

On recommended mouthwashes during COVID-19 pandemic: A review

Seyyed Amirhossein Mirhashemi, Rashin Bahrami *

Department of Orthodontics, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran.

ARTICLE INFO	ABSTRACT
Article Type: Review Article Received: 8 Feb. 2021 Revised: 5 Apr. 2020	Aim and Objective: One of the challenges we are currently facing is the COVID-19 pandem- ic. With its rapid spread around the world, it has become an unprecedented major health, human and financial crisis. The saliva of COVID-19 patients contains the virus that can be transmitted Various studies have shown the effect of mouthwashes in reducing the rate of transmission of the virus and, consequently, reducing the likelihood of infection. Therefore, we considered it important to examine the effect of using different mouthwashes by studying the existing data and articles.
Accepted: 19 May. 2021 *Corresponding author: Rashin Bahrami	Materials and Methods: The study was conducted by the review method. The keywords "coronavirus, SARS-CoV-2, COVID-19, mouthwash, hydrogen Peroxide, chlorhexidine, povidone-iodine, cetylpyridinium chloride" were searched in articles and protocols in the following databases: PubMed, Scopus, Embase, Dimensions. The searched articles were submitted from January 2019 to April 2021. Only the articles in English were studied.
Department of Orthodontics, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran.	Results: Among 23 reviewed studies, there were 15 review study, 4 in vitro study, two clinical trial, one letter to the editor in chief, and two studies that are, in fact, instructions of Australian and American dental community. 4 studies were published in 2021, 18 articles in 2020, and 1 article in 2019. By investigating 16 reports, Povidone-Iodine mouth wash was the most effective mouthwash ever mentioned. Hydrogen peroxide mouth rinse with nine mentions, chlorohexidine with seven mentions, cetylpyridinium chloride with four mentions, Essential oils with three mentions, and mouth rinses contains Citrox and beta-cyclodextrin, and Methylene blue with one mention was ranked next. Generally, most of the studies have recommended mouth rinses use in patients in dental clinics (or other recipients of health care services). They have emphasized their effectiveness in reducing the viral load in saliva and oral secretions.
	Conclusion: The results of the review showed that povidone-iodine mouthwash and hydrogen peroxide mouthwash can be the first and the second candidates to reduce viral load and, consequently, reduce disease transmission. However, more clinical studies are needed to confirm the results.
<i>Tel:</i> +98-21-84902473 <i>Fax:</i> +98-21-84902473 <i>Email:</i> bahramirashin@Yahoo.com	Keywords: Covid-19; Coronavirus; 2019-nCoV; Mouthwash; Mouth rinse; Hydrogen peroxide Chlorhexidine; Povidone-iodine; Cetylpyridinium chloride.

Introduction

Since early 2020, coronavirus has caused a rapid propagation of acute respiratory syndrome worldwide and is now an extreme well-being, human, health, and economic crisis [1]. The novel coronavirus belongs to a group of RNA viruses that are able to penetrate host cells through interactions between the protein coating and the angiotensin-converting enzyme (ACE) receptors [2-4]. ACE2 receptors are present in numerous body areas, such as mucosal tissue, gingiva, non-keratinized squamous epithelium, tongue epithelial cells, and salivary glands [4-7].

Copyright © 2021 Tehran University of Medical Sciences.

This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International license (https://creativecommons.org/licenses/by-nc/4.0/). Non-commercial uses of the work are permitted, provided the original work is properly cited.

A fact about Coronavirus is that the disease severity depends on the virus's infiltration into the cells. A protease named Furin has an essential role in this matter. This protease exists in different parts of the body, including the mouth and lung [8]. Furin is the name of a protein that is coded in humans by (FURIN) gene. This protein is also known by the name of (PACE). Some proteins are inactive at the production time, and for becoming the active form, some of their structural parts should be removed [9]. Furin protein cuts and removes these additional parts. And it converts them to their functional format. Some of the crucial proteins that the Furin transforms them from their initial inactive precursor form to the active state are Parathyroid hormone, Albumin, Nerve growth factor, and von Willebrand factor [10]. Some pathogens use this property of Furin for their activation in the cell. For example, Furin should trim protein envelopes of viruses such as HIV, Influenza, Dengue fever, and Filoviruses such as Ebola virus disease and Marburg virus to transform them into the active form [11]. Also, Furin should process the protein toxin of Anthrax and exotoxin of the Pseudomonas and papillomaviruses before their entrance to the host cells. Coronavirus is one of the viruses that Furin converts it to its active form, and then it enters the host cell [12]. Thus, oral secretions are one of the infected sources of the virus, and it is one of the significant ways of transmitting the disease. In fact, coughing, sneezing, and talking (at less than 1-meter distance) can quickly transfer the Covid-19 because of its existence in saliva and respiratory particles of carriers and patients. And it may infect other persons [13,14].

Upper respiratory tract infection (RTI), fever, dry cough, asthma, severe viral pneumonia with respiratory failure, and even death may develop in patients with COVID-19 disease. However, a percentage of the population has only minor symptoms, including digestive problems, nasal congestion and lowered sense of smell, or are asymptomatic [15,16]. Nevertheless, the saliva and periodontal pockets of infected individuals produce elevated virus levels, and aerosol production-related dental therapy may also be an origin of viral transmission and infection distribution [17,18]. These aerosols include 5-10 microns of microbes and can remain in the air for up to 20 minutes, increasing the likelihood of inhalation and potential infection [19].

Using masks and avoiding attendance to the communities, and observing the interpersonal distances are highly emphasized because the oral secretions and respiratory system can quickly transfer the virus. For some health care providers, watching the interpersonal space is not possible because they should be at a close distance to the patients for providing the services [20]. Dentists are among those health care providers who are unprotected and close to the patients and potentially, the possibility of contact with infected secretions and saliva is high [8]. In these conditions, the solutions that reduce the viral load in saliva and the oral cavity are beneficial [20,21]. One of these solutions is using mouth rinses. Some of the available evidence demonstrates that using mouthwashes before receiving dental services can reduce the mouth's viral load. Therefore, it provides safer conditions for dentists against infection of the Covid-19 [22-25].

Thus, this situation should lead to the development of practical dental guidelines during this period. These guidelines involve mouthwashing before the start of dental therapy. However, no scientific trial has so far demonstrated the possibility of preventing SARS-CoV-2 propagation by using mouthwashes [26]. Nevertheless, it is recommended to use mouthwash previous to dental procedures by the American Dental Association (ADA) and the Center for Disease Control and Prevention (CDC) [27,28]. In this research, we evaluated the effect of mouthwash suggested during this time interval, owing to the unavailability of a thorough and accessible protocol and the concentration and time differences proposed for mouthwash usage.

Materials and Methods

1. Study design

The analysis method and inclusion criteria were determined before, which were based on a PRISMA-based guideline [29].

2. Eligibility criteria

Is mouth rinsing with mouthwash useful for decreasing covid-19 transmission during pandemic?

The search strategy was done due to PICO.

Population: all articles that evaluate this subject

Intervention: mouthwash (such as hydrogen Peroxide, chlorhexidine, povidone-iodine, cetylpyridinium chlo-ride)

Comparison: comparison between different mouthwashes-control group without receive mouthwash.

Outcome: antimicrobial effect (viral infection or % of virus inactivation).

Study design (clinical trials, in vitro or review studies).

3. Inclusion and exclusion criteria

The criteria for inclusion were as follows:

1- Papers assessing mouthwash antibacterial effect.

2- Papers assessing the mouthwash effect on the coronavirus.

3- Papers that include mouthwash procedures before dental therapy.

4- Publications for the time of review.

- 5- English papers.
- 6- Major Publications forms for full-text papers.

4. Search strategy

This research is an analysis of evidence in electronic libraries. Using the keywords "coronavirus, covid 2019, SARS2, SARS-CoV-2, severe acute respiratory syndrome coronavirus 2, coronavirus infection, covid-19, 2019 novel coronavirus disease, SARS-CoV-2 infection, COVID-19 virus disease, 2019 novel coronavirus infection, 2019-nCoV infection, coronavirus disease 2019, coronavirus disease-19, 2019-nCoV, SARS-CoV-2, novel cov,sars cov2, mouthwash, mouth rinse, hydrogen Peroxide, chlorhexidine, povidone-iodine, cetylpyridinium chloride" a review of articles and protocols in the following databases was performed: PubMed, Scopus, Embase, Dimensions. The search time scope for the paper was from January 2019 to April 2021. Only the articles in English were studied. Search: Searches were tailored to the specific databases. An example of a search on PubMed is: ((("SARS-CoV-2") OR ("COVID-19") OR ("2019-nCoV") OR ("coronavirus")) AND (("mouthwash") OR ("mouth rinse") OR ("hydrogen Peroxide") OR ("chlorhexidine") OR ("povidone-iodine") OR ("cetylpyridinium chloride"))).

5. Selecting the articles

For evaluation of selected articles, titles (independently), abstract and full text of articles was read by two individuals. In case of disagreement between individuals about inclusion or exclusion of article from study, the third individual read the article. Overall, 68 article was found which evaluate the effect of different mouthwash on virus load. Eventually, 23 full-text articles which met the inclusion criteria were selected for rest of research. Original and review articles were used to identify the additional studied clinical trials. Moreover, to prevent several publications of data, only the original articles were studied. Presentation methods of data in this study, including identification of research problem, data collection, and analysis and interpretation of data, were conducted according to the checklist for systematic reviews, i.e., PRISMA. The details of inclusion criteria are shown in Figure1.

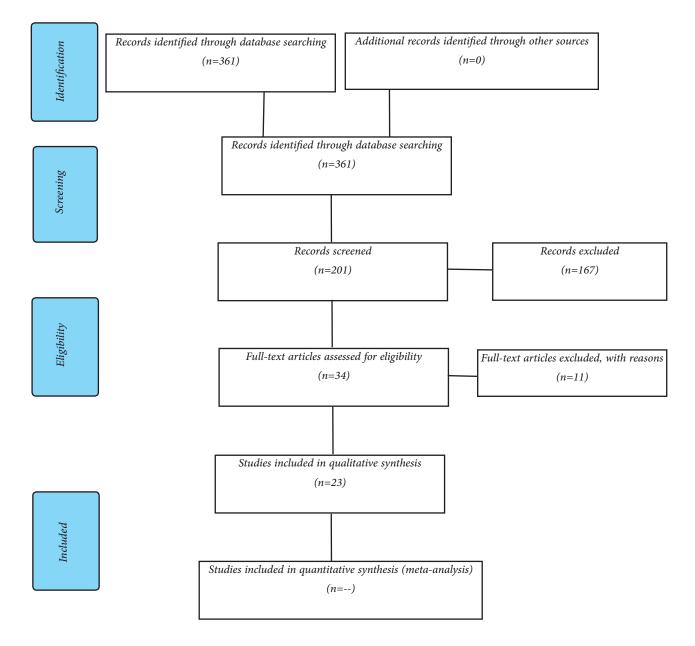


Figure 1. PRISMA flow-chart of selected criteria for the included article reports.

6. Different types of search

We tried to independently use information sources, all the relevant studies with inclusion criteria. Non-randomized clinical trial (NRCT) and controlled studies (pre and post-treatment data) were used. Moreover, randomized clinical trials (CRTs) were considered as potential studies. However, only the treatment group were considered. Review articles, laboratories (invitro study), and protocols provided by health organizations in different countries were also allowed to enter the study.

7. Participants

All articles and protocols presented to evaluate the effect of mouthwashes on reducing coronavirus transmission, including review, clinical and laboratory stud-

ies.

8. Extraction and management of data

The studies that fulfilled the inclusion criteria were collected in an electronic database (Excel). The following data were extracted by each browser in its relevant database: Author, year of publication, title, research design, results, and conclusion, and the full text (Yes or No), and including (Yes or No). Then the qualitative quality of the recovered articles was discussed by the authors to reach an agreement. The results data were extracted by two judges to validate and control data.

9. Duplicate data

The data published several times, was considered a duplicate. In the case of any doubts or ambiguity, the

original article was always considered the final solution. This reduces any overestimation of the effect of the intervention since there are no duplicate data exceptions.

10. Investigating the missing or defective data

The strategies for missing/defective data in the present study are as follows:

1. Contact the author if possible.

2. Analyze only the current data (overlooking the missing data).

3. Finally, we discussed the possible effects of the missing data on the understudy findings in the discussion.

11. Intervention

Application of different mouthwashes including hydrogen peroxide, chlorhexidine, povidone-iodine, cetylpyridinium chloride.

12. Summary measures

Any outcome measure was considered, provided that the outcome of interest was assessed.

Table 1. Summary of articles from 2019 to 2021.

Results

Among 23 reviewed studies, there were 15 review study, 4 in vitro study, two clinical trial, one letter to the editor in chief, and two studies that are, in fact, instructions of Australian and American dental community. 4 studies were published in 2021, 18 articles in 2020, and 1 article in 2019. By investigating 16 reports, Povidone-Iodine mouth wash was the most effective mouthwash ever mentioned. Hydrogen peroxide mouth rinse with nine mentions, chlorohexidine with seven mentions, cetylpyridinium chloride with four mentions, Essential oils with three mentions, and mouth rinses contains Citrox and beta-cyclodextrin, and Methylene blue with one mention was ranked next. Generally, most of the studies have recommended mouth rinses use in patients in dental clinics (or other recipients of health care services). They have emphasized their effectiveness in reducing the viral load in saliva and oral secretions. Table 1 summarizes these articles.

Year of publication	Author	Country	Type of study	Title/ Topic	Suggestion
2019	Grover [44]	India	Review	Managing airborne isolation and precautions in orthodontic practice during the outbreak of coronavirus disease 2019: An orthodontist perspective	Rinsing the mouth with chlorhexidine 0.2-0.12% before each procedure can help minimize the number of microbes in the oral cavity.
2020	Caruso [31]	Italy	Review	Hydrogen peroxide and viral infections: A litera- ture review with research hypothesis definition in relation to the current covid-19 pandemic	Two puffs of 1.5% hydrogen peroxide nasal spray (about 0.28 ml) in each nostril two times a day accompanied by mouthwash and gargling hydrogen peroxide solution for one minute twice a day
2020	Bidra [32]	America	In-Vitro	Rapid In-Vitro Inacti- vation of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Using Povidone-Iodine Oral Antiseptic Rinse	Treatment with 0.5% Povi- done-Iodine for 15 seconds.

2020	Turkistani [13]	Saudi Arabia	Review	Precautions and recom- mendations for orthodontic settings during the COVID-19 outbreak: A review	Rinse the mouth with 0.2% or 0.12% chlorhexidine mouthwash to reduce the number of microbes in oral cavities.
2020	Zi-yu GE [19]	China	Review	Possible aerosol trans- mission of COVID-19 and special precautions in dentistry	Despite the effect of mouth- washes on Corona being unknown, the use of 0.12% chlorhexidine and 0.05% cetylpyridinium chloride ha been suggested considering the impact of cetylpyridin- ium chloride and chlor- hexidine on reducing the microbial load and aerosol.
2020	Basam [20]	India	Review	Institutional approach for the management of patients in orthodontic office during COVID 19 pandemic	1% Povidone-Iodine and 0.05-0.10% cetylpyridiniun chloride were recommended to the patients to reduce th microbes in aerosols in- duced by dental treatments
2020	Herrera [35]	Germany	Review	Is the oral cavity relevant in SARS-CoV-2 pandem- ic?	Mouthwashes contain- ing Povidone-Iodine and cetylpyridinium chloride (19 solution for 15 seconds per in vitro studies, and 7.5% solution diluted with water to a ration of 1:30 for 15 seconds according to other it vitro studies) and chlorhex idine can reduce the chance of transmission by reducing the number of viruses in ora cavities.
2020	Kim [36]	South Korea	In-vitro	Post-COVID-19 Clinical and Management Guide- lines for Orthodontic Practices	Application of 0.2% Povi- done-Iodine or 1.5% hydro gen peroxide for 15 second before the procedure.
2020	Bayley [37]	London	Review	The use of Povidone Iodine nasal spray and mouthwash during the current COVID-19 pandemic may reduce cross infection and pro- tect healthcare workers	Treatment with 0.5% Povi done-Iodine for all patients and healthcare workers.

2020	Muhamed Khan [38]	India	Review	Repurposing 0.5% povidone iodine solution in otorhinolaryngology practice in Covid 19 pandemic	Using 0.5% Povidone-Iodine for patients and healthcare workers minimizes the risk of infection.
2020	Guo [39]	China	Review	Control of SARS-CoV-2 transmission in ortho- dontic practice	 1.Chlorhexidine ineffec- tivenes 2. Using mouthwashes con- taining oxidative properties with 1% hydrogen peroxide concentration and 0.5% Povidone-Iodine for 2-3 minutes due to the vulner- ability of SARS-CoV-2 to oxidation.
2020	Bidra [40]	America	In-vitro	Comparison of In Vitro Inactivation of SARS CoV-2 with Hydrogen Peroxide and Povi- done-Iodine Oral Anti- septic Rinses	Preference of 0.5% Po- vidone-Iodine to 1.5% or 3% hydrogen peroxide (respective studies indi- cated that 1.5% or 3% hydrogen peroxide has the most insignificant impact), recommendation to use 0.5% Povidone-Iodine for 15 min- utes before the procedure.
2020	Carrouel [41]	France	In-vitro	COVID-19: A Recom- mendation to Examine the Effect of Mouthrinses with β -Cyclodextrin Combined with Citrox in Preventing Infection and Progression	Respective studies revealed that mouthwashes contain- ing beta-cyclodextrin and Citrox can eliminate the
2020	Jamal [42]	Emirates	Review	Overview of transnation- al recommendations for COVID-19 transmission control in dental care settings	1% Hydrogen peroxide, 0.2% chlorhexidine, 0.2% Povidone-Iodine, and 2% Listerine.
2020	Buenaventura [43]	Peru	Review	Use of mouthwashes against COVID-19 in dentistry	Gently gargle ml of 1.5% or 3% hydrogen peroxide mouthwash, 9ml 0.2%, 0.4%, or 0.5% Povidone-Iodine mouthwash, 15ml 0.12% chlorhexidine mouthwash, or 15ml Cetylpyridinium chlo- ride mouthwash 30 seconds in the mouth and 30 seconds at the back of the throat.

2020	Peng [44]	China	Review	Transmission routes of 2019-nCoV and controls in dental practice.	Treatment with mouth- washes containing oxida- tive agents such as 1-1.5% hydrogen peroxide or 2% Povidone-Iodine.
2020	Gurzawska- [45] Comis	America	Review	Recommendations for Dental Care during COVID-19 Pandemic	Rinsing the mouth with disinfectants such as 0.2% chlorhexidine and alco- hol-containing Listerine can be effective against the virus, while 0.1% or 0.2% non-al- coholic chlorhexidine are deemed ineffective against the virus.
2020	Australian Dental Association [46]	Australia		ADA COVID-19 Risk Management Guidance	All patients must use 1% hydrogen peroxide mouth- wash, 0.2% chlorhexidine mouthwash, 0.2% Povi- done-Iodine mouthwash, or essential oil mouthwashes before treatment.
2020	American Dental Association [27]	America		Coronavirus Frequently Asked Questions	Application of 1.5% hydro- gen peroxide before each appointment. The Corona- virus is vulnerable against oxidation; this will reduce the salivary oral microbe loading.
2021	Choudhury [47]	Bangladesh	Randomized clinical trial	Effect of 1% Povidone Iodine Mouthwash/Gar- gle, Nasal and Eye Drop in COVID-19 patient	The use of Povidone Iodine 1% as a mouthwash or nasal and ophthalmic drops, decrease the mortality rate of Covid-19.
2021	Oliveira [48]	Brazil	Review	COVID-19 - Mouthwash in dental clinical prac- tice: review	The efficacy of cetylpyridin- ium chloride and Povi- done-Iodine 1% mouthwash were better than other solutions. However, further in vivo analysis needed for better Interpretation of mouthwash efficacy.

2021	Guenezan [49]	France	Randomized clinical trial	PovidoneIodineMouth- wash, Gargle, andNasal Spray to ReduceNaso- pharyngeal Viral Load in Patients With COVID- 19:A Randomized Clinical Trial	In the case of Povi- done-Iodine mouthwash, the Covid-19 virus load decreased. However, it has caused thyroid problems in a number of patients. Further studies needed for optimal concentration of Povidone Iodine to maintain its antiseptic properties and minimize its side effects.
2021	Cavalcante-Leão [50]	Brazil	Systematic review	Is there scientific evidence of the mouth- washes effectiveness in reducing viral load in Covid-19? A systematic review	The 1% and 7% of Povi- done-Iodine mouthwash was a positive effect of Covid-19 virus load in human saliva. In the present study we emphasize that, although the use of hydrogen peroxide mouthwash is recommended in dental guidelines, there is no credible evidence for it.
2021	Arakeri [51]	India	Letter to editor	Methylene blue as an anti-COVID-19 mouth- wash in dental practice	Saliva is a potential source of Covid-19 virus infection. Methylene blue 0.5% mouth- wash is a safe, strong and cost-effective mouthwash that can be a good alterna- tive to other mouthwashes to reduce the Covid-19 virus load in saliva. It is recom- mended that mouthwash be used 10 minutes before receiving dental services and repeated every 5 to 10 min- utes to eliminate new viruses that have just emerged in the saliva.

Discussion

1. Chlorhexidine

Using chlorhexidine mouthwash before dental procedures reduces the number of microorganisms in the aerosols produced during the dental procedures [52,53]. Chlorhexidine could cause bacterial lysis (including gram-negative and gram-positive, aerobic, and anaerobic bacteria) and the fungi by increasing their cell wall permeability [54-59]. The antiviral effect of various chlorhexidine concentrations on viruses with lipid capsid such as the influenzas virus is well-established [60,61]. However, there is controversy in the case of the coronavirus despite its lipid capsid. Using mouthwashes is accessible, but the ADA does not recommend it for reducing the chance of transmitting the COVID-19 as the chlorhexidine has had minimal effect on the SARS-CoV-2 compared with other viruses [36,39]. However, some studies have shown the efficacy of 0.12-0.2% chlorhexidine in 47 C for 30 minutes before the orthodontic procedures [2,13,33]. A clinical study by Yoon et al. showed that the viral load of saliva temporarily decreased for two hours after using chlorhexidine mouthwash and increased again afterwards [2]. The side effects of chlorhexidine include the discoloration of the teeth, formation of gum calcification, and changes in the sense of taste [62]. However, the short-term use of chlorhexidine mouthwash has not been associated with these side effects, although longterm use (more than two weeks) can be.

2. Hydrogen peroxide

The virus is sensitive to the activities of the free oxygen resulting from the peroxide hydrogen, which will lead to the deactivation of the virus functions in vitro and in vivo. However, it has shown no effects on the viruses in the respiratory system [36]. The side effects, such as the irritation of the mouth soft tissue, are rare in low hydrogen peroxide concentrations (e.g. 1% and 1.5%) [63]. ADA27 has recommended a concentration of 1.5% as effective, while some studies have recommended 3%31. In this regard, Bidra et al. studied the 1.5% and 3% concentrations for two periods of 15 and 30 seconds; 40 they concluded that both concentrations are inadequate even after 30 seconds, and further study is required. In fact, the CDC does not recommend the mouthwash due to the lack of scientific evidence.28 although the antimicrobial effects of hydrogen peroxide 1.5% are well-known, it is chemically unstable. No studies have shown that the SARS-VoV-2 virus is deactivated by increasing the consumption time for up to one minute [64].

3. Povidone-iodine

The antimicrobial effects of povidone-iodine mouthwash initiate with the separation of the free iodine from polyvinyl pyrrolidone; this iodine rapidly penetrates the microbes to destroy the proteins and oxidate the nucleic acid structures which, therefore, lead to the death of the microbe [37,65]. The concern on the use of povidone-iodine is on the mucosal absorption of the iodine. The studies have shown that intraoral use of the substance up to a 5% concentration has no side effects on the mucus and a 6% concentration would lead to a minimal raise in the levels of thyroid hormones, which would not cause any health issue [37,66]. Guenezan and colleagues in their clinical study showed that, povidone-iodine mouthwash decreases the Covid-19 virus load. Although, in the number of patients thyroid problems was reported [49]. Therefore, there are no concerns about using the mouthwash with the mentioned concentration and it will not lead to any changes in the taste or discoloration of the teeth [67]. In two studies by Bidra et al., it was shown that there was no significant difference in two periods of 15 and 30 seconds in the concentrations of 0.5, 1, and 1.5% percentages and no toxicity was observed in any of the percentages [32,40]. Moreover, it was shown that povidone-iodine had a stronger antimicrobial effect compared with hydrogen peroxide. It is recommended to be used in its minimum concentration (0.5%) and in the shortest time (15 seconds) for the ease of use and reducing the chance of swallowing [32,40,68,69].

4. Cetylpyridinium chloride

Cetylpyridinium chloride mouthwash, which is usually used to reduce plaques and inflammation of the gums in dentistry and reduce the influenza virus in medicine, destroys viruse's lipid capsid through a lysosomotropic mechanism and is therefore recommended to destroy the virus with capsid of the coronavirus [35,70-72]. Baker et al. suggested 15ml of 0.05% cetylpyridinium chloride mouthwash which requires further clinical studies [73]. Dental discoloration is one of the side effects which could be prevented by a short-term use of this mouthwash [74].

5. Mouthwashes containing Citrox and beta-cyclodextrin

Recently, French scientists have claimed that mouthwashes containing Citrox and beta-cyclodextrin could destroy the coronavirus. In their laboratory study, they showed that the molecule could absorb the virus and destroy its walls. The perio plus is an example of these mouthwashes which could be the best choice in dental procedures due to its accessibility and cost-efficiency. However, no study has been conducted in this regard and further research is needed [41].

6. Essential oil mouthwashes

The essential oil mouthwashes have antiviral properties by damaging the viruses> membranes with envelopes such as influenza and herpes [41,75-76]. One of such mouthwashes is Listerine, which has been shown to decrease the viral load in the mouth in at least 30 minutes after use [77]. However, its antiviral effects are lower compared with chlorhexidine [78]. The Australian Dental Association 46 claimed that the mouthwash could be used against the coronavirus due to having an envelope. Gurzawska-Comis et al. mentioned the possible effects of the mouthwash on the coronavirus in their review study [45]. Due to the lack of in-vitro and in-vivo studies, a definite opinion on the mouthwash is not yet possible.

7. Other

Arakeri et al. reported that, 0.5% methylene blue mouthwash is a safe, strong and cost-effective mouthwash that can be a good alternative to other mouthwashes to reduce the Covid-19 virus load in saliva. It is recommended that mouthwash be used 10 minutes before receiving dental services and repeated every 5 to 10 minutes to eliminate new viruses that have just emerged in the saliva [51].

Conclusion

According to the results, our recommendations on the use of mouthwash in the coronavirus pandemic are as follows: 9ml povidone-iodine mouthwash 0.5%, 15 seconds, 15ml of 1.5-3% hydrogen peroxide, 15-30 seconds and 15ml of chlorhexidine mouthwash with a concentration of 0.2-0.12% at a temperature of 47 °C for 30 seconds. Further studies are needed regarding other mouthwashes. It is not possible to comment definitively on these mouthwashes until clinical studies are conducted in this field.

Conflict of Interest

There is no conflict of interest to declare.

References

- Suri S, Vandersluis YR, Kochhar AS, Bhasin R, Abdallah MN. Clinical orthodontic management during the COVID-19 pandemic. Angle Orthod. 2020 Apr 27. DOI:10.2319/033120-236.1.
- [2] Yoon JG, Yoon J, Song JY, Yoon SY, Lim CS, Seong H, Noh JY, Cheong HJ, Kim WJ. Clinical Significance of a High SARS-CoV-2 Viral Load in the Saliva. J Korean Med Sci. 2020 May 25; 35(20).
- [3] Li F. Structure, function, and evolution of coronavirus spike proteins. Annu Rev Virol 2016; 3:237–61. DOI:10.1146/annurev-virology-110615-042301.
- [4] Chen Y, Guo Y, Pan Y, et al. Structure analysis of the receptor binding of 2019-nCoV. Biochem Biophys Res Commun 2020; 525 (February):135–40. DOI:10.1016/j.bbrc.2020.02.071.
- [5] Xu H, Zhong L, Deng J, et al. High expression of ACE2 receptor of 2019- nCoV on the epithelial cells of oral mucosa. Int J Oral Sci 2020; 12:8. DOI:10.1038/s41368-020-0074-x.
- [6] Wan Y, Shang J, Graham R, et al. Receptor recognition by the novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS coronavirus. J Virol 2020; 94:e00127–220. DOI:10.1128/JVI.00127-20.

- [7] Hamming I, Timens W, Bulthuis ML, et al. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol 2004; 203:631–7. DOI:10.1002/path.1570.
- [8] IMRAN, Eisha, et al. Dental Practitioners' Knowledge, Attitude and Practices for Mouthwash Use 10- Thomas G (Oct 2002). «Furin at the cutting edge: from protein traffic to embryogenesis and disease». Nat. Rev. Mol. Cell Biol. 3 (10): 753–66. doi:10.1038/nrm934.
- [9] Amidst the COVID-19 Pandemic. Risk Management and Healthcare Policy, 2021, 14: 605.
- [10] Shiryaev SA, Remacle AG, Ratnikov BI, Nelson NA, Savinov AY, Wei G, Bottini M, Rega MF, Parent A, Desjardins R, Fugere M, Day R, Sabet M, Pellecchia M, Liddington RC, Smith JW, Mustelin T, Guiney DG, Lebl M, Strongin AY (Jul 2007). «Targeting host cell furin proprotein convertases as a therapeutic strategy against bacterial toxins and viral pathogens». J. Biol. Chem. 282 (29): 20847–53. doi:10.1074/jbc. M703847200. PMID 17537721. DOI:10.1074/jbc.M703847200.
- [11] Rocca JAr What is the most effective mouthwash in patients infected with covid-19 to minimize possible transmission by saliva? Update. J Dent Maxillofacial Res. 2020; 3(1):1-5.
- [12]Mallapaty S. Why does the coronavirus spread so easily between people? Nature. 2020 Mar; 579(7798):183. Doi: 10.1038/d41586-020-00660-x.
 PMID: 32157230. DOI: 10.1038/d41586-020-00660-x.
- [13] Jin YH, Cai L, Cheng ZS, Cheng H, Deng T, Fan YP, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Mil Med Res. 2020; 7:4. DOI: 10.1186/s40779-020-0233-6.
- [14]Vinayachandran D, Saravanakarthikeyan B. Salivary diagnostics in COVID-19: Future research implications. J Dent Sci. 2020; 15:364-366. doi: 10.1016/j.jds.2020.04.006.
- [15] Guan, W.J.; Zhong, N.S. Clinical Characteristics of Covid-19 in China. Reply. N. Engl. J. Med. 2020,

382,1861–1862. DOI: 10.1056/NEJMc2005203.

- [16]Lovato, A.; de Filippis, C. Clinical Presentation of COVID-19: A Systematic Review Focusing on Upper Airway Symptoms. Ear Nose Throat J. 2020, 0145561320920762. DOI: 10.1177/0145561320920762.
- [17] To KK, Tsang OT, Chik-Yan Yip C, et al. Consistent detection of 2019 novel coronavirus in saliva
 [published online ahead of print Feb 12, 2020].
 Clin Infect Dis 2020. DOI: 10.1093/cid/ciaa149.
- Badran Z, Gaudin A, Struillou X, et al. Periodontal pockets: a potential reservoir for SARS-CoV-2? Med Hypoth 2020; 143:109907. DOI: 10.1016/j. mehy. 2020.109907.
- [19] Harrel SK, Molinari J. Aerosols and splatter in dentistry: A brief review of the literature and infection control implications. J Am Dent Assoc 2004; 135:429-37. DOI: 10.14219/jada.archive.2004.0207.
- [20]Cavalcante-Leão BL, de Araujo CM, Basso IB, Schroder AGD, GuarizaFilho O, Ravazzi GC, Gonçalves FM, Zeigelboim BS, Santos RS, Stechman-Neto J. Is there scientific evidence of the mouthwashes effectiveness in reducing viral load in Covid-19? A systematic review. J Clin Exp Dent. 2021; 13(2):e179-89. doi: 10.4317/jced.57406.
- [21] Oliveira, Mirlany Mendes Maciel, et al. COVID-19-Mouthwash in dental clinical practice. Archives of health investigation, 2021, 10.1: 6-10. DOI:10.21270/archi.v10i1.5283.
- [22] Meng L, Hua F, Bian Z. Coronavirus Disease 2019 (COVID-19): Emerging and Future Challenges for Dental and Oral Medicine. J Dent Res. 2020; 99:481-87. doi: 10.1177/0022034520932149.
- [23]Peng X, Xu X, Li Y, Cheng L, Zhou X, Ren B. Transmission routes of 2019-nCoV and controls in dental practice. Int J Oral Sci. 2020; 12:9.
- [24]Carrouel F, Conte MP, Fisher J, Gonçalves LS, Dussart C, Llodra JC, et al. COVID-19: A Recommendation to Examine the Effect of Mouthrinses with beta-Cyclodextrin Combined with Citrox in Preventing Infection and Progression. J Clin Med. 2020; 9:1126. doi: 10.3390/jcm9041126.

- [25] Gururaj Arakeri, Vishal Rao US. Methylene blue as an anti-COVID-19 mouthwash in dental practice. Br J Oral Maxillofac Surg. 2021, 59.1: 135. doi: 10.1016/j.bjoms.2020.09.018.
- [26] Turkistani KA. Precautions and recommendations for orthodontic settings during the COVID-19 outbreak: A review. Am J Orthod Dentofacial Orthop AM J Orthod Dentofac. 2020 May 13. DOI: 10.1016/j.ajodo.2020.04.016.
- [27] American Dental Association. ADA interim guidance for minimizing risk of COVID-19 transmission; 2020. Available from URL: https://www. kavo.com/en-us/resource-center/ada-interim-guidaceminimizing-risk-covid-19-transmission [last accessed 13.08.20].
- [28] Centers for Disease Control and Prevention. Interim infection prevention and control guidance for dental settings during the COVID-19 response. Available from URL: https://www.cdc.gov/coronavirus/2019-ncov/hcp/dental-settings.html [last accessed 13.08.20].
- [29] Moher D, Liberati A, Tetzlaff J, Altman DG, PRIS-MA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med. 2009; 6(7):e1000097. DOI: 10.1371/journal.pmed.1000097.
- [30] Grover I, Agrawal A, Kaur H, Soni R, Mihani L, Grover M. Managing airborne isolation and precautions in orthodontic practice during the outbreak of coronavirus disease 2019: An orthodontist perspective. Int Dent J. 2020 Jan 1; 4(1):11.
- [31] Caruso AA, Del Prete A, Lazzarino AI. Hydrogen peroxide and viral infections: a literature review with research hypothesis definition in relation to the current covid-19 pandemic. Med. Hypotheses. 2020 Jun 1:109910. DOI: 10.1016/j. mehy.2020.109910.
- [32] Bidra AS, Pelletier JS, Westover JB, Frank S, Brown SM, Tessema B. Rapid In-Vitro Inactivation of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Using Povidone-Iodine Oral Antiseptic Rinse. J. Prosthodont. 2020 Jun 8. DOI: 10.1111/jopr.13209.
- [33] Ge ZY, Yang LM, Xia JJ, Fu XH, Zhang YZ. Possi-

J Craniomaxillofac Res 2021; 8(3): 101-115

ble aerosol transmission of COVID-19 and special precautions in dentistry. J. Zhejiang Univ. Sci. B. 2020 Mar 16:1-8. DOI: 10.1631/jzus.B2010010.

- [34]Basam LC, Peddu R, Tamineedi S, Basam RC. Institutional approach for the management of patients in orthodontic office during COVID-19 pandemic. Saint Int Dent J. 2020 Jan 1; 4(1):4.
- [35]Herrera D, Serrano J, Roldán S, Sanz M. Is the oral cavity relevant in SARS-CoV-2 pandemic?. Clin Oral Investig. 2020 Aug; 24(8):2925-30. DOI: 10.1007/s00784-020-03413-2.
- [36] Kim j H, Kai A, Rogowski L, Liu A. Post-Covid-19 Clinical and Management Guidelines for Orthodontic Practices.
- [37]Kirk-Bayley J, Challacombe S, Sunkaraneni S, Combes J. The Use of Povidone Iodine Nasal Spray and Mouthwash During the Current COVID-19 Pandemic May Protect Healthcare Workers and Reduce Cross Infection. Available at SSRN 3563092. 2020 Mar 28.
- [38]Khan MM, Parab SR, Paranjape M. Repurposing 0.5% povidone iodine solution in otorhinolaryngology practice in Covid 19 pandemic. Am J Otolaryngol. 2020 Sep 1; 41(5):102618. DOI: 10.1016/j.amjoto.2020.102618.
- [39] Guo Y, Jing Y, Wang Y, To A, Du S, Wang L, Bai D. Controls of SARS-CoV-2 transmission in orthodontic practice. Am J Orthod Dentofacial Orthop AM J Orthod Dentofac. 2020 Jun 5. DOI: 10.1016/j.ajodo.2020.05.006.
- [40] Bidra AS, Pelletier JS, Westover JB, Frank S, Brown SM, Tessema B. Comparison of in vitro inactivation of SARS CoV-2 with hydrogen peroxide and povidone-iodine oral antiseptic rinses. J. Prosthodont. 2020 Aug; 29(7):599-603. DOI: 10.1111/ jopr.13220.
- [41]Carrouel F, Conte MP, Fisher J, Gonçalves LS, Dussart C, Llodra JC, Bourgeois D. COVID-19: A recommendation to examine the effect of mouthrinses with β -cyclodextrin combined with citrox in preventing infection and progression. DOI: 10.3390/jcm9041126.
- [42] Jamal M, Shah M, Almarzooqi SH, Aber H, Kha-

waja S, El Abed R, Alkhatib Z, Samaranayake LP. Overview of transnational recommendations for Covid-19 transmission control in dental care settings. Oral Dis. 2020 Apr 20. DOI: 10.1111/ odi.13431.

- [43] Vergara-Buenaventura A, Castro-Ruiz C. The Use of mouthwashes against COVID-19 in dentistry. British Journal of Oral and Maxillofacial Surgery. 2020 Aug 15. DOI: 10.1016/j.bjoms.2020.08.016.
- [44] Peng X, Xu X, Li Y, Cheng L, Zhou X, Ren B. Transmission routes of 2019-nCoV and controls in dental practice. Int. J. Oral Sci. 2020 Mar 3; 12(1):1-6.
- [45] Gurzawska-Comis K, Becker K, Brunello G, Gurzawska A, Schwarz F. Recommendations for Dental Care during COVID-19 Pandemic. J Clin Med. 2020 Jun; 9(6):1833. doi: 10.3390/jcm9061833.
- [46] Australian Dental Association. ADA COVID-19
 Risk Management Guidance; 2020. Available from URL: https://www.ada.org.au/Covid-19-Portal/ Files/pdf/COVID-19-Risk-Management-Guiance. aspx.
- [47] Choudhury, Md Iqbal Mahmud, et al. Effect of 1% povidone iodine mouthwash/gargle, nasal and eye drop in COVID-19 patient. BRC. 2021, 7.1: 919-923.
- [48] Oliveira MM, de Almeida AC, de Castros Rodrigues CM, Sol I, Meneses-Santos D. COVID-19-Mouthwash in dental clinical practice. Archives of Health InvestigatioN. 2021; 10(1):6-10. DOI:10.21270/archi.v10i1.5283.
- [49] Guenezan, Jeremy, et al. Povidone Iodine Mouthwash, Gargle, and Nasal Spray to Reduce Nasopharyngeal Viral Load in Patients With COVID-19: A Randomized Clinical Trial. JAMA Otolaryngol. Head Neck Surg. 2021.
- [50]Cavalcante-Leão BL, de Araujo CM, Basso IB, Schroder AGD, GuarizaFilho O, Ravazzi GC, Gonçalves FM, Zeigelboim BS, Santos RS, Stechman-Neto J. Is there scientific evidence of the mouthwashes effectiveness in reducing viral load in Covid-19? A systematic review. J Clin Exp Dent. 2021; 13(2):e179-89. DOI:10.4317/jced.57406.

- [51] Gururaj Arakeri, Vishal Rao US. Methylene blue as an anti-COVID-19 mouthwash in dental practice. Br J Oral Maxillofac Surg, 2021, 59.1: 135. DOI:10.1016/j.bjoms.2020.09.018.
- [52]Marui VC, Souto MLS, Rovai ES, et al. Efficacy of preprocedural mouthrinses in the reduction of microorganisms in aerosol: A systematic review. J Am Dent Asoc. 2019; 150(12):1015–1026. DOI:10.1016/j.adaj.2019.06.024.
- [53]Wirthlin MR, Marshall GWJr. Evaluation of ultrasonic scaling unit waterline contamination after use of chlorine dioxide mouthrinse lavage. J Periodont. 2001; 72(3):401–410. DOI:10.1902/ jop.2001.72.3.401.
- [54]Balbuena L, Stambaugh KI, Ramirez SG, et al. Effects of topical oral antiseptic rinses on bacterial counts of saliva in healthy human subjects. Otolaryngol. Head Neck Surg. 1998; 118(5):625–629.
- [55] Houston S, Hougland P, Anderson JJ, et al. Effectiveness of 0.12% chlorhexidine gluconate oral rinse in reducing prevalence of nosocomial pneumonia in patients undergoing heart surgery. Am J Crit Care. 2002; 11(6):567–570. DOI:10.4037/ ajcc2002.11.6.567.
- [56] Karpiński T, Szkaradkiewicz A. Chlorhexidinepharmaco-biological activity and application. Eur Rev Med Pharmacol Sci. 2015; 19(7):1321–1326.
- [57]Reddy S, PrasadM S, Kaul S, et al. Efficacy of 0.2% tempered chlorhexidine as a pre-procedural mouth rinse: A clinical study. J Indian Soc Periodontol. 2012; 16(2):213. DOI:10.4103/0972-124X.99264.
- [58] Milstone AM, Passaretti CL, Perl TM. Chlorhexidine: expanding the armamentarium for infection control and prevention. Clin Infect Dis 2008; 46:274–81. DOI:10.1086/524736.
- [59]Vitkov L, Hermann A, Krautgartner WD, et al. Chlorhexidine-induced ultrastructural alterations in oral biofilm. Microsc Res Tech 2005; 68:85–9. DOI:10.1002/jemt.20238.
- [60] BaquiA, KelleyJI, Jabra-RizkMA, et al. In vitro effect of oral antiseptics on human immunodeficiency virus-1 and herpes simplex virus type 1. J

Clin Periodontol. 2001; 28(7):610-616.

- [61] Bernstein D, Schiff G, Echler G, et al. In vitro virucidal effectiveness of a 0.12%-chlorhexidine gluconate mouthrinse. J Dent Res 1990; 69:874–6.
- [62] Karpiński TM, Szkaradkiewicz AK. Chlorhexidine-pharmaco-biological activity and application. Eur Rev Med Pharmacol Sci. 2015 Apr; 19(7):1321-6.
- [63] Walsh LJ. Safety issues relating to the use of hydrogen peroxide in dentistry. Aust. Dent. J. 2000 Dec; 45(4):257-69.DOI:10.1111/j.1834-7819.2000. tb00261.x.
- [64] Kampf G, Todt D, Pfaender S, et al: Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. J Hosp Infect 2020; 104:246-251. DOI:10.1016/j.jhin.2020.01.022.
- [65] Tsuda S, Soutome S, Hayashida S, et al. Topical povidone iodine inhibits bacterial growth in the oral cavity of patients on mechanical ventilation: a randomized controlled study. BMC Oral Health 2020;20:62. DOI:10.1186/s12903-020-1043-7.
- [66] Panchmatia R, Payandeh J, Al-Salman R, et al: The efficacy of diluted topical povidone-iodine rinses in the management of recalcitrant chronic rhinosinusitis: a prospective cohort study. Eur Arch Otorhinolaryngol 2019;276:3373-3381. DOI:10.1007/ s00405-019-05628-w.
- [67] Kovesi G: The use of betadine antiseptic in the treatment of oral surgical, paradontological and oral mucosal diseases. Fogorv Sz. 1999; 92:243-250.
- [68] Challacombe SJ, Kirk-Bayley J, Sunkaraneni VS, et al. Povidone iodine. Br Dent J 2020; 228:656–7.
- [69] Mady LJ, Kubik MW, Baddour K, et al. Consideration of povidone-iodine as a public health intervention for COVID-19: utilization as "Personal Protective Equipment" for frontline providers exposed in high-risk head and neck and skull base oncology care. Oral Oncol. 2020; 105:104724. DOI:10.1016/j.oraloncology.2020.104724.
- [70] Silva MF, dos Santos NB, Stewart B, et al. A clinical investigation of the efficacy of a commercial

mouthrinse containing 0.05% cetylpyridinium chloride to control established dental plaque and gingivitis. J Clin Dent 2009; 20:55–61.

- [71] Feres M, Figueiredo LC, Faveri M, et al. The effectiveness of a preprocedural mouthrinse containing cetylpyridinium chloride in reducing bacteria in the dental office. J Am Dent Assoc 2010; 141:415– 22. DOI:10.14219/jada.archive.2010.0193.
- [72] Popkin DL, Zilka S, Dimaano M, et al. Cetylpyridinium chloride (CPC) exhibits potent, rapid activity against influenza viruses in vitro and in vivo. Pathog Immun 2017; 2:252–69. DOI:10.20411/ pai.v2i2.200.
- [73]Baker N, Williams AJ, Tropsha A, et al. Repurposing quaternary ammonium compounds as potential treatments for COVID-19. Pharm Res 2020;37:104. DOI:10.31219/osf.io/ehsn3.
- [74] Rizwana N. The role of cetylpyridinium chloride mouthwash in the treatment of periodontitis. Int J Pharm Sci Invent. 2013; 2(12):36-7.
- [75] Alshehri FA. The use of mouthwash containing essential oils (Listerine[®]) to improve oral health: a systematic review. Saudi J Dent Res. 2018 Jan 1; 30(1):2-6. DOI:10.1016/j.sdentj.2017.12.004.
- [76] Dorman HJ, Deans SG. Antimicrobial agents from plants: Antibacterial activity of plant volatile oils.
 J Appl Microbiol. 2000; 88:308–16. DOI:10.1046/ j.1365-2672.2000.00969.x.
- [77] Meiller TF, Silva A, Ferreira SM, Jabra-Rizk MA, Kelley JI, DePaola LG. Efficacy of Listerine[®] Antiseptic in reducing viral contamination of saliva. J. Clin. Periodontol. 2005 Apr; 32(4):341-6. DOI:10.1111/j.1600-051X.2005.00673.x.
- [78] Marui VC, Souto MLS, Rovai ES, et al. Efficacy of preprocedural mouthrinses in the reduction of microorganisms in aerosol: A systematic review. J Am Dent Asoc. 2019; 150(12):1015–1026. e1. DOI:10.1016/j.adaj.2019.06.024.

Please cite this paper as: Mirhashemi A, Bahrami R; On recommended mouthwashes during COVID-19 pandemic: A review. J Craniomaxillofac Res 2021; 8(3): 101-115