Short Communication

Evaluation of xerostomia in hematopoietic cell transplantation by a simple capacitance method device

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Abstract

***Goals*:** Hematopoietic cell transplantation (HCT) may lead to the development of xerostomia. However, there have been few reports of xerostomia in HCT patients based on objective data. We investigated moisture in the oral mucosa in patients undergoing HCT by the capacitance method using a convenient device, Moisture Checker for Mucus® (MCM; Life Co., Ltd., Saitama, Japan).

***Subjects and Methods*:** Thirty-six patients undergoing HCT at Okayama University Hospital of Medicine and Dentistry (Male: 22, Female: 14; age: 41.6 ± 16.2 years old) were enrolled in this study. Moisture in the oral mucosa was measured by MCM in accordance with the manufacturer's instructions. The results were obtained as MCM values (%), which are the weight percentage of water content in the oral mucosal epithelium. As controls, moisture of the oral mucosa was also examined in healthy volunteers (Male: 27, Female: 35; age: 43.0 ± 14.6 years old).

***Main Results*:** Throughout the examination period, MCM values were significantly lower in patients who underwent HCT than in controls. The degree of mucosal moisture in HCT patients showed wide interindividual differences.

***Conclusion*:** The degree of mucosal moisture in HCT patients was low and showed wide interindividual differences. Evaluation of xerostomia using such a device may contribute to appropriate oral care with saliva substitute.

Key words: xerostomia, hematopoietic cell transplantation, hyposalivation

Introduction

Anti-cancer treatment regimens, such as chemotherapy and/or irradiation, damage the salivary glands and cause uncomfortable xerostomia [1,3]. Hematopoietic cell transplantation (HCT) may lead to the development of xerostomia. High-dose chemotherapy and total-body irradiation, which are performed as conditioning regimens for HCT, damage the salivary glands. Xerostomia results in not only uncomfortable oral dryness, but may also increase the severity of oral mucositis induced by chemotherapy and/or irradiation. This is because patients with xerostomia lose one of the most important factors in protecting the oral mucosa, saliva, which contains many components of the innate and acquired defense systems, and not only eliminates microorganisms from the oral cavity [2,7] but also moderates mechanical contact between the teeth and the oral mucosa. Indeed, we often see the development of ulcerative mucositis on mucosa in contact with dry teeth clinically. However, there have been few studies of xerostomia in HCT patients using objective data.

The measurement of the flow rate of saliva is a diagnostic test of salivary gland function and is one of the diagnostic methods for Sjögren's syndrome. However, it is a relatively time-consuming procedure to carry out in ordinary clinical practice [4]. The general condition of patients undergoing HCT is often poor, and therefore this method is not appropriate in daily evaluation, because even a few minutes of testing may often be difficult for patients during this period.

The recently developed Moisture Checker for Mucus® (MCM; Life Co., Ltd., Saitama, Japan), a device that measures the weight percentage of water content in the oral epithelium by the capacitance

method, has been reported to be useful in the screening of hyposalivation [8]. This device provides information about the moisture of the oral mucosa itself by touching the mucosa for a few seconds.

In the present study, we investigated the moisture of the oral mucosa in patients undergoing HCT by the capacitance method using the MCM.

Patients and Methods

***Subjects*:**

A total of 36 consecutive patients undergoing HCT at Okayama University Hospital of Medicine and Dentistry (Male: 22, Female: 14; age: 41.6 ± 16.2 years old) were enrolled in this study. Diseases and HCT treatment protocols are shown in Tables 1. The oral cavities of all patients were kept plaque-free by themselves, a nurse, and a dental hygienist. As controls, 62 healthy volunteers from the hospital staff (Male: 27, Female: 35; age: 43.0 ± 14.6 years old) were also enrolled in the study.

Informed consent for examination of oral mucosal moisture was obtained from each subject, and the Ethical Committee of Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences approved this study (No. 187).

***Assessment of moisture of oral mucosa*:**

From day –7 to day +14 of HCT, moisture of the oral mucosa was examined in each patient every day. The moisture of the oral mucosa was measured using a simple capacitance method device, Moisture Checker for Mucus® (MCM; Life Co., Ltd.) in accordance with the manufacturer's instructions. This device was designed to measure the weight percentage of water content in the mucosa with a measurement depth of 30 μm by touching the sensor to the oral mucosa for a few seconds. This device uses the capacitance method by which the water content is measured by determining the dielectric constant of water. As the dielectric constant of water is much higher than those of other substances, the measured value of the mucosal dielectric constant is then used to calculate the water content ratio. Results were obtained as

MCM values (%), representing the weight percentage of water content in the oral mucosal epithelium. As controls, the moisture of the oral mucosa was also examined in healthy subjects.

***Statistical analysis*:**

Differences in moisture of the oral mucosa between patients and healthy controls were compared by Student's *t*-test. *P*-values were calculated using the statistical software, StatFlex (Artech, Osaka, Japan).

Results

Moisture of oral mucosa during HCT

The moisture of the oral mucosa during HCT is shown in Figure 1. Throughout the examination period, MCM values, representing the weight percentage of water content in the oral mucosal epithelium, were significantly lower in patients who underwent HCT (n = 36) than in controls (n = 62, 27.3 ± 3.5%). The degree of mucosal moisture in HCT patients showed wide interindividual differences.

Discussion

The present study, which evaluated xerostomia in HCT patients using a simple capacitance method device, indicated that patients undergoing HCT had lower mucosal moisture contents than healthy subjects throughout the study period. Furthermore, the degree of mucosal moisture showed wide interindividual differences.

Evaluation of xerostomia could contribute to appropriate oral care according to the degree of xerostomia in this period. For example, the commercially available saliva substitute Biotène Oralbalance® (Laclede, Inc. CA. USA) has been reported to alleviate the symptoms of post-radiotherapy xerostomia in head and neck cancer patients [5,9]. Therefore, the MCM value suggested that oral care with this saliva substitute may be effective in HCT patients. Our previous study suggested that this product does not promote infection in patients undergoing HCT [6]. Convenient devices, such as MCM, would be useful in daily evaluation of these patients with regard to appropriate oral care.

Wide interindividual differences in the degree of mucosal moisture may be explained by the differences in the original disease, source of hematopoietic cells (auto or allo), and transplantation regimen. Further studies with regard to differences in leukemia treatment should make it possible to predict the severity of xerostomia. Planning strategies for xerostomia based on its predicted severity by the type of leukemia before starting HCT and daily evaluation of xerostomia during the HCT period using a convenient device, such as the MCM, may enable more effective oral care with regard to problems caused by xerostomia, such as mucositis.

In conclusion, mucosal moisture of patients undergoing HCT evaluated by the capacitance method with MCM was reduced as compared to that in healthy controls.

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References

1. Amerongen AV, Veerman EC (2003) Current therapies for xerostomia and salivary gland hypofunction associated with cancer therapies. Support Care Cancer 11: 226-231.

2. Brandtzaeg P (1989) Salivary immunoglobulins. In: Tenovuo J ed., Human saliva: clinical chemistry and microbiology, Vol. II. CRC Press, Inc.: Boca Raton, FL, pp 1-54.

3. Jensen SB, Pedersen AM, Reibel J, Nauntofte B (2003) Xerostomia and hypofunction of the salivary glands in cancer therapy. Support Care Cancer 11: 207-225.

4. Longman LP, McCracken CF, Higham SM, Field EA (2000) The clinical assessment of oral dryness is a significant predictor of salivary gland hypofunction. Oral Dis 6: 366–370.

5. Shahdad SA, Taylor C, Barclay SC, Steen IN, Preshaw PM (2005) A double-blind, crossover study of Biotene Oralbalance and BioXtra systems as salivary substitutes in patients with post-radiotherapy xerostomia. Eur J Cancer Care (Engl) 14: 319-326.

6. Sugiura Y, Soga Y, Tanimoto I, Kokeguchi S, Nishide S, Kono K, Takahashi K, Fujii N, Ishimaru F, Tanimoto M, Yamabe K, Tsutani S, Nishimura F, Takashiba S (2008) Antimicrobial effects of the saliva substitute, Oralbalance®, against microorganisms from oral mucosa in the hematopoietic cell transplantation period. Support Care Cancer 16: 421-424.

7. Tenovuo J (1998) Antimicrobial function of human saliva - how important is it for oral health? Acta Odontol Scand 56: 250-256.

8. Yamada H, Nakagawa Y, Nomura Y, Yamamoto K, Suzuki M, Watanabe NY, Saito I, Seto K (2005) Preliminary results of moisture checker for Mucus in diagnosing dry mouth. Oral Dis 11: 405-407.

9. Warde P, Kroll B, O'Sullivan B, Aslanidis J, Tew-George E, Waldron J, Maxymiw W, Liu FF, Payne D, Cummings B (2000) A phase II study of Biotene in the treatment of postradiation xerostomia in patients with head and neck cancer. Support Care Cancer 8:203-208.

Fig. 1

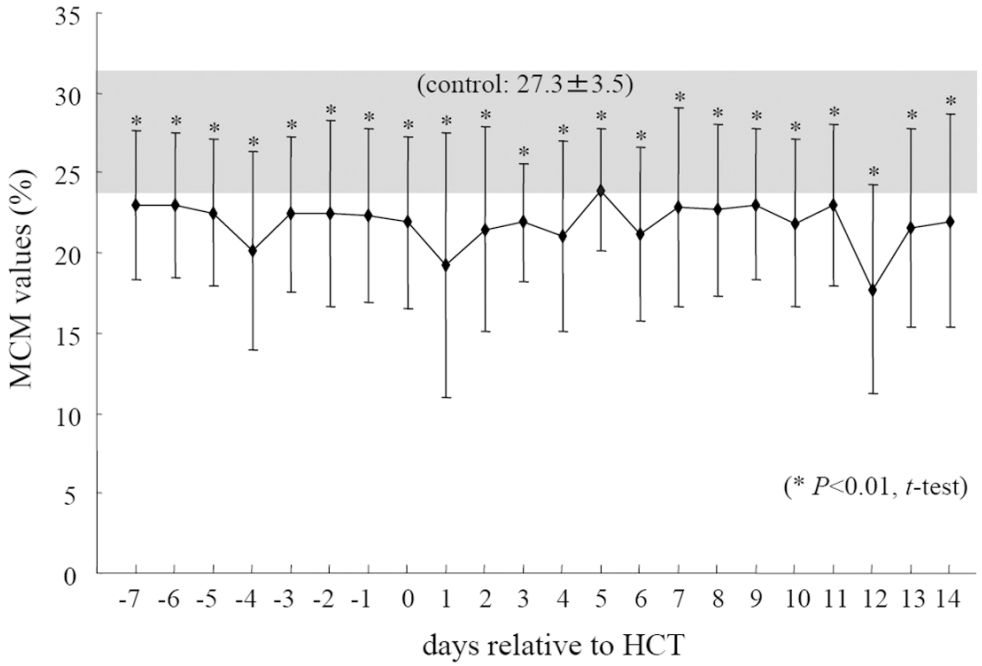
35
30
25
20
15
10
5
0
MCM values (%)
(control: 27.3±3.5)
(* P<0.01, t-test)
-7 -6 -5 -4 -3 -2 -1 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
days relative to HCT

Figure legends

Figure 1: Moisture of the oral mucosa during HCT

MCM values, indicating the weight percentage of water content in the oral mucosal epithelium of the patients (n = 36), were measured on days –7 to +14 and are shown as means ± SD. MCM values of healthy controls (n = 62) are also shown as the grey area (27.3 ± 3.5%). Throughout the examination, the MCM values of patients were significantly lower than those of healthy controls ($P<0.01$, *t*-test). The degree of mucosal moisture in HCT patients showed wide interindividual differences.

Table

Table 1: Diseases of patients and HCT protocols

Diseases	HCT protocols				Total
	Autologous	Allogeneic			
		Conventional		Reduced-intensity	
		with TBI	without TBI		
Malignant lymphoma	4	5	1	6	16
Acute myeloid leukemia		2	1	4	7
Acute lymphoblastic leukemia		5	1		6
Multiple myeloma	2			1	3
Myelodysplastic syndromes				1	1
Aplastic anemia				1	1
Renal cell carcinoma			1		1
Small intestinal carcinoma				1	1
Total	6	12	4	14	36