Dental Developmental Defects in Survivors of Childhood Acute Lymphoblastic Leukemia

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Background

- The American Academy of Pediatric Dentistry (AAPD) recognizes that the pediatric dental professional plays an important role in the diagnosis, prevention, stabilization, and treatment of oral and dental problems that can compromise the child's quality of life before, during, and after immunosuppressive therapy and/or head and neck radiation.[1]
- Cancer treatment, both chemotherapy and radiation in childhood can result in long-term dental developmental defects, including microdontia, V-shaped roots and taurodontism. [2]
- Risk factors for developmental disturbances include: young age at diagnosis (≤3 years of age), h/o hematopoietic stem cell transplantation, use of multiple class of chemotherapeutic agents (≥ 4 classes) and the use of heavy metal agents (e.g. cisplatin).[2]
- Holtta's Defect Index (HDI) was developed in 2002 by Holtta to assess dental defects in recipients of childhood bone marrow transplantation (BMT).
- The method uses an orthopantomogram (OPG) to assess each tooth systematically, and expresses, using a single figure, the total defects of the permanent dentition.[3]
- The HDI comprises 3 components: tooth aplasia, microdontia, and root/crown ratios.[3]
- The following table depicts the defect points given per tooth.

Defect	Defect Points per Tooth
Not determined due to poor visibility, incomplete root formation or breakdown of crown	0
Root-crown ratio	
>1.6 (no disturbance)	0
1.2-1.6 (mild disturbance)	1
0.9-1.1 (severe disturbance)	2
<0.9 (very severe disturbance)	3
Microdontia	4
Missing tooth (not extracted)	5

(Hsieh SG 2011)[4]

Objectives

Specific Aim: To describe the prevalence of dental defects as measured through HDI in survivors of childhood acute lymphoblastic leukemia

Exploratory Aim: HDI for subgroups of survivors based on age at ALL diagnosis (greater than or less than 4 years of age at diagnosis) and history of cranial radiation.

Hypothesis: When compared to an age/gender matched control of a normative population, children with ALL will have a greater HDI, most significantly correlated to patient's age at diagnosis of ALL

Methods

This case-controlled, retrospective chart review evaluated panoramic radiographs of patients treated for ALL by the Dana-Farber Cancer Institute (protocols 05-001 and 11-001) and seen in the Boston Children's Hospital Department of Dentistry.

A descriptive analysis of 21 patients' panoramic radiographs were performed using the HDI. Two examiners reviewed each panoramic radiograph, and their results were averaged together to get the calculated HDI score. The study group was all 21 patients on protocols 05-001 and 11-001 that were evaluated. Within the study group, there was a more defined inclusion group that is described below.

- Fourteen of the 21 patients evaluated meet the following inclusion criteria:
  - General
    - Treated on DFCI ALL Consortium Protocols 05-001 or 11-001
    - Diagnosed with ALL prior to age 16 years
    - In continuous remission and s/p completion of ALL-directed therapy for at least 1 year at time of radiograph
  - Dental
    - A tooth was deemed missing if a second premolar or molar was not visible on the OPG by age 5 years
- Descriptive analysis of the non-qualifying seven patients was also performed to evaluate HDI for patients undergoing transplants, relapsed cancer treatment, CAR T-cell therapy, and other care.
- The study group was compared to an age/gender matched control group of a normative population
- A chi-squared analysis was performed comparing the rates of dental development defects in the study and control groups.

Results

Average Age	Years
At Diangosis	4.3
At Panoramic Radiograph	11.3

Received Cranial Radiation?	n
No	13
Yes	8
Total	**21**

Sex	n
Female	10
Male	11
Total	**21**

Received Stem Cell Transplant?	n
No	17
Yes	4
Total	**21**

Study Group	n
05-001	13
11-001	8
Total	**21**

Had Relapse Event?	n
No	15
Yes	6
Total	**21**

Table 1. Summary of descriptive characteristics of the study group

Root-Crown Ratio Affected?	Study Group (n)	Control Group (n)
No	11	19
Yes	10	1
Total	**21**	**20**

Microdontia?	Study Group (n)	Control Group (n)
No	11	20
Yes	10	0
Total	**21**	**20**

Agenesis?	Study Group (n)	Control Group (n)
No	19	19
Yes	2	1
Total	**21**	**20**

Table 2. Summary of the number of patients with a dental developmental defect in the study and control groups

Top Five Most Common Teeth Affected:

A. Root-Crown Ratio

Tooth #	# of Times Affected
24	5
25	5
26	4
23	3
3	2

B. Microdontia

Tooth #	# of Times Affected
15	7
31	4
18	4
2	2
16	2

C. Agenesis

Tooth #	# of Times Affected
20	2
29	2
13	2
26	1
23	1

Table 3. Summary of most common teeth affected per HDI component in the study group

Description		Average HDL Score
Study Group		9.7
By Age		
	≤ 3 years	10.3
	≥ 4 years	8.9
Inclusion Group		9.4
Received Cranial Radiation		11.0

Table 4. Comparisons of the average HDI for different subgroups within the study group. First the average HDI for all 21 study group patients was calculated. Second, the average HDI was calculated for patients ≤ 3 years and ≥ 4 years in age. Third, the average HDI for the inclusion group, the 14 patients who met all inclusion criteria, was calculated. Lastly, the average HDI was calculated for patients who received cranial radiation.

Of the 299 patients treated on the protocol, 49 patients had panoramic radiographs taken at the Department of Dentistry. Of the 49 patients with a panoramic radiograph, 28 were excluded due to non-diagnostic imaging or because the radiograph was taken prior to oncology treatment. The patients evaluated were diagnosed with cancer between 2007 and 2014. The average age at ALL diagnosis was 4.3 years (range 1-15) **(Table 1)**

- In the study group **(Table 2)**
  - 10 patients (48%) demonstrated root-crown ratio defects
  - 10 (48%) had at least one microdont
  - 2 (9%) presented with agenesis of teeth
- Compared to healthy age/gender matched controls, only 2 of 20 (10%) demonstrated any of the 3 measured defects **(Table 2)**

- The most likely teeth to have a root-crown ratio disturbance were the mandibular central incisors, followed by the mandibular lateral incisors. The second molars (#15, 18, 31) had the highest occurrence of microdontia. Lastly, the second premolars (mandibular and maxillary arch) were the most frequent missing teeth seen in the study group. **(Table 3)**

- Patients ≤ 3 years old at cancer diagnosis had an average HDI of 10.3, compared to patients diagnosed ≥ 4 years old, had an average HDI of 8.9. While the patients that received cranial radiation had an average HDI of 11.0 **(Table 4)**

Root-crown ratio defects were significantly higher in the study population (P >.004) and microdontia was significantly higher in the study population (p >0.001). There is no significant association between oncology treatment and agenesis.

Conclusions

Oncology treatment (chemotherapy, cranial radiation, and other care) may result in long-term dental developmental defects, including microdontia, agenesis, and root/crown ratio defects. The results of this study, were comparable to, but higher, than a previous study that found the following incidences of microdontia (30.76%) and agenesis (20.4%) in patients with varying cancer diagnoses[2]. Differences can be attributed to our small sample size used. In our study, the patients who received cranial radiation and that were diagnosed at a younger age, had a higher average of dental developmental defects compared to their comparison groups. Future studies should continue to assess these defects and evaluate their incidence with more modern oncology treatments.

References:

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