



PII: S0959-8049(98)00169-5

Original Paper

Oral Complications during Treatment of Malignant Diseases in Childhood: Effects of Tooth Brushing

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During anticancer treatment, oral lesions considerably aggravate the child's clinical condition and increase the risk of infection. This prospective study evaluated the incidence, nature and chronology of oral complications arising during the first 6 weeks of chemotherapy. 131 children were included in this study, and their oral and dental health evaluated on enrolment. Each child was observed once a week, for 6 weeks. Fifty-two per cent (68/131) of the children presented with at least one oral lesion. Two oral healthcare regimens (with or without tooth brushing) were evaluated. Tooth brushing significantly reduced the number of children affected. Standardised multicentre studies should permit the definition of oral care regimens which would eliminate pain and reduce the risk of infection in children hospitalised for cancer. © 1998 Elsevier Science Ltd. All rights reserved.

Key words: cancer, oral complications, tooth brushing

Eur J Cancer, Vol. 34, No. 10, pp. 1588–1591, 1998

INTRODUCTION

ORAL LESIONS arising during cancer chemotherapy remain a frequent complication [1, 2]. These lesions may produce discomfort and pain which interfere with eating and therapies and increase the potential risk of oral infection [3]. They depend mainly on the mode of treatment (agents, sequencing, rate of delivery, dosage) and to some extent also on host factors [4]. Few studies dealing with oral complications arising during stays at paediatric oncology facilities have undertaken a longitudinal and retrospective follow-up [1, 5], to the extent that the incidence of such complications and the influence of oral healthcare measures are poorly understood. The beneficial effects of chlorhexidine in the prevention of oral lesions during chemotherapy or bone marrow grafting are already known [6–8]. Conversely, the effects of tooth brushing during courses of chemotherapy have never been analysed. Tooth brushing has been broadly proscribed during chemotherapy, due to risks of infection and haemorrhage. In this present study, we evaluated the influence of tooth brushing by comparing the frequency, severity and progress

of oral lesions among two populations of children, only one of which brushed their teeth, three times a day after meals.

PATIENTS AND METHODS

Patients

For 4 years, all patients admitted for the first time to the Oncology Paediatric Department at Rennes (France) for a 6 week hospital stay for the treatment of malignant disease were included in the study. Consent was obtained from the parent or guardian of each patient.

A clinical examination and a baseline oral examination were performed on every patient by the same resident paediatric dentist. This examination included a systemic and precise oral examination. The assessment recorded on the patient file indicated whether urgent measures were required before or during chemotherapy, such as removal of orthodontic appliances, or extraction of primary teeth.

Subsequent oral/dental examinations were carried out once a week, during the 6-week hospitalisation after the initial examination (week 0) at the patient's bed with a mirror, a tongue depressor and a portable frontal lamp. During these examinations, the condition of the teeth and mucosae were observed. The aspect, location and extent of lesions were

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Received 29 Sep. 1997; revised 17 Mar. 1998; accepted 6 Apr. 1998.

carefully described. Clinical examination of the mucosa of the oral cavity was assessed by assigning an modified ulcerative-mucositis score (WHO index: 0 = no ulcers, 1 = mucosal redness with one or two small ulcers (< 1 cm), 2 = mucosal ulcerations with one or two large ulcers (> 1 cm)).

Oral hygiene regimen

During courses of chemotherapy, each child systematically received oral care three times a day after meals. A regimen based on a chlorhexidine (0.12%) oral mouth rinse and a topical fungizone (2.5 ml) were used. Two groups were observed, one without toothbrushes during the years 1993 and 1994, and one with toothbrushes (7/100 Nylon toothbrush, Inava, France) during the years 1995 and 1996 (Table 1). In the group that brushed, tooth brushing was carried out by trained care-givers for children under 7 years of age and for children older than 7 years who were not able to care for themselves. After use, the toothbrush was stored in a chlorhexidine solution (2%) and rinsed in sterile water before use. In all cases, oral care was supervised by a care-giver for the entire 6 weeks of the study.

Statistical analysis

A chi-square test was used to test for significant differences in frequency of oral complications between groups with and without tooth brushing. Statistical significance was accepted for $P < 0.05$.

RESULTS

131 children participated in the study. Of all children enrolled, 4 required extractions of primary teeth or loose teeth, and 8 required orthodontic appliances to be removed before treatment. 31 required non-urgent dental care, 26 of whom were treated and 5 of whom were never treated. 100 were free of caries. For the next 6 weeks, each child was observed once a week: the total number of examinations was 917.

The two groups with and without tooth brushing comprised 67 and 64 children, respectively, and were comparable for age and type of disease (Table 2). The age of the children varied from 1 to 17.15 years.

During treatment, for both groups combined, 48% of children did not develop oral lesions. The distribution of children without lesions was 25/64 (39%) in the group that did not brush and 38/67 (57%) children in the group that brushed. The other 52% presented at least one lesion during chemotherapy.

Over the 6 weeks, there was a significant difference between the two groups when the number of lesions was analysed. The lesions were more numerous in the non-brushing group compared with the group that brushed ($\chi^2 = 4.08$, $P < 0.05$). This difference was highly significant when the analysis was confined to the patients who showed no oral lesions in the first week ($\chi^2 = 6.10$, $P < 0.02$).

Table 2. Patient characteristics

	Total	Regimen without tooth brushing*	Regimen with tooth brushing*
Total children	131	64	67
Males	74	39	35
Females	57	25	32
Age (years)			
Mean	6.61	6.64	6.57
Standard deviation	4.73	4.44	5.02
Range	1-17.15	1-15.50	1-17
Type of cancer			
Leukaemia	56	28	28
Brain tumour	8	4	4
Neuroblastoma	9	5	4
Nephroblastoma	13	5	8
Non-Hodgkin's lymphoma	11	8	3
Osteosarcoma	10	3	7
Germ cell tumour	6	3	3
Rhabdomyosarcoma	5	3	2
Hodgkin's disease	7	3	4
Other tumours	6	2	4

*The two groups are comparable for these characteristics.

In order to analyse the frequency, severity and development of lesions during the 6 weeks of therapy, those children presenting a pathology on at least one occasion were considered separately, by comparing the populations of 39 children in the group that did not brush with 29 in the group that did brush. The comparative criterion was the frequency of scores of 0, 1, or 2 during the 6 weeks.

In the group that did not brush, a comparison of the frequency of scores between week 1 and the following weeks always showed a significant increase in lesions (Figure 1a). In the group that brushed, this increase in lesions was seen during weeks 2 and 3, with a return to normal during weeks 4 and 5. At week 6, there was a slight excess of lesions compared with week 1 (Figure 1b). This slight increase of oral lesions never reached the same level as in the group that did not brush.

A comparison within each group of the frequency of lesions as a function of caries showed that the presence of caries at the outset ($n = 31$) increased the probability of oral lesions during chemotherapy (group with brushing: $\chi^2 = 6.32$; $P < 0.05$, group without brushing: $\chi^2 = 7.90$, $P < 0.01$). An intergroup comparison showed that brushing had no influence on this parameter (group free of caries $\chi^2 = 1.62$, $P = 0.05$; group with caries $\chi^2 = 0.32$, $P = 0.05$). Caries favour lesions with or without tooth brushing.

DISCUSSION

According to the literature, the incidence of oral complications during chemotherapy is higher in children than in

Table 1. Regimens employed for oral care

Regimen without tooth brushing	Regimen with tooth brushing
Chlorhexidine oral rinse 0.12%*	Tooth brushing§ (toothbrush stored in chlorhexidine 2% solution)
Bicarbonate solution 1.4% v/v diluted 1/5†	Chlorhexidine oral rinse 0.12%*
Fungizone‡ (2.5 ml) oral suspension	Bicarbonate solution 1.4% v/v diluted 1/5†
	Fungizone‡ (2.5 ml) oral suspension

*Hextril Parke Davis; †Aguettan; ‡Squibb; §7/100 Inava toothbrush.

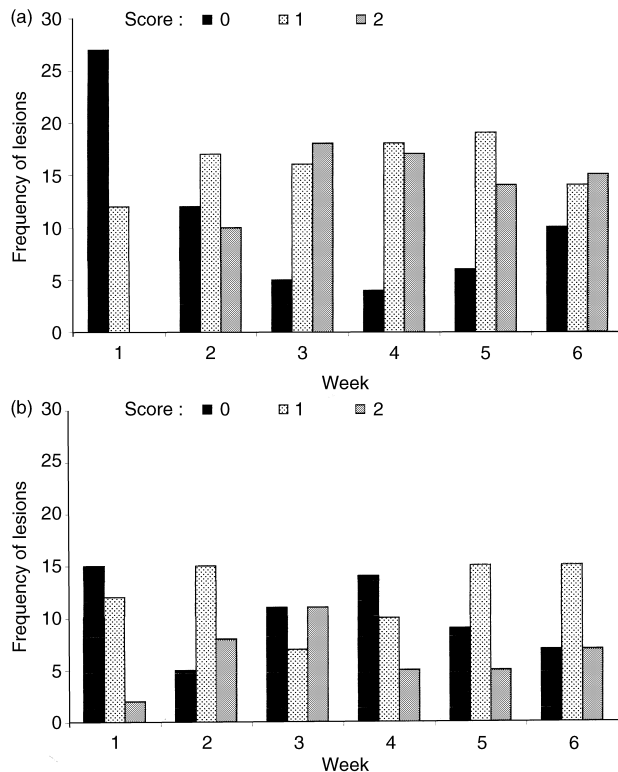


Figure 1. Frequency distribution of lesions and their severity week by week for (a) the non-brushing group; and (b) the group that used toothbrushes.

adults [5, 9]. This difference, which has not been thoroughly analysed, may be due to the higher mucosal cell turnover rate [10]. In the child, the incidence of oral lesions has been reported as 100% [11], 62% [2], 31% [12] and 27% [13] of observed cases. In this study, 52% of children presented with a minimum of one complication confined to the oral cavity during therapy. These disparate results are related to the oral/dental condition at the onset of treatment, to the collection of data, to the frequency of clinical examinations, and to the lesions taken into account by the authors [14]. In this study, children were examined on six occasions during therapy and only lesions of the oral mucosa were taken into account. A precise international classification of lesions and establishment of common scoring and terminology would enable a better understanding of observations and of their preventive and curative treatment. In this study, lesions were analysed according to scores from the WHO Index. These scores, which are easy to use, have the advantage of corresponding to clinical realities compared with classifications based on pain. The classification of Schubert and colleagues [15] was not appropriate for children, because of the high number of measures required. Weekly observation of many children allowed us to monitor the chronology of lesions. A single small ulcer appeared to precede mucositis. This observation contrasts with those of Childers and associates [5], where mucositis preceded ulceration, although the term mucositis is ill-defined in the literature [16, 17].

The most frequently encountered oral complication was one or two ulcers (<1.0 cm). These results corroborate the work of previous studies [1, 18], regardless of prophylactic measures used. We observed that, in conjunction with tooth brushing, limited lesions (score 1) did not necessarily develop

into ulcers (score 2). In this study, the lesions were less numerous in the group that brushed. The difference between the two groups was highly significant when children showing no lesions in the first week were excluded. This result confirms the involvement of plaque bacteria in oral lesions during chemotherapy [19, 20]. Considering the significant differences observed between the two groups, it appears necessary to eliminate dental plaque. Moderate levels of dental plaque and debris can contribute to local infection in immunocompromised patients [21].

For both groups, weeks 2 and 3 appeared critical, although this was more significant for the group that did not brush. This may be explained by the fact that oral mucosal cells are particularly susceptible to various chemotherapeutic regimens as a result of a relatively high renewal rate of 10–14 days [8]. When tooth brushing was practised, we observed a return to normal during weeks 4 and 5. This phenomenon was not seen in the group that did not brush.

The group that brushed showed deterioration during week 6. This was unexpected, even though the deterioration was never as great as that observed in the group that did not brush. This observation may be due to adverse effects of the chlorhexidine rinse used for long periods, notably the increase in numbers of Gram negative bacilli, as has been observed by Ferretti and colleagues [22].

The pretreatment evaluation of the 131 children observed shows that the number of children requiring urgent dental care, before the beginning of therapy, was low compared with the study of Fayle and Curzon [1]. Regardless of the group considered, oral lesions were often found in children with caries. This correlation, shown here for the first time, reinforces the concept of Kamp [12], which indicates that the treatment of paediatric neoplastic disease is multidisciplinary and ideally involves a paediatric dentist for supportive care of oral pathologies. In this study, tooth brushing had no influence on lesions when the child presented with caries at the outset. This lack of difference can be explained by the presence of potential infectious foci related to caries. Moreover, it is essential that all risk of infection from dental sources, i.e. caries or orthodontic appliances [16, 23, 24] be removed before commencing therapy.

Many authors [1, 16, 25] note the importance of oral/dental care during courses of chemotherapy. Different regimens may be proposed, but emphasis should be placed on their rigour, their frequency, and monitoring. Tooth brushing should be included [26, 27].

Moreover, we recommend that throughout chemotherapy, the toothbrush should be placed in a 2% chlorhexidine solution which is replaced after each use in order to prevent bacterial contamination. The toothbrush is then rinsed before use. An understanding of physiopathological and infectious mechanisms should facilitate an improvement in preventive and therapeutic measures. Prospective, standardised and multicentre studies seem necessary in order to halt secondary manifestations, to define regimens for oral care which avoid intense pain, and reduce the risk of oral infection for children hospitalised for cancer treatment.

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Acknowledgements—This work was supported by grants from the Ligue Nationale Contre le Cancer (Ille et Vilaine, France) and from the Comité de Recherche Clinique du CHR-U de Rennes (France). We thank Pascale Thibault and auxiliary nurses for rigorous application of regimens I and II during this study and D. Ní Eidhin for her help in translation.