Disease，慢性閉塞性肺疾患）とは

閉塞性肺疾患の代表として，COPD（肺気腫，慢性気管支炎）および気管支喘息がある。気管支喘息は気道過敏性による喘鳴，息切れ，胸部圧迫感，咳嗽が夜間から早朝に悪化する症状を伴う慢性炎症性疾患で可逆性を有する気流閉塞に特徴づけられるのに対して，COPDは有毒な粒子の吸入（喫煙など）による慢性炎症により末梢気道病変（慢性気管支炎）と肺実質病変（肺気腫）を生じ，不可逆的な気流閉塞を有する疾患であり，労作時呼吸困難，運動耐容能の低下などの症状により特徴づけられる。様々な肺外病変を合併することが多く，肺病変＋肺外病変が相まって病態が進行することが，近年明らかとなってきている。

1．症状・身体所見

当初は症状を呈さないことも多い。一般的には病態の進行とともに慢性咳嗽，喀痰，労作時呼吸困難が生じる。身体所見では，当初は全く所見を認めないことが多いが，病態の進行に伴い肺の過膨張による「ビア樽状胸郭」，努力呼吸に伴う呼吸補助筋（胸鎖乳突筋，斜角筋など）の肥大や鎖骨上窩や肋間腔の陥凹，またチアノーゼなどの呼吸不全症候（低酸素血症）や，浮腫などの症状が出現する。

2．診断

COPDは，肺機能検査（スパイロメトリー）にて不可逆性を有する気流閉塞を認めることにより診断される（気管支拡張剤吸入後（サルブタモール 400μg）の1秒量（FEV_1）/努力性肺活量（FVC）＜0.70）。FEV_1予測値の80%以上 = stage I, 80%未満，50%以上 = stage II, 50%未満，30%以上 = stage III, 30%未満 = stage IVの4段階に重症度分類される。

3．病因

発症要因としては外的因子として，喫煙，職業上の粉塵の吸入，化学物質への曝露および下気道感染などが，内的因子としてはα1アンチトリプシン欠損症，宿主側遺伝子多型性，気道過敏性などが推定されている。長期間の喫煙など有害物質の吸入により，慢性的な炎症が惹起され，この炎症により肺内でプロテアーゼ/アンチプロテアーゼ不均衡，オキシダント/ アンチオキシダント不均衡を生じ，主に末梢気道の線維化と肺胞破壊により，気流閉塞を来す。同時に，慢性炎症により，ガス交換能障害，粘液過分泌，肺高血圧や，類そう，骨格筋疲労，骨粗鬆症，うつ，貧血，心血管病変の合併により病態が形成される。

Potential Benefits of Serum IgG Antibody Titer against Periodontal Bacteria in the Prognosis for Periodontitis Recurrence

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Running title: Prognosis of periodontitis recurrence by serum IgG level

Key words: serum IgG antibody titer; periodontitis recurrence; supportive periodontal therapy; ELISA

Chronic periodontitis is a poly-microbial infectious disease and the patients exhibit high serum IgG titers against periodontal bacteria. We divided the 139 chronic periodontitis patients into 2 groups, normal and high serum IgG titer group after periodontal treatment, and investigated the significant differences between both groups in the recurrence ratio of periodontitis. Interestingly, the recurrence ratio in high IgG titer group against each periodontal bacteria, especially gram-negative obligate anaerobe such as *Prevotella intermedia* and *Treponema denticolla* was higher than that of the normal IgG titer group. Therefore, we conclude serum IgG antibody titer is useful in the prognosis for periodontitis recurrence.

Chronic periodontitis is the most common polymicrobial infectious disease and the disease may result in loss of teeth by inflammation-mediated bone resorption [1]. Infection with periodontal bacteria, especially gram-negative, obligate anaerobe such as *Porphyromonas gingivalis* (*Pg*) leads to humoral immunological responses and elevates the levels of serum IgG antibody titer against the bacteria [2]. There are various reports regarding the usefulness of examination of serum IgG antibody titer during treatment of periodontitis [3-5]. However, it has not been established whether of the level of serum IgG antibody titer can be used to predict periodontitis recurrence after the completion of periodontal treatment.

In the present study, we examined the level of infection of several periodontal bacteria by serum samples from patients using enzyme-linked immunosorbent assay (ELISA) methods and evaluated the relation of serum IgG antibody titer to recurrence of periodontitis during periodontal maintenance phase.

The subjects included 139 chronic periodontitis patients who visited the Department of Periodontics and Endodontics, Okayama University Hospital of Medicine and Dentistry and received dynamic periodontal treatments, followed by supportive periodontal therapy (SPT) for more than 1 year (male: 34, female: 105, average age: 61.4 ± 10.4). The dynamic periodontal treatments include scaling, root planning, under infiltration anesthesia and periodontal surgeries at 1 or more sites. SPT procedures included re-motivation, plaque control guidance, scaling and root planning and removal of local

environmental factors at intervals of a few months. Patients with systemic diseases such as diabetes were excluded from this study because of their known risk factors for periodontal diseases. Additionally, patients were screened for risk behaviors such as smoking, by directed interviews and excluded, as well as any relevant systemic conditions or medication intake. Informed consent was obtained from each subject, and the protocol for the evaluation of serum IgG titer has been approved by the institutional review board. Based on the previous report [6], patients with one or more deepening periodontal pockets with a depth of 3 mm or more in SPT phase were judged to be "with recurrence".

The amount of serum IgG that bound to each pathogenic bacteria antigen causing periodontitis was measured by ELISA as described previously [2]. Since the bacterial antigens include various components, mainly proteins, lipopolysaccharide (LPS) and DNA, the serum IgG antibody titer reflects total results of immune-responses. Therefore, we used sonic extracts of whole bacterial cells as antigens for ELISA assay. In brief, total 1 g (wet weight) of each bacteria, *Actinobacillus actinomycetemcomitans* (*Aa*) Y4, *Aa* ATCC29523, *Eikenerra corrodens* (*Ec*) FDC1073, *Prevotella intermedia* (*Pi*) ATCC25611, *Pg* FDC381, *Pg* SU63, *Treponema denticola* (*Td*) ATCC35405, and *Campylobacter rectus* (*Cr*) ATCC33238 was suspended in 40 ml of 5 mM phosphate buffer (pH 7.4) and disintegrated with 1 g of glass beads (diameter, 0.18 mm; Takashima Shoten, Tokyo, Japan) in an ultrasonic disruptor (Model UR-200P; Tomy Seiko, Tokyo Japan) set at 200 W for 15 min at 4 °C. The sonicated cell suspension was centrifuged at 10, 000 × g for 20 min to remove unbroken cells and cell debris and the supernatant was used as sonic extract.

During the SPT phase, patients were first classified into a "Recurrence group" (with recurrence or progression of periodontitis) and a "Stable group" (without recurrence or progression of periodontal disease) for a case-control study. A total of 139 patients (Stable group: 112, Recurrence group: 27) were evaluated. There were no significant differences between the stable and recurrence group in the score of their plaque control record, bleeding on probing and even averaged pocket probing depth. On the other hand, there were significant differences between

stable and recurrence groups in their age and number of teeth (age, P=0.026; number of teeth, P=0.025; Mann-Whitney U-test). As shown in Figure 1, in 12 strains from 8 bacterial species, the average of serum IgG antibody titer against all periodontal bacteria after periodontal treatment in recurrence group was higher than that of stable group. Importantly, the levels of serum IgG antibody titer against several periodontal bacteria were statistically higher in the recurrence group than that of stable group before transition to SPT phase (*Aa* Y4, P=0.020; *Ec* ATCC23834, P=0.040; *Pg* SUNY67, P=0.020; *Cr* ATCC33238, P=0.025: Mann-Whitney U-test). The serum IgG antibody titer against *Td* ATCC35405 was also clearly higher in the recurrence group than in the stable group (P=0.081: Mann-Whitney U-test) after periodontal treatment.

Next, the patients were classified into "High IgG titer" and "Normal IgG titer" group at the time starting SPT phase for a companion study. We determined the baseline "Normal" IgG titer level by measuring the serum IgG antibody titer in healthy volunteers without chronic periodontitis (n=8, 30.3 ± 4.9 yr). Patients in this study having IgG titer levels significantly above the average (> 2σ) of healthy volunteers were classified as high level-serum IgG antibody titer against periodontal bacteria. The IgG antibody titer obtained from the test was indexed using the width of 2 SD determined from the group of 10 healthy subjests (aged: 20-29 yr). The following formula was applied to the EU value to calculate the diagnostic standardized value:

Test Result (Standardized Value) = {IgG Titer of patient (EUi) – mean IgG titer of healthy control subjects ($\overline{EUx}$)} / 2SD

In the "Normal" group, the level of serum IgG antibody titer was observed to be lower than 1.0 against each type of bacteria. In the "High" group, the level of serum IgG antibody titer exceeds 1.0 against periodontal bacteria.

As shown in Table 1, importantly, we found that there were no significant differences between Normal and High IgG antibody titer group in clinical findings (Mann-Whitney U-test) and confirmed to become healthy clinically in both groups by periodontal treatment. Furthermore, we observed the tendency that the recurrence ratio of high IgG titer group was higher than that of normal group (Normal group: 14.9-19.1 %, High group: 20.5-36.8 %). Especially, the

recurrence ratio of high IgG titer group was statistically higher than that of normal titer group (*Pi* ATCC25611, P=0.021; *Td* ATCC35405, P=0.039; *Cr* ATCC33238, P=0.048: Pearson's χ^2 test). In addition, the recurrence ratio of high titer group against *Pg* SU63 was quite higher than that of normal titer group (P=0.083: Pearson's χ^2 test).

Recently, there have been reports that serum IgG antibody titer was useful for diagnosing periodontitis or judging treatment effects [7,8]. Also, it has been reported that the level of serum IgG antibody titer against *Pg* increases before absorption of alveolar bone, and could predict the progression of periodontitis [9]. The results of this study indicate that serum IgG antibody titer might be useful as a predict marker of periodontitis recurrence.

Taken together, our findings indicate that higher serum IgG titer against obligate anaerobe even after active periodontal treatment is an important factor to predict the periodontitis recurrence and this approach will contribute to create the prognostic systems in periodontitis recurrence.

ACKNOWLEDGEMENTS

We greatly thank Scott Messenger at NASA Johnson Space Center for the revision of the manuscript and for encouragement in our research. This study was supported by Grant-in-Aid for Scientific Research (A) (No. 18209061) from the Japan Society for the Promotion of Science and Health and Labour Sciences Research Grants (Comprehensive Research on Aging and Health) from the Ministry of Health, Labour and Welfare of Japan.

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FIGURE LEGEND

Figure 1. Levels of serum IgG antibody titer against 12 periodontal bacteria.
The significant differences between "Stable" and "Recurrence" group were analyzed using the Mann-Whitney U test. Each dot represents an individual data tested by ELISA assay. The Y-axis in each panel denotes the value determined as [(serum IgG titer tested by ELISA) – (mean titer calculated using that of healthy subjects)] / (2SD calculated using that of healthy subjects).

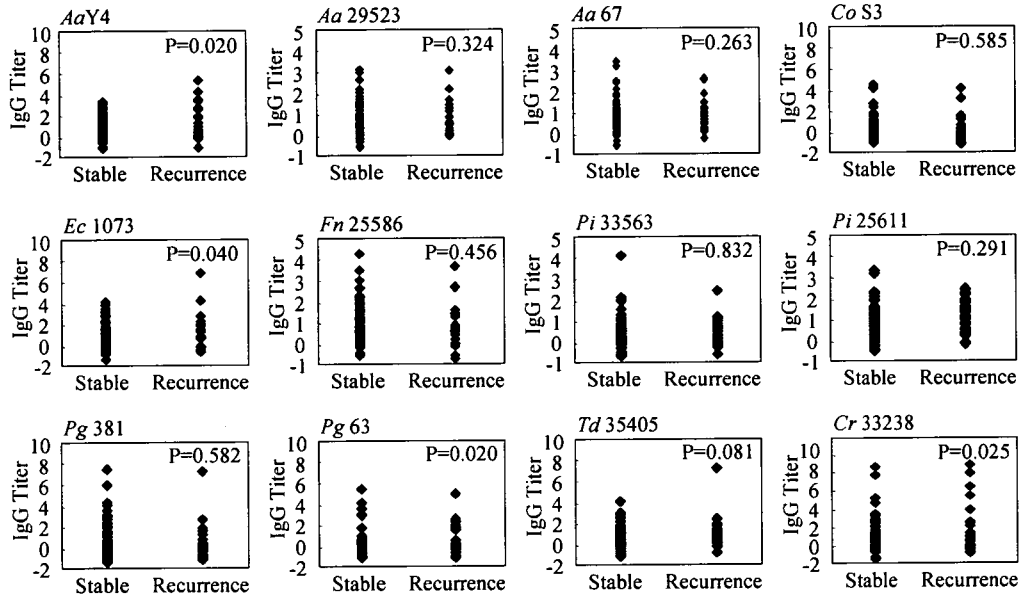
AaY4
P=0.020
Aa 29523
P=0.324
Aa 67
P=0.263
Co S3
P=0.585
Ec 1073
P=0.040
Fn 25586
P=0.456
Pi 33563
P=0.832
Pi 25611
P=0.291
Pg 381
P=0.582
Pg 63
P=0.020
Td 35405
P=0.081
Cr 33238
P=0.025
IgG Titer
Stable
Recurrence

Fig. 1

Table 1. Clinical findings after periodontitis treatment and reccurrence ratio during periodontal maintenance

	Strains	Examination	Normal IgG titer	High IgG titer	*P-Value*
Facultative anaerobic	*AaY4*	Patients number	104	35	
		Age (yr)	60.1 ± 10.7	64.0 ± 9.2	0.16
		Number of teeth	21.8	20	0.17
		PCR (%)	21.3	25.7	0.47
		BOP (%)	11.7	14.4	0.51
		Pocket depth (mm)	2.32	2.29	0.66
		Serum IgG Ab. Titer	0.079	2.51	<0.0001
		Recurrence ratio (%)	17.3	25.7	0.28
	Aa ATCC29523	Patients number	107	35	
		Age (yr)	61.2 ± 10.6	61.5 ± 10.3	0.92
		Number of teeth	22.2	19.2	0.085
		PCR (%)	22.7	21.6	0.54
		BOP (%)	12.4	12.4	0.79
		Pocket depth (mm)	2.28	2.41	0.39
		Serum IgG Ab. Titer	0.11	2.69	<0.0001
		Recurrence ratio (%)	16.8	28.1	0.16
	Ec FDC1073	Patients number	82	57	
		Age (yr)	60.8 ± 10.4	61.6 ± 10.5	0.69
		Number of teeth	22.1	20.2	0.064
		PCR (%)	23.1	21.6	0.41
		BOP (%)	12.4	12.2	0.63
		Pocket depth (mm)	2.31	2.33	0.89
		Serum IgG Ab. Titer	0.11	2.64	<0.0001
		Recurrence ratio (%)	15.9	24.6	0.21
Obligate anaerobic	*Pi ATCC25611*	Patients number	115	24	
		Age (yr)	61.3 ± 10.1	61.1 ± 12.5	0.93
		Number of teeth	21.6	20.2	0.49
		PCR (%)	22.3	23.3	0.84
		BOP (%)	12.2	13.7	0.51
		Pocket depth (mm)	2.31	2.39	0.24
		Serum IgG Ab. Titer	0.02	2.07	<0.0001
		Recurrence ratio (%)	15.8	36.1	0.021
	Pg FDC381	Patients number	100	39	
		Age (yr)	61.7 ± 10.5	60.1 ± 10.5	0.56
		Number of teeth	21.8	20.2	0.43
		PCR (%)	23.1	21.3	0.39
		BOP (%)	12.4	12.4	0.99
		Pocket depth (mm)	2.29	2.38	0.59
		Serum IgG Ab. Titer	0.14	3.14	<0.0001
		Recurrence ratio (%)	19.1	20.5	0.84
	Pg SU63	Patients number	113	26	
		Age (yr)	61.8 ± 10.6	57.8 ± 9.3	0.18
		Number of teeth	21.2	22.1	0.99
		PCR (%)	24.2	12.4	0.29
		BOP (%)	13.1	9.1	0.15
		Pocket depth (mm)	2.31	2.33	0.95
		Serum IgG Ab. Titer	0.004	3.13	<0.0001
		Recurrence ratio (%)	16.8	36.1	0.083
	Td ATCC35405	Patients number	120	19	
		Age (yr)	61.1 ± 10.2	61.3 ± 12.3	0.88
		Number of teeth	21.8	18.8	0.14
		PCR (%)	23.3	17.8	0.24
		BOP (%)	12.7	10.4	0.67
		Pocket depth (mm)	2.33	2.23	0.22
		Serum IgG Ab. Titer	0.21	2.31	<0.0001
		Recurrence ratio (%)	16.7	36.8	0.039
	Cr ATCC33238	Patients number	100	39	
		Age (yr)	61.5 ± 10.1	60.6 ± 11.4	0.79
		Number of teeth	22.1	19.9	0.22
		PCR (%)	22.1	23.3	0.76
		BOP (%)	11.8	13.6	0.65
		Pocket depth (mm)	2.26	2.42	0.13
		Serum IgG Ab. Titer	0.02	3.67	<0.0001
		Recurrence ratio (%)	14.9	29.7	0.048

Data were analysed by Mann-Whitney U test for clinical findings and Pearson's chi-square test for Recurrence ratio between Normal and High IgG titer group.

研究成果の刊行に関する
一覧表

研究成果の一覧表

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	ページ
	なし						

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Sugiura Y et al.	Antimicrobial effects of the saliva substitute, Oral balance, against microorganisms from oral mucosa in the hematopoietic cell transplantation period.	Support Care Cancer			2008, in Press

研究成果の刊行物・別刷

Support Care Cancer
DOI 10.1007/s00520-007-0391-z

SHORT COMMUNICATION

Antimicrobial effects of the saliva substitute, Oralbalance®, against microorganisms from oral mucosa in the hematopoietic cell transplantation period

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Received: 9 September 2007 / Accepted: 12 December 2007

Abstract
Goals The commercially available saliva substitute Oralbalance® has been reported to alleviate symptoms of post-radiotherapy xerostomia in head and neck cancer patients. Oralbalance® may also be effective for xerostomia in patients undergoing hematopoietic cell transplantation (HCT) with high-dose chemotherapy and total-body irradiation. However, HCT patients are severely compromised, and saliva substitute must therefore not promote infection. This study was performed to determine the effects of Oralbalance® on microbial species identified during HCT.
Patients and methods Microbial identification of oral mucosa was performed in 28 patients undergoing HCT. The antimicrobial effects of Oralbalance® against bacteria and fungi detected in the HCT period were examined in vitro. Briefly, bacteria and fungi were spread on agar plates, and 0.1g of Oralbalance® gel was applied (about ϕ1cm). After incubation at 37°C for 24h, the presence of a

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transparent zone of inhibition around Oralbalance® was observed.
Main results Not only bacterial species constituting normal flora of the oral mucosa but also those not usually constituting normal flora, e.g., coagulase-negative *Staphylococcus*, were detected. A transparent zone was observed around Oralbalance® in all bacterial species examined. No transparent zone *was observed* for *Candida albicans*, but growth was inhibited in the area where Oralbalance® was applied.
Conclusions Oralbalance® does not facilitate increases in microorganisms in the HCT period. Oral care with Oralbalance® does not promote infection in patients undergoing HCT.

Keywords Hematopoietic cell transplantation · Xerostomia · Saliva substitute · Antimicrobial activity

Introduction

High-dose chemotherapy and total-body irradiation, which are performed as the conditioning regimen of hematopoietic cell transplantation (HCT), are associated with xerostomia. Xerostomia not only results in uncomfortable oral dryness but also may cause the oral mucositis induced by chemotherapy and/or irradiation to be more severe 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 [1, 8] but also moderates mechanical contact between the teeth and oral mucosa. Indeed, we often see the development of ulcerative mucositis on mucosa in contact with dry teeth clinically. Oral care using saliva substitute may alleviate the symptoms induced by xerostomia.

Oralbalance®, which is a commercially available saliva substitute, has been reported to alleviate the symptoms of post-radiotherapy xerostomia in head and neck cancer patients [7, 9]. Therefore, this product may be effective in HCT patients. However, as these patients are in a markedly compromised condition throughout the period of HCT, saliva substitute must not promote infection.

Therefore, the present study was performed to investigate the effects of the saliva substitute, Oralbalance®, on microbial species identified during HCT.

Patients and methods

Identification of microorganisms from oral mucosa

A total of 28 patients undergoing HCT at Okayama University Hospital (male, 17; female, 11; 38.9 ± 16.6 years old) were enrolled in this study. Microbial samples were obtained from oral mucosal swabs. Culture and identification of microorganisms were performed at the Central Clinical Laboratory of Okayama University Hospital. Microbial samples from mucosal swabs were plated onto brain heart infusion agar plate and cultured in aerobic condition at 37°C. Identification of obtained colonies was performed by rapid ID 32 STREP API®, rapid ID 32 E API® or ID 32 GN API® identification kits (Japan bioMerieux, Tokyo, Japan) according to the manufacturer's instructions. Microbial identification was performed three times (first: day −7 ~ −1; second: day 0 ~ +7; third: day +8 ~ +14) for each patient (a total of 84 examinations in 28 patients).

Antimicrobial test of Oralbalance®

The antimicrobial effects of Oralbalance® against microbial species in the HCT period, with the exception of those detected only once throughout the total of 84 examinations of microorganisms, were examined in vitro. Antimicrobial tests were performed against the following standard strains: *Streptococcus sanguis* American Type Culture Collection (ATCC) 10556, *Streptococcus salivarius* Japan Collection of Microorganisms (JCM) 5707, *Neisseria mucosa* ATCC 19695, *Stomatococcus mucilaginosus* JCM 10910, *Staphylococcus epidermidis* National Institute of Technology and Innovation Biological Resource Center (NBRC) 12993, *Staphylococcus aureus* Food and Drug Administration 209, and *Candida albicans* NBRC 1385. Aliquots of these bacteria and fungi at concentrations of McFarland turbidity standard No. 0.5 were spread on brain heart infusion agar plates (Difco Laboratories, Detroit, MI, USA) or Sensitivity Disk Agar-N plates (Nissui Pharmaceutical, Tokyo, Japan). Then, 0.1g (about ϕ1cm) of Oralbalance® and an equal amount of Oralbalance® that had been pre-incubated at 90°C for 30min to denature the antimicrobial enzymes contained in the gel were applied separately to the same plates. Tetracycline disks for antimicrobial ability test (BD Sensi-Disk Tetracycline 30; BD Biosciences, Franklin Lakes, NJ, USA) or paper containing 100μg of amphotericin B (Invitrogen, Grand Island, NY, USA) were also applied to the plates as positive controls. After incubation at 37°C in air for 24h, bacterial and fungal growth on the plates was examined.

Results

Microorganisms identified on the oral mucosa during HCT

The microorganisms identified on the oral mucosa during HCT are shown in Table 1. No samples were obtained during 13 of the 84 examinations because of the patients' conditions. α- and γ-*Streptococcus* spp. (87.3% and

Table 1 Microorganisms identified from the oral mucosa and detection frequency during HCT

Microorganism	Detection frequency (%)	Number (/71)
Bacterial components of the normal flora		
α-*Streptococcus* spp.	87.3	62
γ-*Streptococcus* spp.	29.6	21
Neisseria spp.	43.7	31
Stomatococcus spp.	23.9	17
Bacteria not usually found in the normal flora		
Coagulase-negative *Staphylococcus* spp.	46.5	33
Staphylococcus aureus	2.8	2
Haemophilus influenzae	1.4	1
Enterococcus spp.	1.4	1
Stenotrophomonas maltophilia	1.4	1
Bacillus spp.	1.4	1
Fungi		
Candida albicans	5.6	4
Torulopsis glabrata	1.4	1

The microorganisms identified on the oral mucosa are shown. Microbial identification was performed three times (first: day −7 ~ −1; second: day 0 ~ +7; third: day +8 ~ +14) for each patient (total of 84 times for 28 patients). No samples were obtained during 13 of the 84 examinations because of the patients' conditions at these time points. Findings from 71 examinations are shown.

29.6%, respectively), *Neisseria* spp. (43.7%), and *Stomatococcus* spp. (23.9%), which are components of normal oral flora, were identified frequently. Coagulase-negative *Staphylococcus* spp. (CNS), which are not constituents of the normal flora, were also identified frequently (46.5%). The fungus, *C. albicans*, was identified at a frequency of 5.6%. *S. aureus*, *Haemophilus influenzae*, *Enterococcus* spp., *Stenotrophomonas maltophilia*, *Bacillus* spp., and *Torulopsis glabrata* were identified at low frequencies (1.4% ~ 2.8%).

Antimicrobial ability of Oralbalance®

The results of antimicrobial tests on Oralbalance® against *S. sanguis*, *S. salivarius*, *N. mucosa*, *S. mucilaginosus*, *S. epidermidis*, *S. aureus*, and *C. albicans* are shown in Fig. 1. The presence of a transparent zone of inhibition was observed around Oralbalance® for all bacterial species examined. No such transparent zone was observed around heated Oralbalance®. With regard to fungi, although there was no transparent zone on *C. albicans* cultures, growth was inhibited in the area where Oralbalance® had been applied.

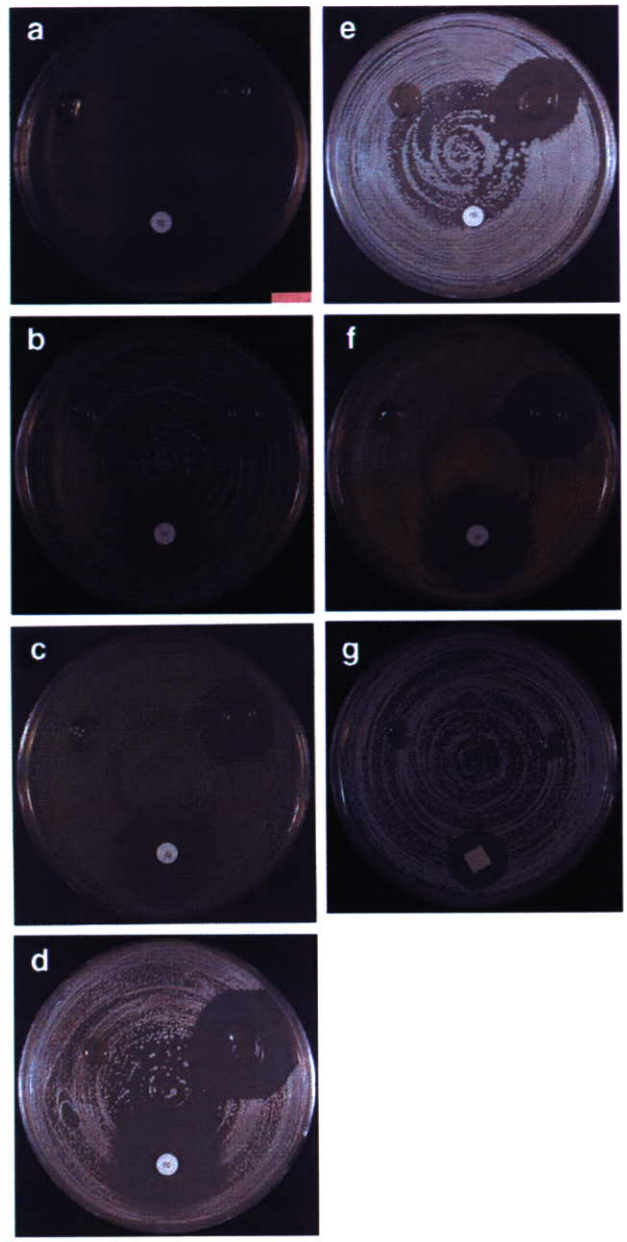

Fig. 1 Antimicrobial ability test of Oralbalance® against bacterial and fungal species isolated from patients during HCT. **a**: *Streptococcus sanguis*, **b**: *Streptococcus salivarius*, **c**: *Neisseria mucosa*, **d**: *Stomatococcus mucilaginosus*, **e**: *Staphylococcus epidermidis*, **f**: *Staphylococcus aureus*, and **g**: *Candida albicans*. Appearance of the entire plate surface; Oralbalance® was applied to the upper right portion of the plates. Heat-incubated Oralbalance® was applied to the upper left portion of the plates. Tetracycline disks (**a**–**f**) or paper containing amphotericin B (**g**) were applied to the lower part of the plates. There was a transparent zone of inhibition around Oralbalance® for all bacterial strains examined. Although there was no apparent transparent zone in *C. albicans* cultures, growth was inhibited in the area where Oralbalance® had been applied

Discussion

The commercially available saliva substitute, Oralbalance®, showed antimicrobial activity against the bacterial species

detected during HCT. Against fungi, although there was no transparent zone observed on *C. albicans* cultures, growth was inhibited in the area where Oralbalance® had been applied in vitro. These result suggested that Oralbalance® would not contribute to the infection in patients undergoing HCT.

There have been some reports regarding the relationships between the bacteria that constitute the normal oral flora, e.g., *Streptococcus* species [6] and *Stomatococcus* species [2, 3], and bacteremia in neutropenic patients. In the present study, bacteria not usually seen in the normal flora in the oral mucosa, e.g., CNS, were also detected with high frequency during HCT, probably because bacterial substitution occurred due to the use of many antibiotics against infections in patients under neutropenic conditions. CNS is the bacterium isolated most frequently from blood cultures of febrile neutropenic patients [5]. The oral mucosa should be considered a potential source of organisms, including CNS, associated with bacteremia in immunocompromised patients [4]. In our in vitro studies, Oralbalance® did not facilitate an increase in such microorganisms related to bacteremia. The antibacterial effect of Oralbalance® is mainly due to antimicrobial enzymes of salivary origin, i.e., lactoperoxidase, lysozyme, and lactoferrin. Indeed, no transparent zone was observed around heat-incubated Oralbalance®. As Oralbalance® does not contain any antibiotics, it does not contribute to the appearance of antibiotic-resistant bacteria.

In conclusion, the saliva substitute, Oralbalance®, would not facilitate an increase in microorganisms during the HCT period.

Acknowledgement This study was supported by Grants-in-Aid for Cancer Research (H15–23) and Comprehensive Research on Aging and Health (H19–008) from the Ministry of Health, Labour and Welfare and a Grant-in-Aid for Encouragement of Scientists (19925028) from the Japan Society for the Promotion of Science.

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