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The Efficacy of Photodynamic Therapy in the Treatment of Halitosis: A Systematic Review

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ABSTRACT

Introduction: Halitosis is a condition of bad breath that can affect the quality of life of sufferers. The main cause of halitosis is the accumulation of bacteria on the dorsum of the tongue that produce volatile sulfur compounds (VSCs). Conventional methods such as the mouthwash and tongue scraping often do not provide long-lasting results and can trigger bacterial resistance.
Objective: This literature review provides information on the efficacy of photodynamic therapy in the treatment of halitosis patients.
Methods: A literature search was conducted in PubMed, Scopus, Cochrane and ScienceDirect databases with inclusion criteria according to the PICOS framework in the period 2020-2024.
Review: Photodynamic therapy (PDT) is an alternative treatment that uses a combination of photosensitizers and light to produce reactive oxygen species that damage bacterial cell membranes. PDT has been widely used in various medical fields, including in the treatment of cancer, infections, and is now being developed for the treatment of halitosis.
Discussion: This study revealed that PDT is able to reduce the concentration of microorganisms that cause halitosis on the dorsum of the tongue significantly compared to conventional methods. However, there are several limitations such as uneven penetration of photosensitizers and the possibility of bacterial recolonization in a short time after therapy.
Conclusion: PDT is an effective method to reduce bacteria that cause halitosis with a low risk of microbial resistance. However, limitations related to bacterial penetration and recolonization indicate that this therapy needs to be done repeatedly for more sustainable results.

KEYWORDS: halitosis, photodynamic therapy, volatile sulfur compound

ARTICLE DETAILS

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INTRODUCTION

Halitosis is a condition characterized by an unpleasant odor that comes from the mouth with various causes such as consumption of food with a strong odor, smoking, alcohol consumption, or poor dental and oral hygiene [1, 2, 3]. Halitosis is produced by anaerobic bacteria that make volatile sulfur compounds such as hydrogen sulfide, dimethyl sulfide, dimethyl disulfide, and methyl mercaptan [4, 5, 6]. Oral bacteria associated with halitosis are *Actinomyces spp., Eubacterium spp., Fusobacterium spp., Porphyromonas spp., and Prevotella spp* [5].

Halitosis often leads to nervousness, embarrassment, and difficulty socializing, such as the inability to approach people and talk to them [7, 8, 5]. Volatile sulfur compounds from halitosis can be toxic to human cells even at low concentrations [2]. Most of the bacteria that cause halitosis are responsible for periodontitis, but they can also affect the development of oral and gastrointestinal cancers [9, 5, 10].

Halitosis is a common condition that affects about 50-65% of the world's population [11]. Several studies show an increasing trend in the prevalence of halitosis worldwide [9]. The prevalence of halitosis in Indonesia reaches 57.6%.

Halitosis is not a disease, but a symptom or disorder that must be unconsciously found out [12]. Intraoral halitosis is caused by coated tongue (43%), gingivitis/periodontitis (11%) or a combination of both (18%) [13].

There are several methods both mechanically and chemically to reduce halitosis. The mechanical method can be in the form of tongue brushing or tongue scraping which is done on the dorsum of the tongue [14]. This mechanical method can reduce the thickness of the coating on the tongue and bad breath itself, but the mechanical method is not able to reach and eliminate the bacteria that produce VSC from the oral cavity [15]. In addition, the effects of tongue scraping are only temporary [16]. Tongue scraping also feels uncomfortable when done. Therefore, an alternative is needed to reduce halitosis that is effective and comfortable in patients.

One of the alternative therapies being studied today is photodynamic therapy. Photodynamic therapy is based on the activation of a photosensitizer by a specific wavelength of light followed by the formation of a reactive oxygen specimen that is lethal to bacteria [17]. Unlike conventional antimicrobial treatments, photodynamic therapy does not cause bacterial resistance [18]. In addition, photodynamic therapy can reduce volatile sulfur compounds in halitosis patients [19]. This literature review provides information about the efficacy of photodynamic therapy in the treatment of halitosis patients.

METHOD

Study Design

This study was compiled based on the guidelines of the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA). This study refers to the following review questions: (1) How does the efficacy of photodynamic therapy compare with *tongue scraper* in halitosis patients?.

Search Strategy

A literature search for this study was conducted on PubMed, Scopus, and Cochrane databases until 6 August 2024. The search using keywords is adjusted to Medical Subject Headings with the following boolean operator keywords ((photodynamic OR photochemotherapies) AND (therapy OR therapies) AND (halitosis OR bad breath OR foul breath)) In detail, the literature search strategy can be seen in **Table 1.**

Table 1. Searching Strategy

Database	Keyword	Retrieved	Date
Pubmed	(("photodynamic" OR "photochemotherapies") AND ("therapy" OR "therapies") AND ("halitosis" OR "bad breath" OR "foul breath"))	22	6 Agustus 2024
Scopus	(TITLE-ABS ("Photodynamic") OR TITLE-ABS ("Photochemotherapies")) AND (TITLE-ABS ("Therapy") OR TITLE-ABS ("Therapies")) AND (TITLE-ABS ("foul breath") OR TITLE-ABS ("halitosis") OR TITLE-ABS ("bad breath")) AND PUBYEAR > 2019 AND PUBYEAR < 2025	23	6 Agustus 2024
Cochrane	"photodynamic" OR "photochemotherapies" in Title Abstract Keyword AND "therapy" OR "therapies" in Title Abstract Keyword AND "halitosis" OR "bad breath" OR "foul breath" in Title Abstract Keyword	22	6 Agustus 2024
ScienceDirect	"photodynamic" OR "photochemotherapies" AND "therapy" OR "therapies" AND "halitosis" AND "clinical trial" AND NOT "review"	25	20 Agustus 2024

Eligibility criteria

The inclusion criteria in this study follow the PICOS (Population, Intervention, Comparison, Outcome, and Study) framework, as follows:

P: patients with halitosis
I: photodynamic therapy (PDT)
C: tongue scraper
O: Hydrogen Sulfide (ppb)

S: Randomized Controlled Trials

In addition, other inclusion criteria include: research published in English-language peer-reviewed journals, and research conducted in the 2020-2024 period. Meanwhile, the exclusion criteria include: full paper restrictions, and data access restrictions.

Data extraction

Data extraction from this study was carried out manually using an extraction table. The extraction items consist of (1) the author's name and year of publication; (2) population characteristics; (3) type of intervention; (4) control type; (5) assessment period; (6) Attractive results. The data extraction process was carried out by three independent reviewers to ensure the consistency and accuracy of the information extracted from each study. If there are differences between the auditors, it is resolved through deliberation and mutual agreement. In addition, the accuracy of the extracted data is also checked by other examiners to ensure the accuracy of the information extracted from each study included in this study.

Item Data

This study uses a quantitative descriptive analysis approach. The extracted articles will be interpreted and analyzed descriptively from the related quantitative results. In addition, all articles included in the study were assessed for risk of bias and the quality of their articles using *RoB 2*.

RESULTS

Study Selection

Based on the search results from three databases, 67 articles were obtained based on keywords. Out of a total of 67 articles, 34 articles were found to be duplicates using *Rayyan.ai tools*. After being filtered by title and abstract, 11 articles were obtained. Articles were searched for collection, and obtained as many as 10. The articles were excluded for several reasons, namely the study design was inappropriate, the intervention was inappropriate, and as many as 5 articles were obtained. In detail, the article search flow can be seen in **Figure 1.**

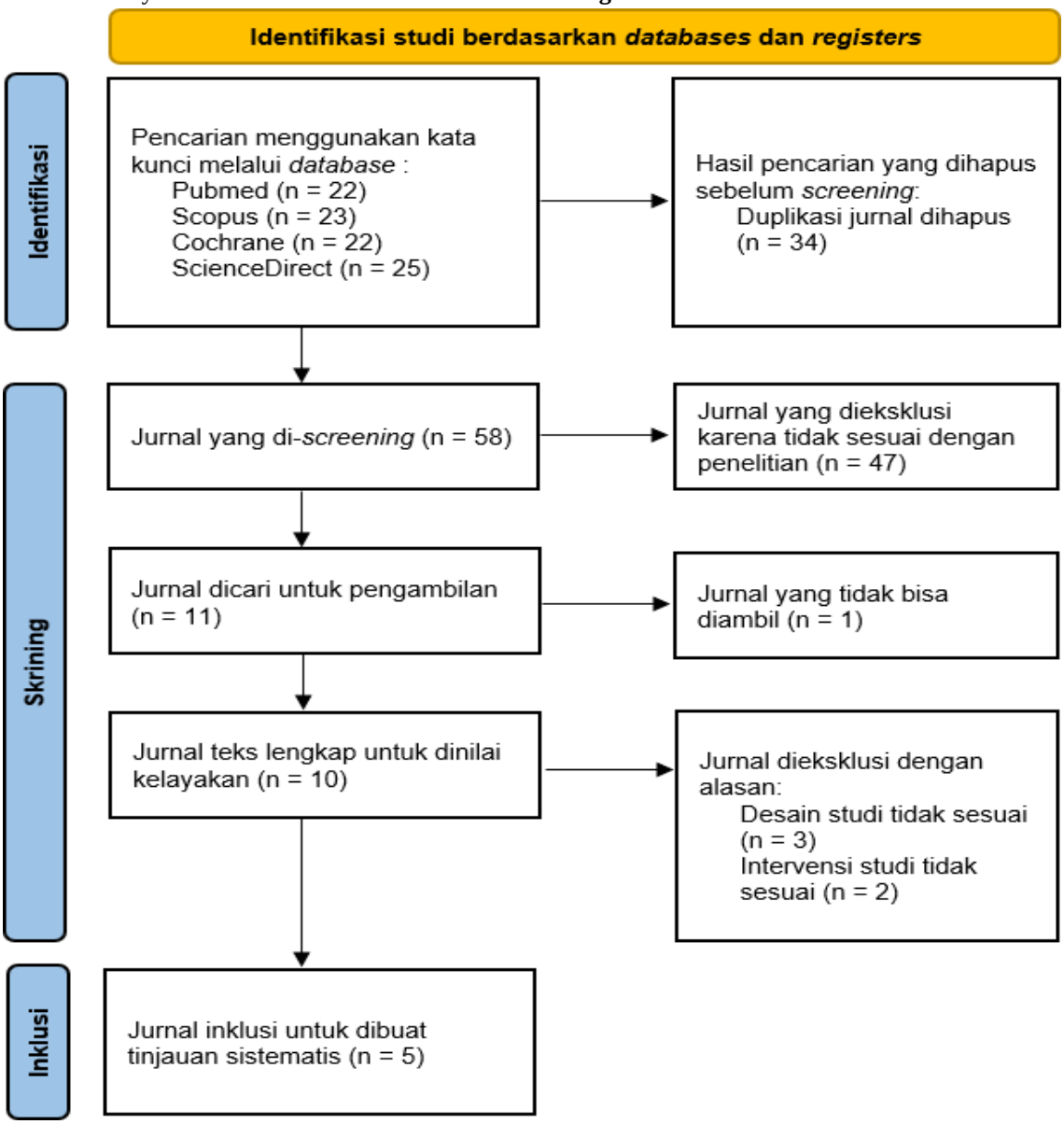

Figure 1. Prisma study flow diagram

Study Characteristics

Of the 5 studies involved, they are randomized controlled clinical trials. The character of the population is a participant Halitosis with h2S >112 ppb. A detailed study of its characteristics can be seen in **Table 2**.

Table 2. Data Extraction

Study, Year	Population Characteristics	Intervention	Control	Period of assessment	Results
Maruyama, et al., 2024	*n* = 22 Age > 20 yo H2S > 112 ppb	Photodynamic therapy (630 nm + 0.01% methylene blue)	No treatment	1 week	- Hydrogen sulfide
Vale, et al., 2021	*n* = 20 Age> 60 yo with complete dentures H2S > 112 ppb	Photodynamic therapy (methylene blue 0,005% + red diode laser)	Tongue scraper	1 week	- Hydrogen sulfide
Romero, et al., 2021	*n* = 40 Age >18 yo H2S > 112 ppb	Photodynamic therapy (660 nm + 0.005 % methylene blue)	Tongue scraper	Immediate, 1 week, 3 months	- Hydrogen sulfide
Alshahrani, et al., 2020	*n* = 45 Age 12-17 yo Fixed orthodontic treatment H2S > 112 ppb	Photodynamic therapy (660 nm + 0.005 % methylene blue)	Tongue scraper	2 week	- Hydrogen sulfide
Labban, et al., 2020	*n* = 40 Age> 60 yo with complete dentures H2S > 112 ppb	Photodynamic therapy (660 nm + 0.005 % methylene blue) + tongue scraper	Tongue Scraper + full mouth disinfection	Baseline, day 5, 15, and 30	- Hydrogen sulfide

Study findings

Research has found that the use of photodynamic therapy to treat halitosis. Photodynamic therapy uses *photosensitizing* agents, which are *non-toxic* dyes with light with a wavelength that matches the *photosensitivity used by the photosensitizer*. The interaction of these three elements forms *reactive oxygen species* (ROS) which results in the death of anaerobic bacterial cells so that hydrogen sulfide and the number of bacteria in the dorsum of the tongue are reduced.

Risk of bias

Results of bias risk assessment in research *randomized controlled trial* showing variation in the quality of research methodologies, **Figure 2.** Overall, most studies have a low risk of bias so the reliability of the articles is high.

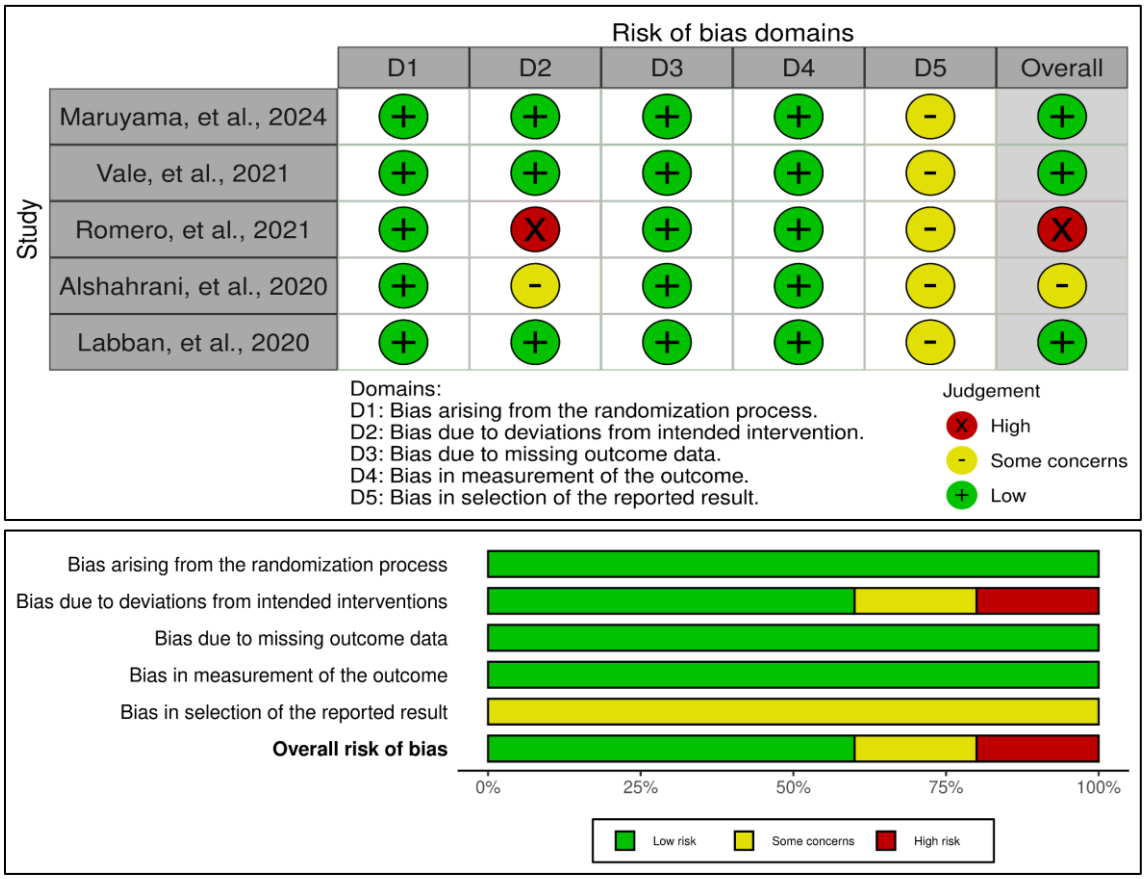

Figure 2. Risk of Bias

LITERATURE REVIEW

Photodynamic Therapy

Photodynamic therapy uses *photodesensitizing* agents, which are *non-toxic* dyes with light with wavelengths that match the *photosensitizer* used [20, 21]. The interaction of these three elements forms *reactive oxygen species* (ROS) which results in the death of cells [22, 23]. In the case of halitosis caused by anaerobic bacteria, hydrogen sulfide and the number of bacteria in the dorsum of the tongue are reduced due to red laser and methylene blue as photosensitizers from PDT [23]. The antimicrobial effect of PDT is only limited to the area affected *by the photosensitizer* and light so that it does not interfere with the surrounding tissues [24]. In addition, the possibility of bacterial resistance is small because singlet oxygen and free radicals formed interact with bacterial cell structures through different metabolic pathways [22].

Bacterial Halitosis

Halitosis is caused by the desquamation of epithelial cells, stagnant saliva, and the accumulation of bacteria [25]. *Fusobacterium nucleatum*, *Porphyromonas gingivalis*, *Treponema denticola*, *Solobacterium moorei*, *Prevotella intermedia*, *Tannerella forsythia*, *Peptostreptococcus*, and *nanobacteria* are closely related to oral hygiene. In addition, in vitro cultures have confirmed that *F. nucleatum*, *P. gingivalis*, and *T. denticola* all break down sulfur-containing amino acid substrates such as cysteine, methionine, tryptophan, arginine and lysine, which then release volatile sulfur compounds (VSCs) to produce bad breath [26]. The number of bacteria in the oral cavity that is a microflora can change due to factors such as dietary changes, reduced saliva rate, and increased acidity of the oral cavity. Changes in the composition of microflora further change the composition of dental microbes in the biofilm. These changes affect the occurrence of halitosis because some bacteria such as *Porphyromonas gingivalis* produce VSC which is the cause of halitosis [27].

Volatile sulfide compounds (VSC)

Volatile sulfide compounds (VSCs) are one of the biggest causes of halitosis. The chemical compounds that make up VSC are hydrogen sulfide, methyl mercaptan, and dimethyl sulfide [28]. VSC is a metabolite product of anaerobic Gram-negative bacteria in the oral cavity such as *Fusobacterium nucleatum* and *Porphyromonas gingivalis* [27, 28].

DISCUSSION

Effectiveness of Photodynamic Therapy in Overcoming Halitosis

Photodynamic Therapy (PDT) has been explored as a method to overcome halitosis through the reduction of bacteria in the dorsum of the tongue, which is one of the main sources of bad breath. PDT is able to significantly destroy microbial biofilms, especially anaerobic bacteria that play a major role in the occurrence of halitosis [29]. PDT with photosensitizer agents activated by light at certain

wavelengths produces reactive oxygen species that damage bacterial cell membranes, making it effective in lowering the concentration of microorganisms that cause halitosis [30].

However, there was no statistically significant difference between the intervention and control groups after one week, suggesting that PDT may not be effective enough for halitosis reduction in the long term [31]. PDT has limitations related to the penetration of photosensitizers into biofilms on the rough surface of the tongue, which can reduce the effectiveness of therapy. The effectiveness of PDT may be limited by factors such as exposure time and the intensity of the light used in therapy, which affect overall clinical outcomes [32].

Advantages of Photodynamic Therapy Compared to Conventional Methods

Compared to conventional methods such as the use of antiseptic mouthwashes or mechanical cleaning of the tongue, PDT offers several unique advantages. PDT has the ability to target specific bacteria without disrupting the oral microbiota as a whole, thereby reducing the risk of dysbiosis often associated with potent antiseptics [32]. In addition, PDT is non-invasive and provides faster results in reducing the concentration of halitosis-causing bacteria without causing significant side effects to patients [30].

One of the main advantages of PDT over conventional methods is its ability to target biofilms with higher precision without causing bacterial resistance [29]. Unlike antibiotics or antiseptic mouthwashes, PDT does not trigger microbial resistance and is safer to use repeatedly [29, 31]. In addition, PDT is more effective in penetrating bacterial biofilms compared to conventional methods, mainly due to the ability of light-activated photosensitizers to reach deeper bacteria on the biofilm, unlike *tongue scraping* which only temporarily clears the bacterial layer on the dorsum of the tongue. These bacteria can quickly redevelop and produce VSCs after the tongue has been cleaned [29].

Limitations of Photodynamic Therapy in Overcoming Halitosis

The limitation of PDT in overcoming halitosis is the possibility of bacteria recolonizing the dorsum area of the tongue that is not exposed to the laser from PDT. The oral microbiota also increased again as before the PDT after 1 week of treatment. Continuous implementation of PDT may be effective in fighting halitosis [31]. This is a limitation of PDT in overcoming halitosis because just like other conventional methods, PDT must be done repeatedly to get long-lasting results.

CONCLUSION

Based on the studies that have been conducted, Photodynamic Therapy (PDT) has been proven to be effective in reducing the number of halitosis-causing bacteria found in the dorsum of the tongue, but the long-term effectiveness of PDT is still debated because the results showed that there was no significant difference between the group that received PDT and the control group after one week of therapy. PDT works through the production mechanism of reactive oxygen species that can damage the cell membranes of bacteria that cause halitosis. One of the main advantages of PDT is its ability to target bacteria without triggering microbial resistance, which is often a problem with the use of other methods.

However, PDT also has some limitations. One of them is the penetration of a photosensitizer into the biofilm on the rough surface of the tongue, which can reduce the effectiveness of therapy. In addition, bacteria can undergo recolonization in areas not exposed to laser exposure from PDT, so the oral microbiota tends to return to its original state within one week. Therefore, to maintain optimal results, treatment with PDT needs to be carried out repeatedly.

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