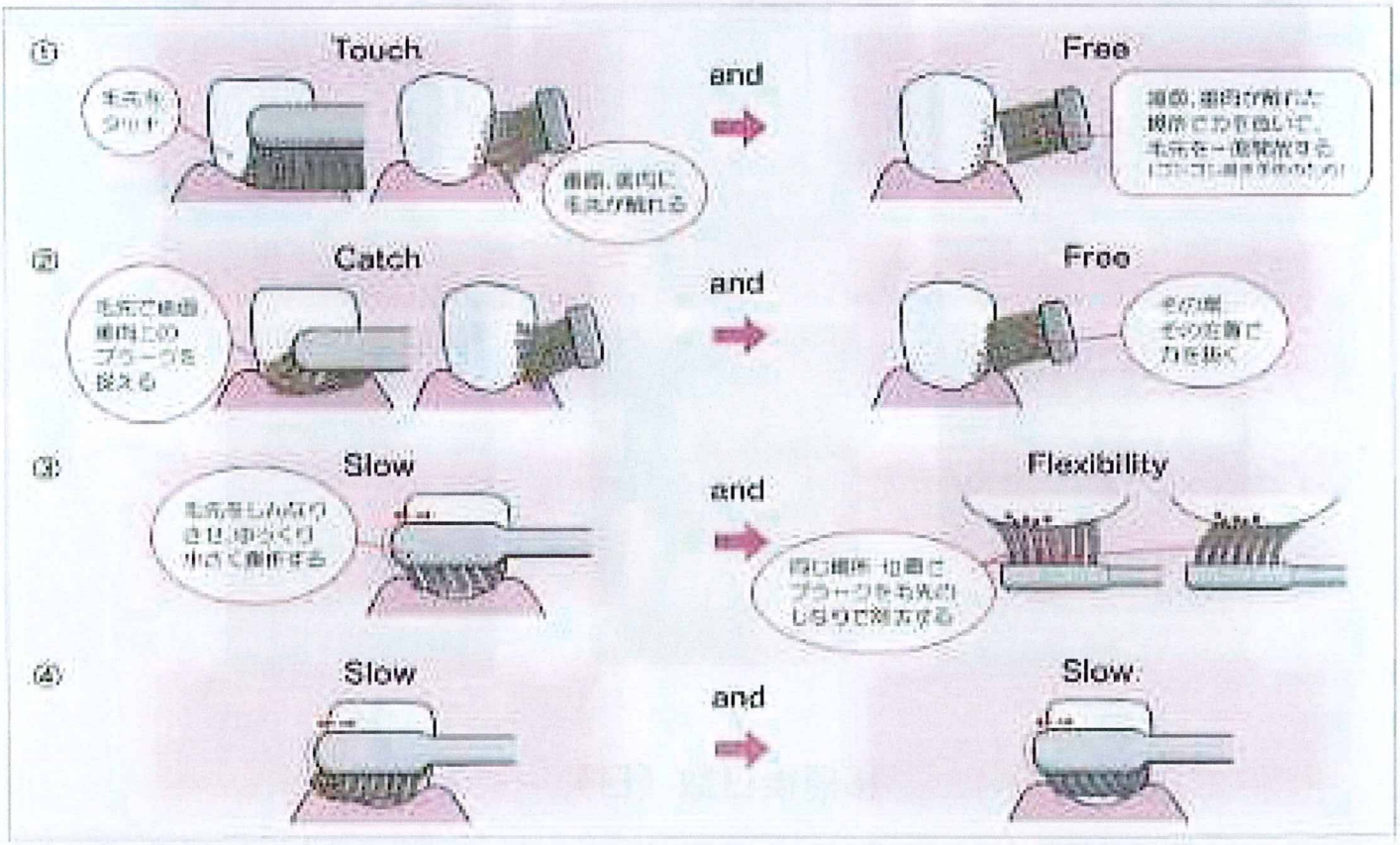
3-2　ブラッシングの方法

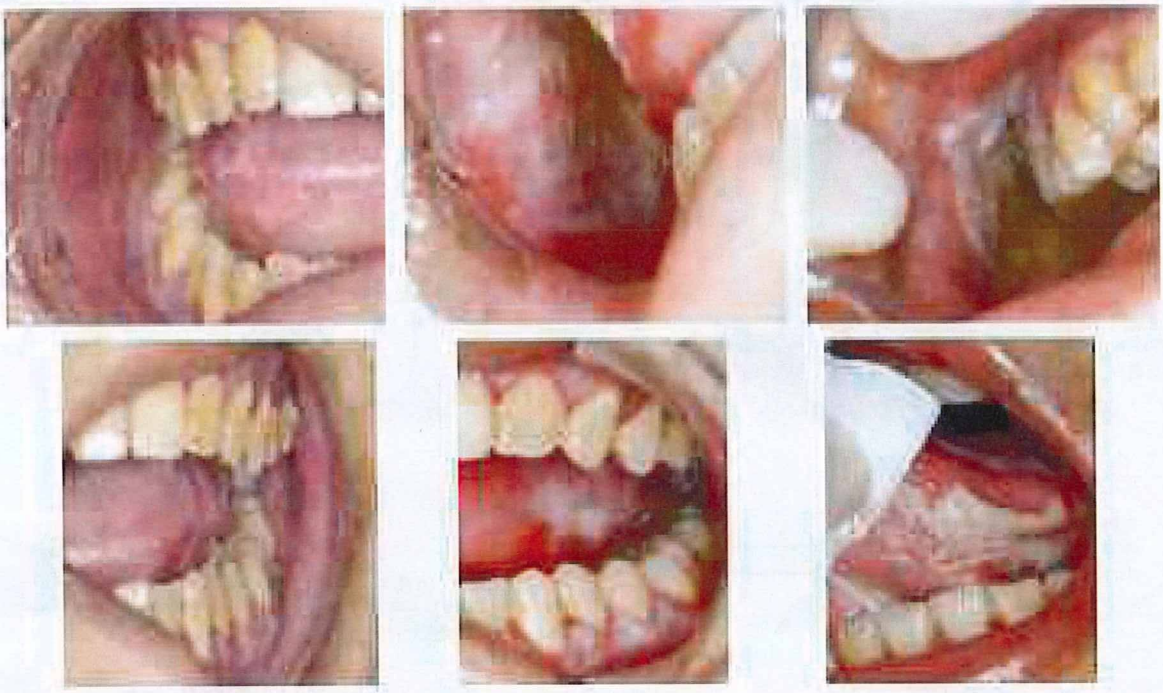
毛先法＝Touch and Free＝ブラッシング



歯科衛生士，Vol.31,No.8,p84,2007より引用

④ 口腔粘膜の乾燥

保清をしっかり行った、ある患者さんの口腔内の経過



5　　7　　10

移植後日数（日）

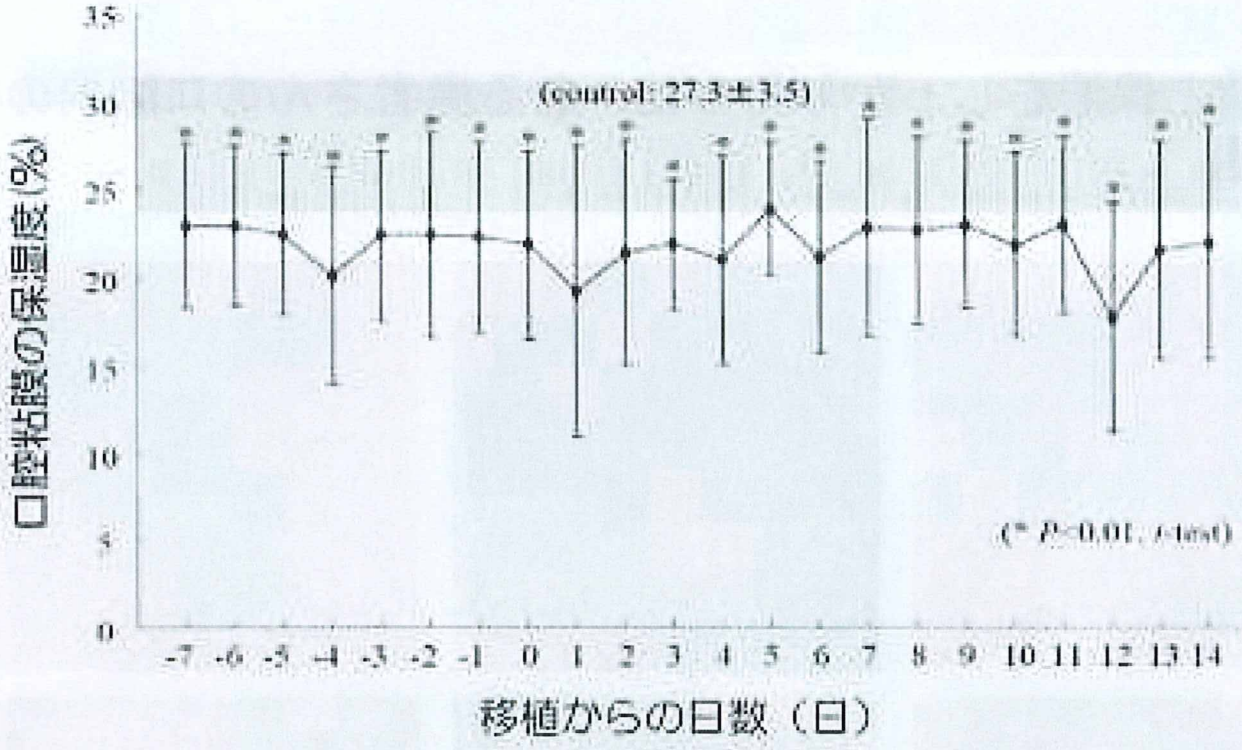
2ページ目と比べると、保清を行ったことで口腔内が非常に清潔になっています。これにより、感染源も減少しました。

しかし、移植後5日目には頬粘膜のほぼ全面にびらんが形成されています。その白変範囲は、7日目、10日目と広がっていることがお分かりいただけると思います。舌のびらんも重度です。感染経路があるとともに、耐え難い痛みを来たしています。

よく見ると、特に7日目の写真で、びらんは硬い歯の接触部に一致して形成されています。

写真からはわかりにくいですが、口腔乾燥も著明です。

口腔水分計を用いて、移植期の口腔粘膜の保湿度を測定してみました。



(Sugita Y et al. *Support Care Cancer*; 2008)

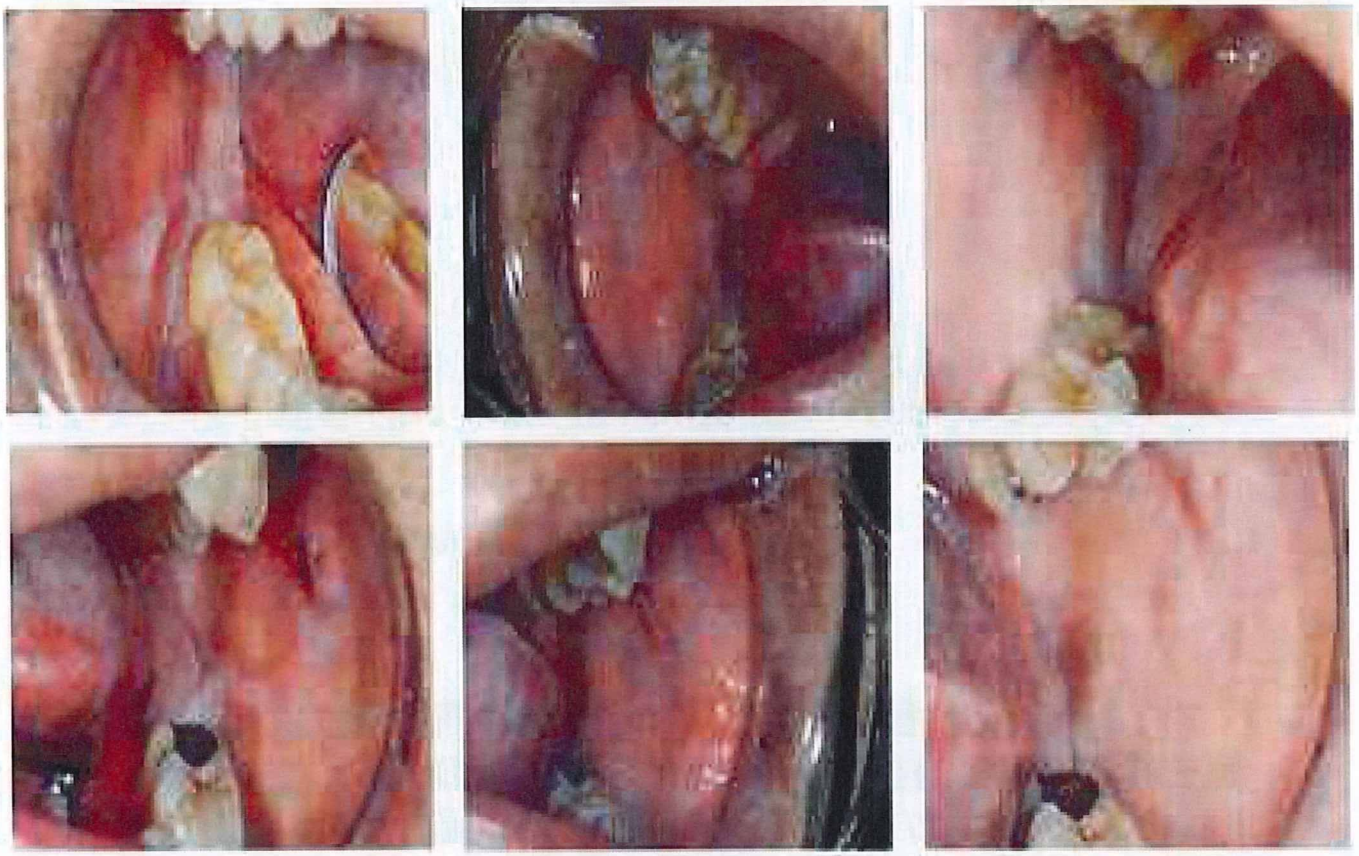
対象とした患者さんは36人です。移植前後の各日の平均値±標準偏差の推移を示します。図中の網掛け部分は、健康な人（62人）の口腔粘膜の保湿度の範囲を示します。

健康な人と比べ，移植を受けた患者さんは、すべての日において口腔粘膜が乾燥していることがわかります。

このことから、移植を受けた患者さんでは唾液による口腔粘膜の保護作用が弱いと予想されます。

4-1　口腔ケアの第二ポイント：保湿
すなわち口腔内の粘膜の保護

保清と保湿をしっかり行った、ある患者さんの口腔内の経過



5　　7　　10

移植後日数（日）

保清をしっかり行うとともに、市販の保湿剤を使って粘膜保護を重視したケアを行いました。

こうすることで、清潔になるとともに傷・びらんが大幅に軽減しています。

これは、乾燥して傷がつきやすかった粘膜と歯の接触が、保湿により緩和され保護されたためと考えられます。

白血球数がゼロ近くで推移する造血幹細胞移植の患者さんにおいては,

保清による菌量減少は ⟹ 感染源の減少
保湿による粘膜保護は ⟹ 感染経路の遮断

という、とても大事な意味があると考えられます。

5) 口腔ケアの実際

造血幹細胞移植患者の標準的口腔ケア

Ⅰ　移植早期からケアを開始する

1）歯科的処置を行う

・歯科を受診し、う歯・歯周炎のチェックと治療を行う。

・正しいブラッシング方法を指導する。

2）ブラッシングが効果的に行えているか評価する。

Ⅱ　患者自身による自己管理が行えるように支援する。

1）日中は2時間毎、夜間は覚醒時に含嗽を行う。

2）含嗽には水や生理食塩水など、使用しやすいものを使う。

3）少なくとも1日3回は歯ブラシを使用してブラッシングを行う。

4）嘔吐後は必ず含嗽する。

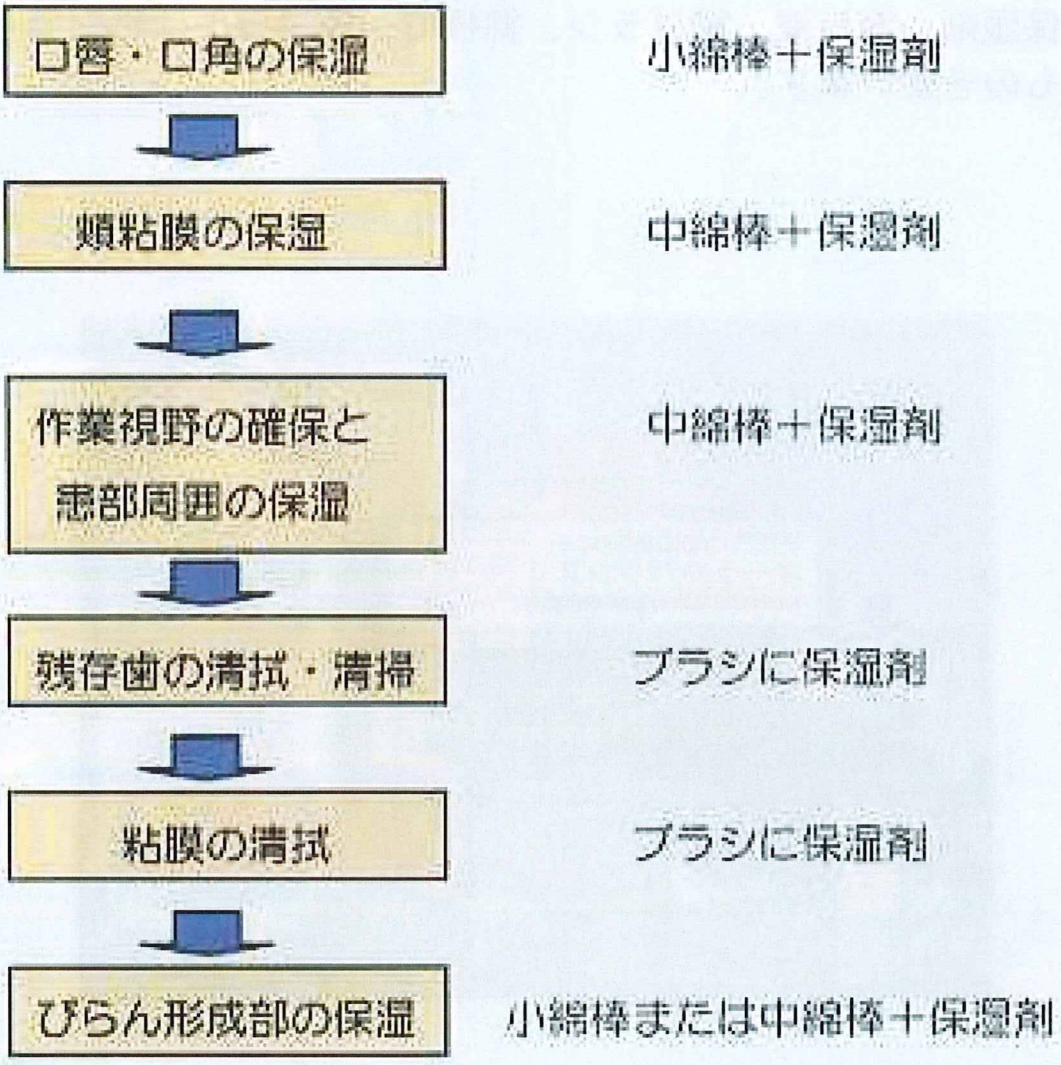
5）口唇の乾燥を防ぐ。

＊義歯装着の場合、口腔ケア時と睡眠時は義歯を外します。義歯もブラッシングします。

＊ケアを継続するためには、疼痛コントロールを十分に行う必要があります。

6) 口腔ケアの流れ

介助が必要な状態にある造血幹細胞移植患者

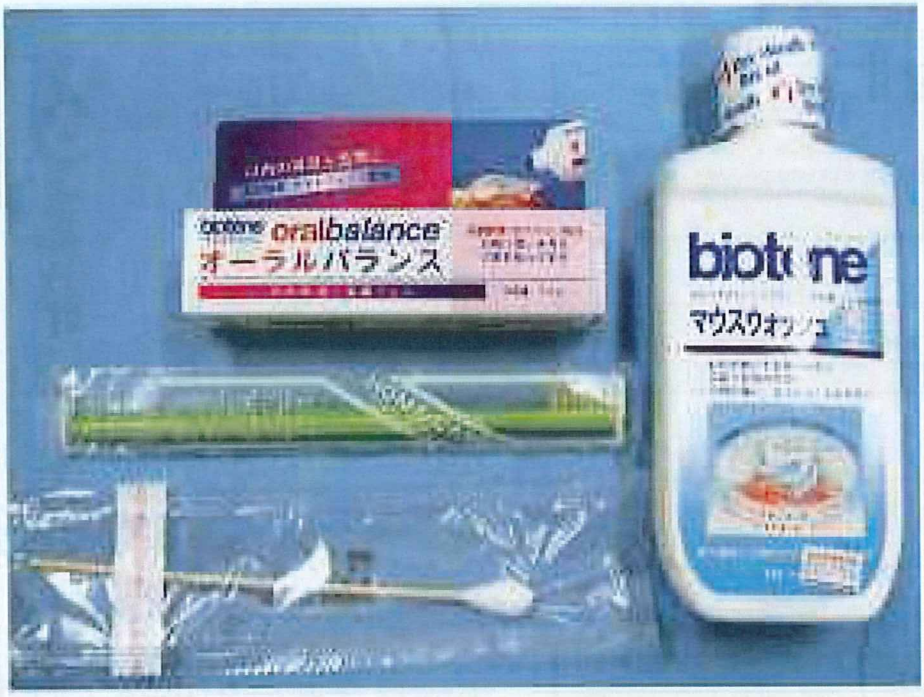


注：びらんがひどいときや粘膜障害に伴う強い痛みがあるとき大量に保湿剤を塗布すると、上層表皮の剥離・出血など患部や表面に損傷を与えることもあるため、ケア前半では使用量についての注意が必要です。

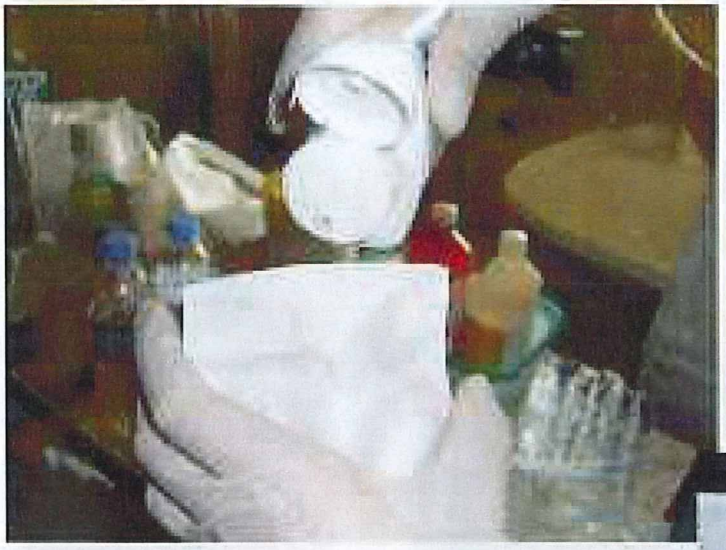
保湿剤を用いた口腔ケア、粘膜保護

わたし達が使っている道具類です。

保湿剤、洗口液、歯ブラシ、綿棒で、歯ブラシは特別柔らかいものを使います。



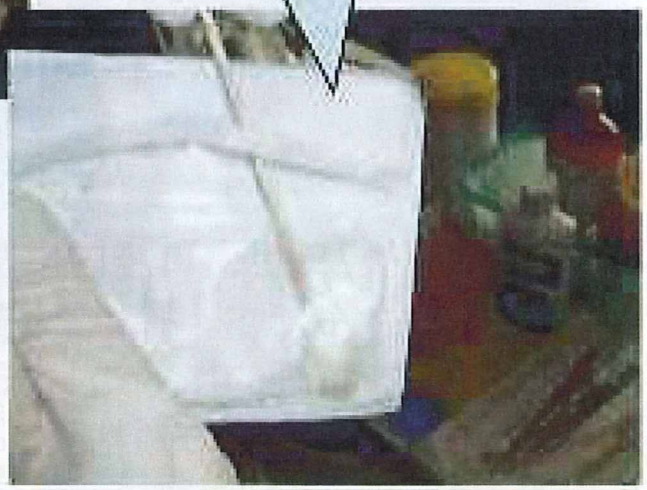
1



洗口液を袋に注ぐ

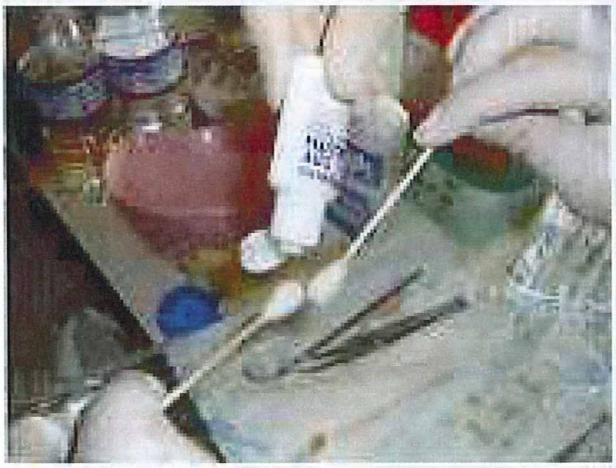
洗口液に滅菌綿棒を浸す

2



さらにジェルタイプまたは乳液タイプの保湿剤をつける

3



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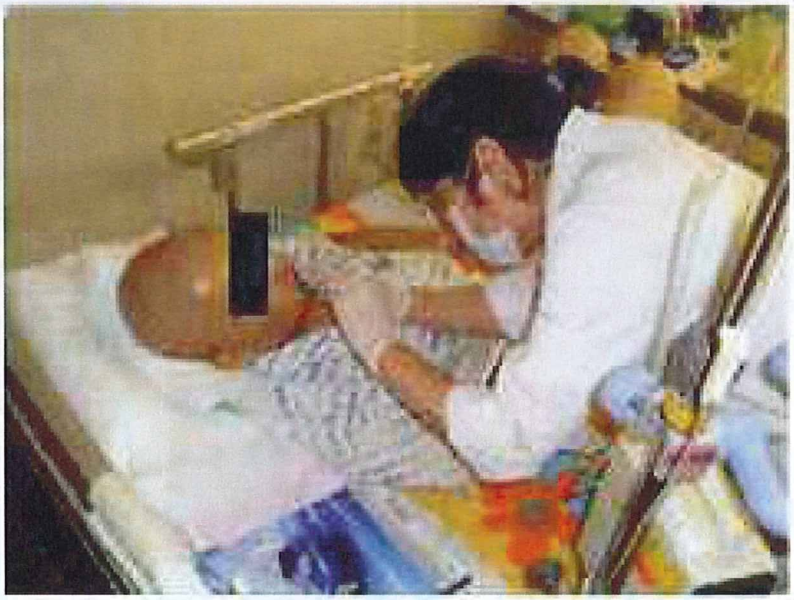
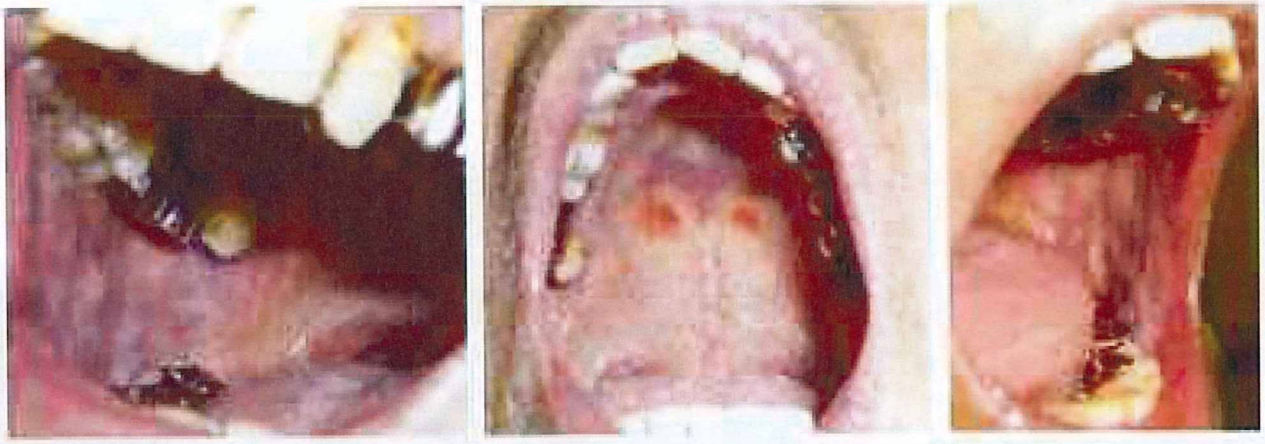


7) 口腔ケアを行った症例

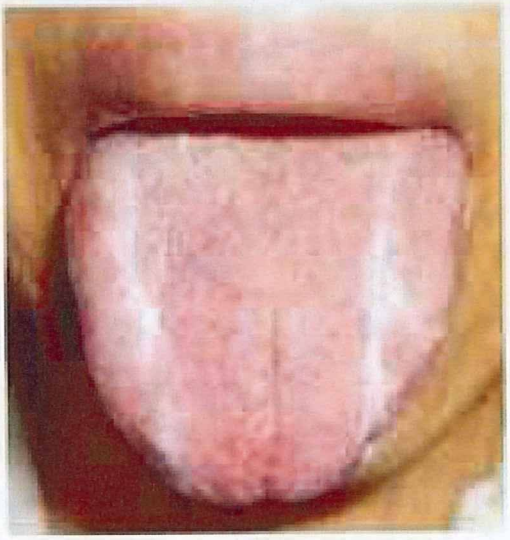
口腔ケア開始前

症例１



移植後7日目、口腔内にびらんが現れ、著しく乾燥がみられた患者さんです。感染予防と粘膜保護・疼痛緩和のための保湿ケアを積極的に開始しました。洗口液での含嗽を頻回に行い、歯牙接触部の頬粘膜，舌側面，舌背に保湿剤を塗付しました。

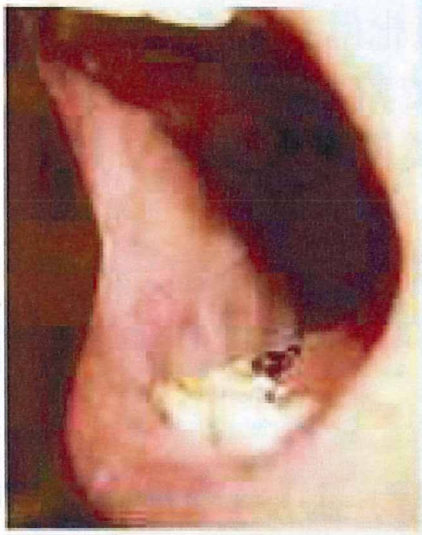
症例２

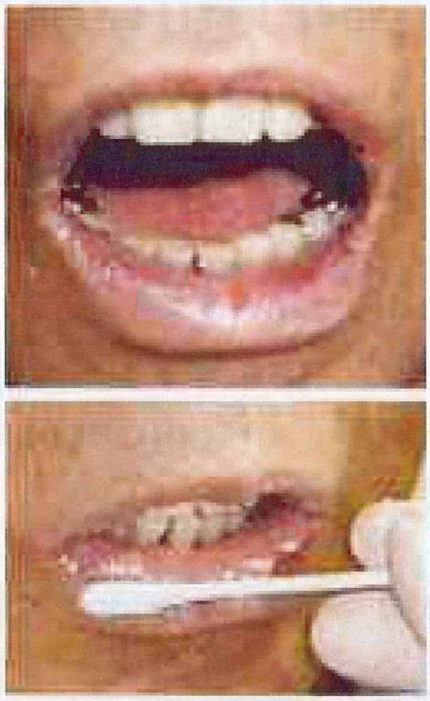


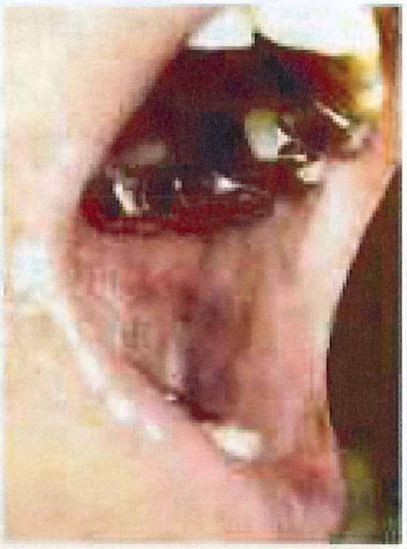
移植を控え，化学療法中に口腔内に乾燥がみられた患者さんです。舌背が乾燥し，唾液が粘性泡状になっています。洗口液で含嗽を行い、保湿剤と舌ブラシを用いて保清を開始しました。

口腔ケア開始後

症例１

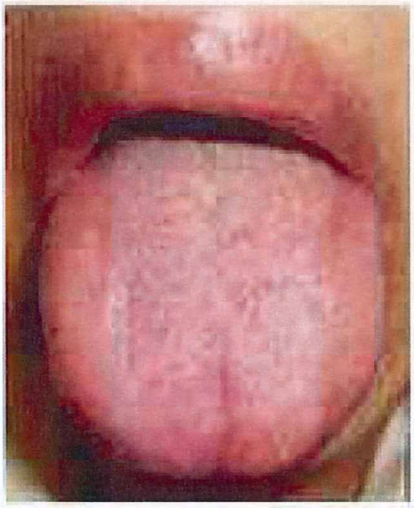






口腔粘膜のびらんや乾燥、疼痛は1週間程で改善傾向となりました。口唇乾燥に対しては、保湿剤を薄く塗布した後、その上からワセリンを塗ることで、より保湿が持続します。

症例２



口腔内が乾燥傾向で、さらに化学療法のため乾燥が増悪した状態でしたが、保湿ケアを行なった翌日には口腔内の乾燥と違和感が軽減されました。移植前のセルフケアにも自信をもたれました。

8 より楽に、安全に

造血幹細胞移植を乗り切っていただきたい…。

保湿剤の使用によって口腔粘膜痛の悪化はなくなり、使用した患者さんからは、口腔粘膜障害で荒れた粘膜と歯などの接触痛が和らいだという感想をよく聞きます。

唾液の役割には、口腔内の微生物の排出および歯牙との接触の緩衝作用があり、口腔内の組織に対して優れた保護作用をもたらします。

保湿剤による保湿・湿潤作用は、粘膜と歯などの物理的な直接の接触を防ぐことにより口腔粘膜障害の増悪防止に貢献している可能性があります。

幹細胞移植期には多種の抗菌剤が使用されることが多くそれにより抗菌剤耐性菌が高頻度に出現します。このことを考えれば、本来唾液に含まれる酵素の抗菌性を口腔粘膜の感染管理に利用することは合理的ではないでしょうか。

9) 口腔ケアに必要なもの

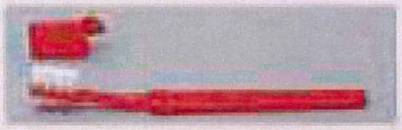
参考

歯ブラシ
特別柔らかい毛の歯ブラシを使います。

PHB ウルトラスワーブ

バイオティーン
スーパーソフト歯ブラシ

PHB ウルトラスワーブ
エリート



義歯ブラシ
歯ブラシで汚れが落ちにくい場合は義歯用ブラシを使います。

PHB義歯ブラシ

スポンジブラシ
柄の長さ、形状など色々な種類があります。

メドライン
スポンジブラシ

吸引ブラシ
吸引歯ブラシや吸引スポンジブラシは、介護者がひとりで口腔ケアを介助する時に便利です。

メドライン吸引ブラシ

洗口液（含嗽剤）

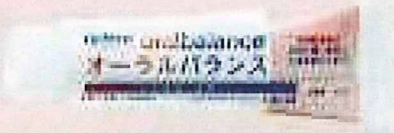
水、0.9%食塩水、2%重曹水、アルコールを含まない市販の洗口液を使います。食塩水や重曹水は作り置きをせず、新しく作ったものを使うようにします。

バイオティーン
マウスウオッシュ

保湿ジェル

水性の保湿剤を使います。唾液の抗菌作用と類似の効果を持つジェルは、免疫能が低下している患者さんに特に効果的です。また、痛みのためジェルの塗布が難しい場合は乳液状のものを使います。

バイオティーン
オーラルバランス



バイオティーン
オーラルバランス
リキッド

歯みがき剤

口腔粘膜への刺激回避のため、ラウリル硫酸ナトリウムが入っていないものを使います。唾液成分と類似の天然酵素を含む歯みがき剤が有効です。

バイオティーン
トゥースペースト

義歯洗浄剤
　金属部分が腐食することが
　あるので、使用説明書の指
　示通りに使います。

超小型ミラー付き無影灯
　口腔内の観察時に便利です。

DenLite照明付きミラー

T&K ティーアンドケー株式会社
〒103-0012
東京都中央区日本橋堀留町1-5-7　ユービル2F
TEL 03-5640-0233　FAX 03-5640-0232
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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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Present address:
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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.

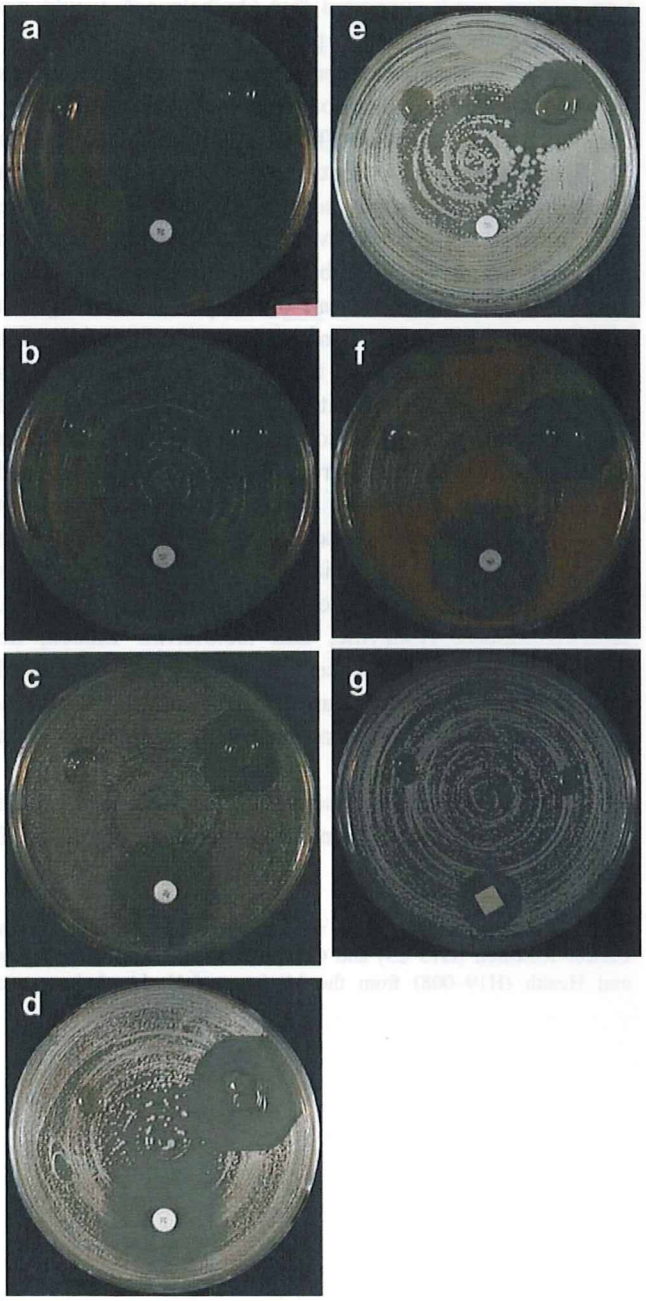

Fig. 1 Antimicrobial ability test of Oralbalance® against bacterial and fungal species isolated from patients during HCT. **a**: *Streptococcus sanguis*, **b**: *Streptococcus salivarius*, **c**: *Neisseria mucosa*, **d**: *Stomatococcus mucilaginosus*, **e**: *Staphylococcus epidermidis*, **f**: *Staphylococcus 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.

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