

Photodynamic Therapy for Halitosis: Could be Possible?

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Abstract: Halitosis is a very frequent condition characterized by an unpleasant odor related to expired air, and 80-90% of the cases originate in the oral cavity. It is a social problem that affects one-third of the population, causing a negative impact on the quality of life. The measurement of volatile sulfur compounds (VSC) at the oral level is very useful for intercepting the problem. Photodynamic Therapy (PDT) is based on the combination of a non-toxic dye and an appropriate wavelength of visible light, which in the presence of oxygen is activated and can promote a phototoxic response. We would like to document a case of oral halitosis diagnosed and treated with photodynamic therapy using a 660 nm diode laser and phenothiazine chloride as a photosensitizer.

Keywords: photodynamic therapy; halitosis; VSC compounds; PDT for halitosis.

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1. Introduction

Halitosis is a term used to describe any unpleasant odor related to expired air, a social problem that affects one-third of the population, causing a negative impact on the quality of life. 80 to 90% of the cases originate in the oral cavity resulting from proteolytic degradation by gram-negative anaerobic bacteria [1,2]. It is mainly caused by the metabolism of the microbiota on the tongue dorsum and periodontium, favored by low salivary flow during the day, food impaction, dental restoration, poor oral hygiene, and diet. Particularly in young patients, the presence of tongue coating seems to be the main cause of halitosis [1].

There are 5 types of halitosis:

Type 1 (oral): this is linked to VSC, volatile organic compounds (VOC), and nitrogen-containing gases (amines) [3]. The principal VSC is hydrogen sulfide (H₂S), methyl mercaptans (CH₃SH), and dimethyl sulfide (CH₃SCH₃) [4, 5]. The gases responsible for oral halitosis derive from protein and glycoprotein putrefaction produced by the oral microbiota. The dorsum of the tongue is the most important halitogenic site, also because it has the largest surface area and the highest bacterial load within a densely populated biofilm [6]. About 85% of oral halitosis cases are linked to poor oral hygiene, plaque stagnation areas, and gingivitis/periodontitis.

Type 2 (airway): originates from the respiratory tract (rhinosinusitis, tonsillitis, pharyngitis, laryngitis, bronchitis, pneumonia). The proportion of this type of halitosis is between 2.9 and 10%. Obstructive nasal pathology causes mouth breathing, often resulting in xerostomia and halitosis. Tonsillitis causes edema and hypertrophy, which may obstruct orifices on the tonsillar surface [4]. This fact disrupts the cleansing flow of secretions and desquamated epithelial and bacterial cells, and food debris becomes harnessed, leading to

stagnation. Anaerobic bacteria found in tonsilloliths include *Eubacterium*, *Fusobacterium*, *Porphyromonas*, *Prevotella*, *Selenomonas*, and *Tannerella* spp., associated with the production of VSCs [7,8]

Type 3 (gastroesophageal): this type of halitosis is due to the leakage of odorant volatiles from the stomach through the esophagus to the mouth and nose. A degree of gastroesophageal reflux is considered normal, occurring in almost all individuals several times per day, but pathologically this halitosis occurs due to gastroesophageal reflux disease (GERD), *Helicobacter pylori*-related gastritis, gastrocolic fistulae and hypopharyngeal diverticula [9,10].

Type 4 (blood-borne): this type of halitosis is due to volatile chemicals in the systemic circulation that during alveolar gas exchange move to exhaled breath and cause halitosis. In pathologic Type 4 halitosis exhaled breath volatiles are reported in patients with diabetes mellitus, sleep apnea, *H. pylori* infection, sickle cell disease, asthma, breast cancer, lung carcinoma, chronic obstructive pulmonary disease, cystic fibrosis, liver diseases, cirrhosis, uremia and kidney failure [11].

Type 5 (subjective): this type can be categorized as psychological or neurologic [12].

The normal tongue coating is characterized by a thin, slightly moist, and whitish substance. The main factors that affect tongue coating are [13]:

1. the age: In the elderly, the tongue coating is more discolored; this could be due to a modification of the diet, a reduction in salivary flow, or poor oral hygiene.
2. the diet: the tongue coating changes according to the type of food ingested.
3. oral hygiene: this is the main factor that influencing the formation of tongue coating. In particular, patients with periodontal disease may accelerate VSC production; in fact, these patients produced higher concentrations of CH₃SH than subjects with healthy periodontal tissues, which produced higher concentrations of H₂S.

The production of VSC metabolites has been considered as the leading cause of intraoral halitosis. Furthermore, short-chain fatty acids (SCFAs), such as propanoic acid and butyric acid, cadaverine, indole, and skatole, may also contribute to the development of halitosis [10].

The sulfur-containing amino acids (cysteine and methionine) are degraded by both Gram-negative and Gram-positive anaerobic bacteria to produce VSCs. A wide range of oral bacteria, including *Porphyromonas gingivalis* (*P. gingivalis*), *Fusobacterium nucleatum* (*F. nucleatum*), *Prevotella intermedia* (*P. intermedia*), *Treponema denticola* (*T. denticola*) and *Tannerella forsythia* (*T. forsythia*), have been regarded to be closely associated with intraoral halitosis [14, 15].

Analysis of VSC is useful for determining levels of H₂S and CH₃SCH₃ so that both the type of halitosis and the intensity can be assessed [11]. The value of 112 ppb H₂S indicates the presence of halitosis, while the value of CH₃SH is normal until 26 ppb, and this gas is found mainly in periodontal pockets [16].

These bacteria develop mainly on the lingual back, as there are deep fissures in this area that facilitate bacterial proliferation, as they provide a low level of oxygen conditions for halitosis-related anaerobic bacteria. For this reason, the lingual back is considered the main source of VSC production [14]. The process for the acquisition of the sample for the heliometric is based on connecting the device to the computer with a specific software program that allows the creation of a graph corresponding to the peaks and concentrations of VSCs. The

results are stored in the program recovered when necessary [17]. In order to properly treat halitosis, it is important to detect its source. If it is a bad breath caused by the oral cavity, it is of primary importance to treat any periodontal disease and instruct the patient to maintain correct oral hygiene at home using the brush and interdental aids such as dental floss and pipe cleaner. Sometimes, however, halitosis can occur even without the presence of periodontal disease; for this reason, it is good practice to instruct patients to clean the tongue daily using the brush and tongue cleaner. However, there are other conditions that can lead to the development of halitosis, such as old restorations, unsuitable prostheses, xerostomia, pericoronitis, oral ulceration, or other types of lesions. First of all, therefore, it is essential to diagnose the cause, treat it and, as the last step, treat halitosis [18].

If instead, the halitosis originates from nonoral causes such as respiratory, gastrointestinal and hepatic, renal, endocrine, or hematological disease, consultation should be done with the specialist. Finally, some people think they have halitosis (halitophobia) even if it is not detected during the diagnosis. In severe cases, these subjects must be treated from a psychological point of view [19].

In addition to mechanical treatment, chemical agents, such as mouthwashes, can be used to help combat halitosis, in particular: chlorhexidine, essential oils, triclosan, hydrogen peroxide, oxidizing lozenges, baking soda, Amine fluoride/Stannous fluoride [20].

Another treatment which, according to the data reported in the literature, can generate good results is photodynamic therapy (PDT). This aid has been widely employed in dentistry, mainly for the decontamination of root canals and periodontal pockets [21, 22]. It is based on the combination of a non-toxic dye and an appropriate wavelength of visible light, which in the presence of oxygen is activated and can promote a phototoxic response. These factors, combined together, can produce lethal cytotoxic ROS that can selectively destroy cells. ROS can cause cell death through several mechanisms, including lipid peroxidation, inhibition of enzymatic systems, and agglutination of proteins. PDT can be repeated several times since it is a non-invasive procedure [21].

Studies in the literature have shown that PDT for the treatment of halitosis is effective, without being an invasive treatment. Through this treatment, the particular reduction of H₂S [23, 24] was found. According to the study of Costa de Mota *et al.*, is found a 7% reduction in bacterial load in the PDT treatment group while reporting a 7% increase for the group that had used only the lingual scraper.

Furthermore, the study by Lui *et al.* reported that the use of PDTs with methylene blue and wavelengths between 635 and 670 nm reduces the levels of *P. gingivalis*, *T. forsythensis* e *T. denticola* [25].

Although PDT leads to good results in reducing the bacterial load on the lingual back and therefore reducing halitosis, the best results in the literature are reported by the synergy between the PDT and the lingual scraper [26].

We would like to document a case of oral halitosis treated with photodynamic therapy.

2. Materials and Methods

A 54 years old man went to our private practice for a normal follow up. He reported good general health and that to have had the sensation of bad breath in the mouth. The patient had good oral hygiene, and he reported to clean every day the tongue. It was therefore decided to carry out a photodynamic therapy session with 660 nm diode laser, 100 mwatt of power, a spot of 1 cm (Helbo, Bredent, Senden, Germany) and phenothiazine chloride 0,1%. This

photosensitizer has been spread along the lingual surface, especially on the posterior side. After 1 minute, the laser light had been activated, with a 2D tip, maintained approximately 0.5 cm from the tongue and making circular movements for a total of 5 minutes (fig 1). Subsequently, the photosensitizer was removed with a cotton ball soaked with a physiological solution 1.



Figure 1. Tongue of the patient during Photodynamic Therapy.

3. Results and Discussion

After a week, the patient felt an improvement in symptoms, and the same results were maintained at 1 month follow up. It is very interesting to evaluate also VSC values. We cannot determine whether the patient improved his condition also for greater lingual cleansing or whether he affected his post-treatment diet. Halitosis plays an important role in the quality of life; for this reason, it is a topic that needs attention to avoid the patient's social isolation. It is a condition that mainly involves anaerobic bacteria, which release VSC during exhalation, are found mainly on the lingual back, and are the cause of the bad smell [27]. According to the literature, halitosis can arise more easily in subjects with poor oral hygiene, wearers of incongruous prostheses, and old restorations. In particular, in elderly subjects wearing prostheses, the correct hygienic maintenance of prosthetic products can be difficult, leading to bacterial colonization, and the onset of bad odors [28].

Therefore, the need for new therapeutic alternatives for the patient is fundamental, as studies have shown that self-cleaning of the tongue alone, using tongue scrapers, is not completely effective for the reduction of halitosis.

Furthermore, the use of mouthwashes as an antimicrobial action is also not completely effective, as they do not eliminate the cause and also cause side effects such as unpleasant taste, alteration of the oral microflora, and coloring of the mucous membranes.

The study conducted by Seerangaiyan *et al.*, analyzed the quality of the tongue microbial in subjects with and without halitosis. From what can be deduced, the test group (with halitosis) presented *Aggregatibacter segnis*, *Campylobacter*, *Capnocytophaga*, *Clostridiales*, *Dialister*, *Leptotrichia*, *Parvimonas*, *Peptostreptococcus*, *Peptococcus*, *Prevotella*, *Selenomonas*, *Treannerella*, while the control group had (without) *Haemophilus parainfluenza* (*H. parainfluenza*), *Moryella*, *Oribacterium*, *Prevotella*, several *Streptococcus*, *Rothia dentocariosa* [29, 30].

Furthermore, from the meta-analysis conducted by Dou *et al.*, it is shown that *H. pylori* infection is related to halitosis. This data can be useful to treat those patients refractory to therapies [31].

PDT, according to the literature, has proven to be a valid alternative, it is also a non-invasive procedure, does not cause side effects, does not cause bacterial resistance, and the effects are immediately visible [6].

Gonçalves' study assessed the presence of halitosis in patients with multiple sclerosis, who showed higher levels of H₂S, compared to the control group not affected by multiple sclerosis. These subjects could be more predisposed to the formation of H₂S for the intake of immunosuppressants, which could alter the salivary flow and, therefore, the oral flora. In this study, it was reported that the combination of the lingual scraper with PDT is more effective in reducing the concentration of VSC than using only the tongue scraper or only the PDT [1].

Another study conducted by Costa da Mota *et al.*, evaluated the clinical and microbiological effect of antimicrobial photodynamic therapy (aPDT) on halitosis in adolescents. They were divided into three groups: group 1 (treatment with photodynamic therapy), group 2 (treatment with tongue scraper), group 3 (treatment with a tongue scraper, and photodynamic therapy). The results reported that the administration of photodynamic therapy alone reduces the concentration of H₂S, therefore of halitosis, compared to the use of tongue scrapers only [26].

A further study, conducted by Garcia Lopes *et al.*, divided adolescents into three groups: group 1 (treatment with photodynamic therapy), group 2 (treatment with a tongue scraper), group 3 (treatment with tongue scraper combined with photodynamic therapy). This study shows that the greatest reduction in sulfides occurs by combining photodynamic therapy with the use of the tongue scraper. [6]. All the data provided in the literature report that photodynamic therapy combined with the correct deduction of the tongue drastically reduces the concentration level of VSC, in particular H₂S, compared to just cleansing the tongue or using antimicrobial agents [32, 33].

4. Conclusions

Phenothiazine derivatives such as methylene blue are very used in the field of chemistry, biology, and pharmacology [34]. In our case, we have used a phenothiazine derivative, and the success of this photosensitizer is well documented in the recent literature [35, 36, 37]. For this reason, the photodynamic therapy treatment can be recommended in halitosis patients, and also, it can be carried out several times as it is a non-invasive treatment capable of immediately generating benefits.

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Conflicts of Interest

The authors declare no conflict of interest.

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