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Comprehensive oral health management of paediatric population with acute lymphoblastic leukemia

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Abstract

Among the childhood oncological conditions, leukemia constitutes 30% with acute lymphoblastic leukemia (ALL) of 75% and peak incidence around 4 years of age. Etiology links to clonal proliferation of lymphoid precursors with arrested maturation, with origin in lymphoid cells of different lineages, resulting in B cell/ T cell/ mixed nature. Due to its response to chemotherapy, acute lymphoblastic leukemia is the first one to be cured in majority of paediatric population.

Keywords: Dental, Acute lymphoblastic leukaemia, Gingiva, Haemorrhage, Pediatric

Introduction

Among the childhood oncological conditions, leukemia constitutes 30% with acute lymphoblastic leukemia (ALL) of 75% and peak incidence around 4 years of age. Etiology links to clonal proliferation of lymphoid precursors with arrested maturation, with origin in lymphoid cells of different lineages, resulting in B cell/ T cell/ mixed nature. Due to its response to chemotherapy, acute lymphoblastic leukemia is the first one to be cured in majority of paediatric population. Oral manifestations should be diagnosed by the dentist and also be aware about the complications of the oncological management in the oral cavity, since the condition occurs due to leukemic cellular infiltration and decreased normal bone marrow characteristics. Clinical manifestations of ALL include lethargy, anemia, irritability, anorexia, petechiae, lymphadenopathy, bone pain, arthralgia, hepatosplenomegaly, sore throat, laryngeal pain, gingival bleeding and oral ulceration. Quality of life of the patients can be improved through the elimination of the pathognomonic oral findings. The malignant disease of the blood forming tissues, leukemia, the sole cause of migration of immature blood cells in the blood stream was discovered by Virchow and Bennet in 1845 [1-3]. Two major classifications, based on duration and cell type, are acute-chronic and myeloid-lymphoid-monocytic [4]. In paediatric neoplasm, ¼ the of the percentage accounts for acute lymphoblastic leukemia. Whereas in the malignancy category, it accounts for ¾ th percentage. Etiology includes, infections, chemicals, ionizing radiation, genetic alterations, habits such as parental smoking and alcohol consumption, non-ionizing electromagnetic and electrical field [5]. Clinical examination reveals fatigue, fever, hepatosplenomegaly and enlarged lymph nodes [6]. Investigations are complete blood count, bone marrow biopsy, cytogenetics and lumbar puncture [7, 8]. Management includes combination of chemotherapy and radiotherapy, chemotherapy alone and bone marrow transplantation [9]. Oral manifestations include gingival hyperplasia, oral mucositis, gingival bleeding, alterations in relation to maxilla and mandible and opportunistic infections, which occur due to thrombocytopenia, neutropenia, or compromised granulocyte function or due to direct leukemic infiltration [10]. The most common complication following chemotherapy and radiotherapy is oral mucositis. In children of less than 9 years of age and high leucocyte count category of 9400 – 400000 leucocyte/mm, oral mucositis was commonly seen [11]. These lesions were commonly seen in children with CT genotype [12]. Alterations in the quantity and quality of saliva occur due to treatment phase [13]. Agnesis, microdontia, tapering roots and short roots are observed in anomalies category. In paediatric patients with graft versus host disease, erosion, oral mucosa ulceration, xerostomia and lichenoid changes are seen [24]. Trismus, mucormycosis, leukemic mandibular infiltration and oral aspergillosis are of rare complications [10, 14-16].

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Four categories of ALL treatment include, a) remission induction for 28 days and consists vincristine, prednisone and L-asparaginase, b) CNS preventive therapy/prophylaxis. Cranial irradiation and/or weekly intrathecal injection of a chemotherapeutic agent, usually methotrexate c) consolidation or intensification focusses on the decreased drug cross resistance through intensified treatment and d) maintenance phase suppress leukemic growth through continuous administration of methotrexate and 6-mercaptopurine. In the initial stage of chemotherapy or radiotherapy, blood count decreases within 5 to 7 days, till 21 days and then rising to normal level in the next cycle. Usually dental treatments should be planned before the commencement of oncology therapy. If not possible, extraction, root canal therapy, periodontal therapy, prosthodontic treatment should be given priority. Early and comprehensive oral hygiene measures need to be implemented to avoid the systemic complications. Achievement of remission is a known prerequisite for prolonged survival. Before leukemia treatment, the concept is to identify and stabilize or eliminate existing and potential sources of infection and local irritants and also educate the patient /parents about the importance of oral care. Initial evaluation includes review of medical history such as, disease/condition (type, stage and prognosis), treatment protocol (conditioning regimen, surgery, chemotherapy, radiation, and transplant), medications(including bisphosphonates), allergies, surgeries, secondary medical diagnoses, haematological status such as Absolute Neutrophil Count (ANC) > 1,000/mm³ without need for antibiotic prophylaxis: antibiotic prophylaxis as per American Heart Association with ANC between 1000 – 2000/cubic mm, complete blood count (CBC)), coagulation status, immune suppression status, and presence of an indwelling venous access line., chemotherapy/radiotherapy protocol, head-neck-dental examination in conjoint with panoramic/bitewing radiographs. Platelet count of > 75,000/mm³: Prolonged bleeding can be controlled by sutures, hemostatic agents, pressure packs and foams. Platelet count is 40,000 to 75,000/mm³: need for platelet transfusions pre and 24 hours postoperatively. Platelet count < 40,000/mm³: avoid elective dental care. Oral hygiene measures, patient education, parent awareness, soft or electric toothbrush, (non-alcohol mouthwashes) 0.12% chlorhexidine mouthwashes, mainly preferred to decrease the incidence of dry mucosa/mucositis, sodium bicarbonate/saline mouthwash, elimination of periodontal disorders to decrease the myelosuppression. Due to carbohydrate rich foods given to maintain weight and oral medications containing increased amounts of sucrose, dental caries usually occurs but has to be treated through fluoride supplements, gels, rinses, in order to avoid further complications. Poor prognosis conditions such as root stumps, impacted teeth, more than 5 mm periodontal pockets, acute infections and non-restorable teeth has to be eliminated before three weeks of chemotherapy in order to avoid the risk of osteoradionecrosis. Atraumatic surgical procedures (50,000 cubic mm platelet for minor and 100,000 cubic mm for major) to be carried out without any sharp margins, thereby facilitating neat closure. Orthodontic measures include decreased root resorption, light forces, earlier treatment completion, simple and basic treatment and treatment limitations pertaining to maxilla. In phase 2, immunosuppression period, maintenance of oral health, management of oral oncological treatment side effects such as mucositis (occurs in two weeks, seen as erythema, erosion,

ulceration, white fibrinous pseudomembrane, gingival bleeding, xerostomia, secondary candidiasis, and herpes simplex and bacterial infections and patient/parent education. Severe pain and weight loss occurs in patients with mucositis. Complications of severe oral mucositis can be reduced by oral hygiene measures. WHO scale measures oral mucositis based on the degree of erythema, soreness and child's normal diet such grade I and II comprising of soft tooth brush, fluoride toothpaste and salt – bicarbonate rinse, grade III of salt-bicarbonate solution dipped gauze for cleaning of oral cavity at least 4 times a day along with oral hygiene measures and grade IV of same oral hygiene measures as that of grade II in addition to salt-bicarbonate solution rinse once in every 4 hours. Chlorhexidine mouthwash also plays an important role in the reduction of oral mucosal lesions. Oral mucositis management protocol includes, nutritional support, pain control, dry mouth palliation, management of oral bleeding and therapeutic interventions and oral decontamination in the form of saline solution-sodium bicarbonate rinses-lidocaine-benzocaine- "magic mouth rinse" containing diphenhydramine, lidocaine, and combinations of aluminum hydroxide, magnesium hydroxide, hydroxypropylcellulose gels or sucralfate solutions, simethicone; parenteral nutrition; water sips-artificial saliva-sugarless chewing gum-cholinergic agents; fibrin glue-gelatin sponge; cryotherapy in the form of ice chips-IV recombinant human keratinocyte growth factor-1-Intravenous human fibroblast growth factor-20-benzylamine hydrochloride mouth rinse - topical oral applicant, RK-0202, consisting of the antioxidant N-acetylcysteine-glutamine-oral sucralfate suspension-recombinant keratinocyte growth factor palifermin-low level LASER therapy (to increase mitochondrial ATP production, fibroblast proliferation, oxygen free radicals detoxification, increase microcirculation and growth factors release) - application of a spray consisting of synthetic collagen precursor amino acids in combination with sodium hyaluronate – fluoride toothpaste, chlorhexidine mouthwash, self applied fluoride gel – oral physiotherapy such as stretching exercises, muscle relaxants, analgesics, trigger point injections - orthodontic care. Most common complications of therapy includes agenesis of teeth, defective mineralization, change in tooth shape and size, malocclusion, change in crown or root shape, delayed tooth eruption, diminished mandibular growth, soft tissue deformities, bony deformities, alteration in pituitary gland function, hypoplasia, microdontia and asymmetrical facial growth^[25]. In this phase, the oral health management includes, detailed clinical and radio graphical assessment, extraction before 10 – 14 days of chemotherapy, scaling, pit and fissure sealant application, fluoride therapy, temporary restoration, oral hygiene instructions, oral prophylaxis measures, twice daily soft tooth brushing and flossing and finally gingival massage^[17-20]. During leukemia treatment, oral health management includes nystatin suspension for fungal infections, topical and systemic acyclovir for herpes simplex infections, artificial saliva and sugar free chewing gum for xerostomia^[19, 21, 22]. Post leukemia treatment, oral health management includes fluoride toothpaste, esthetic – orthodontic – endodontic intervention such as tooth coloured restoration, correction of malaligned teeth and root canal therapy^[18, 23]. Long term success depends on the patient compliance. Caretakers, patient, dietary habits, pediatric medications and nutritional supplements play an important role. The role of the paediatric dentist is crucial along with the haematology/oncology team in reduction of complications arising in the oral cavity before, during and

post leukemic treatment in paediatric population. Oral health education and awareness should be implemented. Thus, the quality of life in paediatric population with leukemia can be improved by preventive and therapeutic approach such as reducing the systemic and oral complications, rapid healing rate and pain alleviation.

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