Oral Malodor--A Detailed Review
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Introduction

Oral malodor has been recognized in the literature since ancient times, but in the last five to six years it has increasingly come to the forefront of public and dental professional awareness[1]. Approximately 40-50% of dentists see 6-7 self-proclaimed oral malodor patients per week[2]. Standard diagnosis and treatment for oral malodor in the routine care of each patient has not been established in the dental or the medical field. However the transfer of knowledge is increasing because of pioneering researchers and clinicians that have developed reputable clinics dealing with this condition. Dental and medical schools must incorporate diagnosis and treatment of oral malodor in their curriculum, so that the future generations of clinicians can effectively treat this condition.

To date, there have been four international conferences where the experts in the field have gathered and published their observations and research findings. The fourth international conference was held at the School of Dentistry, University of California (UCLA) and it a was big success and demonstrated a continued enthusiasm towards further meetings and scientific research in the area of oral malodor. Although this area of research has been ridiculed, at least 50% of the population suffers from a chronic oral malodor condition by which individuals experience personal discomfort and social embarrassment leading to emotional distress. The consequences of oral malodor may be more than social; it may reflect serious local or systemic conditions. Oral Malodor research has gained momentum with increasing suspicions being directed at the sulfur-producing bacteria as the primary source of this condition.

Oral And Non-Oral Causes

Oral malodor can be caused by many localized and systemic disorders. Oral Malodor (OM) caused by normal physiological processes and behaviors is usually transitory. Non pathologic OM may due to hunger, low levels of salivation during sleep food debris, prescription drugs and smoking[3]. Chronic or pathological halitosis stems from oral or non- oral sources. In addition there appear to be

several other metabolic conditions involving enzymatic and transport anomalies (such as Trimethylaminuria) which lead to systemic production of volatile malodors that manifest themselves as halitosis and/or altered chemoreception[4]. Some of the oral causes are periodontal disease, gingivitis, and plaque coating on the dorsum of the tongue. OM may be aggravated by a reduction in salivary flow. Radiation therapy, Sjorrgen's Syndrome, some lung conditions, including cancer, peritonsillar abscess, cancer of the pharynx and cryptic tonsils can also contribute to OM[5]. Nasal problems such as postnasal drip that falls at the posterior dorsum of the tongue may exacerbate the oral malodor condition. Odor generated in this manner can be easily distinguished from mouth odor by comparing the odor exiting the mouth or nose[6]. The non-oral causes of OM include diabetic ketosis, uremia, gastrointestinal conditions, and irregular bowel movement, hepatic and renal failure and certain types of carcinomas such as leukemia. The accurate clinical labeling and interpretation of different oral malodors both contribute to the diagnosis and treatment of underlying disease[7] (Table 9-1). Taste and smell can be altered due to facial injuries, cosmetic surgery radiation and olfactory epithilium located on the dorsal aspect of the nose[8]. A relationship between gastrointestinal diseases such as gastritis and oral malodor has not been established. However, oral malodor has been reported in some patients with a history of gastritis, or duodenal and gastric ulcers[9].

Saliva plays a central role in the formation of oral malodor. Such formation has its basis due to bacterial putrefaction, the degradation of proteins, and the resulting amino acids produced by microorganisms[10]. Many patients with a chief complaint of oral malodor have some level of gingival and or periodontal pathology sufficient to be the etiology, but clearly periodontol pathology is not a prerequisite for production of oral malodor[11]. Medications such as antimicrobial agents, antirheumatic, anti hypertentive, antidepressants and analgesics may cause altered taste and xerostomia.

OM in healthy patients arises from the oral cavity and generally originates on the tongue, dorsum[5,12,13,14,15]. The sulfur producing anaerobic bacteria appears to be the primary source of this odors[16]. The large surface area of the tongue and its papillary structure allow it to retain food and debris. This is an excellent putrefactive habitat for gram negative anaerobes that metabolize proteins as an energy source. The bacteria hydrolyze the proteins to amino acids, three of which contain sulfur functional groups and are the precursors to volatile sulfur compounds (VSC's). These gaseous substances, responsible for malodor, consist primarily of hydrogen sulfide (H_2S), dimethyl sulfide [$(CH_3)_2S$], methyl mercaptan (CH_3SH) and sulfur dioxide (SO_2)[10,12,14,15] . Cadaverine levels have been reported to

be associated with oral malodor and this association may be independent of VSC[17] . Subjects challenged with cysteine rinses produced high oral concentrations of VSC, which thus seems to be a major substrate for VSC production. The other sulfur-containing substrates had much less effect. It was found that the tongue was the major site for VSC production[18].

The Tongue Plaque Coating

Research suggests that the tongue is the primary site in the production of OM. The dorsoposterior surface of the tongue has been identified as the principal location for the intraoral generation of VSC's[19]. The tongue is a haven for the growth of microorganisms since the papillary nature of the tongue dorsum creates a unique ecological site that provides an extremely large surface area, favoring the accumulation of oral bacteria. The proteolytic, anaerobic bacteria that reside on the tongue play an essential part in the development of oral malodor. The presence of tongue coating has been shown to have a correlation with the density or total number of bacteria in the tongue plaque coating[20]. The weight of the tongue coating in periodontal patients was elevated to 90 mg, while the VSC was increased by a factor of four. The CH_3SH/H_2S fraction was increased 30-fold when compared with individuals with healthy periodontium. This high ratio of amino acids can be due to free amino acids in the cervicular fluid when compared with those of L-cysteine[19]. The BANA (Benzoyl-DL-arginine-2 napthylamide) test has been used to detect *T.denticola and P.gingivalis*. The two organisms that may contribute to oral malodor can be easily detected by their capacity to hydrolyze BANA a trypsin-like substrate. BANA scores are associated with a component of oral malodor, which is independent of volatile sulfide measurements, and suggest its use as an adjunct test to volatile sulfide measurement[21]. Higher mouth odor organoleptic scores are associated with heavy tongue coating and correlate with the bacterial density on the tongue and it also correlates to BANA-hydrolyzing bacteria--*T.denticola, P.gingivalis*, and *Bacteroides forsythus*[22].

Microbiota Associated With Oral Malodor

The actual bacterial species that cause OM have yet to be identified from among the 300 plus bacterial species in the mouth. Putrefaction is thought to occur under anaerobic conditions, involving a range of gram-negative bacteria such as *Fusobacterium, Veillonella, T.denticola, P. gingivalis, Bacteroides* and *Peptostreptococcus*[22,23]. Studies have shown that essentially all odor production is a result of gram-negative bacterial metabolism

and that the gram-positive bacteria contribute very little odor[24]. *Fusobacterium nucleatum* is one of the predominant organisms associated with gingivitis and periodontitis and this organism produces high levels of VSC's. The nutrients for the bacteria are provided by oral fluids, tissue and food debris. Methionine is reduced to methyl mercaptan and cysteine. Cysteine is reduced to cystine, which is further reduced to hydrogen sulfide in the presence of sulfhydrase-positive microbes. This activity is favored at a pH of 7.2 and inhibited at a pH of 6.5 [10,12,14,15]. Isolates of *Klebsiella* and *Enterobacter* emitted foul odors in vitro which resembled bad breath with concomitant production of volatile sulfides and Cadaverine both compounds related to bad breath in denture wearers[25]. The amounts of volatile sulfur compounds (VSC) and methyl mercaptan/hydrogen sulfide ratio in mouth air from patients with periodontal involvement were reported to be eight times greater than those of control subjects[15].

Oral Malodor Assessment Parameters

Organoleptic Measurements

One major research problem that must be tackled is the lack of an established gold standard for rapidly measuring OM condition. The objective assessment of oral malodor is still best performed by the human sense of smell (direct sniffing-organoleptic method) but more quantifiable measures are being developed. At present, confidant feedback and expert odor (organoleptic) judges are the most commonly used approaches. Both assessments use a 0-5 scale in order to consistently quantify the odor (0= No odor present, 1= Barely noticeable odor, 2= Slight but clearly noticeable odor, 3= Moderate odor, 4= Strong offensive odor, 5= Extremely foul odor). Individuals are instructed to refrain from using any dental products, eating or using deodorants of fragrances four hours prior to the visit to the clinic Individuals are also advised to bring their confidante or friends to assess their oral malodor. (Table 9-2)

In order to create a reproducible assessment, subjects are instructed to close their mouth for two minutes and not to swallow during that period. After two minutes the subject breathes out gently, at a distance of 10 cm from the nose of the their counterpart and the organoleptic odors are assessed[26]. In order to reduce inter-examiner variations, a panel consisting of several experienced judges is often employed. A study on the inter-examiner reproducibility indicates that there is some co-relation, albeit poor[27]. Gender and age influence the performance of an organoleptic judge. Females have a better olfactory sense and it decreases with age. Dentists and periodontists may not be ideal

judges if they do not use masks on a daily basis[28].

OM can be analyzed using gas chromatography (GC) coupled with flame photometric detection[29]. This allows separation and quantitative measurements of the individual gasses. However the equipment necessary is expensive and requires skilled personnel to operate it. This equipment is also cumbersome and the analysis is time consuming. As a result, GC cannot be used in the dental office and is not always used in OM clinical trials. Recently a closed-loop trapping system followed by off-line high resolution gas chromatography ion trap detection was used for detection of compounds from saliva and tongue coating samples[30]. Numerous volatile components were detected ranging from ketones to many unknowns. Adding casein (to provide cysteine and methionine) during incubation led to the appearance of nine new sulfur-containing compounds.

Portable Sulfide Meter

The portable sulfide meter (Halimeter®--Interscan Corporation, Chatsworth, CA.) has been widely used over the last few years in OM testing. The portable sulfide meter uses an electrochemical, voltammetric sensor which generates a signal when it is exposed to sulfide and mercaptan gases and measures the concentration of hydrogen sulfide gas in parts per billion. The halimeter is portable and does not require skilled personnel for operation. The main disadvantages of using this instrument are the necessity of periodic re-calibration and the measurements cannot be made in the presence of ethanol or essential oils[27]. In other words, the measurements may be affected if the subject is wearing perfume, hairspray, deodorant, etc. In addition, this limitation does not allow the assessment of mouthwash efficacy until after these components have been thoroughly rinsed out or dissipated.

The Electronic Nose

The "Electronic Nose" is a hand held device, being developed to rapidly classify the chemicals in unidentified vapor. Its application by scientists and personnel in the medical and dental field as well as it is hoped that this technology will be inexpensive, miniaturizable and adaptable to practically any odor detecting task[31]. If the Electronic Nose can learn to "smell" in a quantifiable and reproducible manner, this tool will be a revolutionary assessment technique in the field of OM. This device is based on sensor technology that can smell and produce unique fingerprints for distinct odors. Preliminary data indicates that this device has a potential to be used as a diagnostic tool to detect odors.

Management Of Oral Malodor

A large number of so called "Fresh Breath Clinics" are offering diagnostic and treatment services for patient complaints of oral malodor. There are no accepted standards of care for these services, and the clinical protocols vary widely.

A thorough medical, dental and halitosis history is necessary to determine whether the patient's complaint of bad breath is due to oral causes or not[32]. It is important to determine the source of oral malodor; complaints about bad taste should be noted. In most cases patients that complain of bad taste may not have bad breath. The taste disorders may be due to other causes[33]. It has been reported that in approximately 8% of the individuals the odor was caused by tonsilitis, sinusitis, or a foreign body in the nose[34]. This percentage of individuals may be higher, additional research is needed in this area. Approximately 80-90% of the oral malodor originates from the dorsum of the tongue. Therefore the treatments targeted towards reduction of the oral malodor will require antimicrobial components directed against the tongue microbiota.

Treatment of OM is important not only because it helps patients to achieve self-confidence but also because the evidence indicates that VSC's can be toxic to periodontal tissues even when present at extremely low concentrations[35]. The best way to treat OM is to ensure that patients practice good oral hygiene and that their dentition is properly maintained[36] (Table 9-3). Traditional procedures of scaling and root planing can be effective for patients with OM caused by periodontitis[37]. All patients should be instructed in proper tooth brushing and flossing and tongue cleaning. Mouthrinses should be recommended based on scientific evidence. Caution should be exercised and professional advice should be sought as to administration and type of mouthrinse to be used. Tongue scraping should be demonstrated and patients should be asked to demonstrate to the dental hygienist the appropriate use of tongue scrapers. The tongue has a tendency to curl up while tongue scraping therefore a combination of flexible tongue scrapers and tongue scrapers with handles should be recommended to the patients.

The saliva functions as an antibacterial, antiviral, antifungal, buffering and cleaning agent[38] and so any treatment that increases saliva flow and tongue action, including the chewing of fibrous vegetables and sugarless gum, will help decrease OM[39]. Finally, oral rinses can be used as supplement good oral hygiene practices.

Antimicrobial Agents

Mouthwashes have been used as chemical approach to combat oral malodor. Mouth rinsing is a common oral hygiene dating back to ancient times[40]. Antibacterial components such as cetylpyridinium chloride, Chlorhexidine, Triclosan, essential oils, quaternary ammonium compounds, benzalkonium chloride hydrogen peroxide, sodium bicarbonate[41], zinc salts (Table 9-4) and combinations have been considered along with mechanical approaches to reduce oral malodor. Any successful mouthrinse formulation must balance the elimination of the responsible microbes while maintaining the normal flora and preventing an overgrowth of opportunistic pathogens. Most commercially available mouthrinses only mask odors and provide little antiseptic function. Even when these mouthrinses do contain antiseptic substances, the effects are usually not long-lasting[42,43]. The microbes survive antiseptic attacks by being protected under thick layers of plaque and mucus[12].

Many commercially available rinses contain alcohol as an antiseptic and a flavor enhancer. The most prevalent problem with ethanol is that it can dry the oral tissues. This condition in itself can actually induce OM. In addition, there is some controversy as to whether or not the use of alcohol rinses are associated with oral cancer[44,45]. The FDA states that there is no evidence to support the removal of alcohol from over-the-counter products but alcohol-free mouthrinses are becoming increasingly popular.

Zinc Rinses

Clinical trials conclude that zinc mouthrinses are effective for reducing OM in-patients with good oral health[39]. Zinc rinses (in chloride, citrate or acetate form) have been found to reduce oral VSC concentrations for greater than three hours. The zinc ion may counteract the toxicity of the VSC's and it functions as an odor inhibitor by preventing disulfide group reduction to thiols and by reaction with the thiols groups in VSC's. It has been reported a zinc-based rinse was more effective as compared to chlorinedioxide based rinse when both rinses were used twice a day for 60 seconds over a 6-week period[46]. Zinc containing chewing gum has been shown to reduce oral malodor[47].

Chlorhexidine Rinses

Chlorhexidine digluconate is useful in decreasing gingivitis and plaque buildup. It is one of two active ingredients in mouthrinses that has been shown to reduce gingivitis in long-term clinical trials and appears to be the most effective anti-plaque and anti-gingivitis

agent known today[12,48].

The efficacy of chlorhexidine as a mouthrinse to control OM has not been studied extensively. The primary side effect of chlorhexidine is the discoloration of the teeth and tongue. In addition, an important consideration for long-term use is its potential to disrupt the oral microbial balance, causing some resistant strains to flourish, such as *Streptococcus viridans*[49].

The effect of 1-stage full mouth disinfection in periodontitis patients (Scaling and root planing of all pockets within 24 hrs together with the application of Chlorhexidine to all intra-oral niches followed by chlorhexidine rinsing for 2 months) resulted in a significant improvement in oral malodor when compared to a fractional periodontal therapy (consecutive root planings per quadrant, at a 1 to 2 week interval)[50].

While Chlorhexidine appears to be clinically effective from these open-design clinical studies, it is not an agent that should be used routinely, or for long periods of time, in the control of oral malodor, because of its side effects. Mouth rinse containing Chlorhexidine, Cetylpyridium chloride and Zinc lactate was evaluated in a clinical study for two weeks. Eight subjects participated in this pilot study and this formulation showed improvement in organoleptic scores and a trend to reduce tongue and saliva microflora[51].

Antimalodor properties of chlorhexidine spray 0.2% chlorhexidine mouthrinse 0.2% and sanguarine-zinc mouthrinse were evaluated on morning breath. Oral malodor parameters were assessed before breakfast and four hours later after lunch. Results indicated that a sanguarine-zinc solution had a short effect as compared to chlorhexidine that lasted longer[52].

Chlorine Dioxide Rinses

Chlorine Dioxide (ClO_2) is a strong oxidizing agent that has a high redox capacity with compounds containing sulfur. Chlorine dioxide is also used in water disinfection and in food processing equipment sanitation and functions best at a neutral pH. Commercially available mouthrinses are a solution of sodium chlorite since chlorine dioxide readily loses its activity[39]. Further independent clinical investigations are needed to substantiate the effectiveness of sodium chlorite containing rinses for the control of OM. In fact, chlorine dioxide, the agent most widely touted on the Internet, has no published clinical studies (as of December, 1999) to substantiate the claims to reduce oral malodor. Benzalkonium chloride in conjunction with sodium chlorate has been shown to be effective in reducing oral malodor. In this pilot study subjects with mild to severe periodontitis were

instructed to use the mouthwash twice a day for a period of six weeks and periodontal and oral malodor parameters were assessed[53].

Triclosan Rinses

Triclosan (2,4,4'-trichloro-2'-hydroxydiphenylether) is a broad spectrum nonionic antimicrobial agent. This lipid soluble substance has been found to be effective against most types of oral cavity bacteria[54]. A combined zinc and triclosan mouthrinse system has been shown to have a cumulative effect, with the reduction of malodor increasing with the duration of the product use[39].

Two-Phase Rinses

Two-phase oil-water mouthrinses have been tested for their ability to control OM. A clinical trial reported significant long-term reductions in OM from the whole mouth and the tongue dorsum posterior [55]. The rinse is thought to reduce odor-producing microbes on the tongue because there is a polar attraction between the oil droplets and the bacterial cells. The two-phase rinse has been shown to significantly decrease the level of VSC's eight to ten hours after use, although not as effectively as a 0.2% chlorhexidine rinse[56]. Positive controls such as Chlorhexidine and Listerine® that had previously shown to reduce organoleptic scores were used in these clinical studies.

Hydrogen Peroxide

The potential of hydrogen peroxide to reduce levels of salivary thiol precursors of oral malodor has been investigated. Using analytical procedures, percent reduction in salivary thiols levels post treatment compared to baseline was found to be 59%[57].

Topical Antimicrobial Agents

Azulene ointment with a small dose of Clindamycin was used topically in eight patients with maxillary cancer to inhibit oral malodor that originates from a gauze tamponade applied to the postoperative maxillary bone defect. The malodor was markedly decreased or eliminated in all cases. Anaerobic bacteria such as *Porphyromonas* and *Peptostreptococcus* involved in generation of malodor also became undetectable[58].

Other Products

Breathnol is a proprietary mixture of edible flavors, which was evaluated in a clinical study, and this formulation reduced oral malodor for at least 3 hours[59]. Certain lozenges, chewing gums, and mints have been reported to reduce tongue dorsum malodor[60].

Alternative Remedies

Some of the natural controls for oral malodor include gum containing tea extract. Also recommended are natural deodorants such as copper chlorophyll and sodium chlorophyllin. Alternative dental health services suggest the use of chlorophyll oral rinses in addition to spirulina and algae products.

Conclusions

Many of the mouthrinses available today are being used for the prevention and or treatment of oral malodor. Much more research is required to develop an efficacious mouthrinse for the alleviation of oral malodor. The treatment of oral malodor is relatively a new field in dentistry and many of the treatments thus far have involved a trial and error approach, but the knowledge and experience gained so far will hopefully facilitate clinical investigations in this field and eventually lead to improved diagnostic techniques and treatment products.

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Table 9-1 **Seven Common Sources of Oral Malodor**
1. Mouth and tongue sources
2. Nasal, nasopharyngeal, sinus, and oropharyngeal sources
3. Xerostomia-induced oral malodor
4. Primary lower respiratory tract and lung sources

5. Systemic disease-induced malodor
6. Gastrointestinal diseases and disorders-induced malodor
7. Odiferous ingested foods, fluids, and medications

Table 9-2 Oral and Non-Oral Detection Methods
1. Self-monitoring oral malodor tests
2. Spousal and friend/confidante feedback
3. Spoon Test
4. Home microbial testing
5. Wrist-lick test
6. In-office oral malodor testing
7. Odor Judges
8. Microbial and fungal testing
9. Salivary incubation test
10. Artificial noses including the Halimeter®

Table 9-3 Management of Oral and Non-Oral Malodor
1. Local chemical/antibacterial methods
2. Systemic antibacterial methods
3. Mechanical debridement of the tongue
4. Salivary stimulation and/or substitutes
5. Nasal mucous control methods
6. Avoidance of foods, fluids and medications
7. Correction of anatomic abnormalities
8. Medical management of systemic diseases