Randomized Controlled Trial of 0.454% Stannous Fluoride Dentifrice to Treat Gingival Bleeding

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ABSTRACT

PURPOSE: To evaluate the effects of a highly bioavailable 0.454% stannous fluoride dentifrice on established gingival bleeding over a 3-month period. MATERIALS AND METHODS: A randomized controlled clinical trial was conducted. In total, 100 adults with mild-to-moderate gingivitis and an average of 15 bleeding sites were assigned to either the stannous fluoride or regular control pastes for at-home use. Of these, 99 received study treatment and 97 completed the study. RESULTS: The stannous fluoride group experienced 50% to 74% reductions in bleeding sites relative to baseline or the control, differing significantly ($P < 0.001$) at all time points. Most subjects in the stannous fluoride group (94%) had measured improvements in bleeding, and nearly one half completed treatment with one or no bleeding sites. CONCLUSION: These study results suggest that incorporation of this 0.454% stannous fluoride dentifrice into daily oral hygiene may be expected to yield less gingival bleeding at subsequent dental check-ups, and therefore reduce the risk of progressive periodontal disease.

Gingivitis is characterized by marginal redness, swelling, and bleeding—the latter of which can be readily measured by clinicians, and occasionally observed by patients during daily oral hygiene. Plaque accumulation plays a prominent etiological role, as evidenced by the rapid onset of clinical disease following suspension of daily oral hygiene.[1] Along with plaque accumulation, "systemic" factors such as pregnancy, diabetes, immune deficiency, and others have been shown to modulate the clinical expression of gingivitis.[2]

Routine prophylaxis is recognized to reduce or eliminate gingivitis, although plaque can accumulate quickly with inadequate oral hygiene, and gingivitis can reappear soon thereafter. Antibacterial agents can play an important adjunctive role in plaque and gingivitis inhibition, as exemplified by use of prescription chlorhexidine rinses with routine toothbrushing. In addition to professional care and prescription products, systematic review recognizes long-term antiplaque and antigingivitis effects of various over-the-counter dentifrices and rinses used as part of daily oral hygiene.[3] One of these agents is stannous fluoride, which has a 50-plus-year history of use in dentifrices for anticaries activity, and more recently, for its antigingivitis effects.[4]

Over the past decade, research has focused on new stannous fluoride dentifrices that use cosmetic agents to improve in-tube stability and in-use esthetics. Clinical outcomes with these dentifrices have included reductions in plaque and gingivitis versus regular toothbrushing during the 6-month period that coincides with normal dental recall.[5] Contemporary research has focused on highly bioavailable stannous fluoride dentifrice options to improve clinical response. This new clinical trial

was conducted to evaluate the clinical practice implications of a novel, highly bioavailable stannous fluoride dentifrice in the treatment of existing gingivitis.

STUDY POPULATION AND METHODOLOGY

A 3-month randomized controlled trial was conducted to evaluate a new multi-benefit 0.454% stannous fluoride dentifrice. Eligibility was limited to adult volunteers with at least 16 natural teeth and mild-to-moderate gingivitis. Written informed consent for participation in this study was obtained from all subjects in accordance with the Declaration of Helsinki II, and the protocol was approved by the Bio-Sci Research Canada, Ltd (BRCL) Institutional Review Board.

This study assessed dentifrice effects on natural gingivitis treatment; therefore, no dental prophylaxis was performed. The evaluation period was 3 months, which allowed for normal recall and professional care after the study ended. After baseline measurements, subjects were randomized to either the experimental group treatment, a novel multi-benefit dentifrice containing 0.454% stannous fluoride (Crest® Pro-Health Clinical Gum Protection, Procter & Gamble, www.crestprohealth.com), or the control-group treatment, a regular anticavity dentifrice (Colgate® Cavity Protection Toothpaste, Colgate-Palmolive, www.colgateprofessional.com) without stannous fluoride. Daily oral hygiene was completed at home and unsupervised, and for standardization, both groups were provided a regular manual toothbrush (Oral-B® Indicator Soft, Procter & Gamble, www.pg.com) for use throughout the study. The assigned paste and brush was dispensed in a blinded kit box with manufacturer-specific instructions (experimental: 1-inch strip of paste, brush teeth thoroughly for at least 1 minute twice a day; control: brush thoroughly twice daily).

Clinical response was evaluated monthly over a 3-month period by a trained dentist examiner, who was blinded to treatment assignment. For the clinical practice implications, efficacy was assessed from the number of marginal gingival bleeding sites measured using the Gingival Bleeding Index (GBI). With this method, the marginal gingivae were evaluated 30 seconds after gentle probing to assess bleeding on a simple 3-point scale (0 = absence of bleeding after 30 seconds; 1 = bleeding observed after 30 seconds; 2 = immediate bleeding observed). Six sites were measured per evaluable tooth (up to 168 sites per person excluding third molars). Sites with GBI scores of 1 or 2 were classified as "bleeding," and these positive bleeding sites were summed to determine the total number of bleeding sites per subject. In addition, gingival inflammation was measured (initially to determine eligibility) using the non-contact Modified Gingivitis Index (MGI), and safety was assessed from clinical examination. All assessments followed standard methods, such as those used previously in a 3-month clinical trial to evaluate different types of oral hygiene products.[6]

Treatment groups were compared for baseline demographics using analysis of variance (ANOVA) for age, and Fisher's Exact Test for gender. Within-group comparisons of the number of bleeding sites (GBI) to baseline were made using a paired-difference *t*-test. Between-group comparisons used ANOVA with baseline as a covariate. All treatment comparisons were two-sided with a significance level of 0.05.

RESULTS

Of the total 109 subjects who were screened, 100 were enrolled, 99 were treated, and 97 completed the 3-month study. Mean (SD) age was 33.6 (11.1) years, with females comprising 60% of the study population (Table 1). Mean (SD) bleeding sites were 15.5 (9.3) at baseline, ranging as high as 36 total sites. Groups were balanced ($P > 0.52$) on age, gender, the number of gingival bleeding sites (GBI), and gingival inflammation (MGI).

TABLE 1

Baseline Demographics and Gingival Heal

	Regular *n* = 50	Stannous Flouride *n* = 50	Overall *n* = 100	*P* Value
Age (Years)				
Mean (SD)	33.6 (11.29)	33.5 (11.11)	33.6 (11.14)	0.96
Range	18–66	19–54	18–66	
Female				
Number (%)	29 (59%)	30 (60%)	59 (60%)	0.99
Bleeding Sites				
Mean (SD)	16.1 (9.72)	14.9 (8.88)	15.5 (9.28)	0.53
Range	0–36	0–33	0–36	
MGI				
Mean (SD)	2.19 (0.10)	2.18 (0.10)	2.19 (0.10)	0.64
Range	1.9–2.3	1.8–2.3	1.8–2.3	

Relative to baseline, the 0.454% stannous-fluoride group experienced significant ($P < 0.001$) improvement in gingival bleeding each month (Table 2). In contrast, the control group was essentially unchanged and did not differ significantly ($P > 0.55$) from baseline at any time point. Between-group comparisons, adjusting for baseline values, showed significant ($P < 0.001$) differences in bleeding sites favoring the stannous-fluoride group, ranging from approximately 52% at Month 1 to 73% at Month 3.

For individual subjects, the majority assigned the 0.454% stannous-fluoride group had a measured reduction in bleeding, and this response was evident irrespective of the starting bleeding level. As illustrated in the control chart, 46 of 49 subjects (94%) assigned to the 0.454% stannous-fluoride group had reductions in the number of bleeding sites at Month 3 (Figure 1). Nearly one-half (24 of 49) of all stannous-fluoride users had one or fewer bleeding sites at study completion, approximately four-fold greater than the control dentifrice.

Significant outcomes were obtained for gingival inflammation, both with respect to changes from baseline and between-group comparisons, while safety outcomes were generally unremarkable and did not impact on response. In the stannous-fluoride dentifrice group, two subjects reported minor oral soft-tissue desquamation, while one had mild oral irritation, all of which resolved during or after treatment.

TABLE 2

Adjusted Mean Number of Bleeding Sites by Treatment Group and Visit

Group	*N*	BLEEDING SITES		
		Adjusted Mean	Change from Baseline	
			P Value	Improvement
Month 1				
Control	49	16.1	0.551	-3%
Stannous Fluoride	49	7.9	< 0.001	50%
Month 2				
Control	48	15.9	0.839	-1%
Stannous Fluoride	50	5.5	< 0.001	65%
Month 3				
Control	48	15.4	0.846	2%
Stannous Fluoride	49	4.2	< 0.001	74%

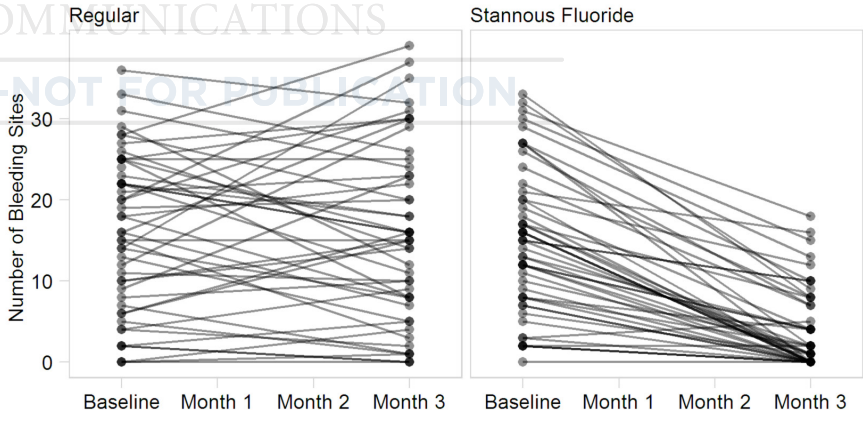

Fig 1.

Fig 1. Three-month change in number of bleeding sites by subject and treatment group.

DISCUSSION

Stannous fluoride has a long history in dentifrices, in part, due to the recognized inhibition of dental plaque metabolism. More contemporary products have stannous fluoride and anti-tartar/whitening agents to improve cosmetic outcomes, and in clinical trials, use of a stannous-fluoride dentifrice has been shown to reduce gingivitis after prophylaxis by 20% or more relative to a regular dentifrice control.[5] A novel, highly bioavailable 0.454% stannous-fluoride dentifrice was developed, and a new randomized controlled trial was conducted to assess the clinical implications on established gingival bleeding.

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The 0.454% stannous-fluoride dentifrice group had appreciable bleeding improvement after 1 month of at-home use relative to both baseline and the control dentifrice, and response improved with continued use at all subsequent evaluations. End-of-study outcomes at Month 3 included a 73% reduction in the number of bleeding sites for the stannous-fluoride group relative to the regular dentifrice control. Individual subject response was favorable. The overwhelming majority (94%) of subjects assigned the stannous-fluoride dentifrice had measureable improvement in bleeding, and 49% had little-to-no bleeding (0 to 1 bleeding sites) after 3 months' use. This improvement in gingival health was achieved without clinical evidence of stain accumulation or meaningful adverse events from the introduction of the novel stannous-fluoride dentifrice into the daily oral hygiene routine.

> "Because toothpaste selection may occur in the absence of professional consultation, the authors designed this study to assess the impact of self-adoption of a new dentifrice on clinical presentation at the time of the next recall visit."

This clinical trial was designed to model conditions that are most common within the contemporary dental practice relative to population selection, evaluation methods, and product use. With respect to the population, study subjects averaged 15 bleeding sites—a mild-to-moderate level of disease occurrence that is generally consistent with prevailing disease levels.[7] Bleeding has long been identified as an important objective sign of gingival inflammation.[8] Accordingly, the evaluation focused on gingival bleeding sites as an effectiveness variable of interest, not just because of its objectivity for research, but also because this endpoint can be readily measured in practice to monitor progress. Further, persistent gingival bleeding is recognized as a risk factor for progressive periodontal disease and tooth loss.[9] Finally, dentifrice use was at home and unsupervised without other interventions. Because toothpaste selection may occur in the absence of professional consultation, the authors designed this study to assess the impact of self-adoption of a new dentifrice on clinical presentation at the time of the next recall visit. This was a gingivitis treatment study without a baseline prophylaxis, so study duration was limited to 3 months in order to allow for normal post-study recall treatment.

This randomized controlled trial of a novel 0.454% stannous-fluoride dentifrice demonstrated significant reductions in gingival bleeding at 1 month, and improving through 3 months of at-home use. Based on the outcomes from this trial, the simple incorporation of this 0.454% stannous-fluoride dentifrice into daily oral hygiene may be expected to yield less gingival bleeding at subsequent dental check-ups, and, therefore, reduce the risk of progressive periodontal disease.

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DISCLOSURE

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REFERENCES

1. Loe H, Theilade E, Jensen SB. Experimental gingivitis in man. *J Periodont*. 1965;36:177-187.
2. Tatakis DN, Trombelli L. Modulation of clinical expression of plaque-induced gingivitis. I. Background review and rationale. *J Clin Periodontol*. 2004;31(4):229-238.
3. Gunsolley JC. A meta-analysis of six-month studies of antiplaque and antigingivitis agents. *J Am Dent Assoc*. 2006;137(12):1649-1657.
4. Tinanoff N. Progress regarding the use of stannous fluoride in clinical dentistry. *J Clin Dent*. 1995;6(spec no):37-40.
5. Mankodi S, Bartizek RD, Winston JL, et al. Anti-gingivitis efficacy of a stabilized 0.454% stannous fluoride/sodium hexametaphosphate dentifrice. *J Clin Periodontol*. 2005;32(1):75-80.
6. Goyal CR, Qaqish J, He T, et al. A randomized 12-week study to compare the gingivitis and plaque reduction benefits of a rotation-oscillation power toothbrush and a sonic power toothbrush. *J Clin Dent*. 2009;2(3):93-98.
7. Lang NP, Schatzle MA, Loe H. Gingivitis as a risk factor in periodontal disease. *J Clin Periodontol*. 2009;36(suppl 10):3-8.
8. Chaves ES, Wood RC, Jones AA, et al. Relationship of "bleeding on probing" and "gingival index bleeding" as clinical parameters of gingival inflammation. *J Clin Periodontol*. 1993;20(2):139-143.
9. Lang N, Joss A, Orsanic T, et al. Bleeding on probing. A predictor for the progression of periodontal disease? *J Clin Periodontol*. 1986;13(6):590-596.