Chlorhexidine Varnish Application and Fluoride Self-administration for Dental Caries Control in Head and Neck Irradiated Patients. A Three-year Follow-up

M. Carmen Llena[a], José V. Bagan[b]

[a]*Faculty of Experimental and Health Science Cardenal Herrera, CEU University, Moncada, Valencia, Spain.*
[b]*Stomatology Department, Faculty of Medicine and Dentistry, University of Valencia, Valencia, Spain.*

Purpose: Head and neck irradiated patients are at greater risk of dental caries due to lack of protection resulting from quantitative and qualitative changes in their saliva. The purpose of this study was to assess the effectiveness of the application of a chlorhexidine varnish every three months and the daily use of a high-concentration fluoride in a group of head and neck irradiated patients, and to compare the rise in caries in this group with that of a control group.

Materials and Methods: A total of sixty-four patients were examined: 32 were head and neck irradiated and 32 were general clinic patients without any systemic pathology. We determined the clinical/radiological DMFS index and measured the salivary flow and pH in stimulated whole saliva at the outset of the study and after three years of three-monthly applications of a 1% chlorhexidine and thymol containing varnish (Cervitec©), and self-administered high-concentration fluoride. At the start and end of the study the DMFS scores of this group of patients were compared with those of the control group.

Results: Salivary flow was significantly higher in the patients who had received lower doses of radiotherapy and the lower the saliva flow, the lower the pH values observed. Except for the number of missing teeth, which was significantly higher in the group of patients who had been treated for squamous cell carcinoma, the caries indicators did not differ significantly by sex, diagnosis or radiotherapy dose. The rise in the number of new caries lesions and the progress of the existing untreated lesions in the study group did not differ significantly from those of the control group.

Conclusions: Caries risk in irradiated patients who followed a strict caries-prevention protocol is comparable to that of the general population.

Key words: radiation therapy, dental caries, cariostatic agents

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INTRODUCTION

Saliva is the main regulator of the oral ecosystem and the best protection against dental caries. Patients with an impaired salivary function constitute a population at higher risk for dental caries and other oral diseases. This population includes head and neck irradiated patients, whose salivary secretion is altered, both quantitatively and qualitatively, for the rest of their lives (Dreizen et al, 1976; Shannon et al, 1977, Epstein et al, 1992).

The main oral health consequences of the lack of saliva are the frequent appearance of oropharyngeal candidiasis, an increased fragility of the mucosa and an increased risk for caries, with a distribution pattern of preference for the neck and cusps of the tooth (Dreizen et al, 1977; Mandel, 1987; Rossie et al, 1987). These patients have higher levels of cariogenic bacteria, specifically Streptococcus mutans (SM) and Lactobacillus (LB); these bacteria are acid-producing and their presence is directly related to the increased risk of

caries (Brown et al, 1975; Keene et al, 1981, Keene et al, 1987).

Various preventive regimes based on the continuous regular use of fluorides and/or chlorhexidine, at different concentrations and with different forms of administration, have been used in these patients (Epstein et al, 1981; Epstein et al, 1989; Joyston-Bechal et al, 1992; Vissink et al, 2003); most have proved effective in reducing caries over the medium term although a beneficial effect in reducing acid-producing bacteria has not always been demonstrable. Specifically, applications of high-dose fluorides have proved effective in SM reduction but not in LB reduction, while chlorhexidine application has proved effective in reducing both SM and LB (Emilson, 1977; Keene et al, 1987).

Additionally, it cannot be assumed that the preventive measures that have demonstrated their usefulness in the general population can be easily extrapolated to these types of patients, some of whom have a zero capacity to produce saliva (Meraw et al, 1998).

In these patients, the salivary factors already mentioned are joined by cariogenic dietary habits, owing to their frequent ingestion of carbohydrates, which increase their susceptibility to caries (Specht et al, 2002).

As well as general rigorous oral hygiene control measures, these patients require specific, individualised preventive measures. It is therefore necessary to conduct studies to assess the effectiveness of different preventive protocols to control the development of caries in these patients and keep the patients motivated to complete them (Andrews et al, 2001; Bader, 2001).

In order to assess the effectiveness of a protocol based on the application of a chlorhexidine varnish every three months and the daily use of high-concentration fluoride, this study determined the DMFS index and its components at the start and end of a three-year follow-up period. It also compared the rise in caries in this group of patients with that of a general population with no specific risk factors over the same period of time.

MATERIALS AND METHODS

The sample studied numbered 64 patients: 32 in the study group and 32 in the control group. The patients in the study group had received radiotherapy in the head and neck area and after completing this treatment had been referred to a Preventive Dentistry Area Unit (PDU), where they were followed up for three years. The control group was made up of a further 32 patients without systemic or oral diseases that could condition changes in the salivary flow rate, who were followed up regularly for three years at a dental office. All procedures were performed by the same examiner in both study and control groups.

The distribution of the study population was as follows: 17 women (53.1%) and 15 men (46.9%), with an average age of 46.8±14.7 (40.3±15.9 for the women, 54.2±9.0 for men). As regards their diagnoses, 21 had been diagnosed with squamous cell carcinoma (SCC) in different oropharyngeal sites; the average age for this group was 52.8±8.9 years, 8 were women (average age 50.2±9.0) and 13 were men (average age 54.3±8.8). Ten of the patients had been diagnosed with different types of lymphoma; their average age was 32.5±14.9, 8 were women (average age 27.3±10.3) and 2 were men (average age 53.0±14.1). The remaining patient had an adenoid cystic carcinoma (cylindroma) of the right sub-maxillary gland. The average radiation dose received by the sample as a whole was 51.45±12.13 Gy. By sex, the women had received a significantly lower dose than the men (47.4±14.3 and 56.0±6.9 respectively, $p=0.038$).

The average age of the control group was 45.2±10.0. Distribution by sex was 16 women with an average age of 42±8.2, and 16 men with an average age of 53.4±11.3.

The protocol followed by the patients in the study group began with a clinical and radiological examination with two bite-wing X-rays to determine the clinical/radiological DMFS index. Lesions ranging from demineralisation lesions in the form of a white spot to cavitated lesions were counted as clinical caries; radiological caries covered lesions that were confined to the enamel as well as lesions that affected the dentine (Hintz, 1993). The stimulated whole saliva flow (stimulated by chewing a paraffin tablet for 5 minutes) was determined and the flow per minute was calculated by dividing the total saliva collected by 5 (Makkonen, 1986). The pH of the saliva was determined, immediately after collection, by the Dentobuff system (Vivadent), which is a semi-quantitative system that enables the pH to be classified as low (<5.5), medium (5.5-6.5), or high (≥7). All determinations were performed at least 2 hours after having eaten. Following these examinations, the patients were instructed in basic oral hygiene practice, tartar removal was performed if necessary and a 1% chlorhexidine and thymol containing varnish (Cervitec©) was applied. Patients were also instructed in the use, daily or weekly depending on whether their stimulated saliva flow was below or

above 0.7 ml/min, of high-concentration fluoride. Every three months the patients were reassessed, their oral hygiene condition was checked, prophylactic measures were taken (dental polish and/or tartar removal) and the chlorhexidine varnish was reapplied. Bite-wing X-rays were repeated annually in order to evaluate the progress of the interproximal caries lesions. After the 12th visit, the same parameters as used at the start of the study were assessed and compared to the initial measurements.

For the patients in the control group, the initial clinical/radiological caries diagnosis was carried out in an identical manner and the DMFS was calculated. Tartar removal was performed if necessary; patients were given oral hygiene instructions individually; the necessary treatments were performed and these were then included in a preventive protocol consisting of a high-concentration fluoride application, yearly or twice-yearly depending on the caries risk. At the end of the study period all the initial parameters were reassessed.

Univariate and bivariate data analyses were performed with the SPSS 11.0 statistics package; ANOVA was used to compare the qualitative variables with the quantitative variables; the chi-square test was used to compare the qualitative variables with each other; and the Wilcoxon test for two paired samples was used to compare the initial and final data of the study. Significance was claimed at $p<0.05$.

RESULTS

Table 1 shows the percentages of low, medium and high pH levels among the irradiated patient group. Over the study period, the number of low pH patients fell and that of medium pH patients rose. The differences between the initial and final measurements were significant except in the group of patients who had been treated for lymphoma. The average stimulated saliva flow was 0.48±0.58 ml/min at the start and 0.55±0.47 ml/min at the end of the study, with no significant differences between men and women. On analysing the variations between the start and end of the study by sex, a significant rise in salivary flow over the study period was found among the women (0.15 ml/min. $p=0.23$). The DMFS index and its components showed very slight differences between the start and end of the study, as can be observed in Table 2. Although treatment was not received systematically by the patients who needed it, the average D value fell while the M and F values both rose. It should also be mentioned that of the caries lesions which were not treated, either because they were incipient or because the patient voluntarily decided against treatment, only 2.1% showed signs of having progressed. By sexes, the fall in the average D component value was higher in women, where it was largely counterbalanced by the rise in the average F value. Among the men it was counterbalanced by the rise in the average M value. The differences in the F component of the DMFS index at the start and end of the study were significant for the women but not for the men.

On analysing the results by diagnosis, it was found that the radiation dose received by the patients diagnosed with lymphoma was considerably lower than for those diagnosed with squamous cell carcinoma, with average values of 35.28±6.41 Gy and 58.93±4.35 respectively ($p=0.00$). The average D component of the DMFS index fell between the start and end of the study in both groups, while the component with the highest rise in average value was M. At both the start and end of the study, the DMFS scores and those of its M component were significantly lower in the lymphoma group, as can be observed in Table 3. Equally, saliva flow, both initial and final, was significantly higher in the patients treated for lymphoma than in those

Table 1 Variations in the percentages of patients presenting the different qualitative pH values at the start (initial) and end (final) of the study by sex and diagnosis. The variables that present significant differences between the start and end of the study are shown in bold type

pH values	<5.5		5.5-6.5		≥7		p
	Initial	Final	Initial	FinalInitial	Final		
Men	43.8 %	37.5%	31.3%	56.3%	25.0%	6.3%	**0.005**
Women	41.2%	35.3%	47.1%	47.1%	11.8%	17.6%	**0.015**
SCC	57.1%	47.6%	33.3%	47.6%	9.5%	4.8%	**0.002**
Lymphoma	18.2%	9.1%	54.5%	54.5%	27.3%	36.4%	0.170
Total	42.4%	36.4%	39.4%	51.5 %	18.2%	12.0%	**0.000**

Table 2 DMFS index and component values by sex and diagnosis of the patient and control groups at the start (initial) and end (final) of the study. The variables that present statistically significant differences are shown in bold type

		D			
		Initial	Final	Increment	p
Patient group	Men	5.06	5.33	0.27	0.465
	Women	5.76	4.29	−1.48	0.065
	SCC	4.95	4.61	−0.34	0.599
	Lymphoma	6	4.70	−1.30	0.293
	Total	5.43	4.78	−0.66	0.233
Control group	Total	5.20	4.60	−0.60	0.234
		M			
		Initial	Final	Increment	p
Patient group	Men	29.73	34	4.27	0.109
	Women	17.05	18.17	1.12	0.180
	SCC	29.47	32.04	3.57	0.109
	Lymphoma	6.30	9.20	2.90	0.317
	Total	23	25.59	2.6	**0.043**
Control group	Total	14.2	12.1	2.1	0.061
		F			
Initial	Final	Increment	p		
Patient group	Men	7.13	8.06	0.93	0.600
	Women	5.24	6.78	1.83	**0.007**
	SCC	5.90	7.85	1.95	0.236
	Lymphoma	7.10	7	−0.10	0.343
	Total	6.28	9.40	1.40	0.078
Control group	Total	11.10	12.30	1.20	0.092
		DMFS			
		Initial	Final	Increment	p
Patient group	Men	24.51	25.80	1.33	0.345
	Women	22.52	23.81	1.59	0.106
	SCC	40.33	41.69	1.28	0.352
	Lymphoma	19.30	20.90	1.60	0.279
	Total	34.68	25.29	1.47	0.068
Control group	Total	30.50	29.18	1.32	0.071

treated for squamous cell carcinoma (0.84±0.48 ml/min and 0.41±0.42 ml/min respectively, p=0.017). Within each diagnostic group, neither the decay score nor the saliva flow exhibited significant differences between the initial and final measurements.

On comparing the pH values with the remaining variables it was observed that the lower the average stimulated saliva flow values, the lower the pH levels, and that all the pH levels differed significantly from the salivary flow values at the end of the study (Table 4).

On comparing the rises in the average DMFS and index component scores of the study group and the control group over the study period, no significant differences between the two groups were observed (Table 5).

DISCUSSION

In this study we assessed stimulated rather than unstimulated salivary flow because patients with squam-

Table 3 Values of the parameters studied at the start (initial) and end (final) of the study compared by diagnosis of the pathology that required radiotherapy. The variables that present statistically significant differences are shown in bold t

	Lymphoma	Squamous Cell Carcinoma	p
Initial D	6	4.95	0.581
Initial M	6.30	29.47	**0.005**
Initial F	7.10	5.90	0.724
Initial DMFS	19.30	40.33	**0.018**
Initial FLOW	0.78	0.35	0.060
Final D	4.70	4.61	0.967
Final M	9.20	32.04	**0.010**
Final F	7	7.85	0.820
Final DMFS	20.90	41.61	**0.027**
Final FLOW	0.84	0.41	**0.017**

Table 4 Relation between pH and salivary flow at the start (initial) and end (final) of the study

	Average flow
Initial pH	
Low	0.2564*
Medium	0.4969+
High	1.4000*+
Final pH	
Low	0.2642***
Medium	0.6306***
High	1.1750***

* Statistically significant difference between the variables
\+ Statistically significant difference between the variables
*** Statistically significant difference between the variables

Table 5 Variation in rise in caries between the study group and the control group

	IRRADIATED	CONTROL	p
D Increment	−0. 66	−0.60	0.172
M Increment	2.6	2.1	0.231
F Increment	1.40	1.20	0.112
DMFS Increment	1.47	1.32	0.145

ous cell carcinoma had no initial salivary flow in most cases. Since our objective was to determine the caries development in a high-risk population group (with diminished salivary flow) following specific preventive care, and to compare it with the general population group without pathology and having no drug intake (that could reduce their salivary flow) and following a program of preventive visits to the dentist, we did not assess salivary flow in the control group.

Together with the preventive protocol, the patients were given hygiene and dietary recommendations. However, the extent to which the latter were put into practice was difficult to control, given that some of these patients had serious feeding difficulties due to functional incapacity and lack of saliva. This study did not control these factors and it is therefore not possible to determine whether part of the results might be attributable to other reasons, e.g. dietary habits, or the use of fluoridated tooth paste in daily tooth brushing. In order to standardize these factors to a certain extent, we gave basic dietetic advice to the patients, oriented to caries prevention, that was repeated at each visit, as well as noting the conditions for plaque control, e.g. method, frequency and toothpaste (fluoride type). Nonetheless, there is evidence to show that patients who do not follow a preventive regime following radiotherapy develop caries that progresses very rapidly over short periods of time (Epstein et al, 1975; Epstein et al, 1992; Duggal et al 1997; Epstein et al, 1999; Andrews et al, 2001; Vissink et al, 2003). In this sense, our results show that, at least from a general point of view, patients responded well to the suggested hygienic-dietetic instructions.

Various fluoride and chlorhexidine application regimes have been presented in the literature (Banting et al, 2000; Brailsford et al, 2002; Frentzen et al, 2002; Matthijs et al, 2002), which has demonstrated their effectiveness, both in reducing the appearance of new lesions and in remineralizing white spots, or arresting lesions that are confined to the enamel. The application of high-concentration fluoride alone, despite being the only measure to reduce the risk of caries in the general population for which there is sufficient scientific evidence (Rozier et al, 2001), has not proved effective in controlling the appearance of new lesions in irradiated patients (Katz, 1982; Makkonen et al, 1986). Oral environmental conditions are extremely adverse in these types of patients and high concentration fluoride application alone is not sufficient.

As regards the ability of these treatments to reduce cariogenic bacteria, fluoride application (particularly tin fluoride) reduces SM levels but not LB levels in irradiated patients (Keene et al, 1987; Millard, 1989).

Caries reduction in patients who follow continuous programmes of chlorhexidine application, in various forms and concentrations, has been demonstrated in

the literature (Giertsen et al, 1993; Baca et al, 2003). However, when these are interrupted their effectiveness disappears and the patients' risk of caries rises again (Baca et al, 2003). The majority of these studies has been conducted in children with normal salivary flow, pointing to the importance of following-up the preventive protocols in extremely high-risk patients (Hutton et al, 1982; Mackie et al, 2000; Caribe-Gomes et al, 2003). In general, the combination of professional applications of fluorides and chlorhexidine proves effective in reducing caries in high-risk patients but not in low-risk patients (Hausen et al, 2000). The present study confirms the effectiveness of combining the two measures.

Studies have demonstrated the effectiveness of chlorhexidine in arresting dentine caries lesions and in reducing the proteolytic activity of the cariogenic bacteria (Garcia et al, 2001). This study demonstrates the stabilisation of incipient lesions, in so far that 98% of the lesions at the start of the study that were not filled did not progress further, either because they were incipient or because the patient voluntarily decided against this treatment.

The differences in DMFS scores between the patients treated for lymphoma and those treated for squamous cell carcinoma were due, in essence, to the M component. This was increased in the latter group as caries was considered to have been the cause of all the missing teeth. In many cases another possible reason could have been their extraction to extend the surgical resection margin, although this factor could not be assessed as dental records prior to surgery were not available. However, the D component of the index did not differ significantly between the two groups either at the start or end of the study, despite the significant difference in the radiation dose received, and in the salivary flow of the two groups of patients.

The preventive protocol proposed, which combines three-monthly chlorhexidine applications at the clinic and daily applications of high-concentration fluorides, has shown itself to be effective: only 15 newly affected surfaces appeared among the 32 patients followed up over the three-year study period; existing lesions progressed to the point of requiring restoration treatment or extraction in only one patient; the remaining fillings and extractions that were performed had already been prescribed at the start of the study, owing either to decay or to periodontal pathologies.

The rise in the average decay indicator values assessed was not found to differ significantly between the study group and the control group. It may be concluded that the risk of caries in irradiated patients who follow a strict caries-prevention protocol is comparable to that of the general population.

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Reprint requests:
M. Carmen Llena Puy
Albuixech 8, 2ª
46021 Valencia
Spain
E-mail: llena@uv.es