



Surveillance Spotlight: Current Concepts in Oral-Systemic Health

Use of Alcohol-Containing Rinses to Reduce Oral Microbial Burden: Safety and Efficacy

By Anthony M. Iacopino, DMD, PhD

The previous *Surveillance Spotlight* addressed the importance of reducing or eliminating oral biofilm (oral microbial burden).¹ The strong relationship between oral inflammation and elevated levels of systemic inflammatory markers is the basis for current theories on the mechanistic linkages between gingivitis/periodontitis and systemic inflammation linked to chronic inflammatory diseases and conditions such as diabetes, atherosclerosis, arthritis and adverse pregnancy outcomes.^{2,3} Future policy and practice guidelines for interprofessional clinical care models will most likely be based on approaches to reduce oral biofilms. Research has shown that the pathogenic nature of dental plaque biofilm can be diminished by oral hygiene procedures that include daily toothbrushing, flossing and rinsing with an antimicrobial mouthrinse.⁴

The safety of alcohol-containing mouthrinses has been called into question, and 3 recent papers⁵⁻⁷ have fuelled the controversy. Two of the studies,⁵⁻⁶ which appear to establish a relationship between the use of these rinses and oral cancer, are significantly flawed. Based on existing data, results in the most recent review⁷ have either been misinterpreted or overstated.

To fully evaluate the potential association of alcohol-containing mouthrinses and oral cancer, one must consider various factors. First, there is a difference between pure ethanol (the alcohol that is used in mouthrinses as a solvent for flavouring and active agents and as a preservative) and the alcohol that is ingested from alcoholic beverages. These beverages contain many contaminants and congeners from the distillation and fermentation process such as nitrosamines, polycyclic hydrocarbons and aflatoxins.⁸ The carcinogenicity of these contaminants and congeners is well established; however, pure ethanol has never been shown to be carcinogenic in any animal, human or cell culture system.⁸

Second, it has been shown that alcohol exposure can increase the permeability of oral mucosal cells through alteration of lipid membrane components, making these cells more susceptible to carcinogens in alcoholic beverages and in cigarette smoke, an important consideration since social drinking and tobacco use often co-exist.⁹ However, these findings are based on long durations of exposure (one hour or longer) and large concentrations of alcohol that would mimic social drinking. These findings do not consider the extremely short exposure to mouthrinses (30–60 seconds) with extremely small amounts of alcohol, or the flushing effect of saliva that would rapidly dissipate any residual rinse. In fact, studies that examined alcohol-containing mouthrinses under actual conditions of usage reported no effect on oral mucosal permeability barriers.¹⁰

Third, one of the main linkages between alcohol use and oral cancer is the conversion of alcohol to acetaldehyde, a carcinogenic metabolite. This conversion is accomplished through the alcohol dehydrogenase enzyme in oral bacteria. Thus the conversion occurs more quickly and to a greater degree with poor oral hygiene and a large oral microbial burden. In fact, a study¹¹ done in 1995 showed there was only a trace amount of acetaldehyde produced by oral bacterial biofilms in response to alcohol-containing mouthrinses compared to the amounts produced by social drinking or eating a small container of yogurt. This same study showed that use of antimicrobial mouthrinses significantly reduced acetaldehyde production in both scenarios.

Notably, 8 epidemiologic studies were undertaken before 1995 to determine whether the use of alcohol-containing mouthrinses was associated with an increased incidence of oropharyngeal cancer.¹² None of these studies found any relationship whatsoever. Additionally, the U.S. Food and Drug Administration (FDA) investigated the relationship between alcohol-containing mouthrinses and oral cancer in 1996¹³ and in 2003¹⁴ and concluded that there was no relationship. This was once again confirmed in an evaluation of epidemiologic literature over a 25-year period.¹⁵ Two of these studies^{14,15} consisted of the highest level of scientific evidence: systematic reviews and meta-analysis. The majority of the other studies were rigorously designed with large numbers of patients and thorough documentation of frequency, duration and specific details of mouthrinse usage.

In contrast, the 3 recent publications⁵⁻⁷ which allege a relationship between alcohol-containing mouthrinses and oral cancer suffer from some serious scientific flaws in experimental design and data interpretation. To understand these shortcomings, one must consider the following factors:

- self-report data for oral hygiene, smoking and drinking (known to be unreliable data)
- less than adequate control for heavy smokers and drinkers (no surrogate markers were used to validate self-report data)

- controls were only required to live in study areas for one year (this time period is too short to control for environmental factors that may contribute to oral cancer)
- no data was collected on smokeless tobacco use or diet (other known contributors to oral cancer risk)
- no information as to whether mouthwash use was to conceal tobacco or drinking-related breath odours (mouthwash use could have been an indicator of heavy smoking and drinking)
- no information on how long the mouthwash was used, frequency of use, or how long the mouthwash was retained in the mouth during use lack of dose–response data (amounts of actual mouthwash used and oral alcohol concentration were not measured)
- inconsistent findings among males and females (no biological basis for differences)
- improper classification of pharyngeal cancer as oral cancer (no biologic plausibility for mouthwash exposure and an over-estimation of the number of cancer cases by 70%)
- no information as to whether mouthwash use began after presence of oral lesions as an attempt at self resolution (mouthwash use could have been a consequence, instead of the cause, of disease)
- very small numbers of patients in non-smoking groups (greatly limiting valid statistical analysis)

In summary, there is no reason to avoid the use of alcohol-containing mouthrinses, and all antimicrobial rinses, including those containing alcohol, have been shown to be safe and effective in reducing oral biofilms. Thus, they should remain an important part of a comprehensive oral health care regimen that also includes brushing and flossing to reduce the oral and systemic inflammatory burden.¹⁶ ♦

References

1. Iacopino AM. Oral biofilms: the origin of cross-reactive antibodies involved in systemic disease? *J Can Dent Assoc* 2009; 75(3):180–181.
2. Seymour GJ, Ford PJ, Cullinan MP, Leishman S, Yamazaki K. Relationship between periodontal infections and systemic disease. *Clin Microbiol Infect* 2007; 13(Suppl 4):3–10.
3. Van Dyke TE. Inflammation and periodontal disease: a reappraisal. *J Periodontol* 2008; 79(8 Suppl):1501–2.
4. Thomas JG, Nakaishi LA. Managing the complexity of a dynamic biofilm. *J Am Dent Assoc* 2006; 137 Suppl:105–155.
5. Guha N, Boffetta P, Wunsch Filho V, Eluf Neto J, Shangina O, Zaridze D, Curado MP, and others. Oral health and risk of squamous cell carcinoma of the head and neck and esophagus: results of two multicentric case-control studies. *Am J Epidemiol* 2007 15;166(10):1159–73. Epub 2007 Aug 30.
6. Marques LA, Eluf-Neto J, Figueiredo RA, Góis-Filho JF, Kowalski LP, Carvalho MB, and others. Oral health, hygiene practices and oral cancer. *Rev Saude Publica* 2008; 42(3):471–9.
7. McCullough MJ, Farah CS. The role of alcohol in oral carcinogenesis with particular reference to alcohol-containing mouthwashes. *Aust Dent J* 2008; 53(4):302–5.
8. Garro AJ, Lieber CS. Alcohol and cancer. *Annu Rev Pharmacol Toxicol* 1990; 30:219–49.
9. Squier CA, Cox P, Hall BK. Enhanced penetration of nitrosonornicotine across oral mucosa in the presence of ethanol. *J Oral Pathol* 1986; 15(5):276–9.
10. Bhageerutty Y, Cruchley AT, Williams DM. Effect of an alcohol-containing mouthwash on mucosal permeability. *J Dent Res* 1998; 77 (Spec No B):768.
11. Homann N, Jousimies-Somer H, Jokelainen K, Heine R, Salaspuro M. High acetaldehyde levels in saliva after ethanol consumption: methodological aspects and pathogenetic implications. *Carcinogenesis* 1997; 18(9):1739–43.
12. Elmore JG, Horwitz RI. Oral cancer and mouthwash use: evaluation of the epidemiologic evidence. *Otolaryngol Head Neck Surg* 1995; 113(3):253–61.
13. FDC Reports. Alcohol-containing mouthwash concern alleviated by existing data. *The Tan Sheet* 1996; 4(24):1–5.
14. Department of Health and Human Services, Food and Drug Administration. Oral health care drug products for over-the-counter human use: antigingivitis/antiplaque drug products; establishment of a monograph; proposed rules. Part III. *Federal Register* 2003 May 29; 68:32241–32243.
15. Cole P, Rodu B, Mathisen A. Alcohol-containing mouthwash and oropharyngeal cancer: a review of the epidemiology. *J Am Dent Assoc* 2003; 134(8):1079–87.
16. Silverman S Jr, Wilder R. Antimicrobial mouthrinse as part of a comprehensive oral care regimen. Safety and compliance factors. *J Am Dent Assoc* 2006; 137(Suppl):225–265. ♦

Dr. Iacopino is dean and professor of restorative dentistry, and director of the International Centre for Oral–Systemic Health, faculty of dentistry, University of Manitoba, Winnipeg, Manitoba. Email: iacopino@cc.umanitoba.ca

Dr. Iacopino has provided expertise and consultancy over the past several years to various dental and health care companies related to oral-systemic health, including Colgate–Palmolive and Johnson and Johnson.