome or acute lymphoblastic leukaemia. The disorder also causes increased pigmentation and hypopigmented areas, short stature, skeletal anomalies involving the thumb, radius, and long bones, microcephaly, eye anomalies, deafness, hyperreflexia, developmental delay, and renal and cardiac anomalies. Patients with Fanconi anaemia are predisposed to both hematologic and non-hematologic malignancies. Very rarely, it shows an X-transitive recessive trait. The average age at which haematological disorder is observed is seven years old. Bone marrow destruction occurs in 90% of cases by age 40. The haematological disorder is usually macrocytosis followed by thrombocytopenia. Progressive pancytopenia is observed, and severe aplastic anaemia is present. Patients with Fanconi anaemia have a risk of developing myelodysplastic syndrome or acute lymphoblastic leukaemia. Patients have increased pigmentation and hypopigmented areas. Short stature, skeletal anomalies involving the thumb, radius and long bones, microcephaly, eye anomalies, deafness, hyperreflexia, developmental delay, renal and cardiac anomalies can be observed. Patients are predisposed to haematological and non-haematological malignancies (21).

Oral and Dental Health

Sickle Cell Anemia patients may experience a crisis due to fear of dental treatment. Therefore, it is essential to keep patient appointments short to reduce potential stress (10). Pain in the jaw during sickle cell crises may be mistaken for toothache or osteomyelitis. Sickle cell crises can also affect pulp tissue, leading to pulp necrosis, even in patients without a history of trauma or caries (14,15). A strict preventive program is implemented in sickle cell anaemia patients to minimize the risk of oral inflammation. If treatment is required during a crisis, only a relaxing treatment is applied. Orthodontic treatment may be necessary due to skeletal changes in sickle

cell patients. The most important thing to pay attention to in Sickle Cell Anemia patients is that the patient has a crisis due to fear of dental treatment. Therefore, it is important to keep patient appointments short to reduce potential stress on the patient. Pain in the jaw during sickle cell crises may be perceived as toothache or osteomyelitis. Pulp tissue can be affected by sickle cell crises. It has been determined that pulp necrosis may occur in patients with sickle cell disease who do not have a history of trauma or caries (10).

A strict preventive program is implemented in sickle cell anaemia patients, and thanks to such a program, the patient's risk of developing oral inflammation is minimized. If treatment is required in case of crisis, only a treatment that will relax the patient is applied. Many skeletal changes in sickle cell patients may require orthodontic treatment (12). When erythropoiesis is not functioning properly, the bone marrow becomes reactive. Which leads to an increase in bone growth, causing the maxilla and skull to widen. The widening of the skull dipoles gives a hairy appearance, which can be observed on lateral head radiographs. Patients with major thalassemia may develop a chipmunk-like facial appearance due to bone marrow expansion in the maxilla. The expansion can cause teeth spacing and forward sliding of the maxillary incisors, which may require orthodontic treatment (18,19). Although the teeth can move quickly during treatment, sometimes, they may shift back to their previous position because of the ease of movement. Ensuring that the teeth remain in their new condition after the treatment can be challenging. On radiography, areas of rarefaction in the alveolar bone can create a honeycomb appearance. Though it may not seem significant, iron accumulation can result in painful swellings caused by parotids and xerostomia. Furthermore, folate deficiency may lead to burning of the tongue. Children with thalassemia who have low IgA levels in their saliva may be more susceptible to developing a high number of caries. Another recent study found that the endocrine function is responsible for dental caries. In addition, patients neglect dental care due to diseases that affect their lives. For this reason, poor oral hygiene, lack of proper nutrition and lack of motivation are the most important causes of tooth decay in children with thalassemia, just as in healthy children. Regular dental check-ups and preventive treatments are recommended for patients. It is important to consult with the patient's haematologist prior to any dental treatment. It is recommended that dental treatment should not be performed when haemoglobin levels are below 100g/l. Patients with spleen removed should use prophylactic antibiotics (18). Local anaesthesia will be sufficient for pain control during dental treatment for patients with iron deficiency anaemia. It is important to ensure full oxygenation and conscious sedation may be applicable. In people with normal physical conditions, a burning sensation in the tongue may occur as a result of below-normal iron levels. The most well-known effect of severe anaemia is atrophic glossitis.

Depopulation, burning and discolouration of the tongue are observed. Candida infection may occur or is at risk of occurring along with anaemia. Treating anaemia alone without antifungal therapy can trigger infection. Although it affects a very small population, angular cheilitis is also a well-known indicator of iron deficiency anaemia. Aphthous stomatitis may also be associated with iron deficiency anaemia. Iron discoloration on teeth can be prevented by using sodium ironedate. Iron discolouration on teeth may be confused with caries or may be aesthetically disturbing to the child and family. Compared to ferrous sulfate, it can be preferred because it does not contain sugar and is more delicious. Iron discolouration on teeth may be confused with caries or may be aesthetically disturbing to the child and family. Local anaesthesia is successful in vitamin B12 deficiency. If haemoglobin levels are moderately suppressed, conscious sedation can be performed by giving supplemental oxygen, but sedation with nitrous oxide is theoretically

contraindicated. General anaesthesia is contraindicated until haemoglobin levels recover. Patients may physically feel burning and pain in the normal tongue(20).

Some studies argue that there is a relationship between anaemia caused by folate deficiency, local anaesthesia, conscious sedation, and general anaesthesia, which are applied in the same way as pernicious anaemia. Alternatively, nitrous oxide can be easily applied. Sensitivity may be observed without depopulation of the tongue, or colour change may occur in the early period. Angular stomatitis is the most well-known indicator, although it does not appear much. Aphthous stomatitis may be associated and sometimes requires treatment (2).

For aplastic anaemia, anaemia, susceptibility to haemorrhage and infections, corticosteroid use, hepatitis B and other viral infections should be included in the dental treatment plan. Local anaesthesia should be applied. Conscious sedation and general anaesthesia should be avoided due to anaemia. Oral findings of aplastic anaemia are similar to leukaemia. Ulcerations, haemorrhage, susceptibility to infection, and oral lichen lesions are observed. If a graft versus host reaction occurs to bone marrow transplantation after anaemia, this may lead to a Sjögren's-like syndrome (2).

Conclusion

Hemoglobinopathies can cause dental diseases, which can be particularly concerning for children with this condition. While dentists have a responsibility to treat dental diseases, prevention is the best approach. Physicians with adequate knowledge of the diseases can address this issue safely and effectively. It is important to pay attention to this matter to ensure the best possible outcomes for patients.

Individuals with β-thalassemia should undergo regular dental check-ups, whether they have undergone splenectomy or not. These check-ups should include both preventive and therapeutic measures to address the underlying and contributing factors of oral diseases. It is important to educate and support affected children and their parents about the side effects of the disease and its treatment, which may include subclinical or hidden oral health problems

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