Halitosis: Its Intraoral Factors and Mechanism Relating to Formation

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Abstract

Various factors contribute to halitosis, such as smoking, food smell, etc., but intraoral factors are significant. There are many niches for bacteria in oral cavity, so they are suitable for the growth of microorganism. Oral anaerobes can produce volatile sulfur compounds (VSCs) including hydrogen sulfide, methyl mercaptan, dimethyl sulfide and minor components including amines and acids, which may be associated with halitosis. Hydrogen sulfide and methyl mercaptan are considered as major ingredients of VSCs responsible for halitosis. This review of literature illustrates the formation and the affiliated intraoral factors to halitosis.

Keywords

Halitosis; Intraoral factor; Mechanism; Oral anaerobes; Volatile sulfur compounds

Introduction

Halitosis, alternatively named as oral malodor (foul breath, breath malodor, and foetor oris) [1], is an abnormal symptom characterized by a foul or offensive odor emanating from the oral cavity with breath air [2]. It is considered as indicators of health status and oral cleanliness with the problems of producing social and psychological handicap [3]. From Greek and Roman times, it has been well recognized in the literature and its remedies can be traced to Hippocrates [4]. With the improvement of life quality and the enhancement of awareness for oral health, more and more people pay attention to halitosis, visiting dentists as a chief complaint and spent a lot of hundred millions in developed countries on breath fresheners. Several studies reported that no significant differences had been found between male and female participants in terms of oral malodour values [5,6]. One recent study shows that halitosis has a worldwide occurrence with a prevalence range of 22% to 50% [7] whereas severe cases are restricted to 5% [8]. Some estimation suggests that approximately 50% the North American population [9], 24% of Japanese individuals [10], 27.5% Chinese population [11], and 15% among Brazilian population [12] are suffered from halitosis [9,10,11,12]. It was demonstrated that the predominant composition of halitosis is VSCs and that some 82 commensal species of microorganisms in oral environment that were named as VSCs-producing bacteria could engender H₂S, CH₃SH, and acids in the process of metabolism that are in first place in composite of VSCs [20,23]. Of which, some have a close bearing on halitosis, principally, *Fusobacterium*, *Veillonella*, *T.denticola* (T.d.), *Porphyromonas gingivalis* (P.g), *Bacteroides forsythus* (B f) and *Peptostreptococcus*, etc. [16,24]. In the oral cavity of elderly people, *Fusobacterium* and *P. melaninogenica* were illustrated to be involved in the production of H₂S [25]. Furthermore, oral gram-negative anaerobes were verified to be responsible for halitosis, such as P.g, *Veillonella parvula*, *Prevotella intermedia* (P.i), *Actinomyces* (A.a) [16,21], *Peptostreptococcus*, *Eubacterium*, *Selenomonas*, *Centipeda*, *Bacteroides*, *Fusobacterium* and T.d [26]. All pathogens to halitosis can give out VSCs when they metabolize by taking advance of their especial enzyme such as trypsinlike, collagenic hydrolase, L-cysteine desulhydral and L-methionine-α-deamino-γ-mercaptomethane-lyase (METase) [18,20,21,27]. The halitosis-associated bacteria metabolize protein [15], cysteine [18,28], L-methionine and other amino acids as substrates to produce H₂S and CH₃SH that are converted to VSCs, but some authors showed that the ratio of methionine to whole free amino acids was significantly higher than that of cysteine [17].

There were remarkable differences of anaerobes between halitosis patients and healthy people, especially P.g. which could use sulphur-containing amino acids as substrates to produce a great deal of H₂S [29,30] with collagenic hydrolase and gingivain [21]. Persson, Edlund et al. [26] reported that the genera *Peptostreptococcus*, *Eubacterium*, *Selenomonas*, *Centipeda*, *Bacteroides* and *Fusobacterium* formed significant amounts of H₂S from L-cysteine while CH₃SH from L-methionine was formed by some members of the genera *Fusobacterium*, *Bacteroides*, *Porphyromonas* and *Eubacterium* [26].

The enzymatic reactions involved in the formation of H₂S and CH₃SH are predicted to be as follows: L-cysteine + L-cysteine + L-cysteine → pyruvate + ...
氨气 + H₂S, L-甲硫氨酸→H₂S + L-甲硫氨酸→α-酮戊二酸 + 氨气 + CH₃SH [20]. Moreover, these oral gram-negative anaerobes are able to cause a corresponding decrease in oxidation-reduction potentials (Eh) and at the same time a low Eh favours oral putrefaction and halitosis occurrence [28].

Additionally, H. pylori have been shown to produce H₂S and CH₃SH, which could contribute to the development of halitosis [31]. H. pylori presence in the oral cavity may be only transient due to the gastric reflux [32]. A recent study showed clear association between gastric H. pylori and occurrence of halitosis and coated tongue, and eradication of this infection on the contrary significantly improve halitosis and coated tongue [33]. Other recent studies have indicated a possible involvement of H. pylori in the pathogenesis of halitosis and glossitis, and even periodontitis as well [34].

**Intraoral related factors to halitosis**

The mouth harbors hundreds of bacterial species with various nutritional preferences and provides various microbiological niches in human ecology, such as saliva, dental plaque, periodontal pocket, gingival crevicular fluid (GCF), gingival pocket and tongue etc. [2,16,23,35]. Recently, some researchers [2,29,22] found that the process of developing bad breath is similar to that noted in the progression of gingivitis/periodontitis. Meanwhile, many investigations and experiments focused on the intraoral factors of halitosis respectively.

**Intraoral niches for VSCs-producing flora**

The main anatomical sources of VSCs identified in the oral cavity are the tongue and gingival sulcus [36]. Researchers suggest that the tongue plays an important role in the production of halitosis [7,16,27]. The surface morphologic characteristics of the tongue dorsum provide additional irregularities such as fissures, grooves and depapillated areas that may serve as retention areas for harboring bacteria, and the papillary structure on the dorsum represents a unique ecological niche in the oral cavity, offering a large surface area that favors the accumulation of oral debris and microorganism [16,20,37]. Furthermore, there is a visible white-brownish layer adhered to the dorsum of the tongue, which is named tongue coating or tongue biofilm, and is considered as a particular niche on the dorsum of tongue composed of desquamated epithelial cells, blood cells and metabolites, nutrients and bacteria [20,38]. Tongue biofilm is anyhow much more of importance by a wide variability and diversity of bacteria, with a high proportion of anaerobic bacteria [39], including P.g, A.a, S. sanguinis, P. i, E. Corrodens and oral spirochetes [40]. Gordon et al. [41] were the first to analyze the tongue microbiota and they identified several anaerobic species (Bacteroides, Fusobacteria spp, Peptococcus and Peptostreptococcus) among the prominent cultivable microorganisms [42]. In 80%-90% of cases, bacterial activities especially on the dorsum of the tongue are implicated [7], so that tongue coating is the major factor in halitosis [16,38]. Thus, with its anatomic and formative characteristics, tongue coating is referred to as one of the major sources of VSCs responsible for main components of halitosis [2,20,34,43,44]. In addition a Brazilian study [44] has found that high tongue coating levels were related with more VSCs counts and found a significant correlation between VSCs and tongue coating scores for all age groups, which was the similarly reported by Hinode et al. [45] and Liu et al. [11] whom also found that no statistically significant relation was observed among the VSCS levels considering age, bleeding and periodontal pockets sites. In a Japanese study, the numbers of total bacteria and H₂S-producing bacteria in the tongue biofilm in the malodorous group were statistically higher than those in the non-odorous group [16,43]. Another research investigated the relationship between halitosis and tongue microbiota in tongue biofilm samples via real-time PCR and found that anaerobes like P.g, T. forsythia, P. i, Prevotella nigrescens and T.d might contribute greatly to VSCs production [46], while other study reported that an increase in the number of H₂S-producing bacteria such as Prevotella spp as well as Veillonella and Actinomyces in tongue coating sample responsible for oral malodour [47]. The most studies showed a positive correlation between the clinical parameters of halitosis and total bacterial numbers, as well as that and Prevotella intermedia, Fusobacterium nucleatum and Campylobacter rectus concentrations in the tongue coating samples. However, there was no similar correlation with respect to the saliva samples [5]. Some researchers stated that the tongue dorsum and tongue coating played a more important role in the formation of halitosis than periodontal diseases [6,27]. José R et al. [48] also reported that tongue biofilm seems to be directly involved in the production of oral halitosis and may have an important role in the success of periodontitis therapy since it is a potential reservoir for periodontal pathogens. Other structures on the tongue dorsum were confirmed that the presence of deep fissures was related to the twice counts of bacteria and to the noticeable higher mouth and tongue odor scores [16,27].

Saliva played a positive role in the formation of halitosis [49]. Saliva, containing a multitude of desquamated oral epithelial cells, leukocytes, bacteria, food residues and a little of proteins and enzymes, is a feasible culture for oral bacteria. As a result, external degeneration of saliva provides substrates to be oxidized as VSCs [49,50]. Besides, the pH, Eh and the quantity of saliva also are effective in the formation of malodor [51]. The higher density of hydrogen ions and the larger quantity of saliva refrain or mitigate oral malodorous formation, whereas neutrality and alkalinity of saliva promote production of malodor. The pH value on the surfaces of oral mucosa is mainly determined by the fermentative and putrefactive activities of the adhered bacteria, and these acid-base processes are of importance for regulating the formation of halitosis [49]. According to microbiota in saliva, the previous reports suggested that P. g and F. i in saliva contribute to oral malodour [52]. However, recently it has been found that there was no positive correlation between specific oral bacterial species in resting saliva and VSCs concentrations [5]. The comparison of microbial profile with VSCs levels showed a weak positive correlation of P. g, F. n and T. f count with Organoplectus and Tanita score. A quantitative analysis of P. g, F. n, T. f and T. d in the saliva, on the tongue coating, and in the subgingival plaque of patients with oral malodor using real time PCR showed correlation between increased VSCs levels and increased levels of P. g and T. f in subgingival sample and F. n in tongue coating [53].

Dental plaque especially materia alba, gingival pocket, periodontal pocket, and gingival crevicular fluid serve the formation of halitosis as important niches for VSCs-producing bacteria. These niches provide suitable microbial ecosystem for the development and growth of diverse and plentiful oral flora.

**Periodontal diseases and halitosis**

By the examination of gas chromatography, the amount of VSCs and CH₃SH/H₂S ratio in mouth air from patients with periodontal involvement were 8 times greater than those of control subjects [17] and these two parameters increased in proportion to the bleeding...
index and probing depth in another investigation [38]. Many studies confirmed that the primary causative microbes for halitosis were similar to the periodontopathic bacteria to some extent [16,41,48], such as P. g. P. i, A. a, and T. d [2,21,29,54], so that periodontal disease–associated bacteria are capable of producing large amounts of VSCs [20]. Furthermore, gingival diseases and periodontitis might lead to halitosis [3,17,54] due to the maturation of subgingival plaque suitable for the growth of anaerobes in periodontal pocket. Meanwhile, VSCs could destroy periodontal tissues in turn [29,55]. An increasing volume of evidence is demonstrating that extremely low concentrations of many of these compounds are highly toxic to tissues [55]. It can increase the permeability of the oral mucosa [56] and decrease protein or collagen synthesis [57,58]. These compounds are highly toxic, especially CH₃SH [10]. H₂S, CH₃SH and other substances could prevent fibroblasts or collagen from synthesis [22,55] and inhibit cell migration in periodontal ligament cells [59], then invade into deeper tissue directly to make kinds of toxin devastate periodontal tissues. The presence of CH₃SH within a periodontal pocket was involved in the induction or progression of periodontal disease [22]. The increase in the ratio of CH₃SH to H₂S in human gingival crevicular sites was correlated with deeper pockets or bleeding pockets [60]. In addition, CH₃SH also increases permeability of intact mucosa and stimulates production of cytokines which have been associated with periodontal disease [55]. Consequently, some periodontopathic bacteria produce VSCs, which cause halitosis, aggravate periodontal diseases as well in the same time. Some studies, however, showed that there was a much weaker association between VSCs and periodontal conditions [44,61]. These observations tend to suggest that oral malodour is not caused by periodontal disease alone, but by a combination of factors, including periodontal conditions and tongue coating.

Oral healthcare is obviously paying more and more attention along with more attention nowadays. Due to the psychological and physical harm as a kind of oral disease, halitosis is drawing more and more attention from dentists and researchers. From mouth access, external supplies of various foods are passed and nearly 400 species of microorganisms could be identified [29]. Oral cavity provides a favorable condition for the survival and development of diverse and numerous oral flora, owing to its proper temperature, humidity and food remnants. Of these oral flora, anaerobes such as P.g, Veillonella parvula, P.i and Actinomyces, etc. are found in dental plaque, periodontal pocket, tongue coating and saliva, and confirmed as the pathogens for halitosis to engender H₂S, CH₃SH, indole, etc. in the periodontal pocket. Meanwhile, VSCs could destroy periodontal tissues in turn [29,55]. The oral ecology and periodontal diseases.

Considering the formation and related factors of halitosis, the initial treatment strategy should focus on the exact cause and on oral hygiene [63]. Except for oral health instruction, necessary treatments are used for the patients with halitosis [64]. The patients with halitosis should destroy oral niches for VSCs-producing, using mechanical and medical means. Most approaches were found to be inefficient and/ or short lasting. The most successful treatment involved mechanical debridement (including tooth brushing, flossing, chewing gums and tongue cleaning), possibly combined with the use of an antimicrobial mouth rinse, such as chlorhexidine, cetipiridinium chloride and zinc lactate [22,48,64,65]. Several previous and recent studies reported that breath odor and tongue coating status, tongue coating scores, concentrations of CH₃SH and total VSCs are improved after instructions on tongue brushing or with patients who had the habit of tongue cleaning [5,66]. Investigators have showed that the mouth rinse is efficient, which contains metal ions, especially zinc, that inhibit odor formation because of its affinity to sulphur compounds [63,67]. Thus, tongue cleaning is an effective method for preventing or improving halitosis.

Better education of both the public and dental professionals as to the most frequent cause of halitosis, insufficient oral hygiene, might elevate the level of compliance by patients [64]. It is necessary to make oral examination regularly for them. Also, the patients with halitosis should avoid smell-producing foods and habit with those such as garlic, onion, smoke, etc.

The formation and mechanism of VSCs for halitosis are partially crystallized according to the current literature. The oral ecology and the interaction among microorganisms and saliva, tongue coating, the dorsum of tongue and embrasure of gingival papilla are expected for further researches on mechanism, prevention and treatment of halitosis. Halitosis caused by oral pathologic causes is associated with anaerobes in the oral niches including periodontal area, dental plaque, tongue, GCF and saliva, which can produce VSCs in metabolism. This article concludes the formation mechanisms of halitosis and its intraoral related factors, such as niches for VSCs-producing bacteria and periodontal diseases.

References


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