

Caries Experience of Leukemic Children During Intensive Course of Chemotherapy

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Objective: To determine the incidence of dental caries in 64 leukemic children who received dental treatment before the initiation of chemotherapy and had intensive oral care during the course. **Design:** Caries experience (deft/DMFT), white-spot lesions (enamel demineralization), premature primary molar extractions and carious first permanent molars were investigated before and after intensive therapy. **Setting:** Pediatric Dental Care Unit and Department of Pediatric Hematology, Faculty of Medicine, Uludağ University. **Results:** The dental caries level was insignificantly higher following chemotherapy compared to the initial caries level. However, the prevalence of white-spot lesions was significantly increased during the course. Caries level in 30 subjects (47%) remained stable. **Conclusion:** Caries level in leukemic children, who were not caries-free before chemotherapy, could be stabilized by caries prevention methods such as frequent topical fluoride applications and fissure sealants, intensive oral care and improved self-care practices.

Keywords: caries experience, intensive chemotherapy, childhood leukemia

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INTRODUCTION

Chemotherapy has been widely used for the treatment of leukemia and may have adverse effects on the oral cavity.¹ Various reports have indicated the relationship between dental caries prevalence and chemotherapy.²⁻⁵ These studies suggested that leukemic children had more carious teeth compared to healthy subjects. Oral mucositis, xerostomia, oral fungal infections, gingival bleeding, and dental abnormalities are also frequent.^{1,6,7} Therefore, children with leukemia are considered to be a high risk group for dental care. However, there has been limited amount of research focusing on effective prevention of dental caries during the intensive course of chemotherapy as a part of leukemia nursing. Thus, the purpose of this study was to determine the caries experiences of leukemic children who received urgent dental treatment prior to chemotherapy and intensive oral health care during the intensive course.

METHODS

There were 144 children admitted with the diagnosis of cancer de novo to Uludağ University Hospital for the treatment. Of them, 64 children diagnosed as leukemia [Acute lymphoblastic leukemia (ALL) (n=35) and acute myeloblastic leukemia (AML) (n=29)] were eligible for the study. Informed written consent was obtained from each family before chemotherapy. The study was approved by the ethics review committee of Uludağ University, Faculty of Medicine, Bursa, Turkey.

All children with ALL were treated according to chemotherapy protocol of BFM-95 of which the intensive period ranged between 6 to 8 months before the initiation of maintenance therapy. On the other hand, children with AML received MRC-UK-12 protocol of which this period was considered to be over after completing the whole courses, usually taking 7 to 10 months.

A systematic and precise dental examination was performed on every child by a pediatric dentist. The first dental examination was performed as soon as possible before chemotherapy was initiated. The visual oral findings included caries experience indices for decayed-missed-filled teeth in the permanent dentition (DMFT) and decayed-exfoliated-filled teeth for primary dentition (deft) were collected according to the criteria of the WHO Oral Health Surveys Basic Methods.⁸ Panoramic radiographs were taken to identify the present dental health status of all subjects. Then, children continued their urgent dental treatments prior to intensive course initiated. Light-cured glass-ionomer cement and compomer material were chosen for the restorations of primary teeth whereas composites were preferred for the restorations of permanent teeth. All the sound permanent

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first primary molars were sealed with fissure sealants. Then, the deft and DMFT indices were recalculated for each subject. These scores obtained after urgent dental treatments were considered as the caries status of all subjects prior to intensive therapy. An individual oral care guideline specific to oral mucositis prevention, basic oral health activities about tooth-brushing and flossing, fluoride usage, and adequate nutrition was instructed to parents. Brush-on neutral sodium fluoride gel applications were repeated every day before bed-time during the course. Fluoride gel application was interrupted during the period of which the subjects had oral mucositis and the application was followed as soon as the lesions resolved (Table 1). Children were monitored once a week to reinforce a high standard of oral hygiene, to be sure that all children and parents were following the guideline, and reduce the severity of the mucositis while they were on chemotherapy. In the case of thrombocytopenia ($<50 \times 10^9/L$), the children were not allowed to brush their teeth and the trained parents were suggested to use a sterile gauze embedded in sodium bicarbonate solution to clean the teeth, gums and tongue. All children received oral antifungal agents when needed during the intensive course. The final dental examination of 64 patients was performed after successfully completing intensive therapy to determine the effects of oral health care activities on caries experience.

White-spot lesions (enamel demineralization) were also investigated in both examinations (before the onset and after the completion of therapy) to reveal current caries activity of the children following the course. The prevalence of pre-

ture loss of primary molars and caries on first permanent molars were investigated as an indicator of inadequate dental health care during the therapy.

The data was analyzed using SPSS (13.0). Parametric and/or non-parametric tests were chosen by using Kolmogorov-Smirnov and Shapiro-Wilk tests. Paired student t-test was used to compare the caries scores which were obtained before intensive course and maintenance therapy. A probability value less than 0.05 were considered significant.

RESULTS

Mean age was 8.9 ± 3.2 years ranging between 4 and 13 years. Of 64 children, 39 were males and 25 were females. At the beginning of the study, eight children (12 %) were in permanent dentition stage whereas 18 (28%) of the subjects had primary teeth. The rest ($n=38$, 60%) were in mixed dentition.

Dental health prior to intensive chemotherapy course

Initial dental examination

The mean score of deft was found 6.7 ± 0.8 revealed that approximately 6 primary teeth of all subjects were carious ($dt=6.3 \pm 0.8$). et and ft scores were constituted the minor part of deft index and determined as 0.4 ± 0.2 and 0.02 ± 0.0 in respectively. The score of DMFT index was 4.2 ± 0.3 . The DT component (3.6 ± 0.6) constituted the most of the index indicated that at least 4 permanent teeth were carious in all subjects. MT and FT were also constituted the insignificant part

Table 1. Intensive oral care guideline specific to oral mucositis followed by leukemic children during intensive course of chemotherapy.

Perform oral care instructions according to the following procedures at the 1st, 2nd and 3rd week after the initiation of intensive chemotherapy (Days 1-21):

After waking up

- Brush teeth with a suggested toothbrush and toothpaste*. Place the brush on your teeth at a 45-degree angle against the gums and move it back and forth gently in short strokes for 90 seconds. Gently clean and massage your tongue with the toothbrush.
- Rinse your mouth with 60 ml sodium bicarbonate solution for 30 seconds. Swish and spit out. Do not swallow the solution.

Within 30 minutes after each meal

- Brush teeth with a suggested toothbrush and toothpaste*. Place the brush on your teeth at a 45-degree angle against the gums and move it back and forth gently in short strokes for 90 seconds. Gently clean and massage your tongue with the toothbrush.
- Rinse your mouth with 60 ml sodium bicarbonate solution for 30 seconds.

Before bed time

- Brush teeth with a suggested toothbrush*. Place the brush on your teeth at a 45-degree angle against the gums and move it back and forth gently in short strokes for 90 seconds. Gently clean and massage your tongue with the toothbrush.
- Rinse your mouth with 60 ml sodium bicarbonate solution for 30 seconds. Swish and spit out. Do not swallow the solution.
- Brush the teeth with a suggested amount (pea-size) of neutral sodium fluoride gel for 60 seconds*. Spit out and do not swallow the solution. Do not drink or eat anything after brushing for at least 30 min.

* If the platelet counts of your child are below $50 \times 10^9/L$, consult your nurse, dentist or physician.

Table 2. The mean caries experiences in both dentitions before the onset and after the completion of chemotherapy.

Caries Experience	Following the urgent dental treatment (Before the onset of chemotherapy) (I)	After chemotherapy (II)	P
	Mean±sd	Mean±sd	
deft	5.6±0.7	6.35±0.3	NS
dt	4.3±0.5	4.7±0.5	NS
et	0.0±0.0	0.35±0.0	NS
ft	1.3±0.2	1.3±0.2	NS
DMFT	3.1±0.6	3.8±0.5	NS
DT	1.8±0.1	2.5±0.5	NS
MT	0.3±0.0	0.3±0.0	NS
FT	1.0±0.2	1.0±0.2	NS

NS: P>0.05 (Non-significant).

of the index as in the deft index and calculated 0.1 ± 0.0 and 0.5 ± 0.2 , respectively. Forty-six children out of 64 (72%) had at least one first permanent molar teeth erupted ($n=138$) at the beginning of the study. Out of the 138 teeth, 47 (34%) were carious.

Following the urgent dental treatment

The scores of deft and DMFT are presented in Table 2. The mean carious primary teeth score (dt) was decreased to 4.3 ± 0.5 . The DT score was found 1.8 ± 0.1 after the urgent dental treatment showed that almost two permanent teeth were left carious prior to intensive chemotherapy. The prevalence of white-spot lesions (enamel demineralization) was found 23.7%. Following the urgent dental treatments were completed, twenty-two children (35%) required extraction of at least one primary molar tooth ($n=25$) prematurely because of profound caries and/or dental root infection. Ninety-one sound first permanent molars (66%) were sealed.

Dental health after completing intensive chemotherapy course

Higher dt (4.7 ± 0.5) and DT (2.5 ± 0.5) scores were collected compared to the initial scores of the children. This finding was indicated non-significance ($P>0.05$). However, the mean numbers of filled (f & F) and exfoliated (e) and missed (M) teeth was calculated same as the previous values presented in the manuscript. Therefore, these scores were transferred same as the initial values since there was no change in the scores between the two evaluation periods. The higher carious teeth means (dt & DT) after the therapy were increased total caries experiences (deft & DMFT) in the study. However, the difference between the evaluation periods was insignificant ($P>0.05$, Table 2).

Re-examination of the subjects who had caries on their first permanent molars before the intensive course revealed no recurrence. In addition to that, all the sealed first permanent molars were detected caries free during the examination. White-spot lesions (enamel demineralization) were detected 64.8% of all the subjects which was significantly higher prior to intensive course ($P<0.001$). Premature extrac-

tion (loss) of primary molar was not required since there were no root infections and/or profound caries involving primary molars during chemotherapy. Thirty subjects out of 64 (47%) remained stable for their caries status.

DISCUSSION

This cohort provided data on dental caries experience of leukemic children before and after intensive chemotherapy courses. The other reports for this subject were usually related to the late dental effects of the therapy, but not considered the specific changes in a period of time as presented in this study.¹⁰⁻¹⁶

According to the data from WHO, Turkey had high caries prevalence, which was in contrast to the reports from western countries where the prevalence of the entire population was low.¹⁷⁻¹⁸ The child population receives low level of dental care and do not have the benefit of advice to prevent caries starting from an early age, indicating dental caries is a major public health problem in Turkey.¹⁹⁻²¹ In addition to that, children with blood diseases such as hemophilia or leukemia also do not receive regular dental recalls as in the healthy child population. However, this situation is different in developed countries where all pediatric hemophiliacs and leukemic children attended for dental care during their follow-up and received a more vigorous dental prevention program than the entire healthy population. Therefore, caries scores of all subjects in this study were prominent prior to chemotherapy.

Caries activity of leukemic children can be increased by various factors such as the harsh effects of the stomatotoxic therapy on dental and oral tissues, the alteration in chemical structure and viscosity of saliva, and the health of the teeth at the diagnosis of leukemia.^{2,22,23} Therefore, the final dental examination performed after the intensive course revealed that dental caries scores increased in both dentitions compared to the initial scores. However, the increase was non-significant ($P>0.05$, Table 2). The percentage of premature loss of primary molars also determined was found as same as prior to intensive course. Same ft and FT scores following chemotherapy revealed that there was no newly formed

active caries requiring filling. All of these findings could be explained by the positive effects of intensive oral care and improved self-care practices. In addition to that, frequent fluoride applications and former treatments using glass-ionomer cements, compomers and composite materials that can release fluoride ions to oral environment might contribute the positive effects of oral care.²⁴ Parents also could easily access to dental health information during their follow-ups since the hospital had a full-time resident pediatric dentist. Thus, the mean number of carious teeth scores did not increase significantly in these subjects.

Caries prevalence of first permanent molars and the percentage of premature loss of primary molars determined during the final dental examination was found as same as prior to intensive course. This can be attributed to the caries preventive effect of fissure sealants which was applied to the occlusal surface of the molars before the course was initiated. Caries level of 30 subjects (47%) also remained stable. However, white-spot lesions could not be prevented despite of fluoride usage and intensive oral care. This can be explained by the decreased salivary flow, and being reluctant to perform oral care because of pain during the course.

In conclusion, the findings of the study is clearly showed that dental caries activity in leukemic children with poor dental health could be stabilized by intensive oral care, improved oral health knowledge and self-care.^{10,12,13,16,25,26} Adequate oral care is out of discussion during cancer therapy in developed countries. However, treatment of dental diseases before chemotherapy, monitoring the children during the course and establishing intensive oral care are unordinary interventions in our country. Therefore, results of our study also highlighted the importance of the integration of dental services into the medical care structure for children with malignancy. More attention should be paid to prophylaxis and dental treatment for leukemic children with caries before therapy was initiated. Collaboration with a pediatric dental specialist at the hematology-oncology unit could achieve this objective. Dental health information and advice should be provided and be easily accessible to children, parent, the medical team, and providers of primary health care.

REFERENCES

1. Minicucci EM., Lopes LF., Crocci AJ. Dental abnormalities in children after chemotherapy treatment for acute lymphoblastic leukemia. *Leukemia Res*, 27: 45–50, 2003.
2. Purdell-Lewis D.J., Stalman M.S., Leeuw J.A., Homphrey G.B., Kalsbeek H. Long term results of chemotherapy on the developing dentition: caries risk and developmental aspects. *Community Dent Oral Epidemiol*, 16: 68–71, 1988.
3. Pajari U., Larmas M., Lanning M. Caries incidence and prevalence in children receiving antineoplastic therapy. *Caries Res*, 22: 318–20, 1988.
4. Clarkson J.E., Eden O.B. Dental health in children with cancer. *Arch Disease Child*, 78: 560–1, 1998.
5. Pajari U., Ollila P., Lanning M. Incidence of dental caries in children with acute lymphoblastic leukemia is related to the therapy used. *ASDC Journal of Dent Child*, 62: 349–52, 1995.

6. Kaste S.C., Hopkins K.P., Bowman L.C., Santana V.M. Dental abnormalities in children treated for neuroblastoma. *Med Pediatr Oncol*, 30: 22–7, 1998.
7. Bonnaure-Mallet M., Bunetel L., Tricot-Doleux S., Guerin J., Bergeron C., LeGall E. Oral complications during treatment of malignant diseases in childhood: effects of toothbrushing. *Eur J Cancer*, 34: 1588–91, 1998.
8. World Health Organization. *Oral Health Surveys-basic methods*. 3rd ed. Geneva: WHO, 1987.
9. Armitage P., Berry G. Inferences from proportions. In: *Statistical methods in Medical Research* (eds Armitage P. & Berry G.), Oxford, UK: Blackwell Scientific, 118–32, 1994.
10. Kinirons M.J., Fleming P., Boyd D. Dental caries experience of children in remission from acute lymphoblastic leukaemia in relation to the duration of treatment and the period of time in remission. *International Journal of Paed Dent*, 5: 169–72, 1995.
11. Sepet E., Aytepe Z., Ozerkan A.G., Yalman N., Güven Y., Anak S., Devecioglu O., Agaoglu L., Gedikoglu G. Acute lymphoblastic leukemia: dental health of children in maintenance therapy. *J Clin Pediatr Dent*, 22: 257–60, 1998.
12. Fleming P., Kinirons M.J. Study of the dental health of children in remission from acute lymphoblastic leukemia in Northern Ireland. *Community Dent Oral Epidemiol*, 21: 309–12, 1993.
13. Nunn J.H., Welbury R.R., Gordon P.H., Kernahan J., Craft A.W. Dental caries and dental abnormalities in children treated by chemotherapy for malignant disease: a study in the north of England. *Int J Paediatr Dent*, 3: 131–5, 1991.
14. Tagliabue R., Ebanista P., Pignanelli C., Adamoli L., Fracchini D., Pignanelli M. DMFT index values in patients treated for leukemia during growth. *Ital Odontologica Infant*, 2: 47–51, 1990.
15. Maguire A., Craft A.W., Evans R.G., Amineddine H., Kernahan J., Macleod R.I., Murray J.J., Welbury R.R. The long-term effects of treatment on the dental condition of children surviving malignant disease. *Cancer*, 60: 2570–5, 1987.
16. Nasman M., Bjork O., Soderhall S., Ringden O., Dahllof G. Disturbances in the oral cavity in pediatric long-term survivors after different forms of antineoplastic therapy. *Pediatr Dent*, 16: 217–23, 1994.
17. World Health Organization. *Oral health information systems, 2006*. Available at: who.int/oral_health/action/information/surveillance/en.
18. Petersen P.E. Changing oral health profiles of children in Central and Eastern Europe-challenges for the 21st century, 2006. Available at: who.int/oral_health/action/information/.
19. World Health Organization. *Oral health for the 21st century*. Copenhagen: WHO/ORH/Oral C21, 1994.
20. Saydam G., Oktay I., Möller I.G. A situation analysis of oral health in Turkey. *Tur-Oral-Health* (WHO). Printed in Turkey, 1990.
21. World Health Organization. *Health for all targets. The health policy for Europe*. Copenhagen: WHO Regional Office for Europe, 1991.
22. Dahlöf G., Modeer T., Bolme P. Oral health in children treated with bone marrow transplantation: a one-year follow-up. *J Dent Child*, 55: 196–200, 1988.
23. Pajari U., Lanning M., Larmas M. Prevalence and location of enamel opacities in children after anti-neoplastic therapy. *Community Dent Oral Epidemiol*, 4: 222–6, 1988.
24. Hamilton I.R., Bowden G.H.W. Fluoride in the oral environment. In: *Fluoride in dentistry*. (eds Fejerskov O., Ekstrand J., Burt B.A.) 2nd ed., Munksgaard, 232–6, 1996.
25. O'sullivan E.A., Duggal M.S., Bailey C.C. Changes in the oral health of children during treatment for acute lymphoblastic leukaemia. *Int J Paediatr Dent*, 4: 31–4, 1994.
26. Pajari U., Yliniemi R., Möttönen M. The risk of dental caries in childhood cancer is not high if the teeth are caries-free at diagnosis. *Pediatr Hematol Oncol*, 18: 181–5, 2001.