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ORIGINAL ARTICLE

Oral health is an important issue in end-of-life cancer care

Petter Wilberg · Marianne J. Hjermstad · Stig Ottesen · Bente B. Herlofson

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Abstract
Purpose This study aims to assess the prevalence of oral morbidity in patients receiving palliative care for cancers outside the head and neck region and to investigate if information concerning oral problems was given.
Methods Patients were recruited from two Norwegian palliative care inpatient units. All patients went through a face-to-face interview, completed the Edmonton Symptom Assessment System (ESAS) covering 10 frequent cancer-related symptoms, and went through an oral examination including a mouth swab to test for *Candida* carriage.
Results Ninety-nine of 126 patients (79 %) agreed to participate. The examined patients had a mean age of 64 years (range, 36–90 years) and 47 % were male. Median Karnofsky score was 40 (range, 20–80) and 87 % had metastatic disease. Estimated life expectancy was <3 months in 73 %. Dry mouth was reported by 78 %. The highest mean scores on the modified 0–10 ESAS scale were 4.9 (fatigue), 4.7 (dry mouth), and 4.4 (poor appetite). Clinical oral candidiasis was seen in 34 % (86 % positive cultures). Mouth pain was reported by 67 % and problems with food intake were reported by 56 %. Moderate or rich amounts of dental plaque were seen in 24 %, and mean number of teeth with visible carious lesions was 1.9. One patient was diagnosed with bisphosphonate-related osteonecrosis of the jaw. Overall, 78 % said they had received no information about oral adverse effects of cancer treatment.
Conclusion Patients in palliative care units need better mouth care. Increased awareness among staff about the presence and severity of oral problems is necessary. Systematic information about oral problems is important in all stages of cancer treatment.

Keywords Palliative care · Neoplasms · Drug therapy · Oral health · Xerostomia · Dysgeusia · Dental caries

P. Wilberg · S. Ottesen · B. B. Herlofson (✉)
Department of Oral Surgery and Oral Medicine,
Faculty of Dentistry, University of Oslo (UiO),
P.O. Box 1109, Blindern,
0317, Oslo, Norway
e-mail: b.b.herlofson@odont.uio.no

M. J. Hjermstad · S. Ottesen
Regional Centre for Excellence in Palliative Care,
Oslo University Hospital, Ullevaal,
Oslo, Norway

M. J. Hjermstad
European Palliative Care Research Centre,
Department of Cancer Research and Molecular Medicine,
Norwegian University of Science and Technology,
Trondheim, Norway

B. B. Herlofson
Department of Maxillofacial Surgery and Hospital Odontology,
Cancer Clinic, Oslo University Hospital,
Oslo, Norway

Introduction

According to the Norwegian Cancer Registry, more than 26,000 persons are annually diagnosed with cancer in Norway [1], about 11,000 people die of cancer every year, and more than 190,000 are alive with a cancer diagnosis [1]. About 95 % of the patients treated at palliative care centers in Norway have a cancer diagnosis. A major goal of palliative care is to relieve pain and other distressing symptoms [2]. Studies have shown that poor symptom assessment is the single most important barrier for adequate symptom management [3]. Oral problems are not systematically assessed in oncology, unless specific interventions such as tooth extractions are necessary for infection control before

the initiation of oncological treatment [4]. Nevertheless, many patients may suffer from stressful oral side effects resulting from the disease and/or from the treatment regardless of whether they have been declared disease-free or not.

Anticancer treatment has profound acute and long-term side effects on healthy tissue with a high proliferation rate, i.e., in the gastrointestinal tract. The epithelium of the oral mucosa is affected by most therapeutic agents, resulting in mucositis, xerostomia, and taste alterations [5–12]. A recent review [5] showed that chemotherapy often induce temporary salivary gland hypofunction and xerostomia. Saliva is an integral part of taste perception, while taste is also important for the formation of saliva [5, 6]. Thus, loss or impairment of one function will influence the other. Adverse effects of cancer therapy may be dose-limiting and consequently compromise prognosis. Furthermore, they may cause severe pain and long-standing nutritional problems that often contribute to weight loss, fatigue, impaired quality of life, and a persisting negative effect on social function [7–12].

Oral complications caused by cancer and/or its treatment are significant and well-documented, especially in patients with head and neck cancer [13, 14]. However, in cancers outside this area, oral problems are less well-documented. Oral status and oral care are often insufficiently documented in the patient's medical records and systematic oral care protocols seldom exist. It has been claimed that physicians and nurses show less attention to the mouth than to other parts of the body [11]. Oral problems may be underreported by the patients and inadequately addressed by physicians. This may be truer in the late stages of disease, and we have only been able to identify a few studies assessing oral morbidity in patients with cancers outside the head and neck region receiving palliative care [15–19]. Furthermore, personnel with special training in oral or dental care are not routinely included in oncology or palliative teams in Norway.

According to the literature, 30–77 % of palliative care cancer patients will experience xerostomia as an adverse effect due to cancer treatment and medication [15]. In addition, an association between xerostomia and the presence of oral candidiasis in these patients has been reported. Oral candidiasis in advanced cancer patients has previously been reported with vastly differing prevalence rates, ranging from 8 to 94 % [15, 16]. Furthermore, several drugs frequently given for symptom relief have powerful anticholinergic and immunosuppressive effects that may lead to quantitative and qualitative changes in saliva and saliva flow. This in turn may lead to xerostomia, infections, stomatitis, caries, nutritional disturbances, fungal infections, and insomnia [11, 17, 18]. Taste alterations (dysgeusia) have been reported in 25–50 % of patients with advanced cancer [18]. Hong et al. [19] showed a prevalence of dental caries of 21 % in patients treated with chemotherapy and radiation with a mean decayed, missing, or filled teeth (DMFT) score [20, 21] of 4.5 in the post chemotherapy group. Osteonecrosis of the jaw (ONJ) has emerged as a new, debilitating adverse effect due to extended use of high potent intravenous bisphosphonates for bone metastases [22]. The cumulative incidence of ONJ is still uncertain but is estimated to range from 0.8 to 12 % after intravenous bisphosphonate treatment [23]. ONJ has also been associated with new targeted oncology medication with antibone resorptive activity, such as bevacizumab, sunitinib, and denosumab [24].

The present study was launched in order to investigate the prevalence of oral and dental problems in cancer patients receiving palliative treatment. The primary study aim was to examine the oral health and the prevalence of oral morbidity by means of patient self-report and an oral examination in palliative care cancer patients. The secondary aim was to investigate if information regarding oral problems was received by the patients.

Materials and methods

Study design

This was a cross-sectional, descriptive study conducted at the Cancer Center, Oslo University Hospital HF, Ullevaal (OUS) and at Hospice Lovisenberg, Norway from September 2007 through July 2008. Eligible patients, as assessed by the attending palliative care physician, were approached by the principal investigator (PW) and asked for their willingness to participate. The study consisted of two parts: the first being a semistructured interview supplemented by the completion of a self-report symptom assessment tool and the second being a clinical oral examination.

Patients

A convenience sample of 126 palliative care cancer inpatients was recruited, based on inclusion once a week at the two sites alternately, when the dentist (PW) was on duty. The inclusion criteria were (1) a diagnosis of advanced cancer outside the head and neck region, (2) admittance as a palliative care inpatient, (3) age ≥18 years, (4) ability to give informed consent, and (5) cognitive and physical ability to complete the questionnaire as judged by the patient's attending physician.

Measures

Interview and questionnaires

A face-to-face registration form developed by the investigators based on a previous pilot study on oral morbidity in

cancer patients at OUS (unpublished data; Herlofson BB poster presentation, European Association of Oral Medicine, Berlin 2004) was used for the semistructured interview. The registration form included items on gender, age, nationality, previous and current disease, cancer diagnosis and treatment, medication, tobacco and alcohol use, oral care, oral problems (including specific questions about the patient's perception of general oral morbidity, xerostomia, taste disturbances, problems eating, and dental health), and whether information about oral issues was given to the patient before and during treatment. The majority of questions had dichotomous answer categories, but categorical scales were used where appropriate, i.e., weight loss and hydration status. Karnofsky Performance Status (KPS) score [25], hydration, weight loss, and life expectancy were assessed by one of two experienced palliative care physicians based on their clinical experience. The number of medications per patient were counted and grouped according to registered general oral side effects, xerostomia, and taste changes according to multiple national and international databases for drug information such as http://www.felleskatalogen.no/ and http://www.fass.se/.

All patients completed the Norwegian version of the Edmonton Symptom Assessment System (ESAS) [26]. The ESAS was designed for quantitative assessment of symptom intensity with minimal patient burden and is among the most frequently used symptom assessment tools in advanced cancer [26, 27]. The modified Norwegian version used in the present study included 10 common symptoms of advanced cancer (pain at rest, pain when moving, fatigue, nausea, dyspnea, xerostomia, appetite, anxiety, depression, and general well-being) [28]. All symptoms were scored on a 0–10 numerical rating scale, with higher scores implying higher symptom intensity.

Oral examination

All patients underwent a bedside oral examination according to standard clinical practice with a systematic registration of oral findings including mucosa, teeth, dental plaque, gingival bleeding, and mirror test friction. Test of mirror friction on the oral mucosa is a simple bedside method for checking the lubricating effect of saliva and saliva replacement. It is performed by drawing the back of a mouth mirror along the buccal mucosa. The friction was registered according to a frequently used three-point scale [29]. Examination of the oral mucosa focused on the clinical expression of a fungal infection, based on the classification of oral candidiasis proposed by Axell et al. [30], and other mucosal alterations. Registrations of teeth included the number of remaining teeth, decayed teeth, missing teeth, and teeth with fillings based on the DMFT index, a functional dentition was defined as 20 or more remaining teeth [31]. Plaque and gingiva were evaluated by the mucosal-plaque index, an index developed for the evaluation of oral health and oral hygiene in hospitalized patients [32]. If oral treatment was needed, the patient was informed and assisted in getting contact with a hospital or private dentist. Oral mucosal swabs were taken for possible identification of fungal carriage and swabs were inoculated on Sabouraud's dextrose agar for 4 days at 37°C. If oral candidiasis was suspected clinically and confirmed by culture, treatment was given in collaboration with the attending physician.

Data analysis

SPSS 16.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for data analysis. Variables were described by means, standard deviations, and percentages. The dependent variable "oral morbidity" was determined by the patients' answer to the dichotomous (yes/no) question: "Do you suffer from discomfort or pain from the oral cavity at present?". For the univariate analysis, chi-square tests and *t* tests were used as appropriate. The significant factors associated with oral morbidity in the univariate analysis (nausea, appetite, anxiety, taste alterations, well-being, and xerostomia) were entered as predictors in a multivariate logistic regression analysis using backward variable selection. *Candida* carriage was not entered as a predictor in the model as it is just a marker of carriage of a microbe, not a manifest disease. A p value of 0.05 or less was taken to indicate statistical significance.

Ethical considerations

Ethical approval was obtained from the Regional Committee for Medical Research Ethics, Health Region South–East Norway. Data storage and conduct of the study were performed according to the regulations set forth by the Norwegian Data Inspectorate, the Data Protection Supervisor, and the Research Committee at OUS. Written informed consent was obtained from all participants.

Results

Ninety-nine of the 126 eligible patients (79 %) (mean age, 64 years; range, 36–90 years; 47 % males) agreed to participate. The predominant causes for declining participation were reduced general condition (38 %), fatigue (29 %), and no interest in the project (13 %). The most prevalent diagnoses were gastrointestinal cancer (21 %), lung cancer (19 %), and prostate cancer (11 %). Median KPS score was 40 (range, 20–80), all patients had either locally advanced, metastatic, or generalized disease, and in 73 %, the estimated life expectancy was <3 months. Seventy-three percent of the patients died within 3 months of examination (Table 1).

Table 1 Demographic and medical characteristics of the study population

Variable		Reported oral morbidity			*p* value
		Yes (*n*=66) *n* (%)	No (*n*=33) *n* (%)	Total (*n*=99) *n* (%)	
Gender	Male	29 (44)	17 (52)	46 (47)	0.48
	Female	37 (56)	16 (49)	53 (54)	
Age	Mean (SD)	62.4 (±12.7)	66.9 (±11.2)	63.9 (±12.3)	0.09[a]
	Range	36–90	36–88	36–90	
Smoking habits	Smoker	16 (24)	9 (27)	25 (25)	0.74
	Nonsmoker	50 (76)	24 (73)	74 (75)	
Taste alterations	Yes	51 (80)	14 (45)	65 (68)	0.001
	No	13 (20)	17 (55)	30 (32)	
Xerostomia	Yes	62 (94)	15 (46)	77 (78)	<0.001
	No	4 (6)	18 (55)	22 (22)	
Problems eating	Yes	40 (61)	15 (45)	55 (56)	0.15
	No	26 (39)	18 (55)	44 (44)	
Karnofsky score ≤40	Yes	35 (53)	17 (52)	52 (53)	0.89
	No	31 (47)	16 (49)	47 (48)	
Dehydrated	Yes	37 (56)	15 (46)	52 (53)	0.32
	No	29 (44)	18 (55)	47 (48)	
Lost >5 kg last 6 months	Yes	32 (49)	13 (39)	45 (46)	0.39
	No	34 (52)	20 (61)	54 (55)	
Estimated life expectancy	<3 months	51 (77)	21 (64)	72 (73)	0.15
	>3 months	15 (23)	12 (36)	27 (27)	
Actual time until death	<3 months	52 (79)	20 (61)	72 (73)	0.06
	>3 months	14 (21)	13 (39)	27 (27)	

[a] *t* test

Xerostomia was reported by 78 % of the patients, with 41 % reporting that they had experienced xerostomia for more than 3 months, 70 % of the patients showed increased mucosal friction on a mirror test, and 53 % of the patients were considered moderately dehydrated. General oral discomfort was reported by 67 % of the patients. Taste changes were reported by 68 % of the patients, while 56 % had problems with food intake and 46 % had lost more than 5 kg during the last 6 months (Table 1). The highest mean scores on the ESAS were found with fatigue (4.9), xerostomia (4.7), and poor appetite (4.4) (Table 2). No significant differences were seen in the total number of drugs taken or drugs with registered oral side effects when comparing patients who reported oral morbidity, xerostomia, or taste alterations, respectively, and those who did not report these adverse effects.

Table 2 ESAS symptom scores in patients with and without oral morbidity

ESAS symptom	Prevalence[a] (%)	Severity of symptom distress			*p* value
		ESAS all patients (*n*=99); mean (SD)	Oral morbidity		
			Yes (*n*=66); mean (SD)	No (*n*=33); mean (SD)	
Pain at rest	31.3	2.5 (±2.3)	2.6 (±2.2)	2.3 (±2.5)	0.46
Pain when moving	43.4	3.4 (±2.7)	3.6 (±2.5)	3.2 (±3.0)	0.51
Fatigue	62.6	4.9 (±2.9)	5.2 (±2.7)	4.4 (±3.2)	0.16
Nausea	23.2	2.0 (±2.4)	2.4 (±2.6)	1.3 (±1.7)	0.04
Dyspnea	41.4	3.1 (±3.0)	3.3 (±3.0)	2.6 (±3.0)	0.24
Xerostomia	65.7	4.7 (±3.0)	5.7 (±2.6)	2.8 (±2.9)	<0.001
Appetite	60.6	4.4 (±2.8)	5.0 (±2.7)	3.2 (±2.7)	0.002
Anxiety	34.3	2.9 (±2.5)	3.3 (±2.5)	2.2 (±2.4)	0.04
Depression	34.3	3.1 (±2.6)	3.2 (±2.5)	2.7 (±2.7)	0.34
General well-being	57.6	4.1 (±2.4)	4.5 (±2.3)	3.3 (±2.4)	0.02

[a] Based on the percentage of patients with a score above 3 on the ESAS 0–10 scale

Microbial evidence of *Candida* carriage was found in 86 % of the patients, while 34 % had both clinical and microbiological evidence of oral candidiasis. Nine (27 %) of the patients with both clinical and microbiological evidence of oral candidiasis were already receiving antifungal treatment. Partial or complete dentures were used by 14 (14 %) patients. Moderate or rich amounts of dental plaque were seen in 24 (24 %) patients. The mean number of decayed teeth was 1.9, missing teeth was 5.7, filled teeth was 13.2, and remaining teeth was 22.6. Mean DMFT for the whole patient group was 20.7, with a caries prevalence of 50.5 %. A functional dentition was registered in 96 % of the patients <60 years, while 69 % of those ≥60 years had ≥20 remaining teeth. Having a functional dentition was not associated with oral morbidity in this study (Table 3). Twelve patients (12 %) had received intravenous bisphosphonate therapy. One of these was diagnosed with ONJ triggered by an extraction of a maxillary molar 16 months prior to the examination.

Twenty-two percent of the patients stated that they had received information about adverse effects in the oral cavity caused by cancer and cancer treatment prior to or during therapy, while 38 % had received information about measures to reduce xerostomia. Of those reporting xerostomia as a problem, 43 % said that they had received such information. Information about the importance of oral hygiene during treatment had been received by 31 % only. However, 81 % of the patients were satisfied with the overall information they had received (Table 4).

The multivariate analysis showed that only xerostomia ($p<0.001$) and taste alterations ($p=0.03$) were significantly associated with oral morbidity (Table 5).

Discussion

The present study is one of a few combining palliative care patients' self-report of oral problems with a clinical examination. Our results showed that two thirds of the patients reported oral discomfort at the time of examination and interview. Xerostomia, taste alterations, appetite, *Candida* carriage, nausea, impaired feeling of well-being, and anxiety were all associated with oral morbidity in the univariate analysis, but only xerostomia and taste alterations were significantly associated with oral morbidity in the multivariate analysis. Oral morbidity in palliative care cancer patients may not necessarily result from the cancer treatment, but can be an expression of advanced, progressive disease [33]. Nevertheless, the treatment should focus on alleviating all symptoms, treating infections, patient information and education, and interventions that could be helpful on a day to day basis. Most of the patients in this study were very ill at the time of examination, and 73 % died within 3 months after the interview which may explain some of the results.

Xerostomia has been reported as a problem in 77 % of terminally ill cancer patients [18], almost the same as in the present study (78 %). Taste changes has been reported as a problem in 25–50 % in advanced cancer [18, 33], whereas 68 % of our study population reported it as a significant problem. This is a well-known side effect from chemotherapy, but only 14 % of our patients received chemotherapeutic drugs with taste changes as a known side effect at the time of the examination. It is important to recognize that other drugs, such as analgesics, beta-blockers, bisphosphonates, and antidepressants that are frequently used in the

Table 3 Clinical characteristics related to oral morbidity

Variable		Reported oral morbidity			*p* value
		Yes (*n*=66) *n* (%)	No (*n*=33) *n* (%)	Total (*n*=99) *n* (%)	
Mirror test friction	Yes	57 (86)	12 (36)	69 (70)	<0.001
	No	9 (14)	21 (64)	30 (30)	
Candida carriage	Yes	60 (91)	24 (75)	84 (86)	0.04
	No	6 (9)	8 (25)	14 (14)	
Candida infection	Yes	24 (36)	10 (30)	34 (34)	0.55
	No	42 (64)	23 (70)	65 (66)	
Plaque	No/small amount	49 (74)	26 (79)	75 (76)	0.62
	Moderate/large amount	17 (26)	7 (21)	24 (24)	
Gingivitis	No/mild	57 (86)	31 (94)	88 (89)	0.26
	Moderate/severe	9 (14)	2 (6)	11 (11)	
Caries	Yes	30 (46)	18 (62)	48 (51)	0.14
	No	36 (55)	11 (38)	47 (50)	
DMFT	Mean number of teeth (SD)	20.4 (±5.6)	21.3 (±5.8)	20.7 (±5.6)	0.49[a]
Functional dentition (≥20 teeth)	Yes	52 (80)	22 (71)	74 (77)	0.33
	No	13 (20)	9 (29)	22 (23)	

[a] *t* test

Table 4 Patients' perception of the information received

Variable		Report oral morbidity			*p* value
		Yes (*n*=66) *n* (%)	No (*n*=33) *n* (%)	Total (*n*=99) *n* (%)	
About measures to reduce xerostomia	Yes	27 (42)	10 (30)	37 (38)	0.28
	No	38 (59)	23 (70)	61 (62)	
About oral adverse effects of cancer treatment	Yes	15 (23)	6 (18)	21 (22)	0.55
	No	49 (77)	27 (82)	76 (78)	
About oral hygiene during and after cancer treatment	Yes	21 (32)	10 (30)	31 (31)	0.88
	No	45 (68)	23 (70)	68 (69)	
Satisfied with information in general	Yes	54 (82)	26 (79)	80 (81)	0.72
	No	12 (18)	7 (21)	19 (19)	

palliative setting do have taste changes reported as an adverse effect. In our study, we found that 92 % of the patients used one or more drug with taste alterations as a known adverse effect.

The patients in this study did not differ much from the general population of Norway [31] with regards to functional dentition, and functional dentition was not associated with oral morbidity. However, 50.5 % of the patients had dental caries and mean DMFT was 20.7. This is far more than that reported by Hong et al. [19] in their study in a general cancer sample after treatment with chemotherapy. The higher rate in our study may be explained by the high mean age of the study population, that the patients were in an advanced stage of disease, and that there might have been a lack of systematic assessment and treatment of dental problems during previous treatment.

The prevalence of clinically manifest oral candidiasis was 34 % in the present study. This is in accordance with a previous study by Davies et al. [16] in patients with advanced cancer in a palliative medicine unit, while our yeast carriage numbers were somewhat higher. Most of the patients who were given antifungal treatment were receiving this on a prophylactic indication (systemic fluconazole, in combination with local therapy with nystatin and/or clotrimazole). Although a number of different drugs are used against candidiasis, a recent Cochrane review showed a disputable effect of many of these drugs [34]. Thus, the uncertain effect of antifungal therapy might explain why the nine patients receiving antifungal treatment for their candidiasis still had a manifest clinical infection.

Table 5 Factors predicting oral morbidity

Predictor	*df*	*p* value	Exp(*B*)	95 % CI for Exp(*B*)	
				Lower	Upper
Xerostomia	1	<0.001	17.553	4.466	68.984
Taste alterations	1	0.031	3.471	1.124	10.725
General well-being	1	n.s.			
Appetite	1	n.s.			
Anxiety	1	n.s			
Nausea	1	n.s			

Multivariate logistic regression model using backward variable selection

n.s. not significant

Few patients reported that they had received information about oral side effects of cancer and cancer therapy prior to or during treatment, measures to relieve xerostomia at any time, or the importance of oral hygiene during and after treatment. On the other hand, most patients were generally pleased with the information they had received. No difference could be seen on any information variable between those with and those without oral morbidity, probably because very few had received such information in either group. This is a disturbing finding because all of these patients were supposed to have received a standardized information booklet at the start of treatment including a segment concerning oral complications. This shows that written information may not be sufficient and that health care personnel should be attentive to the possibility that patients do not read and/or understand all the information they are given. Inclusion of or collaboration with oral health professionals in the palliative team would increase the focus on oral problems. Bedside oral examinations could be conducted to identify problems and start prophylaxis or treatment early. It is important to follow-up each patient and to evaluate the effectiveness of the treatment.

Conclusion

This study showed that oral morbidity, xerostomia and taste changes in particular, are highly prevalent in palliative care cancer patients. This may lead to nutritional problems and impaired quality of life. Relatively few patients reported that they had received information about oral side effects. Increased awareness of and systematic information about oral problems is important in all phases of the cancer disease.

Systematic collaboration with dental professionals may increase the detection of oral morbidity at an early stage, thereby improving symptom management.

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