Progress of oral care and reduction of oral mucositis

-A pilot study in a hematopoietic stem cell transplantation ward-

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Abstract

Purpose

Oral mucositis is a common symptomatic complication associated with hematopoietic stem cell transplantation (HCT). We use simple strategies aimed to reduce oral mucositis by keeping the oral cavity clean and moist. Here, we report on the progress of oral care and the changes in the degree of oral mucositis. The purpose of this pilot study is to evaluate the effects of our strategies on the prevalence and the severity of oral mucositis.

Methods

Fifty-three consecutive patients from 2003–2006 administered conventional allogeneic HCT were enrolled in this study. Degree of oral mucositis was evaluated daily in all patients. Our oral care program was divided into two periods: “examination and trial period (2003 and 2004)” and “intensive oral care period (2005 and 2006). In the latter, an oral care regimen was carried out systematically by a multidisciplinary team.

Results

Using our oral care strategies, the prevalence of ulcerative oral mucositis was decreased significantly. The rate was reduced from 76% (10 of 13) of patients with ulcerative oral mucositis in 2003 to only 20% (3 of 15) in 2006.

Conclusions

Our pilot study suggests that oral mucositis in HCT patients can be alleviated by simple strategies aimed at keeping the oral cavity clean and moist.

Introduction

Oral mucositis is one of the most common symptomatic complications associated with high-dose chemotherapy, especially hematopoietic stem cell transplantation (HCT) [1,2]. Severe mucositis is associated with not only intolerable pain but also the risk of systemic infection. Oral mucositis is a significant cause of suffering and morbidity in patients receiving myeloablative chemotherapy [3]. Effective interventions to alleviate this complication are needed [3].

Keeping the oral cavity clean is one of the important interventions because this prevents both mucositis itself and infection associated with oral mucositis. The Multinational Association for Supportive Care/ International Society of Oral Oncology mucositis guidelines [4] and the National Cancer Center Network task force report [5] both recommend good oral hygiene in these patients.

Keeping the oral cavity moist may also be important. Oral dryness is caused by high-dose chemotherapy and total-body irradiation (TBI) performed as part of the conditioning regimen for HCT. Oral dryness not only results in discomfort, but may also exacerbate oral mucositis. We have often seen the development of ulcerative mucositis on dry mucosa in contact with dry teeth clinically. One of the reasons may be that saliva is necessary to maintain oral mucosal health. Additionally, moisture in oral cavity may moderate irritation caused by mechanical contact between the teeth and oral mucosa.

We began attempts to implement oral care in our ward from 2003. Our strategy includes a multidisciplinary approach prior to and during cancer treatment aimed at reducing the oral microbial load and keeping the oral cavity moist. Here, we describe the effect of intensive oral care on the degree of oral mucositis in HCT recipients.

Materials and Methods

Patients

Fifty-three consecutive patients administered conventional allogeneic HCT at Okayama University Hospital of Medicine and Dentistry between April 2003 and March 2007 (23 men, 30 women; mean age ± SD, 34.3 ± 11.8 y) were enrolled in this study. Patients administered autologous and reduced-intensity HCT (RIST) were excluded. Numbers of patients and diseases according to year are shown in Table 1.

The Ethics Committee of Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences approved this study.

HCT conditioning regimens

Most patients with related or unrelated donors received total-body irradiation (TBI) at a dose of 12 Gy in six fractions followed by cyclophosphamide (CY) at a dose of 60 mg/kg once daily for 2 days. Alternatively, patients received a combination of busulphan (BU) (4 mg/kg/day ×4 days) and CY (60 mg/kg/day ×2 days). Patients with unrelated cord blood donors were treated with TBI at 12 Gy, CY (60 mg/kg/day ×2 days) and cytarabine (Ara-C; 6 g/m^2/day ×2 days). Numbers of patients, sources of hematopoietic stem cells and HCT protocols (conditioning regimen) according to year are shown in Tables 2 and 3.

General infection control

Fluoroquinolone for prophylaxis against bacterial infection and fluconazole for prophylaxis against fungal infection were administered orally. Prophylaxis against

herpes virus infection with acyclovir was also given. Neutropenic fever was managed according to the guidelines of Hughes *et al*. [6].

Assessment of oral mucositis

The severity of oral mucositis in patients undergoing HCT was evaluated daily according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 3.0 [7]. The criteria for oral mucositis were as follows:

Grade 1: Erythema of the mucosa

Grade 2: Patchy ulcerations or pseudomembranes

Grade 3: Confluent ulcerations or pseudomembranes; bleeding in response to minor trauma

Grade 4: Tissue necrosis; significant spontaneous bleeding; life-threatening consequences

Grade 5: Death

Assessments were performed as part of daily nursing care by nurses who were trained by dentists and dental hygienists. The consistency of these assessments was checked by the dental team at least once per week.

Progress of our oral care regimen

Implementation of our oral care program was divided into two periods: “examination and trial period (2003 and 2004)” and “intensive oral care period (2005 and 2006).” Throughout this study period, the core oral care providers consisting of an experienced dentist, dental hygienists, and nurses were the same.

Examination and trial period (2003 and 2004):

We provided oral care interventions when oral mucositis developed clinically in HCT patients. On the other hand, there was no consensus within our ward regarding the precise method of oral care, and sometimes some points were missed.

Intensive oral care period (2005 and 2006):

We provided preventive oral care interventions keeping the oral cavity clean and moist. The core oral care providers educated all ward staff members, including new personnel. The oral care regimen included:

1) All subjects were referred to dentists with experience in treating medically compromised patients, and necessary dental treatment aimed at reducing pre-existent oral infection and the oral microbial load was completed as much as possible before HCT.
2) All subjects were instructed regarding self management including performing meticulous oral hygiene geared to their individual needs. Staff members, including nurses and dental professionals performed oral hygiene measures to patients in poor general condition. In patients with severe mucositis who could not tolerate tooth brushing, dental and mucosal debris was gently removed using saline drenched gauzes, aimed at keeping the oral cavity as clean as possible.
3) Oral rinsing with saline was performed every 3 h during daytime. In addition, patients used a commercial saliva substitute, Oralbalance® when they experienced oral dryness. Oral rinsing with chlorhexidine is not recommended in Japan. Oral rinsing with amphotericin B was indicated only when fungi were detected on the oral mucosa.

Statistical analysis

The frequencies of patients with oral ulcerative mucositis (NCI-CTCAE version 3.0 $\geq$ 2) during transplantation period for each year were analyzed statistically with Fischer's exact test. Mucositis frequencies of 2004, 2005, and 2006 were compared with that of 2003, and the period 2003-2004 and 2005-2006 were compared. *P*-values were calculated using StatFlex statistical software (Artech, Osaka, Japan).

Results

Progress of oral care and oral mucositis

The frequencies of all grades of mucositis by year are shown in Fig. 1A. Subjects were categorized as follows: non-oral ulcer, < Grade 1; oral ulcer carrier, > Grade 2, since mucositis ≥ Grade 2 suggests disruption of the oral mucosal membrane barrier and formation of an infection route (Fig. 1B). With progress of oral care, the frequency of patients with ulcerative oral mucositis decreased significantly ($P \leq 0.05$, Fischer's exact test), whereas there were no significant changes relative to diseases or conditioning regimens (Tables 1 and 2); mucositis rate was reduced from 76% (10 of 13) of patients with ulcerative oral mucositis in 2003 to only 20% (3 of 15) in 2006. When the historical control group (2003+2004) was compared with the intensive oral care regimen group (2005+2006), also a significant reduction in ulcerative mucositis was observed (Fig. 1C; $P \leq 0.05$, Fischer's exact test).

Discussion

Our oral care strategy aimed at keeping the oral cavity clean and moist reduced the degree of ulcerative oral mucositis in our ward. Borowski *et al.* reported the superiority of intensive oral care in patients with and without TBI and in patients with good or poor oral hygiene; the observed risk of mucositis was reduced by 70% in each of these four subgroups in their study [8]. Our results were very similar to those reported in this study. The ulcerative mucositis rate in our study was reduced from 76% (10 of 13) of patients in 2003 to only 20% (3 of 15) in 2006. Therefore, the rate of ulcerative mucositis in 2003 was reduced by 73.7% in 2006 by our intensive oral care regimen (Fig. 1B).

The Multinational Association for Supportive Care in Cancer/ International Society of Oral Oncology mucositis guidelines recommend systematic oral care with brushing, flossing, bland rinses, and moisturizers [4]. This guideline recommends a multidisciplinary approach to oral care including nurses, physicians, dentists, dental hygienists, dieticians, pharmacists, and others when relevant. Furthermore, dental examination and treatment are considered important prior to the start of cancer therapy [4]. The present pilot study supports these recommendations. Our oral care regimen included application of Oralbalance, which has been shown to have an antimicrobial effect [9]. However, the use of additional antimicrobial agents may be indicated in patients who cannot continue tooth brushing. In our regimen we used wet gauzes to clean the oral cavity in these patients, but this has been shown to be ineffective to remove dental plaque [10].

The shifts in some of the diagnoses (Table 1) and associated treatment regimens between the two periods evaluated may have had an impact on the outcomes.

A prospective intervention study including large numbers of subjects and controls may provide more detailed information on optimal oral care measures and may demonstrate the significance of oral care in HCT patients to reduce oral mucositis and related outcomes including pain, fever and infection, length of hospital stay and costs.

In conclusion, our results suggest that oral mucositis in HCT patients can be alleviated by intensive multidisciplinary oral care starting prior to HCT and aimed at keeping the oral cavity clean and moist in the immediate post transplant phase.

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Tables

Table 1. Diseases of patients

Diseases	Year				Total
	2003	2004	2005	2006	
Acute myelogenous leukemia	5	4	3	4	16
Acute lymphoblastic leukemia	5	3	1	2	11
Chronic myelogenous leukemia	1	0	1	0	2
Malignant lymphoma	1	4	6	4	15
Aplastic anemia	1	0	1	0	2
Myelodysplastic syndromes	0	0	2	5	7
Total	13	11	14	15	53

Table 2. Source of hematopoietic stem cells

Source	Year				Total
	2003	2004	2005	2006	
Related donors	7	4	2	6	19
Unrelated donors (without cord blood donors)	4	7	7	4	22
Unrelated cord blood donors	2	0	5	5	12
Total	13	11	14	15	53

Table 3. Conditioning regimen of HCT

Conditioning regimens	Year				Total
	2003	2004	2005	2006	
With TBI					
CY/TBI	6	5	6	9	26
L-PAM/TBI	2	2	3	2	9
CA/TBI	1	0	0	0	1
CA/CY/TBI	0	1	3	2	6
CY/TBI/ATG	0	0	1	0	1
Without TBI					
BU/CY	3	3	1	1	8
CY/ALG	1	0	0	0	1
Flu/BU	0	0	0	1	1
Total	13	11	14	15	53

TBI, Total-body irradiation; CY, cyclophosphamide; L-PAM, melphalan; CA, cytarabine; ATG, anti-thymocyte globulin; BU, busulfan; ALG, anti-lymphocyte globulin; Flu, fludarabine.

Figure legend

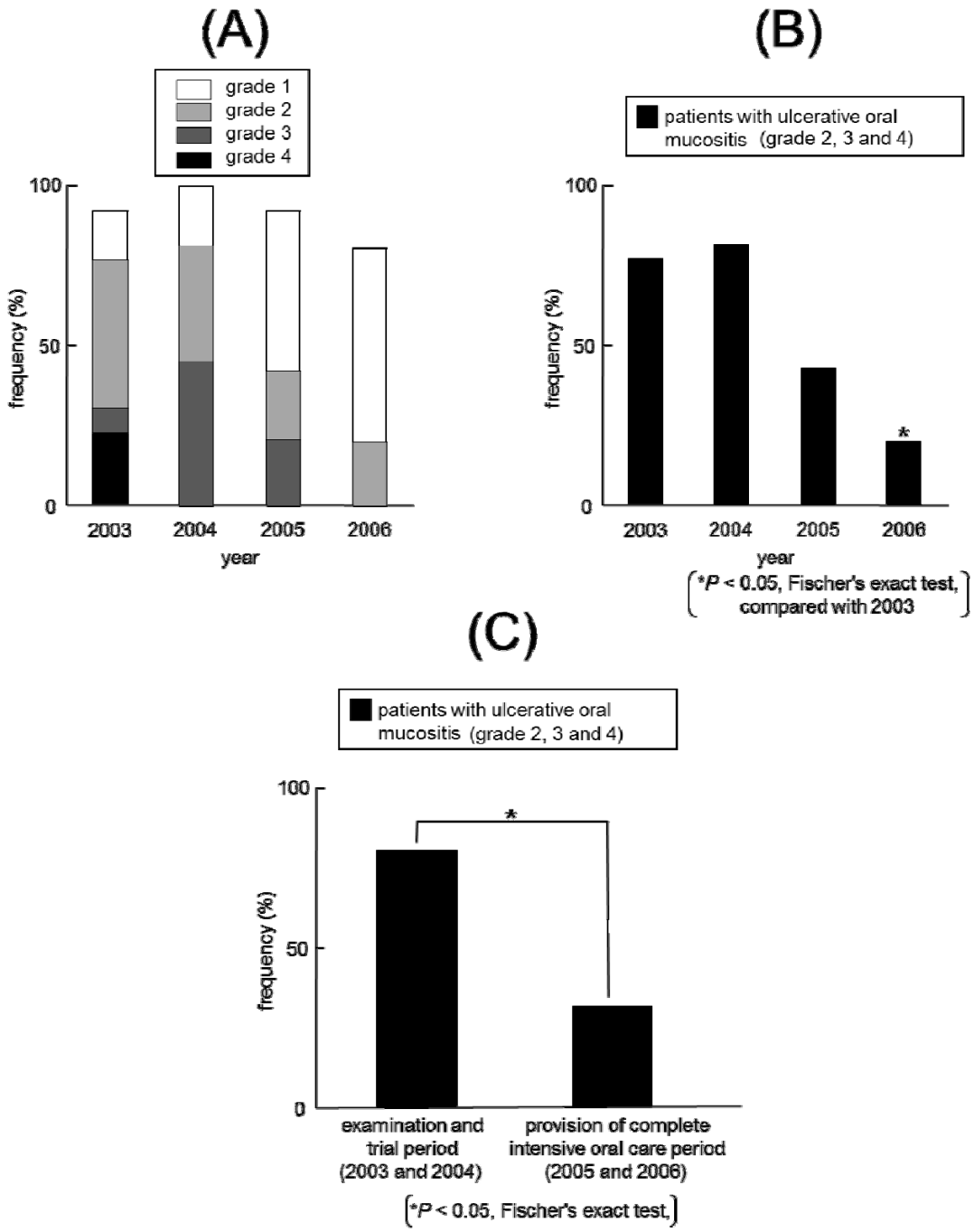
Fig. 1 Frequencies of oral ulcerative mucositis by year.

(A): Frequencies of all grades of mucositis by year.

(B): Frequencies of patients with ulcerative oral mucositis (grade > 2). Numbers of patients with ulcerative oral mucositis according to the year of their HCT were as follows: 10 of 13 in 2003; 9 of 11 in 2004; 6 of 14 in 2005; 3 of 15 in 2006.

(C): The historical control group (2003+2004) was compared with the intensive oral care regimen group (2005+2006). A significant reduction of ulcerative mucositis was observed.

Fig. 1


(A)
grade 1
grade 2
grade 3
grade 4
100
50
0
frequency (%)
2003
2004
2005
2006
year
(B)
patients with ulcerative oral mucositis (grade 2, 3 and 4)
100
50
0
frequency (%)
*
2003
2004
2005
2006
year
(*P < 0.05, Fischer's exact test, compared with 2003)
(C)
patients with ulcerative oral mucositis (grade 2, 3 and 4)
100
50
0
frequency (%)
*
examination and trial period (2003 and 2004)
provision of complete intensive oral care period (2005 and 2006)
(*P < 0.05, Fischer's exact test,)