Oral Health Programme
Ministry of Health Malaysia

ORAL HEALTH TECHNOLOGY REVIEW

Mouthwash and Its Effect on Blood Pressure

1.0 INTRODUCTION

Mouthwash, or mouth rinse, is a liquid product commonly used to rinse oral cavity. Mouthwash can help to prevent bad breath, reduce the risk of gingivitis or reduce plaque build-up to help prevent tooth decay. It is available both over-the-counter at the stores and by prescription, depending on the formulation and concentration.

2.0 METHODS

Articles relevant to the topic of interest was searched across electronic databases which include Ovid interface: Ovid MEDLINE ® ALL year 1946 to present and PubMed. Google search engine was used to search additional web-based materials and information. Additional articles were identified from reviewing the references of retrieved articles. The terms used for search strategy (either in singular or in different combinations) were blood pressure, hypertension, cardiovascular problems, mouth rinse and mouthwash. The last search was conducted on 31 January 2022 and limited to English language.

3.0 TYPES OF MOUTHWASH

Mouthwash can be classified into three main types, which is antiseptic, plaque-inhibiting and preventive. Despite the different types of mouthwash, there is no one single mouthwash that can replace routine tooth brushing with toothbrush and toothpaste.

i. Antiseptic

Antiseptic mouthwash acts on bacteria, spores and fungi and used as a short-term adjunct to regular tooth brushing. The most commonly prescribed antiseptic mouthwash and considered to be a gold standard is chlorhexidine-containing mouthwash with 0.2% concentration. It is normally prescribed for two weeks to one month with the rinsing frequency of twice daily. Most commonly reported side effects include brown staining of teeth and oral appliances, formation of calculus, temporary taste alteration, oral dryness and burning sensation of oral mucosa. These side effects

will typically resolve once the use is discontinued. Emphasis should be made on the duration and directions of use as to ensure the benefits of this mouthwash greatly outweigh the side effects. [1]

ii. Plaque-inhibiting

The main focus of this type of mouthwash is to improve plaque control by tackling oral plaque biofilm at different stages of colonisation, subsequently, restrain the onset and progression of gingivitis and dental caries. The plaque-inhibiting mouthwash is recommended for use of twice daily. The side effects are known to be fewer than that of antiseptic mouthwash. [1]

iii. Preventive

The most widely used preventive mouthwash contains fluoride which helps to prevent dental caries and reverse initial caries in certain cases. This fluoride mouthwash is suitable to be used by patients above 8 years old and those who are identified to have high-caries risk. It can be used in two ways, either daily rinses using 0.05% sodium fluoride, or weekly rinses using 0.2% sodium fluoride. The adverse reactions of preventive mouthwash tend to be mild and uncommon, provided the user follows the directions for use. [1]

4.0 NITRATE (NO_3) – NITRITE (NO_2) – NITRIC OXIDE (NO) REDUCTION PATHWAY

There has been an argument saying that antiseptic mouthwash, also known as, chlorhexidine mouthwash has an effect on blood pressure, particularly involving the nitrate (NO_3) – nitrite (NO_2) – nitric oxide (NO) pathway. It was claimed that daily use of antiseptic mouthwash disrupted the ability of oral bacteria to convert nitrate into nitrite. The decrease in nitrate-reducing oral bacteria concentration resulted in lower circulatory nitrite bioavailability. Subsequently, this leads to the reduction of NO, which plays a major role in preserving vascular homeostasis. [2] In order to investigate the basis of the argument, one must understand the pathways of nitric oxide syntheses.

Nitric oxide (NO) is a free radical, multifunctional signalling molecule. NO moves from vessels to the surrounding muscle cells and causes muscle relaxation. Subsequently, it leads to vasodilation, increases blood flow and reduces blood pressure (BP). NO is produced endogenously by endothelial cells in vascular endothelium by means of enzymes called NO synthases (NOS). Alternatively, NO is also derived from various sources via Nitrate (NO_3) - Nitrite (NO_2) - Nitric Oxide (NO) Reduction Pathway, involving: [2, 3]

i. Dietary / Exogenous NO3

Dietary sources such as meat, vegetables and drinking water contains inorganic NO_3. Only 25% of exogenous NO_3 is absorbed by salivary glands via enterosalivary cycle and converted into NO_2 by means of oral bacteria. NO_2 is then reduced to NO via several reactions, including: [2, 3]

- nitration ($-NO_2$);
- direct NO signaling;
- nitrosation (-NO); and
- other proteins such as mitochondrial enzymes

ii. Reduction to ammonia

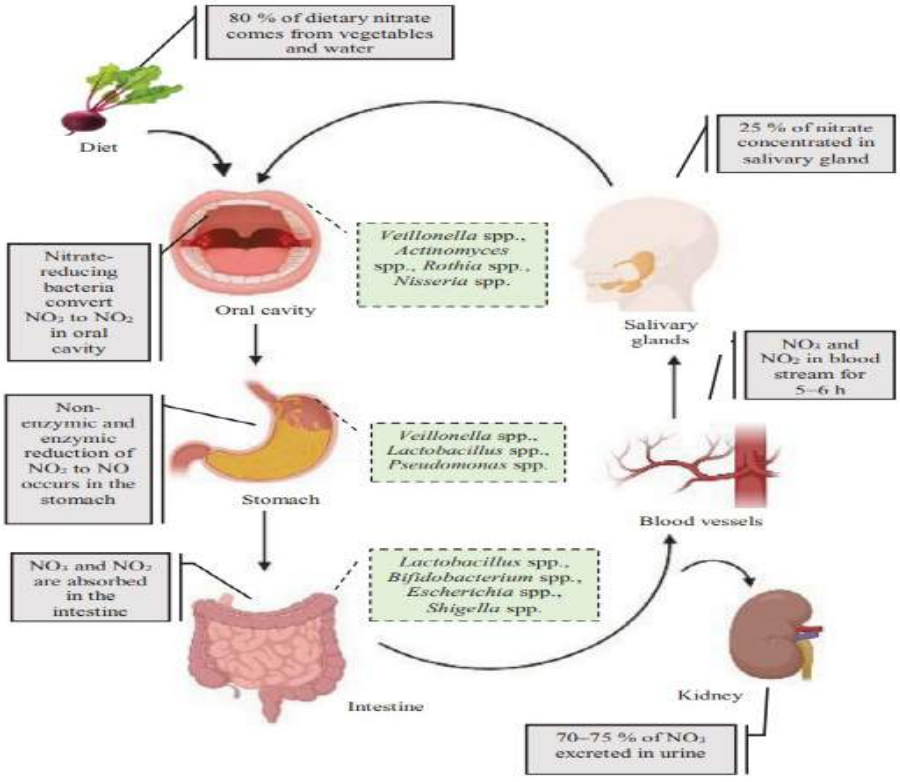
Faecal microbiota can reduce NO_3 to NO via denitrification.

iii. Nitroso-redox alteration in cardiovascular system

Xanthine oxidoreductase (XOR) is a key enzyme of purine degradation pathway. It also reduces NO_3 to NO_2 and then to NO, which acts as a protective mechanism to hypertension.

5.0 RECYCLING OF NITRIC OXIDE (NO)

NO is oxidised into NO_2 and NO_3 immediately after its production via enterosalivary cycle. About 24 hours after the consumption of nitrate-rich diet, three-quarters of the nitrate will be excreted in the urine. Despite the short-life of NO and immediate oxidisation into NO_2 and NO_3, NO can be stored in red blood cells and plasma. It maintains a physiological effect and acts as a marker of NO availability. Imbalance in NO bioavailability has been associated with some cardiovascular (CVS) and metabolic diseases. [2, 3]



6.0 MOUTHWASH EFFECT ON BLOOD PRESSURE

Antiseptic mouthwashes act to reduce the concentration of oral bacteria in general. There is conflicting evidence on the action of mouthwash on NO_3 metabolism and the influence on blood pressure. A systematic review investigated the relationship between mouthwash use, salivary or plasma NO_2/NO_3, and blood pressure. The review included five human studies and crossover trials that compare antiseptic mouthwash with placebo or water, but the outcomes were discordant. [4] Three studies reported significant increase in blood pressure, whereas two others found no significant difference. [5-7] Bondonno et al. recruited 15 hypertensive participants and they were instructed to use 1.28mg/mol chlorhexidine (CHX) mouthwash twice a day for three days. They reported an increase in systolic blood pressure (SBP) by 2.3mmHg and reduce in salivary NO_2 level, but no difference in diastolic blood pressure (DBP) and plasma NO_2 level. [5] Another study that supported this finding was by Kapil et al., which involved 19 normotensive participants that were instructed to use 0.2% CHX mouthwash twice daily for one week. It was found that the SBP increased by 1.5-4.5mmHg, DBP increased by 1.2-3.2mmHg and reduce in both salivary and plasma NO_2 levels. [6] Similarly, Woessner et al. reported increase in SBP by 2-5mmHg after 4 hours of using CHX and Cepacol mouthwashes hourly, compared with Listerine mouthwash and water. [7] Although significant findings were reported in these studies, conclusion should be made with caution considering the small sample size and influence of confounders. On the contrary, two other studies in the review involving 12 [8] and 17 healthy individuals [9] found that the use of CHX mouthwash resulted in significant reduction of salivary NO_2 levels. One of the studies also reported significant reduction of plasma NO_2. [8] However, both studies showed no statistically significant change in SBP and DBP. [8, 9]

In a more recent review by Alzahrani et al., another 3 human studies were included. [10] A study by Mitsui and Harasawa found that CHX-based mouthwash reduced the bacterial count of oral nitrate-reducing bacteria compared to Listerine and povidone-iodine mouthwashes in normotensive participants. [11] Comparably, Govoni et al. reported that rinsing with CHX twice daily would decrease salivary and plasma NO_2 levels. [12] However, Tribble et al. found inconsistent effect of CHX mouthwash on SBP in healthy individuals, when used twice daily for 7 days. From their study, nine participants had at least 5mmHg increase in SBP, whereas a decrease was observed in four participants. [13]

In addition to the findings from both reviews, a recent crossover design study involving 36 healthy individuals found that the use of CHX mouthwash twice daily for 7 days led to lower saliva and plasma nitrite availability. However, no significant increase in SBP was seen. [14]

7.0 CONCLUSION

The chlorhexidine mouthwash may disrupt oral microbiome that have direct role in enterosalivary pathway of NO production and mediate the blood pressure effect of dietary nitrate. However, there are various other pathways for NO production and multiple confounding factors that may also contribute to an increased risk of hypertension. It remains to be clarified whether the use of antiseptic mouthwash solely would have a significant effect on the blood pressure. Since the benefits of mouthwash greatly outweigh the risks, it should strictly be used according to prescription and directions. To reiterate, mouthwash does not replace tooth brushing or flossing and is not recommended for children under 6-years-old due to the risk of swallowing. Patients should discuss with their dentists the type of mouthwash suitable for use.

REFERENCE

1. Wilson N, Patel R, Gallagher J, Chapple I. How to select the right mouthwash. Pharmaceutical Journal. 2014;292(7795):119-21.
2. Pignatelli P, Fabietti G, Ricci A, Piattelli A, Curia MC. How Periodontal Disease and Presence of Nitric Oxide Reducing Oral Bacteria Can Affect Blood Pressure. International journal of molecular sciences. 2020;21(20).
3. Lundberg JO, Weitzberg E, Gladwin MT. The nitrate-nitrite-nitric oxide pathway in physiology and therapeutics. Nature reviews Drug discovery. 2008;7(2):156-67.
4. Senkus KE, Crowe-White KM. Influence of mouth rinse use on the enterosalivary pathway and blood pressure regulation: A systematic review. Crit Rev Food Sci Nutr. 2020;60(17):2874-86.
5. Bondonno CP, Liu AH, Croft KD, Considine MJ, Puddey IB, Woodman RJ, et al. Antibacterial mouthwash blunts oral nitrate reduction and increases blood pressure in treated hypertensive men and women. Am J Hypertens. 2015;28(5):572-5.
6. Kapil V, Haydar SM, Pearl V, Lundberg JO, Weitzberg E, Ahluwalia A. Physiological role for nitrate-reducing oral bacteria in blood pressure control. Free Radic Biol Med. 2013;55:93-100.
7. Woessner M, Smoliga JM, Tarzia B, Stabler T, Van Bruggen M, Allen JD. A stepwise reduction in plasma and salivary nitrite with increasing strengths of mouthwash following a dietary nitrate load. Nitric Oxide. 2016;54:1-7.
8. McDonagh ST, Wylie LJ, Winyard PG, Vanhatalo A, Jones AM. The Effects of Chronic Nitrate Supplementation and the Use of Strong and Weak Antibacterial Agents on Plasma Nitrite Concentration and Exercise Blood Pressure. Int J Sports Med. 2015;36(14):1177-85.
9. Sundqvist ML, Lundberg JO, Weitzberg E. Effects of antiseptic mouthwash on resting metabolic rate: A randomized, double-blind, crossover study. Nitric Oxide. 2016;61:38-44.
10. Alzahrani HS, Jackson KG, Hobbs DA, Lovegrove JA. The role of dietary nitrate and the oral microbiome on blood pressure and vascular tone. Nutr Res Rev. 2021;34(2):222-39.
11. Mitsui T, Harasawa R. The effects of essential oil, povidone-iodine, and chlorhexidine mouthwash on salivary nitrate/nitrite and nitrate-reducing bacteria. J Oral Sci. 2017;59(4):597-601.
12. Govoni M, Jansson EA, Weitzberg E, Lundberg JO. The increase in plasma nitrite after a dietary nitrate load is markedly attenuated by an antibacterial mouthwash. Nitric Oxide. 2008;19(4):333-7.

13. Tribble GD, Angelov N, Weltman R, Wang BY, Eswaran SV, Gay IC, et al. Frequency of Tongue Cleaning Impacts the Human Tongue Microbiome Composition and Enterosalivary Circulation of Nitrate. Front Cell Infect Microbiol. 2019;9:39.
14. Bescos R, Ashworth A, Cutler C, Brookes ZL, Belfield L, Rodiles A, et al. Effects of Chlorhexidine mouthwash on the oral microbiome. Sci Rep. 2020;10(1):5254.

Prepared by:
Oral Health Technology Section
Oral Health Programme
Ministry of Health Malaysia
31 January 2022