ISSN 2706-6819 Vol.5, Issue 8: 115-120, DOI: 10.25236/IJFM.2023.050816

Oral health and oral health management in children with acute lymphoblastic leukemia

Lan Lan[1], Yuwei Han[1], Yishan Liu[1,2,*]

[1]Department of Pediatric Prevention of Stomatology, The First Affiliated Hospital (Affiliated Stomatological Hospital) of Xinjiang Medical University, Urumqi, 830054, China
[2]Xinjiang Uygur Autonomous Region Institute of Stomatology, Urumqi, Xinjiang Uygur Autonomous Region, 830054, China
[*]Corresponding author

Abstract: *Acute lymphoblastic leukemia is the most common type of childhood leukemia, and most children with acute lymphoblastic leukemia show impaired oral health, high risk of dental caries, altered caries related factors and oral flora disorders, with significantly higher periodontitis status and oral mucous inflammation. Dental morphological disorders are more common in children with ALL than in healthy children. In children with ALL, malocclusion due to small dental clusters may also trigger TMJ disorders. In recent years, the treatment and prognosis of children with acute lymphoblastic leukemia have been significantly improved, but the disease and its therapeutic measures can lead to a variety of oral complications, which affects further treatment and is not conducive to disease control. Maintaining oral health, improving related symptoms of patients and reducing the occurrence of complications has received much attention. In order to improve the quality of life of children, this paper reviews the oral health status and oral health management of children with acute lymphoblastic leukemia, providing clinical reference.*

Keywords: *Acute lymphoblastic leukemia; Childhood leukemia; Chemotherapy; Complications; Oral care; Oral disease; Oral infection; Oral health management*

1. Introduction

Acute lymphocytic leukemia is the most common malignant tumor, children make up about 27.3% of childhood cancer ALL is the most common cancer in children, incidence of a disease at the age of 1 to 4 years old [1]. The initial manifestations of ALL may be gum swelling, gum bleeding, or even tooth loosening in severe cases [2].After starting chemotherapy, children with ALL often suffer from the toxicity of chemotherapy drugs, such as methotrexate. Adverse reactions of chemotherapy are often related to the oral cavity, such as destroying oral mucosal tissue, inhibiting the immune function of patients, and causing bacterial flora imbalance and infection. Due to the effects of chemotherapy drugs, oral mucosal barrier is damaged and bone marrow suppression is caused, and patients are more susceptible to fungal virus infection, and are more likely to develop sepsis and sepsis[3].Oral complications include oral mucositis, opportunistic infections, gum inflammation and bleeding, and dry mouth [4].Oral health management of children should run through the whole process before, during and after treatment, and targeted prevention should be carried out according to the causes of various oral complications. Oral health problems of children with leukemia have attracted more and more attention [5].

2. Oral health Status of Children with ALL

2.1 Oral mucosa status in children with ALL

Some leukemia in children with ALL first appears in the mouth [6,7]. The common oral manifestations of ALL patients include gingival bleeding, oral ulcers, gum swelling, candidiasis and periodontitis [8,9,10], and the adverse reactions of chemotherapy for ALL often involve the mouth, such as destroying oral mucosal tissue, inhibiting the immune function of patients, causing bacterial imbalance and infection, and changing the dietary habits and oral hygiene of patients [11,12].

The nature and treatment of ALL can have a direct and indirect impact on the oral health of patients. Leukemia cells can invade the gums and deep periodontal tissues [13], and the incidence of oral mucitis

ISSN 2706-6819 Vol.5, Issue 8: 115-120, DOI: 10.25236/IJFM.2023.050816

in children with ALL is as high as 80% [14]. The clinical manifestations of oral mucositis are mucosal atrophy, swelling, erythema, and even oral mucosal ulcer [15].Oral mucositis usually appears 5 to 7 days after the start of antitumor therapy and persists throughout the treatment cycle. The main reason is the use of chemotherapeutic cytotoxic drugs [14], which have non-specific interference on mitotic cells and reduce the cell renewal rate of oral mucosal epithelial base layer, leading to mucosal atrophy, erosion and ulcers. Bacterial, viral and fungal infections are also common complications in children with ALL. Among them, Candida is the most common fungal infection. The researchers conducted a study on children with oral ulcers receiving chemotherapy and found that 30% of the children's mucosal damage was caused by Candida albicans, and the incidence of oral fungal infection in ALL children was 27%-50% [16-17].Figliolia et al. [18] analyzed the oral status of 169 children with ALL, in which herpes simplex virus was detected in the mouths of 23 children, 13 of whom also suffered from oral mucositis. At present, it is believed that the effect of chemotherapy drugs leads to the destruction of oral mucosal barrier and bone marrow suppression, and the immune system of patients is damaged, and they are more susceptible to fungal virus infection and sepsis and sepsis [19].

2.2 Periodontal status of children with ALL

The initial manifestation of ALL in children is periodontal abnormality and gum swelling caused by cancer cells infiltrating the gum, periodontal membrane and alveolar bone. Kapoor et al. [20] evaluated the periodontal status of 110 children diagnosed with ALL and 110 healthy children, and the results showed that the average OHI-S of the children in the ALL group was 1.158 and that of the healthy group was 1.252.The average modi-fiedgingivalindex (MGI) was 0.6779 in ALL group and 0.4783 in healthy group. Although the children in the ALL group strictly followed the doctor's advice for oral care, the mean plaqueindex (PI) score of 0.675 was still higher than that of the healthy group, whose mean PI was 0.655, which was speculated to be due to the use of chemotherapy drugs leading to immunosuppression, promoting bacterial colonization and increasing plaqueindex. Studies have found that the gingival index of children with ALL is higher than that of healthy children [21]. On the one hand, the gingival swelling is caused by cancer cells infiltrating the periodontal tissue of children with ALL; on the other hand, chemotherapy damages the periodontal tissue and weakens the gingival tissue, resulting in increased gingival index.

2.3 Tooth morphology of ALL children

It has been reported that ALL may negatively affect the alveolar process complex during its formation. However, this association depends on a variety of factors, including the age of the patient at diagnosis, the type of drug used in chemotherapy, and the dose of radiotherapy (if used as an adjunct to chemotherapy in severe cases) [21-26]. Chemotherapy is selectively toxic to actively proliferating cells by interfering with DNA synthesis and replication, RNA transcription, and cytoplasmic transport mechanisms [22].The ideal chemotherapy drug would destroy only malignant cells. However, since chemotherapeutic drugs are not selectively toxic to tumor cells; They may also affect healthy cells in the proliferative stage [27]. There have been reports [28] of enamel and dentin disturbances caused by chemotherapy. Studies [22-24] have shown that chemotherapeutic drugs (such as cyclophosphamide and vincristine) interfere with cell cycle and intracellular metabolism, thereby causing residual changes in tooth development that may lead to small tooth groups, deformities and changes. Kaste et al. [29] reviewed the clinical records and panoramic radiographs of 423 children with ALL, and found that dental deformities in ALL children mainly included root dysplasia, microdental deformities, tooth loss, bovine teeth and decidary teeth retention, among which root dysplasia accounted for 24.4% of dental deformities and was the most common dental deformities in ALL children. Studies have shown that radiotherapy and chemotherapy in the early stages of tooth development can lead to dental hypoplasia or microdental malformation, and may interfere with tooth root development in the later stages [30]. Some patients receive radiation therapy as an adjunct to chemotherapy for ALL [31]. A radiation dose of 10 gray (Gy) has been reported to permanently damage ameloblasts, while a radiation dose of 30Gy stops tooth development from the time the tooth is irradiated. Sonis et al. [32] studied the dental-facial development of 97 children diagnosed with ALL. The children received either (a) chemotherapy and 18gy craniological radiation, or (b) chemotherapy and 24gy craniological radiation. Results showed that 94 percent of patients and 100 percent of children under 5 years of age had dental abnormalities at diagnosis, including blocked root development, enamel dysplasia, alveolar development and dental hypoplasia. Jaw growth was impaired in children who received 24gy irradiation compared to children who received low-dose radiotherapy for ALL.

ISSN 2706-6819 Vol.5, Issue 8: 115-120, DOI: 10.25236/IJFM.2023.050816

In addition, it has been found that diagnosis before age 5 and treatment with anthracyclines (doxorubicin) at cumulative doses >120mg/m2 may lead to more severe dental defects in children with ALL, whereas the proportion of dental deformities in children older than 5 years at diagnosis is relatively low.

2.4 Caries in ALL children

The vast majority of parents believe that children with ALL are young and in poor general condition, and cannot cooperate when brushing and flossing, which will increase the risk of bleeding infection and replacement of baby teeth, so it is unnecessary to take children for oral examination and ask children to brush teeth. Oral mucositis and gingival bleeding caused by chemotherapy also interfere with the normal implementation of daily oral hygiene measures [33-34].In addition, the caries filling rate of children with ALL is significantly lower than that of normal children, which may be due to the fact that medical staff and parents in the hematology department focus too much on the treatment of leukemia and pay insufficient attention to dental caries. When caries are found, they often choose not to treat them in the absence of pain and other discomfort. In addition, the poor general condition of ALL children and the inability to tolerate dental treatment may also be one of the reasons for the low caries filling rate.

Children with ALL diet mainly liquid, semi-liquid diet, food adhesion is strong, easy to adhere to the tooth surface is not easy to remove. Chemotherapy can also cause salivary gland hypoplasia, reduced saliva flow, and reduced scouring of the mouth. In severe cases, this is manifested as dry mouth syndrome [35].According to Hong et al., leukemia patients tend to consume more high-energy foods and drink sugar-rich beverages to relieve dry mouth [36].Due to nausea and vomiting caused by chemotherapy drugs, children with ALL have very little food intake, so the number of meals is significantly increased. Studies have shown that the decrease of saliva pH and flow in children with ALL after chemotherapy, as well as the resulting increase in the consumption of sweet drinks and sweet soft foods (due to oral lesions and mucositis and dysphagia caused by treatment), the intake of high sugar and the increase in eating frequency are not conducive to the oral hygiene of patients, promote the development of dental caries, and increase the risk of dental caries in children with ALL.

2.5 Temporomandibular joint status

Temporomandibulardisorder (TMD) is including the temporomandibular joints (TMJ) and chewing muscles and its re[l]ated structural abnormalities disease. It is one of the most common maxillofacial diseases, often manifested as TMJ pain, occlusal malocclusion, limited mandibular range of motion, joint snap and locking [37].Dahllof et al. [38] studied the temporomandibular joint status of 19 children with bone marrow transplantation who underwent radiation therapy, and found that compared with healthy children, the children who received radiation had a significant decrease in their mouth opening ability, and 53% of children had a decrease in condylar translation movement, while only 5% of the control group. This is because long-term radiotherapy and chemotherapy can cause changes in connective tissue and muscle tissue, leading to inflammation and eventually fibrosis, resulting in TMJ dysfunction [39].

3. Oral health management in children with ALL

3.1 Early warning effect of oral signs in children with ALL before diagnosis

It was reported that only 7% of the 353 leukemia patients were hospitalized with leukemia as the primary disease, and more were hospitalized with other symptoms and diagnosed with leukemia after examination. As mentioned earlier, the initial manifestations of ALL in children may be gum swelling, gum bleeding, and even tooth loosening in severe cases. Therefore, children with abnormal periodontal status should be asked about their systemic status in detail. Children with highly suspected blood diseases should be recommended for routine blood examination to avoid missed diagnosis.

3.2 Oral health management of children with ALL before treatment

For children with diagnosed ALL, whole-course effective oral health education is very important for the prevention of oral diseases in children, and studies have confirmed that oral health education can significantly reduce the dental plaque in children [40].The study of Djuric et al. [41] also showed that oral examination and intervention, oral hygiene guidance and dietary guidance were given to children with ALL before chemotherapy, and the oral health status of children with ALL was significantly better than

ISSN 2706-6819 Vol.5, Issue 8: 115-120, DOI: 10.25236/IJFM.2023.050816

that of other children with ALL. The oral diseases should be treated before anti-tumor therapy. It is recommended that children with ALL should have a comprehensive oral examination at least 10 to 14 days before treatment. Children who can cooperate should try to have a panoramic X-ray examination. For any suspected tooth infection, dental X-ray examination must be performed to detect and deal with oral problems in time. If the general condition permits, all dental and periodontal diseases can be completely cured, periodontal cleaning and curettage can be performed, and the treatment should be completed within 1 month before chemotherapy. For teeth that may cause infection, especially those whose infection has spread to the pulp or even deeper, it is recommended to remove them 3 weeks before treatment. To minimize the risk of oral and systemic complications during anti-tumor treatment, while ensuring full healing of the extraction site [42].At the same time, the examination included the soft and hard tissues of the head, face, neck and mouth of the child, and found caries, gingival bleeding, periodontitis, soft and hard tissue damage and trauma, etc., and made corresponding treatment after assessing the general health status.

It is important to emphasize that blood tests should be performed and risk assessed before any invasive procedures or tests are performed. Therefore, in order to ensure the oral health of children with ALL, oral health education should be strengthened for children with ALL and their parents, and targeted dietary guidance and oral hygiene guidance should be provided to children with ALL and their parents. Meanwhile, patients should be advised to avoid eating sticky, high-sugar or irritating foods.

3.3 Oral health management in children with ALL during treatment

During treatment, oral flushing with 0.12% chlorhexidine gluconate and essential oil formulation is currently a more recognized oral bactericidal and anti-infection method during chemoradiotherapy [43].In addition, povidone iodine is also an effective oral bactericide [44].Sodium bicarbonate or salt water can also be used to gargle to reduce the colonization of oral microorganisms and prevent mucositis and caries. If oral mucosal problems are detected, local anesthesia drugs such as lidocaine or opioids may be used to relieve pain. High-dose radiotherapy to the head and neck has been shown to cause changes in the chemical composition of saliva as well as a reduction in the speed and flow of saliva in adults [45].Xerostomia induced by radiation can also lead to the transformation of oral flora into highly acidic and cariogenic populations [46].

For children in the tooth replacement period, the baby teeth are allowed to fall out naturally, but supervision should be strengthened when the baby teeth are loose and have not fallen out, and timely stop the children from playing with the baby teeth with their hands to avoid infection and even bacteremia. For children undergoing mobile or fixed orthodontic treatment, if oral cleanliness cannot be guaranteed, it is recommended to remove orthodontic devices before cancer treatment. During treatment, children may not be able to brush their teeth due to oral pain. Use wipes soaked with sodium carbonate or chlorhexidine solution to wipe the mouth. In addition, vomiting is a common symptom in the treatment of children with ALL. It is recommended that children rinse their mouths with water after vomiting to wash away the digestive fluid remaining in the mouth as much as possible, so as to avoid the digestive fluid from corroding tooth enamel and causing demineralization, and reduce oral mucosal irritation. Therefore, it is also necessary to carry out oral care and examination on time and maintain good oral hygiene during treatment.

3.4 Oral health management of children with ALL after treatment

At least one dental follow-up every 3 to 6 months is recommended after the end of treatment. Clean your teeth with fluoride toothpaste, floss, toothbrush, and 0.05% sodium fluoride mouthwash. Due to the increased incidence of dental deformities in children with ALL after treatment, TMJ may have functional abnormalities, which may affect the facial aesthetics and occlusal function of children, and orthodontic treatment, aesthetic repair and TMJ treatment can be performed. It should be noted that children are susceptible to secondary primary cancers due to radiation and multi-drug chemotherapy, among which squamous cell carcinoma and mucoepidermoid carcinoma are the second primary oral solid malignancies after allogeneic hematopoietic stem cell transplantation. Therefore, oral examination of children with ALL after treatment is very important [2].

4. Conclusions

Oral complications are common in children with ALL, mainly including oral mucositis, dental

ISSN 2706-6819 Vol.5, Issue 8: 115-120, DOI: 10.25236/IJFM.2023.050816

deformity, gum bleeding and swelling, dental caries, mandibular lesions, etc., which have a serious impact on the life and treatment of children with ALL, and even threaten their lives in severe cases. Dentists should provide targeted oral health education for children with ALL and their parents, and provide them with dietary and oral hygiene guidance. Children with ALL are encouraged to have regular oral examinations before, during and after chemotherapy. Fully understand the systemic condition and blood situation of the child, and carry out appropriate oral intervention. While actively treating ALL, medical staff in the hematology department should pay attention to oral health, strengthen the connection with the stomatology department, and minimize the occurrence of oral complications. Parents should communicate more with hematology and stomatology doctors, improve the importance of oral health, and ensure the normal implementation of oral health measures such as brushing teeth as far as possible under conditions.

References

[1] Duan Y F. Research progress on the relationship between STAT5 and acute lymphoblastic leukemia in children [J]. Chinese Journal of Pediatrics, 2002, 24(8): 942-947.
[2] Tang Yawen, Zhang Lin, Yang Xue et al. Oral health management of children with acute lymphoblastic leukemia [J]. Oral Disease Prevention and Treatment, 2019, 29(8): 572-576. (In Chinese)
[3] Riley P, Glenny AM, Worthington HV, et al. Interventions for preventing oralmucositis in patients with cancer receiving treatment: cytokines and growth factors [J]. Cochrane Database Syst Rev, 2017, 11(11): Cd011990.
[4] Wang Y, Zeng X, Yang X, Que J, Du Q, Zhang Q, Zou J. Oral Health, Caries Risk Profiles, and Oral Microbiome of Pediatric Patients with Leukemia Submitted to Chemotherapy. Biomed Res Int. 2021 Jan 16; 2021: 6637503. doi: 10. 1155/2021/6637503. PMID: 33532491; PMCID: PMC7834790.
[5] Sun Wenmin, Ming Xiuyun, Zhang Xiuyun, et al. Multi-factor nursing intervention of oral lesions after chemotherapy for leukemia [J]. PLA Journal of Nursing, 2006, 23(7): 14-16. (In Chinese)
[6] Garrett WS, Lord GM, Punit S, et al. (2007) Communicable ulcerative colitisinduced by T-bet deficiency in the innate immune system. Cell 131: 33-45.
[7] Barrett AP (1986). Leukemic cell infiltration of the gingivae. J Periodontol 57: 579-581.
[8] Hou GL, Huang JS, Tsai CC (1997). Analysis of oral manifestations of leukemia: a retrospective study. Oral Dis 3: 31-38.
[9] Meyer U, Kleinheinz J, Handschel J, et al. (2000) Oral findings in three different groups of immunocompromised patients. J Oral Pathol Med 29: 153-158.
[10] Javed F, Utreja A, Bello Correa FO, et al. (2012) Oral health status in children with acute lymphoblastic leukemia. Crit Rev Oncol Hematol 83: 303-309.
[11] E. C. de Oliveira Lula, C. E. de Oliveira Lula, C. M. Alves, F. F. Lopes, and A. L. Pereira, "Chemotherapy-induced oral complications in leukemic patients, " International Journal of Pediatric Otorhinolaryngology, vol. 71, no. 11, pp. 1681–1685, 2007.
[12] N. Oosterom, P. H. Griffioen, M. A. H. den Hoed et al, "Global methylation in relation to methotrexate-induced oral mucositis in children with acute lymphoblastic leukemia, " PLoS One, vol. 13, no. 7, article e0199574, 2018.
[13] Mazaheri R, Jabbarifar E, Ghasemi E, et al. Oral health status, salivary pH status, and Streptococcus mutans counts in dental plaques and saliva of children with acute lymphoblastic leukemia. Dent Res J (Isfahan). 2017 May-Jun; 14(3): 188-194.
[14] Ribeiro ILA, Limeira RRT, Dias de Castro R, et al. Oral mucositis in pediatric patients in treatment for acute lymphoblastic leukemia [J]. Int J Environ Res Public Health, 2017, 14(12).
[15] Sroussi HY, Epstein JB, Bensadoun RJ, et al. Common oral complications of head and neck cancer radiation therapy: mucositis, infections, saliva change, fibrosis, sensory dysfunctions, dental caries, periodontal disease, and osteoradionecrosis [J]. Cancer Med, 2017, 6(12): 2918-2931.
[16] Vuciccevicc Boras V, Vidoviccc Juras D, Aurer I, et al. Gingival ulcerations in a patient with acute myeloid leukemia: a case report and literature review [J]. Acta Clin Croat, 2019, 58(3): 556 - 560.
[17] Pereira IF, Firmino RT, Meira HC, et al. Radiation - induced oral mucositis in brazilian patients: prevalence and associated factors [J]. In Vivo, 2019, 33(2): 605-609.
[18] Figliolia SL, Oliveira DT, Pereira MC, et al. Oral mucositis in acute lymphoblastic leukaemia: analysis of 169 paediatric patients [J]. Oral Dis, 2008, 14(8): 761-766.
[19] Riley P, Glenny AM, Worthington HV, et al. Interventions for preventing oral mucositis in patients with cancer receiving treatment: cytokines and growth factors [J]. CochraneDatabaseSystRev, 2017, 11(11): Cd011990.
[20] Kapoor G, Goswami M, Sharma S, et al. Assessment of oral health status of children with Leukemia: a cross-sectional study [J]. Spec Care Dentist, 2019, 39(6): 564-571.

ISSN 2706-6819 Vol.5, Issue 8: 115-120, DOI: 10.25236/IJFM.2023.050816

[21] Krasuska-Sławińska E, Broz·yna A, Dembowska-Bagińska B, et al. Factors influencing caries incidence in permanent teeth in children/adolescents under and after anti-neoplastic treatment [J]. Contemp Oncol (Pozn), 2016, 20(1): 45 - 51.
[22] Goho C. Chemoradiationtherapy: effect on dental development. Pediatr Dent 1993; 15: 6-12.
[23] V ahlsing HL, Kim SK, Feringa ER. Cyclophosphamide-induced abnormalities in the incisors of the rat. J Dent Res 1977; 56: 809-16.
[24] Stene T. Effect of vincristine on odontoblasts in rat incisor. Scand J Dent Res 1978; 86: 346–56.
[25] Maciel JC, de Castro Jr CG, Brunetto AL, et al. Oral health and dental anomalies in patients treated for leukemia in childhood and adolescence. Pediatr Blood Cancer 2009; 53: 361–5.
[26] Dahllöf G, Rozell B, Forsberg CM, et al. Histologic changes in dental morphology induced by high dose chemotherapy and total body irradiation. Oral Surg Oral Med Oral Pathol 1994; 77: 56–60.
[27] Kaste SC, Hopkins KP, Jenkins 3rd JJ. Abnormal odontogenesis in children treated with radiation and chemotherapy: imaging findings. AJR Am J Roentgenol 1994; 162: 1407–11.
[28] Sonis AL, Tarbell N, Valachovic RW, et al. Dentofacial development in long-term survivors of acute lymphoblastic leukemia. A comparison of three treatment modalities. Cancer 1990; 66: 2645–52.
[29] Kaste SC, Hopkins KP, Jones D, et al. Dental abnormalities in children treated for acute lymphoblastic leukemia[J]. Leukemia, 1997, 11(6): 792-796.
[30] Çetiner D, Çetiner S, Uraz A, et al. Oral and dental alterations and growth disruption following chemotherapy in long - term survivors of childhood malignancies[J]. Support Care Cancer, 2019, 27(5):
[31] Anirudhan D, Bakhshi S, Xess I, et al. Ls A. Etiology and outcome of oral mucosal lesions in children on chemotherapy for acute lymphoblastic leukemia. Indian Pediatr 2008; 45: 47–52.
[32] Subramaniam P, Girish Babu KL, Nagarathna J. Oral manifestations in acute lymphoblastic leukemic children under chemotherapy. J Clin Pediatr Dent 2008; 32: 319–24.
[33] Azher U, Shiggaon N. Oral health status of children with acute lymphoblastic leukemia undergoing chemotherapy[J]. Indian J Dent Res, 2013, 24(4): 523.
[34] Kung AY, Zhang S, Zheng LW, et al. Oral health status of chinese paediatric and adolescent oncology patients with chemotherapy in Hong Kong: a pilot study[J]. Open Dent J, 2015, 9: 21-30.
[35] K. P. Dholam, S. Gurav, J. Dugad, and S. Banavli, "Correlation of oral health of children with acute leukemia during the induction phase, " Indian journal of medical and paediatric oncology : official journal of Indian Society of Medical & Paediatric Oncology, vol. 35, no. 1, pp. 36–39, 2014.
[36] C. H. Hong, J. J. Napeñas, B. D. Hodgson et al, "A systematic review of dental disease in patients undergoing cancer therapy, " Support Care Cancer, vol. 18, no. 8, pp. 1007–1021, 2010.
[37] Ouanounou A, Goldberg M, Haas DA. Pharmacotherapy in Temporomandibular disorders: a review [J]. J Can Dent Assoc, 2017, 83: h7.
[38] Dahllöf G, Krekmanova L, Kopp S, et al. Craniomandibular dysfunction in children treated with total - body irradiation and bone marrow transplantation[J]. Acta Odontol Scand, 1994, 52(2): 99 105.
[39] Wu VW, Lam YN. Radiation - induced temporo - mandibular joint disorder in post - radiotherapy nasopharyngeal carcinoma patients: assessment and treatment[J]. J Med Radiat Sci, 2016, 63(2): 124132. doi: 10. 1002/jmrs. 145.
[40] Stein C, Santos NML, Hilgert J. B. , et al. Effectiveness of oral health education on oral hygiene and dental caries in schoolchil-dren: systematic review and meta-analysis[J]. Community Dent Oral Epidemiol, 2018, 46(1): 30-37.
[41] Djuric M, Hillier -Kolarov V, Belic A, et al. Mucositis prevention by improved dental care in acute leukemia patients[J]. Support Care Cancer, 2006, 14(2): 137-146.
[42] Furlong W , Rae C , Feeny D ,et al.Health-related quality of life among children with acute lymphoblastic leukemia[J]. Pediatric Blood & Cancer, 2012, 59(4):717-724.DOI:10.1002/pbc.24096.
[43] Gaetti-Jardim E Jr, Jardim ECG, Schweitzer CM, et al. Supragingi-val and subgingival microbiota from patients with poor oral hy-giene submitted to radiotherapy for head and neck cancer treat-ment[J]. Arch Oral Biol, 2018, 90: 45-52.
[44] Bahrololoomi Z, Sadat-Hashemi A, Hassan-Akhavan-Karbassi M, et al. Evaluating the additive effect of Persica and chlorhexidine mouthwashes on oral health status of children receiving chemotherapy for their hematomalignancy: A randomized clinical trial[J]. J Clin Exp Dent, 2020, 12(6): e574-e580.
[45] Kawashita Y, Soutome S, Umeda M, et al Oral management strategies for radiotherapy of head and neck cancer[J]. Jpn Dent Sci Rev, 2020, 56(1): 62-67.
[46] Lalla RV, Treister N, Sollecito T, et al. Oral complications at 6months after radiation therapy for head and neck cancer[J]. OralDis, 2017, 23(8): 1134-1143.