



# Effectiveness of Different Antimicrobial Agents on Malodor Prevention in Two-Stage Dental Implants: A Double-Blinded Randomized Clinical Trial

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## Abstract

**Objective** Opening of a healing abutment in two-stage implant systems is usually followed by a bad smell. Previous studies have found that presence of bacteria in microleakages of the implant-abutment interface results in further malodor. However, studies focusing on preventive treatments for this issue are scarce. Therefore, the aim of this study is to evaluate the effectiveness of two antimicrobial agents on prevention of malodor followed by opening the healing abutments.

**Materials and Methods** Current double-blinded randomized clinical trial was performed on 51 eligible patients who were referred for their exposure surgery. They were divided equally into three parallel groups. In two groups, either chlorhexidine or tetracycline was added to the internal surface of the fixtures before screwing the healing abutments. One group did not receive any intervention. Three to 4 weeks later malodor was scored by sniffing the healing abutments immediately after uncovering them (odorless = 0/odor = 1). The three groups were then compared regarding malodor scores.

**Results** Our findings showed that malodor was more frequent in the control group (58.82%) in comparison with groups of intervention (17.65 and 23.53%). There was a statistically significant difference between malodor in patients in whom antimicrobial agents (chlorhexidine and tetracycline) were used in their implants and the control group ( $p$ -value = 0.023). However, malodor in the chlorhexidine group and tetracycline group did not show any significant difference ( $p$ -value = 1).

**Conclusion** Based upon the data from this study, it appears that local antimicrobial agents including chlorhexidine and tetracycline result in less malodor production within the implant-abutment interface.

**Clinical Significance** A specific type of malodor is commonly seen after opening the healing abutment of a two-stage dental implant. Not only this issue is noticed by the

## Keywords

- ▶ antimicrobial agents
- ▶ malodorous
- ▶ two-stage dental implant systems

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dentist, but also annoyed the patient. Using local antimicrobial agents in the fixtures is likely to be a simple, easily applicable solution that satisfies both patients and dentists, and eliminates the possibility of further inflammation.

## Introduction

Loss of dentition is still prevalent among societies, especially in the elderly and middle-age people.<sup>1</sup> It is estimated that complete edentulism is seen in 7 to 69% of adults internationally.<sup>2</sup> For this mean, dental implants have been used to improve function and esthetic in edentulous patients.<sup>3</sup> Dental implants are introduced as a treatment with a good prognosis. Most studies indicate a success rate of more than 90% for dental implants.<sup>1,4,5</sup> They are offered in two general types of one-stage (tissue level) and two-stage (bone level) implants.<sup>6</sup>

Although dental implants have a good predictability, both technical and biological complications have been reported.<sup>7-9</sup> Biological complications (i.e., peri-implantitis and bone loss) may occur due to reaction against microorganisms present in oral cavity.<sup>9,10</sup> Beside from implant failure, oral pathogenic bacteria—mostly anaerobic—are also responsible for oral malodor, which is defined as an unpleasant odor coming out of the mouth, nose, sinuses, or pharynx.<sup>11</sup>

Presence of pathogenic bacteria in unavoidable micro-leakages of implant-abutment interface in two-stage dental implant systems may cause further malodor production and peri-implantitis.<sup>12-14</sup> According to studies and clinical observations, transmucosal depth of two-stage implants is associated with anaerobic bacteria population, thereby producing malodor.<sup>15</sup> Several studies have demonstrated effectiveness of chlorhexidine in reducing oral bacteria.<sup>16,17</sup> It has also been indicated that topical administration of tetracycline results in significant reduction of oral bacteria.<sup>18</sup>

Malodorous followed by opening of the healing abutment is usually noticed by both patients and the dentist. Patients may also ask their dentist about the possibility of a persistent malodor. However, there are few studies focusing on malodor prevention in this specific situation. Therefore, the aim of this study is to assess and compare the effectiveness of two harmless topical antimicrobial agents in prevention of the bad odor releasing after opening the healing abutments.

## Materials and Methods

### Study Design

The current study was a controlled clinical trial with “stratified randomization” and “double blinding,” which was performed on patients who were referred to the implant department of Isfahan University of Medical Sciences, Isfahan, Iran, for surgical exposure of their two-stage implants from July 2021 to September 2021. We performed our study using three equal groups, each containing 17 eligible participants.

### Sample Size Calculation

The sample size was calculated based on a similar study<sup>17</sup> and the following formula, which indicated that with a sample of 17 participants per group, the power of 0.8 would be obtained at 0.05 level of significance:

$$n = \frac{\left( Z_{1-\frac{\alpha}{2}} + Z_{1-\beta} \right)^2 [2 \times p(1-p)]}{d^2}$$

### Inclusion Criteria

- ☑ Patients who were referred for surgical exposure of their two-stage implants, and were treated with a SNUCONE implant system were included in this randomized clinical trial.
- ☑ All patients included had healthy periodontal conditions (less than 10% bleeding on probing) and a transmucosal depth—transmucosal depth (gingival height [GH]) evaluation was performed using a color-coded Michigan Williams periodontal probe and was measured at four points and the maximum depth was recorded—of 1 to 3 mm since these factors can affect malodorous in this study.

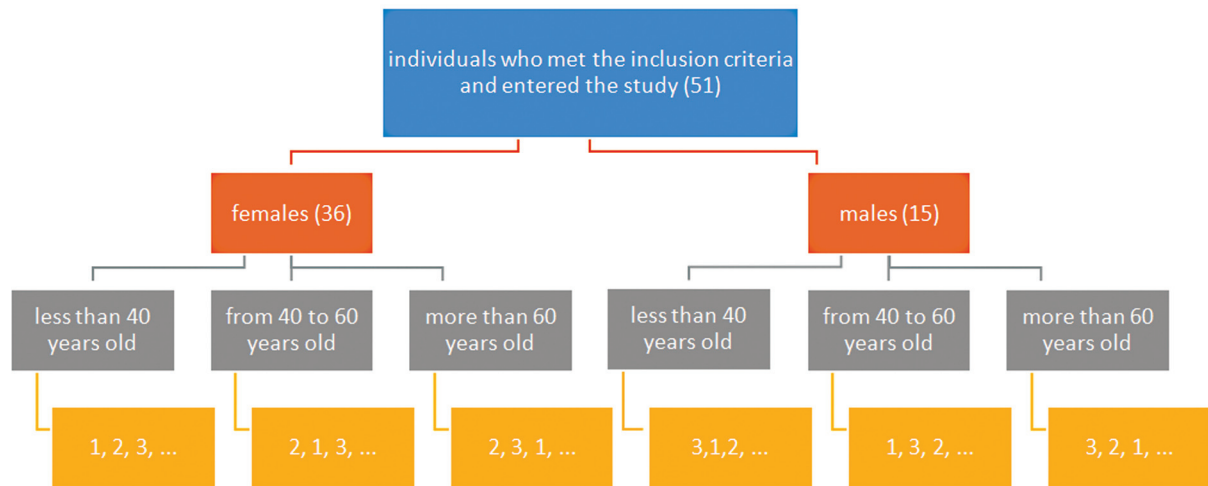
### Exclusion Criteria

- ☒ The individuals who were either smokers or in any specific medical condition were excluded from the study.
- ☒ The individuals who showed current halitosis (halitosis was assessed using an organoleptic method—the organoleptic measurement of breath was taken at a distance of 10 cm from oral cavity by a single investigator who was trained and calibrated for this task, and patients were then scored as follows: – = negative halitosis, + = positive halitosis) during our primary assessment were also excluded.
- ☒ The individuals who had used antibiotics during the past 4 weeks of their visit were also excluded since it could cause bias in our results.

Using the stated criteria, 51 eligible patients were collected as samples, which were then divided into three parallel and equal study groups (group 1, group 2, and group 3). To eliminate potential bias, we engaged in a stratified randomization procedure<sup>19</sup> to divide the samples into three equal subgroups.

### Randomization

At first, samples were stratified (layered) into six blocks; two levels of gender (male and female) and three levels of age (less than 40, between 40 and 60, and more than 60 years old).



**Fig. 1** Stratified randomization procedure.



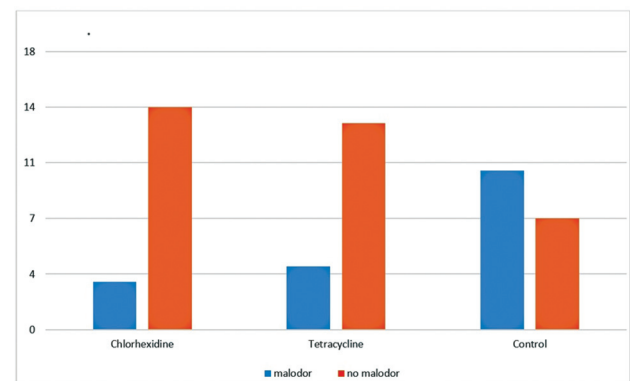
**Fig. 2** Applying chlorhexidine gel on a microbrush.

For assigning the participants within each block to one of the three study groups, six potential sequences are possible. Therefore, a sequence was given to each block randomly (i.e., the first participant of the first block enters group 1, the second participant of the first block enters group 2, the third participant of the first block enters group 3, etc.) (→ Fig. 1).

Eventually, all layers were equally and randomly assigned into three parallel groups of 17 people. Female-male ratio was equal between the three groups and according to one-way analysis of variance, no statistically significant difference was found between age averages of the three groups ( $p$ -value = 0.987).

### Intervention

In the exposure surgery session, fixtures were exposed surgically applying a flap. Then for the first group chlorhexidine 2% gel (Morvabon brand; made in Morvabon Company in Iran) and for the second group tetracycline 3% ointment (made in Hakim Company in Iran) was added to the internal surface of the fixtures with a sterile microbrush (→ Fig. 3). No



**Fig. 3** Frequency distribution of malodor within the study groups.

additional intervention was performed on the third group. Eventually, the healing abutments were screwed into the implants hand-tight using the screwdriver.

After the surgical procedure, patients were asked to brush their teeth (using toothbrush and toothpaste) and floss once a day until their next visit. They were then given postsurgery instructions and followed until their next visit.

### Measurements

Measurements were conducted 4 to 5 weeks following second-stage surgery at the first removal of the healing abutment. Patients were asked to have their breakfast meal properly early in the morning and avoid eating or drinking for 2 hours prior to measurements. Measurements included subjective odor score which was performed by a single independent observer whose functioning of olfaction was tested using The Sniffin' Sticks test.<sup>20</sup> Malodor was scored by sniffing the abutment immediately after uncovering it. Odor emitting from the healing abutment was scored as followed: 0 = odorless; 1 = odor.

- The organoleptic test (subjective assessment of odor) is not only a simple, low-cost method, but is considered to be the gold standard for odor assessment.<sup>21–23</sup>

**Table 1** Mean and standard deviation (SD) of age and gingival height within the study groups

Group category	Age (y) Mean ± SD	Gingival height (GH) (mm) Mean ± SD
Group 1 (chlorhexidine)	55.0 ± 10.18	2.03 ± 0.495
Group 2 (tetracycline)	54.5 ± 8.78	1.99 ± 0.508
Group 3 (control)	54.7 ± 9.50	1.93 ± 0.572
Total	54.7 ± 9.31	1.98 ± 0.517

- The number of fixtures implanted for each patient varied from 1 to 4 fixtures. But when measuring odor, even if only one of the patient fixtures was given a score of 1, we considered point 1 for that person considering that even one smelling fixture can result in dissatisfaction.

**Blinding:** Our method was performed in three steps, each by an individual investigator:

1. The first investigator (A.F.) assessed the participants in terms of inclusion and exclusion criteria and finalized the number of samples. He performed the whole randomization process in the examination session and assigned the participants into the study groups. A code was then given to each patient. Then, he transferred the list of the participants of all three study groups to the surgeon. However, the patients were not informed which group they were participated in.
2. The surgeon (M.R.) attended the exposure surgery session and performed the intervention on the participants based on the group each were participated in. Again, patients were not informed about the exact intervention during the exposure surgery.
3. The last investigator (S.N.) attended only the measuring session (3–4 weeks after the exposure surgery when opening the healing abutments) and assessed the outcomes.

Conclusively, neither patients nor the outcome assessor was informed about the medication used for each particular patient (double-blinded).

**Table 2** Frequency distribution of malodor within the study groups

Scale of malodor		Study groups			Total
		Chlorhexidine	Tetracycline	Control	
No Malodor 0	Count	14	13	7	34
	Percentage	82.4%	76.5%	41.2%	66.7%
Malodor 1	Count	3	4	10	17
	Percentage	17.6%	23.5%	58.8%	33.3%
Total	Count	17	17	17	51
	Percentage	100.0%	100.0%	100.0%	100.0%

## Statistical Analysis

Data was analyzed by IBM SPSS Statistics 24. For comparison of qualitative data between groups, the chi-square test was used. A value of  $p < 0.05$  was indicated as statistically significant.

## Results

The aim of the current study was to evaluate the effectiveness of two antimicrobial agents (chlorhexidine and tetracycline) in preventing malodor associated with two-stage implants. The study sample included 51 patients who were referred to the implant department for surgical exposure of their bone-level implants. Participants were divided into three equal groups. Each group included 12 females (70.6%) and 5 men (29.4%). Baseline and clinical characteristics of the patients are reported in ► **Table 1**.

According to one-way analysis of variance, the difference between mean age and mean GH of the three groups was not statistically significant ( $p$ -value = 0.987 and 0.857).

According to the chi-square test malodor frequency between the three groups was significantly different ( $p$ -value = 0.023). According to Fisher's exact test there was no significant difference between malodor in chlorhexidine and tetracycline group ( $p$ -value = 1). Moreover, chi-square test showed that there was a significant difference between malodor scale in the chlorhexidine group and control group ( $p$ -value = 0.013) and there was also a significant difference between malodor scale in the tetracycline group and control group ( $p$ -value = 0.037) ► **Table 2**.

## Discussion

In this study, we aimed to evaluate the effectiveness of chlorhexidine and tetracycline on preventing malodor associated with dental implants in comparison with the control group. Our findings showed a statistically significant difference between malodor in patients whom antimicrobial agents were used in their implants and the control group. However, malodor in the chlorhexidine group and tetracycline group did not show any significant difference.

Two-stage implants contain two components: the intraosseous (fixture) and the extraosseous component (abutment or healing screw). Most mechanical and biological

issues related to dental implants originate from the implant-abutment interface.<sup>24,25</sup> For instance, bacterial contamination occurs in the microgap between the two components both when the healing screw and when the permanent abutment is applied. When a healing screw is removed, malodorous is a result of the presence of the bacteria and their volatile sulfide compounds.<sup>15,26,27</sup> In 1997, Jansen et al reported that there are unavoidable microleakages at the implant-abutment connection. They suggested that bacterial colonization that occurs in the microleakages, close to the epithelial attachment, will result in further peri-implant bone resorption and implant failure.<sup>24</sup> Furthermore, Resende et al concluded that saliva infiltration and bacterial growth could occur in microgaps and cause inflammation and malodor.<sup>28</sup> Based on a recent pilot *in vitro* study, obtaining a complete seal against bacterial colonization at the implant-abutment interface is unlikely.<sup>29</sup> Scarano et al evaluated the efficacy of an antibacterial coating in the internal chamber of the implant using real-time volatile organic compound measurement technique. Based on their results, the antibacterial coating has been effective in reducing bacterial activity.<sup>30</sup> In the present study, chlorhexidine and tetracycline were effective in prevention of the malodorous when applied topically in the fixtures.

According to a study performed by Scarano et al, larger microgaps will result in more bacterial growth.<sup>31</sup> Based on previous studies, microgap size is affected by materials and fabrication methods, and significantly different microgap sizes have been reported among different implant systems.<sup>32,33</sup> In the current study, a single implant system was assessed considering that various systems are likely to have different sizes of microgaps. Therefore, our results may not be extensible to other implant systems.

Researchers have shown that the anaerobic bacteria located in the back of the tongue play an important role in the production of malodor, since this region is not cleaned properly.<sup>34-36</sup> It has also been reported that the bacteria responsible for malodor are mostly *Fusobacterium nucleatum* and *Porphyromonas gingivalis*.<sup>37-39</sup> There are two general ways for assessing malodor: organoleptic and instrumental technique. In organoleptic method, malodor is evaluated by the examiner's sense of smell. For instrumental measurement, various devices are used. Despite the fact that organoleptic measurement is known to be gold standard for this mean, it is associated with undeniable bias due to its subjectivity, and therefore this was a limitation of the present study.<sup>21-23</sup>

For one thing, our findings provided a better understanding of a common issue with two-stage dental implants, which is particularly annoying for patients as well as dentists. We found that chlorhexidine and tetracycline were both effective in reduction of malodor when applying locally in the fixtures. Whether or not our findings can generally be used as a probable predictive treatment in this condition needs further investigation. It is also suggested for future studies to focus on identifying bacteria responsible for this issue, and use specific antibiotics based on their susceptibility.

In conclusion, based upon the data from this study, it appears that local antimicrobial agents including chlorhexidine and tetracycline result in less malodor production within the implant-abutment interface.

#### Ethical Approval

All patients gave their written and informed consent before entering the study. This study has been approved by the Ethics Committee of the Vice Chancellor for Research, Isfahan University of Medical Sciences (code# IR.MUI.RESEARCH.REC.1400.190) and confirmed in IRCT Web site (code# IRCT20210705051795N1).

#### Conflict of Interest

None declared.

#### References

- Sharma A, Shrestha B, Chaudhari BK, et al. Preferred source and perceived need of more information about dental implants by the undergraduate dental students of Nepal: all Nepal survey. *Int J Dent* 2018;2018:6794682
- Petersen PE, Bourgeois D, Bratthall D, Ogawa H. Oral health information systems—towards measuring progress in oral health promotion and disease prevention. *Bull World Health Organ* 2005;83(09):686–693
- Rajgiri SU, Dayalan M. Full-mouth rehabilitation with implant-supported fixed prosthesis. *In J Oral Implantol Clin Res* 2016;7(03):73–80
- Clementini M, Morlupi A, Canullo L, Agrestini C, Barlattani A. Success rate of dental implants inserted in horizontal and vertical guided bone regenerated areas: a systematic review. *Int J Oral Maxillofac Surg* 2012;41(07):847–852
- Sharma A, Chaudhari BK, Shrestha B, et al. Knowledge and perception about dental implants among undergraduate dental students. *BDJ Open* 2019;5(01):1–5
- Esposito M, Grusovin MG, Chew YS, Coulthard P, Worthington HV. Interventions for replacing missing teeth: 1- versus 2-stage implant placement. *Cochrane Database Syst Rev* 2009;(03):CD006698
- Ferreira PW, Nogueira PJ, de Araújo Nobre MA, Guedes CM, Salvado F. Impact of mechanical complications on success of dental implant treatments: a case-control study. *Eur J Dent* 2022;16(01):179–187
- Hanif A, Qureshi S, Sheikh Z, Rashid H. Complications in implant dentistry. *Eur J Dent* 2017;11(01):135–140
- Passariello C, Di Nardo D, Testarelli L. Inflammatory periimplant diseases and the periodontal connection question. *Eur J Dent* 2019;13(01):119–123
- Berglundh T, Persson L, Klinge B. A systematic review of the incidence of biological and technical complications in implant dentistry reported in prospective longitudinal studies of at least 5 years. *J Clin Periodontol* 2002;29(Suppl 3):197–212, discussion 232–233
- Akaji EA, Folaranmi N, Ashiwaju O. Halitosis: a review of the literature on its prevalence, impact and control. *Oral Health Prev Dent* 2014;12(04):297–304
- Teixeira W, Ribeiro RF, Sato S, Pedrazzi V. Microleakage into and from two-stage implants: an *in vitro* comparative study. *Int J Oral Maxillofac Implants* 2011;26(01):56–62
- Quirynen M, van Steenberghe D. Bacterial colonization of the internal part of two-stage implants. An *in vivo* study. *Clin Oral Implants Res* 1993;4(03):158–161

- 14 Callan DP, Cobb CM, Williams KB. DNA probe identification of bacteria colonizing internal surfaces of the implant-abutment interface: a preliminary study. *J Periodontol* 2005;76(01):115–120
- 15 Sterer N, Tamary I, Katz M, Weiss E. Association between transmucosal depth of osseointegrated implants and malodor production. *Int J Oral Maxillofac Implants* 2008;23(02):277–280
- 16 De Boever EH, Loesche WJ. Assessing the contribution of anaerobic microflora of the tongue to oral malodor. *J Am Dent Assoc* 1995;126(10):1384–1393
- 17 Naveen N, Suhas PG, Vanishree N, Vinitha M, Bharath C, Anushri M. Effectiveness of three different oral hygiene techniques on Viridans streptococci: a randomized controlled trial. *J Indian Assoc Public Health Dent* 2016;14(01):10
- 18 Hayashida S, Funahara M, Sekino M, et al. The effect of tooth brushing, irrigation, and topical tetracycline administration on the reduction of oral bacteria in mechanically ventilated patients: a preliminary study. *BMC Oral Health* 2016;16(01):67
- 19 Kang M, Ragan BC, Park J-H. Issues in outcomes research: an overview of randomization techniques for clinical trials. *J Athl Train* 2008;43(02):215–221
- 20 Hummel T, Sekinger B, Wolf SR, Pauli E, Kobal G. 'Sniffin' sticks': olfactory performance assessed by the combined testing of odor identification, odor discrimination and olfactory threshold. *Chem Senses* 1997;22(01):39–52
- 21 Brunner F, Kurmann M, Filippi A. The correlation of organoleptic and instrumental halitosis measurements. *Schweiz Monatsschr Zahnmed* 2010;120(05):402–408
- 22 Falcão DP, Miranda PC, Almeida TFG, Scalco MGDS, Fregni F, Amorim RFB. Assessment of the accuracy of portable monitors for halitosis evaluation in subjects without malodor complaint. Are they reliable for clinical practice? *J Appl Oral Sci* 2017;25(05):559–565
- 23 Alasqah M, Khan S, Elqomsan MA, Gufran K, Kola Z, Hamza MOB. Assessment of halitosis using the organoleptic method and volatile sulfur compounds monitoring. *J Dental Res Rev* 2016;3(03):94
- 24 Jansen VK, Conrads G, Richter E-J. Microbial leakage and marginal fit of the implant-abutment interface. *Int J Oral Maxillofac Implants* 1997;12(04):527–540
- 25 Kano SC, Binon PP, Curtis DA. A classification system to measure the implant-abutment microgap. *Int J Oral Maxillofac Implants* 2007;22(06):879–885
- 26 Assenza B, Tripodi D, Scarano A, et al. Bacterial leakage in implants with different implant-abutment connections: an in vitro study. *J Periodontol* 2012;83(04):491–497
- 27 Koutouzis T. Implant-abutment connection as contributing factor to peri-implant diseases. *Periodontol* 2000 2019;81(01):152–166
- 28 Resende CCD, Castro CG, Pereira LM, et al. Influence of the prosthetic index into Morse Taper implants on bacterial microleakage. *Implant Dent* 2015;24(05):547–551
- 29 Smojver I, Vuletić M, Gerbl D, Budimir A, Sušić M, Gabrić D. Evaluation of antimicrobial efficacy and permeability of various sealing materials at the implant-abutment interface—a pilot in vitro study. *Materials (Basel)* 2021;14(02):385
- 30 Scarano A, de Oliveira PS, Leo L, Festa F, Carinci F, Lorusso F. Evaluation of a new antibacterial coating of the internal chamber of an implant via real time measurement of Volatile Organic Compounds (VOCs). *Front Biosci (Elite Ed)* 2021;13(02):216–225
- 31 Scarano A, Lorusso C, Di Giulio C, Mazzatenta A. Evaluation of the sealing capability of the implant healing screw by using real time volatile organic compounds analysis: internal hexagon versus cone morse. *J Periodontol* 2016;87(12):1492–1498
- 32 Molinero-Mourelle P, Cascos-Sanchez R, Yilmaz B, et al. Effect of fabrication technique on the microgap of CAD/CAM Cobalt-chrome and zirconia abutments on a conical connection implant: an in vitro study. *Materials (Basel)* 2021;14(09):2348
- 33 Tribst JPM, Dal Piva AMDO, Ausiello P, Kalman L. Influence of implant-abutment contact surfaces and prosthetic screw tightening on the stress concentration, fatigue life and microgap formation: a finite element analysis. *Oral* 2021;1(02):88–101
- 34 Sacco G, Campus G. The treatment of periodontal disease using local oxygen-ozone. *Ozone Therapy* 2016;1(03):45–52
- 35 Rosenberg M. The science of bad breath. *Sci Am* 2002;286(04):72–79
- 36 Mogilnicka I, Bogucki P, Ufnal M. Microbiota and malodor—etiology and management. *Int J Mol Sci* 2020;21(08):2886
- 37 Iatropoulos A, Panis V, Mela E, Stefaniotis T, Madianos PN, Papaioannou W. Changes of volatile sulphur compounds during therapy of a case series of patients with chronic periodontitis and halitosis. *J Clin Periodontol* 2016;43(04):359–365
- 38 Tanda N, Hoshikawa Y, Ishida N, et al. Oral malodorous gases and oral microbiota: from halitosis to carcinogenesis. *J Oral Biosci* 2015;57(04):175–178
- 39 Suzuki N, Nakano Y, Watanabe T, Yoneda M, Hirofujii T, Hanioka T. Two mechanisms of oral malodor inhibition by zinc ions. *J Appl Oral Sci* 2018;26:e20170161