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Review Article

Dentistry Section

Orthodontic Therapy for Paediatric Cancer Survivors: A Review

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ABSTRACT

The paper aims at reviewing the possibilities of orthodontic therapy for paediatric cancer survivors. It is important to understand the fundamental disease, it's treatment protocols, effects on growing skeleton, dental development, oral cavity and oral mucosa, dental caries, bone, orthodontic tooth movement.

Keywords: Brackets, Cancer therapy Oral epithelium, Orthodontic appliance

INTRODUCTION

A cancer survivor refers to any individual who had been diagnosed with cancer till the remaining of his life. A paediatric cancer survivor is any person who has been disease free for five years and without any form of therapy for two years [1-3]. Since, there is increase in survival rate, the need for orthodontic treatment is also increasing. As a result, orthodontist consults more patients who have successfully undergone anti cancer therapy in childhood. There are various oral complications of cancer treatment therapy. Cancer therapy has significant effects on the craniofacial skeleton and oral cavity. Orthodontic treatment is a specific treatment modality aiming patient's of all ages especially children, teenagers and young adults. Cancer survivors are a specific group that an orthodontist would encounter in clinical practice.

The main purpose of this present review is to understand the possibilities of orthodontic treatment in these patients bearing in mind the potential adverse clinical implications and a significant risk of complications during orthodontic treatment. The treatment in the paediatric cancer survivors stands as a challenge to the orthodontist in terms of treatment strategies with thorough understanding of the risk versus benefit factors for the patient.

Paediatric Cancer

Paediatric cancer includes children of ages (0-14) years; around 60,620 cancer survivors. It affects approximately 12 in 100,000 children [4,5]. The types of cancer most commonly diagnosed in children include:

Acute lymphoblastic leukaemia- 26%;

Brain and CNS tumours- 21%;

Neuroblastoma- 7%.

The five year survival rate is as high as 93.5% with improved therapeutics. Therapeutics commonly employed to treat include chemotherapy (general treatment) which is complemented by radiotherapy (local treatment) and surgery (local treatment). These therapies have adverse effects on the craniofacial skeleton and dentition as discussed below [6-8].

Effects of Chemotherapy and Radiotherapy on Growing Skeleton

Most of growth in a child takes place at less than five years of age. Craniofacial, skeletal and dental developmental problems too are frequently reported to occur during this age. The effect of chemotherapy and radiotherapy are most pronounced during puberty [9-11]. A long term survivor encompasses patients who have finished active cancer treatment. A 77-100% of survivors undertaking head and neck radiation therapy report mild to severe radiation damage of soft tissue and bones [12-14]. Damage to the thyroid gland and pituitary axis can affect the overall growth. The various factors affecting growth in children include:

1. Chronic graft versus host disease;
2. Pulmonary dysfunction;
3. General poor health;
4. Steroid therapy;
5. Direct irradiation effects on skeletal growth and thyroid function.

The most pronounced effects of radiotherapy include hypovascularity and cytotoxic effect on epiphyseal chondrocytes [15,16]. There is increase in height of growth plate due to increase in layers and swelling of the chondrocytes. In chemotherapy treated patients, bone mineral density is reduced. Whenever there is injury to remodeling system, it results in atrophy, osteoradionecrosis and pathologic fractures. In a study when 24 Gy cranial radiation was given at ages between 3-13 years, there was decrease in cranial base five years after treatment [17,18].

Disturbances in Dental Development [19]

Chemotherapy and radiotherapy treated cases are presented with:

- Arrested root development;
- Short V shaped roots with premature apical closure;
- Microdontia;
- Increase in incidence of aplasia;
- Reduction in tooth size;

Levander E et al., have reported regarding External Apical Root Resorption (EARR). They have illustrated a substantive genetic factor susceptible to EARR [20]. After termination of active orthodontic treatment, no apparent increase in root resorption was found. Although, a progressive remodeling of the root surface was evident.

Children undergoing chemotherapy are 2.93 times more likely to experience no dental complications [21]. Child undergoing radiotherapy and/or chemotherapy is 5.07 times more likely to cause root stunting or microdontia. When younger than five years; 14.72 times more chances to develop root stunting or microdontia are seen [22]. The risk of developing microdontia or root stunting dropped in patients who had received radiation over the age of 10 years. Anomalies such as hypodontia, microdontia, enamel hypoplasia and root malformation are recognized frequently after childhood cancer treatment [23].

The risks of increase in odontogenesis increases with treatment

at ages younger than five years and with exposure to high doses of chemotherapeutic agents. Chemotherapy causes thinning, shortening of premolar roots and enamel abnormalities [24].

Effects of Radiotherapy on Oral Cells and Cavity

Radiotherapy can cause disruptions in enamel and dentin formation affecting cells in their mitotic phase as well as in non proliferating cells in very high doses. Radiation doses of 4 Gy can result in dental defects. Nearly, 10 Gy of radiation exposure can permanently damage mature ameloblasts. Greater than 20 Gy radiations can significantly increase incidence of one or more dental anomaly [25].

The various effects seen are:

a. Mucositis:

Mucositis, mouth and throat ulceration are common side effects of radiation therapy. With a radiation dose of 20 Gy, around 80% of salivary function is lost. Immediately after therapy, 80 % of salivary function is lost. These changes remain up to three months after completion of radiotherapy and remain more or less constant throughout life.

Care for mucositis

- Proper Oral hygiene maintenance

To maintain oral moistness and decrease pathogenic flora, anti plaque rinses like isotonic saline or sodium bicarbonate solution is recommended.

Antimicrobial agents like nystatin/amphotericin-B is recommended [26,27]. Analgesic rinses like 2% viscous lidocaine is advisable for oral hygiene maintenance.

- Dietary modifications
- Mucosal protectants

b. Dysfunctional Taste and Malnutrition:

The complications include dysguesia, dysphagia, excessive secretions, nausea, loss of appetite and weight loss. The most prevalent late effect of head and neck cancers is xerostomia which may be a contributing factor towards acute mucositis [28].

Moistening agents are recommended for salivary dysfunction disorders. Cholinergic receptor agonists like pilocarpine can be used [29,30]. Parenteral nutrition is required as an early intervention. The taste sensations can be achieved by the use of Zinc supplements [31].

c. Radiation Caries:

Radiation caries is a rapid, rampant carious process which can be prevented by application of 1% neutral sodium fluoride gel. Fluoride prophylaxis is initiated at least one week before radiation therapy [32].

Orthodontic Treatment and it's Effects on Oral Mucosa

Similar access to orthodontic care for children with chronic health conditions should be provided as that received by a healthy child. Orthodontists will encounter children and adolescents who have been long-term survivors of cancer or with a cancer diagnosed during active orthodontic treatment.

Changes in oral health condition like gingival oozing, petechiae, haematomas, ulcerations, gingival pain, gingival hypertrophy, mucosal pallor, pharyngitis, lymphadenopathy raise concern and a physician's referral becomes mandatory especially when a patient exhibits symptoms without accompanying local causative factors.

Chemotherapy usually causes significant oral complications. Orthodontic appliances when placed in the mouth can cause stress to the oral mucosa. Ulcerations may occur as the regenerative capability of the mucous membrane is impaired [33].

Various strategies are incorporated by the orthodontist while dealing with problems of patients with special care needs:

1. Appliance Selection:

Glossitis, metal taste, gingivitis, peeling lips, erythema multiformae and gingival hypertrophy can arise during the course of orthodontic treatment. These manifestations are associated with corrosive products and ion release from the appliances [34]. Heavy metals can cause damage to DNA by interacting directly with DNA or it's replication.

The most common brackets used in orthodontic practice are manufactured from stainless steel which can produce cytotoxicity due to increased production of free radicals. The free radicals enter the cells and reduce the number of cellular functions. Cancer survivors are already immune-compromised as anti cancer treatment additionally results in a significantly lessened resistance to infections and atrophy of oral mucosa, so stainless steel brackets are best avoided.

Thus, appliance choice would include Nickel free brackets (also called stainless steel with manganese or with low nickel content, less than 5%) [35].

Nickel-sensitive patients should be treated with titanium brackets as a first choice, since these have greater resistance to corrosion and do not release nickel into the oral cavity [36].

2. Force Application:

Applied forces should be optimal and kept low. A low force helps to prevent any untoward root resorption. To affect, this outcome, only force ranging from 20 to 150 grams per tooth might be required [37].

3. Treatment Duration:

The duration of treatment must be kept short. Treatment should be terminated as soon as possible.

4. Technique Selection:

The appliance technique employed must be simple and effective. Orthodontic treatment could be started following a two year event-free patient survival period during which there was no recurrence of disease or secondary malignant neoplasms [38].

The frequency of secondary neoplasms has been reported to be 2.6% to 12.1% at 25 years after the initial diagnosis. As the need for orthodontic extraction is a considered possibility in various situations, the healing has been observed to be uneventful in these circumstances [39]. Growth modification procedures are not successful in these patients as maxillary/mandibular growth centres is affected due to radiotherapy and this can compromise maturation of the craniofacial complex.

Orthodontic Treatment Protocols [40]

AAPD 2013 recommends three objectives for oral care once cancer treatment is complete:

a. Maintenance of optimum oral health;

b. Reinforcement to the patient/parents the importance of optimal oral and dental care for life;

c. Treatment of a dental issue that may arise as a result of the long term effects of cancer therapy.

The treatment of neoplasms results in increased susceptibility to infections and atrophy of the oral mucosa. Mucosal irritation may be minimized by using non-irritating orthodontic appliances. Daily topical fluoride application and regular rinsing with artificial saliva is recommended. One of the concerns with longer orthodontic treatment time is root shortening.

It has been demonstrated that a two to three month pause in treatment after the initial six months of active treatment could reduce the number of patients experiencing advanced root resorption [41].

The general recommendation for all orthodontic patients at risk of root resorption is to take periapical film after six months into active treatment. If progression of the resorption is noted, treatment should be interrupted for three months- active tooth movement stopped.

After the completion of treatment, any removable retainers should be fabricated to fit well and not become a source of irritation, ulceration or infection. Newer brackets are available: nickel-free brackets with low toxicity levels. These brackets may be routinely used in cancer survivors.

Orthodontic treatment is performed electively for all patients, and particularly for children and adolescents with cancer. Children with chronic health conditions deserve the same access to orthodontic care as a healthy child. But orthodontists may need special considerations in treatment planning.

The incidence of Osteoradionecrosis (ORN) is reported at 8.2% when considering extractions in adults receiving head and neck radiotherapy and a threefold higher incidence in males than in females. Fifty percent of all cases of ORN were associated with tooth extractions. Atraumatic extraction procedures may reduce the risk.

Cancer survivors have decreased resistance to infections due to anti-neoplastic treatment and consequently, there is atrophy of the oral mucosa. Any external factor has the potential to irritate the mucosal surface. To minimize the risk, non-irritating orthodontic appliances should be considered.

External root resorption creates concern as sequelae of orthodontic treatment. Longer treatment times are associated with increased root shortening which may be minimised by the use of lighter force levels.

Importantly, genetic factors play a significant role in a patient's susceptibility to external apical root resorption. The general recommendation for all orthodontic at risk patients is to take a periapical film after six months of active treatment. If the film reveals progress of the resorption, treatment should be discontinued for three months. It is not necessary to remove the appliances but the arch wires should be adjusted to a passive stage so that there is no active tooth movement.

Relapse Cases:

In cases of recurrence of cancer during active orthodontic treatment, fixed appliances should be removed and treatment should be discontinued. It minimises the potential for oral complications. Once the patient is considered in remission, orthodontic treatment may be reconsidered [42].

Current Update:

The patient's age at receiving cancer therapy plays a role in determining possible dental complications. Anomalies such as hypodontia, microdontia, enamel hypoplasia, and root malformation are recognized frequently after childhood cancer treatment.

The risks for altered odontogenesis increases with treatment at ages younger than five years and with exposure to higher doses of chemotherapeutic agents.

The mainstay of antineoplastic treatments is chemotherapy as the use of radiation therapy has been declining. This is a positive outcome as radiation potentially affects facial growth and tooth development.

CONCLUSION

The fundamental disease needs to be understood by the orthodontist before initiating treatment. The cancer process must be adequately assessed and the aim of treatment modified to achieve treatment objectives based on the general health and well-being of the patient. A comprehensive intervention strategy needs to be followed where the dental concerns of the patients, their parents and their health care providers need to be identified. Evidence based methodology needs to be followed.

REFERENCES

[1] Young JL, Ries LG, Silverberg E, Horm JW, Miller RW. Cancer incidence, survival, and mortality for children younger than age 15 years. Cancer. 1986;58:598–602.
[2] Barbara S, Bryan W. Orthodontic management of patients with hematologic malignancies. Am J Orthod Dentofacial Orthop. 1996;109:575-80.
[3] Dunn NL, Russell EL, Maurer HM. An update in paediatric oncology. Paediatr Dent. 1990;12:10–19.
[4] Sheller B, Williams B. Orthodontic management of patients with hematologic malignancies. Am J Orthod Dentofac Orthop. 1996;109:575-80.
[5] Ottmann OG. Treatment of Ph/BCR-ABL positive ALL. Haematologica 2005.
[6] Linet MS, Ries LAG, Smith MA. Cancer surveillance series: recent trends in childhood cancer incidence and mortality in the United States. J Natl Cancer Inst. 1999;91:1051-58.
[7] Nordic Society of Paediatric Haematology and Oncology. Childhood cancer in the Nordic countries. Report on epidemiologic and therapeuticresults, NOPHO, Aalborg 2000.
[8] Sklar C, Constine LS. Chronic neuroendocrinological sequelae of radiation therapy. Int J Radiation Oncol Biol Phys. 1995;31:1113-21.
[9] Forsberg CM, Dahllöf G, Ringdén O. Facial growth and morphology in long-term survivors after bone marrow transplantation. Eur J Orthod. 1989;11:332-40.
[10] Sonis AL, Tarbell N, Valachovic RW. Dentofacial development in long-term survivors after acute lymphoblastic leukaemia. A comparison of three treatment modalities. Cancer. 1990;66:2645-52.
[11] Denys D, Kaste SC, Kun LE, Chaudhary MA, Bowman LC, Robbins KT. The effects of radiation on craniofacial skeletal growth: a quantitative study. Int J Pediat Otorhinolaryngol 1998; 45:7–13.
[12] Fromm M, Littman P, Raney R. Late effects after treatment of twenty children with soft tissue sarcomas of the head and neck. Cancer. 1986;57:2070-76.
[13] Jahnukainen K, Karsila TS, Peltomäki T. Disturbances in craniofacial morphology in children treated for solid tumours. Oral Oncol. 2001;37:586-92.
[14] Moell C, Garwicz S, Westgren U. Disturbed pubertal growth in girls treated for acute lymphoblastic leukaemia. Paediatr Hematol Oncol. 1987;4:1-5.
[15] De-Smet AA, Kuhns LR, Fayos JV. Effects of radiation therapy on growing long bones. Am J Roentgenol. 1976;127:935-39.
[16] Samuelsson BO, Márky I, Rosberg S, Albertsson-Wikland K. Growth and growth hormone secretion after treatment for childhood non-Hodgkin's lymphoma. Med Pedatr Oncol. 1997;28:27-34.
[17] Dahllof G, Huggare J. Orthodontic considerations in the pediatric cancer patient:A Review. Semin Orthod 10: 266-276.
[18] Dahllöf G, Forsberg CM, Ringdén O et al: Facial growth and morphology in long-term survivors after bone marrow transplantation. Eur J Orthod 1989; 11:332-340.
[19] Mitu KM, Łoboda M, Marcinkowska MA, Durka ZM, Pawłowska E. Orthodontic treatment in oncological patients. Przegl Lek. 2015;72:243-45.
[20] Levander E, Malmgren O, Eliasson S. Evaluation of root resorption in relation to two orthodontic treatment regimens. A clinical experimental study. Eur J Orthod. 1994;16:223-38.
[21] Deboni AL, Giordani AJ, Lopes NN, Dias RS. Long term effects in patients treated with radiochemotherapy for head and neck cancer. Support Cancer Care. 2012;20:555-68.
[22] Gabrielle PA, Bruno CJ, Claudia SM, Luis GS, Addah RF. A review of the biological and clinical aspects of radiation caries. J Contemp Dent Pract. 2009;10:1-11.
[23] Hong CH Fonseca DA. Consideration in the paediatric population with cancer. Dent Clin N Am. 2008;52:155-81.
[24] Kaste SC, Goodman P, Leisenring W, Stovall M, Hayashi RJ, Yeazel M, et al. Impact of radiation and chemotherapy on the risk of dental abnormalities. Cancer. 2009;115(24):5817-27.
[25] Otmani N. Oral and maxillofacial side effects of radiation therapy in children. J Can Dent Associ. 2007;73:257-61.
[26] Kostler WJ, Hejna M, Wenzel C, Zielinski CC. Oral mucositis complicating chemotherapy and/or radiotherapy: options for prevention and treatment. CA Cancer J Clin. 2001;51:290–315.
[27] Hancock PJ, Epstein JB, Sadler GR. Oral and dental management related to radiation therapy for head and neck cancer. J Can Dent Assoc. 2003;69:585–90.
[28] Moller P, Perrier M, Ozsahin M, Monnier P. A prospective study of salivary gland function in patients undergoing radiotherapy for squamous cell carcinoma of the oropharynx. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2004;97:173–89.
[29] Konings AW, Coppes RP, Vissink A. On the mechanism of salivary gland radiosensitivity. Int J Radiat Oncol Biol Phys. 2005;62:1187–94.
[30] Gornitsky M, Shenouda G, Sultanem K, Katz H, Hier M, Black M, et al. Double-blind randomized, placebo-controlled study of pilocarpine to salvage salivary gland function during radiotherapy of patients with head and neck cancer. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2004;98:45–52.
[31] Ripamonti C, Zecca E, Brunelli C, Fulfaro F, Villa S, Balzarini A. A randomized, controlled clinical trial to evaluate the effects of zinc sulfate on cancer patients with taste alterations caused by head and neck irradiation. Cancer. 1998;82:1938–45.
[32] Spak CJ, Johnson G, Ekstrand J. Caries incidence, salivary flow rate and efficacy of fluoride gel treatment in irradiated patients. Caries Res. 1994;28:388–93.

[33] Marucci G, Tabacow LB, Weckx LL. Oral manifestations of leukaemia. Ear Nose Throat J. 1990;69(5):341-42, 345-46.
[34] Deroze D, Camps J, Mockers O. Cytotoxicity of orthodontic bands, brackets and archwires in vitro. Dent Mater. 2002;18:311-17.
[35] Gosch CS, Ribeiro DF, Costa I, Lenza MA, Costa MT. In vitro evaluation of corrosion and cytotoxicity of orthodontic brackets. J Dent Res. 2007;86:441-45.
[36] Hamula DW, Sernetz F, Hamula W. Pure titanium orthodontic brackets. J Clin Orthod. 1996;30:140-44.
[37] Krishnan V, Davidovitch Z. Cellular, molecular and tissue-level reactions to orthodontic force. 2006;129:469e.1-460e.32.
[38] Raber Durlacher JE, Elad S, Barasch A. Oral mucositis. Oral Oncol. 2010; 46:452-6.
[39] Dahllöf G, Jönsson A, Ulmner M, Huggare J. Orthodontic treatment in long term survivors after paediatric bone marrow transplantation. Am J Orthod Dentofac Orthop. 2001;120:459-65.
[40] American Academy of Paediatric Dentistry (AAPD). Guideline on dental management of paediatric patients receiving chemotherapy, hematopoietic cell transplantation, and/or radiation, 2013.
[41] Levander E, Malmgren O, Eliasson S. Evaluation of root resorption in relation to two orthodontic treatment regimens. A clinical experimental study. Eur J Orthod. 1994;16:223-28.
[42] Mullally B, Burden D, Sandler J. Orthodontic treatment of patients with medical disorders. Eur J Orthod. 2001;23:363-72.

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