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Effect of chemotherapy on dental maturity in children with hematological malignancies

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Abstract

Dental maturity or dental age was determined in 44 children with hematological malignancies treated with chemotherapy. No significant difference was observed between the chronological and dental age in children treated with chemotherapy compared to healthy controls. With regard to the number of erupted permanent teeth, no significant differences could be found between the two groups. The results indicate that chemotherapy given to children with hematological malignancies did not interfere with dental maturity or eruption of permanent teeth.

The impressive advances made in treating childhood cancer have resulted in an increasing population of patients who apparently are cured of their disease. With current chemotherapy programs, more than 70% of standard risk patients with hematological malignancies will remain in complete remission (Gustavsson et al. 1981). This progress now has directed interest to the late sequelae as a consequence of both the disease and the therapy given (Byrd 1985). The dental health of this patient group during and after treatment is therefore of importance since it can affect their future quality of life. Children treated with chemotherapy experience a wide range of acute oral complications such as ulcers, bleeding, and fungal and bacterial infections (Fleming and Kinirons 1986; Dahllöf et al. 1988a).

Long-term survivors of childhood cancer treated with chemotherapy alone exhibit normal somatic growth and development (Wells et al. 1983, Robison et al. 1985). When chemotherapy is combined with cranial irradiation, growth hormone deficiency frequently is observed (Shalet et al. 1976) as well as reduced growth measured as height velocity (Wells et al. 1983; Robison et al. 1985).

Data are now accumulating on the long-term effects of childhood cancer treatment on the oral tissues. An increased incidence of dental abnormalities such as enamel hypoplasia and dental root disturbances have been reported (Maguire et al. 1987; Rosenberg et al. 1987; Dahllöf et al. 1988b). A delayed eruption of permanent teeth also has been found in some patients (Adatia 1968; Purdell-Lewis et al. 1988).

The aim of the present investigation was to study dental development and maturity in children treated with chemotherapy for hematological malignancies.

Patients and Methods

The study population consisted of 44 pediatric subjects (32 M and 12 F) who presented to Huddinge Hospital between September 1979 and October 1987 for bone marrow transplantation (BMT) secondary to hematological malignancy (Table 1). Attempts at remission induction (prior to BMT) varied in the study population (1 to 5), as did the time interval from initial diagnosis to BMT (0.1–6.5 years).

TABLE 1. Diagnoses and Numbers of Remission Induction Therapies in 44 Children Treated With Chemotherapy

Diagnosis	*Number of patients*
Acute lymphoblastic leukemia	
1st remission	2
2nd remission	20
3rd – 5th remission	6
Acute myeloid leukemia	
1st remission	9
2nd remission	3
Chronic myeloid leukemia	1
Acute erythrocyte leukemia	1
Lymphoma	2
Total	44

Children with acute lymphoblastic leukemia (ALL) were treated according to regimens that included methotrexate, vincristine, doxorubicin, cyclophosphamide, and prednisolone. Children with acute myeloid leukemia (AML) were treated with daunorubicin, cytarabine, and tioguanine.

A panoramic radiograph was obtained in each child at different intervals (0.1–6.5 years) after initial diagnosis of the disease and start of remission induction therapy. The distribution of subjects relative to the time interval can be seen in Fig 1. For each patient treated with chemotherapy a panoramic radiograph of two age

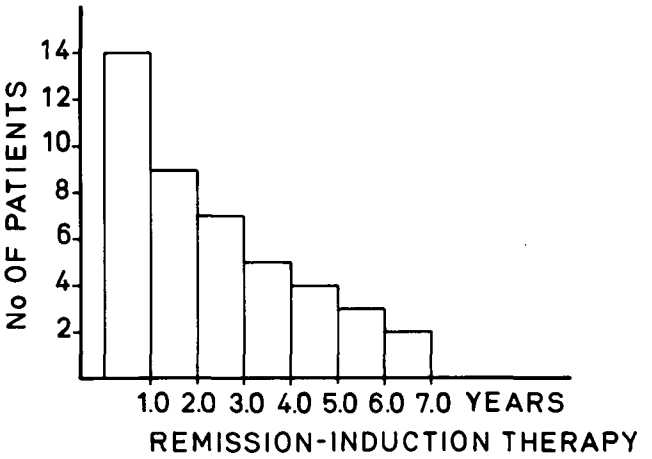

Fig 1. Time interval between diagnosis and end of remission-induction therapy.

and sex matched healthy controls were obtained through the Department of Orthodontics. Dental maturity or dental age was determined according to the seven-teeth method described by Demirjian and Goldstein (1976). When this method is used, the stages of mineralization of the seven left mandibular teeth are assessed using an eight-stage scale. The stage of development of each tooth is given a maturity score. The total dental maturity is the sum of the scores of the individual teeth. Two of the authors rated all 132 radiographs at two different occasions with a three week interval. From the clinical examination of the patients, the number of erupted permanent teeth was recorded.

Results

The mean chronological age was 9.7 years in the chemotherapy and control groups. The mean estimated dental age in the chemotherapy group varied from 10.0 to 10.6 years and between 10.2 and 10.9 years in the control groups (Table 2).

There was no statistically significant difference between the chronological and dental age in the chemotherapy group compared to the two control groups (Table 3, see top of next page). The difference between chronological and dental age varied between -0.44 years and -1.06 in the chemotherapy group, and between -0.49 and -1.10 in the control groups.

The interexaminer variation in the three groups varied from -0.05 to -0.62 years, and the intra-examiner variation varied between -0.06 and -1.16 years. None of the differences were statistically significant.

The use of the Demirjian and Goldstein (1976) scoring system for assessing the dental maturity constantly overestimated the true chronological age in all age groups. There was no correlation between the number of remission induction therapies and difference between chronological and dental age ($r = 0.158$). Neither was there any correlation between the period from diagnosis to examination and difference between chronological and dental age ($r = -0.157$). With regard to the number of erupted permanent teeth, no significant differences could be found between children treated with chemotherapy compared to healthy controls (Table 4, see next page, lower right).

Discussion

The results of this study indicate that chemotherapy given to children with hematological malignancies does not affect the dental development in terms of dental age or dental maturity. Several methods for estimation of chronological age have been devised (review Demirjian 1978). The method described by Demirjian and Goldstein (1976) has been proposed for age determination in adopted children of unknown age by the Swedish Board for Health and Welfare. The difference between chronological and dental age in the present material was of the same magnitude as that reported by Hägg and Matsson (1985) who used this method in healthy Swedish children. The intraexaminer varied in examiner 1 between -0.06 and -0.27 years which is in accordance with the results by Hägg and Matsson (1985). Overestimation of the dental age using the scoring system according to

TABLE 2. Mean Values (*X*) and Standard Deviations (SD) of Chronological Age and Dental Maturity (Age) Scores (Demirijan & Goldstein 1976) in Children Treated With Chemotherapy (N = 44) and Two Control Groups

	Chemotherapy Group (N = 44)		*Control Group 1 (N = 44)*		*Control Group 2 (N = 44)*	
	X	*SD*	*X*	*SD*	*X*	*SD*
Chronological age	9.7	3.2	9.7	3.2	9.7	3.2
*Dental maturity scores**						
Examiner 1, 1st	10.0	3.8	10.3	3.6	10.2	3.4
Examiner 1, 2nd	10.3	3.8	10.3	3.7	10.2	3.8
Examiner 2, 1st	10.6	3.8	10.8	3.6	10.9	3.5
Examiner 2, 2nd	10.5	3.8	10.7	3.6	10.5	3.4

* Dental maturity was assessed by two examiners on two separate occasions.

TABLE 3. Comparison Between Chronological Age and Dental Maturity Scores in Chemotherapy and Control Groups. d = Difference Between Chronological and Dental Age.

	Chemotherapy Group d_1	*Control Group 1* d_2	*Control Group 2* d_3	*t-value** d_1-d_2	d_1-d_3	d_2-d_3
Difference between chronological and dental age						
Chronol-Exam 1:1	−0.44	−0.50	−0.49	0.26	0.20	−0.07
Chronol-Exam 1:2	−0.70	−0.56	−0.76	−0.54	0.23	0.73
Chronol-Exam 2:1	−1.06	−0.97	−1.10	−0.36	0.17	0.53
Chronol-Exam 2:2	−0.89	−0.90	−0.71	−0.04	−0.67	−0.73
Intraexaminer variation						
Exam 1:1-Exam 1:2	−0.26	−0.06	−0.27	−1.43	0.08	1.40
Exam 2:1-Exam 2:2	−1.16	−0.07	−0.39	0.70	−1.35	−2.17
Interexaminer variation						
Exam 1:1-Exam 2:1	−0.62	−0.47	−0.62	−0.94	−0.03	1.00
Exam 1:2-Exam 2:2	−0.19	−0.34	−0.05	0.91	−1.22	−1.88

* Student's *t*-test, * $P < 0.05$.

Demirjian and Goldstein (1976) also has been reported by Hägg and Matsson (1985).

In children treated with chemotherapy for ALL, a temporary reduction of somatic growth was found during active treatment, whereas normal growth is found three years after the first induction therapy (Herber et al. 1985; Clayton et al. 1988). This is in contrast to the observations in children treated with chemotherapy in combination with cranial irradiation. In those patients a permanent reduction of somatic growth is found (Wells et al. 1983; Robison et al. 1985; Kirk et al. 1987).

In the study by Herber et al. (1985), skeletal age was studied using the TW_2-method (Tanner et al. 1975) in 34 children, of whom 29 had received cranial or spinal irradiation. They found no significant difference between chronological and skeletal age in this group of patients. These findings regarding skeletal age are in accordance with the results concerning dental age found in the present study. Two previous studies (Adatia 1968; Purdell-Lewis et al. 1988) have discussed dental maturity in patients treated with chemotherapy. Adatia (1968) found delayed eruption in one of 13 patients treated with cyclophosphamide, methotrexate, and vincristine for Burkitt's tumor. Purdell-Lewis et al. (1988) found a delayed tooth formation in 8 of 45 long-term survivors of childhood cancer treated with chemotherapy. The method for assessing the delayed tooth formation was not described in any of these studies. Data from animal studies suggest that cytotoxic drugs such as cyclophosphamide and vincristine have a temporary effect on amelo- and dentinogenesis (Stene 1979; Adatia and Berkovitz 1981). In contrast to the study by Purdell-Lewis et al. (1988), we could not observe any significant difference regarding the numbers of erupted permanent teeth between the two groups.

In conclusion, the present study indicates that chemotherapy given to children with hematological diseases has no interference with dental maturity or eruption of permanent teeth.

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TABLE 4. Mean Number (X) and Standard Deviations (SD) of Erupted Permanent Teeth in Children Treated With Chemotherapy Compared to Normal Controls

Age	*Number of Patients*	*Chemotherapy Group (N = 44)* X	SD	*Number of Patients*	*Control Group (N = 88)* X	SD
4	2	0.0		4	0.0	
5	2	0.0		4	0.0	
6	2	5.0	1.4	4	8.6	1.9
7	9	8.3	3.2	18	8.7	2.9
8	5	10.8	2.7	10	10.2	5.1
9	6	13.0	2.1	12	13.6	4.8
10	4	15.5	3.3	8	16.8	5.5
11	2	18.0	3.4	4	18.6	5.7
12	3	27.7	0.6	6	26.0	4.0
13	4	27.5	1.0	8	25.5	3.6
14	1	28.0		2	27.3	1.0
15	4	28.0	0.0	8	27.0	1.7

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Health care spending up

Each day this year, Americans will spend $200 million more on healthcare than they did last year. At year end, the total will be $620 billion, up from $550 billion in 1988.

In 1987, doctors and hospitals paid $8 billion in malpractice insurance premiums. In Florida, obstetricians paid annual premiums of $153,000; malpractice insurance costs for each baby delivered in Florida were $921. Almost 60% of the premium dollars go to lawyers, insurers, and the courts.

The $2500 we'll spend this year for each man, woman, and child in the U.S. is 50% more than the next-highest-spending nation, Canada; more than twice that in Japan; and almost triple that in Great Britain. Yet each of these nations has lower infant mortality rates and similar longevity, according to Joseph Califano, Jr., writing in the New York Times.

The cost of dental services rose by an average of 0.7% in March 1989, according to the Cons*umer Price Index*. For all items, the increase was 0.6%.

Also in March, the cost of physician services rose by 0.7%, hospital room rates by 0.5%, medical care by 0.6%, food by 0.5%, commodities by 0.8%, and services by 0.5%.