Efficacy Evaluation of a Chlorine Dioxide Containing Toothpaste (DioxiBrite™) on Plaque and Gingivitis

A Clinical Study

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Study Sponsored By:
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Final Report
Protocol #DBT-100
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ABSTRACT
The efficacy of DioxiBrite™ a Chlorine Dioxide containing toothpaste on plaque and gingivitis was compared to an active control product Colgate Total™ containing Triclosan in a 3 week clinical trial. Fourteen subjects with moderate levels of plaque and gingivitis were randomly assigned to the experimental or positive control groups. Bleeding on probing and noninvasive measures of plaque and gingivitis were assessed at baseline and 3 weeks. Experimental group scores were significantly lower ($p<.0482$) than the positive control scores for plaque at 3 weeks. Both groups showed significant reductions in gingivitis and bleeding ($p<.0001$) over the course of the study. No adverse events were reported for either group. Results indicate that the test product showed good levels of safety and efficacy during the 3 week test period.

INTRODUCTION
Chlorine dioxide is recognized as a highly potent, broad spectrum antimicrobial that has been successfully developed for uses in a variety of areas including municipal water supplies and food processing. In dentistry, chlorine dioxide containing products have demonstrated their ability to oxidatively consume volatile sulfur compounds (VSCs) responsible for halitosis, elevate the oxygen tension in both saliva and plaque, remove residual organic solutes, and suppress the activity of bacterial proteolytic enzymes (Chapek, 1994). However, there is little reference in the literature to its effect on periodontal disease. Yates et al. (1997) investigated the persistence of antimicrobial action and plaque inhibitory properties of ClO_2 mouthrinses by comparison with a positive control, chlorhexidine 0.12%. The results indicated that the ClO_2 rinses have equivalent plaque inhibitory action to chlorhexidine. Other isolated reports have also indicated improved periodontal parameters in gingivitis and periodontitis using stabilized chlorine dioxide (Goultschin, 1989, Spindler, 1998).

The present study evaluated the antiplaque and antigingivitis efficacy and clinical safety of a chlorine dioxide (acidified chlorite) containing toothpaste over a 3 week period. Unlike "stabilized" chlorine dioxide, the acidified nature of DioxiBrite™ releases chlorine dioxide from chlorite which is thought to enhance its effect on both plaque and gingivitis.

MATERIALS AND METHODS

Human Subjects

Subjects participating in the study were 18 years of age or older, in good general health, and had not taken any antibiotics within one month or used any chemical antiplaque products within 2 weeks of study initiation. All subjects had at least 20 natural teeth without dental caries, crowns, orthodontic bands, or severe mutilation and were free from moderate to advanced periodontitis with pockets ≤ 5mm. Subjects were screened for a plaque index score of ≥1.95 using the Turesky modification of the Quigley-Hein Plaque Index, an average gingival score of ≥ 1.5 according to the Lobene Gingival Index, and ≥ 20% sites which bled on probing. Subjects who presented with a history of hypersensitivity to dentifrices or triclosan, were pregnant, nursing, had any metabolic condition that may affect gingival health or require antibiotic premedication prior to examination, had any dental treatment in the week prior to study initiation or were undergoing an extensive oral hygiene program were excluded from the study.

Experimental Design

Two groups of 7 subjects were studied in a randomized, double blind, parallel design. The experimental group received DioxiBrite™ dentifrice containing 0.6% chlorite (pH 4.9), and 0.06% sodium fluoride. The positive control group received the currently marketed Colgate Total® dentifrice containing 0.3% triclosan and 0.24% sodium fluoride. After baseline evaluation, subjects were randomly assigned to one of the two groups. Subjects were instructed to refrain from changing their oral hygiene habits during the study period, and no attempt was made to influence toothbrushing technique. The toothpaste products used in this study were packaged similarly consisting of two parts housed in a dual product dispenser. Both products looked similar in color and consistency. Subjects were instructed to dispense equal quantities of each part from the dual product dispenser onto the toothbrush and brush his or her teeth for 60 seconds. While brushing subjects were asked to make sure that the two parts were mixing. Compliance was monitored by subject diaries and the return of product dispensers, which were weighed to determine amount of unused product.

Clinical Indices - Efficacy

Clinical scoring was carried out by one investigator who is an experienced clinical researcher with an 80% intra-examiner reliability. Originally calibrated by experienced clinical personnel of the Oral Health Research Center, at Fairleigh-Dickinson University, the investigator has calibrated numerous examiners both nationally and internationally on the use of these indices.

Noninvasive measures of plaque and gingivitis were assessed at baseline and 3 weeks. Plaque was scored on six surfaces (mesiobuccal, buccal, distobuccal, lingual, mesiolingual and distolingual) of all teeth using the Turesky et al. Modification of the Quigley-Hein Plaque Index:

0 = no plaque
1 = separate flecks or a discontinuous band of plaque at the gingival margin
2 = thin (up to 1mm) continuous band of plaque at the gingival margin
3 = band of plaque wider than 1mm but covering less than 1/3 of the gingival third of the tooth surface
4 = plaque covering more than 1/3, but less than 2/3 of the gingival third of the tooth surface
5 = plaque covering 2/3 or more of the gingival third of the tooth surface.

Gingival inflammation was scored on the marginal and papillary gingival units associated with scorable teeth. The Lobene et al. Modification of the Loe and Silness Gingival Index was employed using the following criteria:

0 = absence of inflammation
1 = mild inflammation; slight change in color, little change in texture of any portion of but not the entire marginal or papillary gingival unit.
2 = mild inflammation, criteria as above, but involving the entire marginal or papillary gingival unit
3 = moderate inflammation; glazing, redness, edema and/or hypertrophy of the marginal papillary gingival unit
4 = severe inflammation; marked redness, edema and/or hypertrophy of the marginal or papillary gingival unit, spontaneous bleeding, congestion, or ulceration

Bleeding measures were also evaluated at baseline and 3 weeks with the use of a standard periodontal probe that was gently inserted into the sulcus to the base of the pocket. After removal of the probe, the presence or absence of bleeding was noted using the following scale:

0 = no bleeding
1 = pinpoint bleeding present without flow along gingival margin
2 = bleeding with flow along gingival margin
3 = profuse bleeding immediately on probing
4 = spontaneous bleeding in the absence of probing.

Clinical Indices - Safety

Safety parameters were assessed by a soft tissue examination that was conducted at baseline and 3 weeks prior to each plaque and gingivitis evaluation. The soft tissue examination assessed the buccal, labial and sublingual mucosa, tongue, hard and soft palate, uvula and oral pharynx for any abnormalities. Any adverse events were recorded at each clinic visit on an Adverse Event report form, including date of onset and cessation, intensity, relationship to study product, action and outcome.

Statistical Methods
Analyses were performed using a statistical analysis system (SAS) PROC GENMOD, which used a statistical estimation procedure called "Generalized Estimating Equation" to account for the possibility of correlations among the data as well as repeated measures and missing data elements. Changes from baseline values were analyzed for differences between treatment groups utilizing mixed-model analysis of variance (ANOVA).

RESULTS
Fourteen participants completed the 3 week clinical investigation: 7 in the experimental group, and 7 in the positive control group. All patients met all inclusion and exclusion criteria except one patient in the Colgate Total® group whose plaque score (1.48) at baseline was below the inclusion criteria of ≥ 1.95. With regard to demographics, there were no statistically significant differences between groups at baseline.

Analysis of whole mouth mean scores revealed a significant treatment effect $p < 0.0482$ for plaque when comparing groups (see Table I and Graph I). At three weeks, the degree of improvement from baseline in the DioxiBrite™ group for plaque was over six times as great as for the Total® group (DioxiBrite yielded a 14.9% improvement vs. a 2.3% improvement for Total®). When whole mouth means were analyzed for gingivitis and bleeding there were no statistically significant differences noted between groups. Both groups demonstrated a significant reduction in gingivitis $p < .0001$ and bleeding $p < .0001$ (see Tables II, III, and Graph I).

Soft tissue examinations revealed no significant findings. No adverse events were reported during the course of the study by either the investigator or the study participants. According to the completed patient use diaries and product use measurements, there was a high degree of patient compliance and there were not statistically significant differences between the two groups.

Table I
Summary of Baseline and Three Week Means (SD)
for Dental Plaque Index

Parameter	Baseline		3 Week Follow-up		Change from Baseline	
	Mean	SD	Mean	SD	Mean	p-Value
DioxiBrite	2.79	(.15)	2.38	(.09)	-0.41	.0001
Total®	2.63	(.22)	2.57	(.09)	-0.06	.4881
Difference	0.16		-0.19		-0.35	.0482

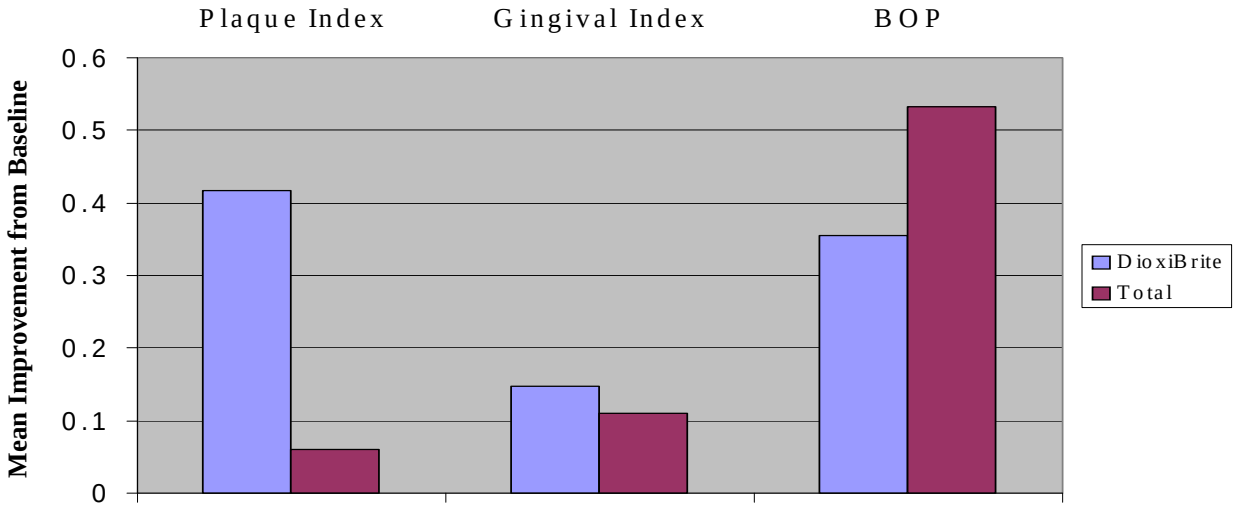
Table II
Summary of Baseline and Three Week Means (SD)
for Gingival Index

Parameter	Baseline		3 Week Follow-up		Change from Baseline	
	Mean	SD	Mean	SD	Mean	p-Value
DioxiBrite	2.12	(.05)	1.97	(.04)	-0.14	.0001
Total®	2.04	(.02)	1.93	(.01)	-0.11	.0001
Difference	0.070		0.04		-0.03	.8817

Table III
Summary of Baseline and Three Week Means (SD)
for Bleeding Index

Parameter	Baseline		3 Week Follow-up		Change from Baseline	
	Mean	SD	Mean	SD	Mean	p-Value
DioxiBrite	1.39	(.14)	1.04	(.06)	-0.35	.0001
Total®	1.57	(.23)	1.04	(.04)	-0.53	.0001
Difference	-0.18		0.00		0.17	.5480

Graph 1. Primary Efficacy Parameters



DISCUSSION

This study demonstrates that DioxiBrite™ toothpaste effectively reduced dental plaque accumulation, gingivitis, and bleeding on probing over the course of a three week clinical trial. The research design compared the efficacy of DioxiBrite (chlorine dioxide) with Colgate's Total® (triclosan). Since Total® is widely accepted as a gold standard antiplaque and antigingivitis toothpaste, when used as a positive control it further supports the results of efficacy. Compared to Total®, DioxiBrite demonstrated an equivalent reduction in both gingivitis and gingival bleeding. However, DioxiBrite demonstrated that it was significantly better in reducing plaque when compared to Total®. Soft tissue examinations revealed no irritation or untoward effects indicating that the test product has a good level of safety. There were no adverse events reported during the course of the study by either the investigator or the participants.

It is recognized that limitations of population size and length of study time reduces the generalizability of the study results. Short-term improvement in the oral health of subjects cannot be completely equated with the use of the products under investigation because the study did not control for the Hawthorne (placebo) effect. Therefore, the initial decrease in indices scores may be the result of eager subjects who became conscientious about toothbrushing because they were involved in a research study. Although the placebo effect was not controlled for, the statistically significant difference in plaque reduction between the two groups is a notable finding.

CONCLUSION

In a short-term clinical trial, DioxiBrite™ toothpaste demonstrated clinical safety and efficacy in reducing dental plaque accumulation, gingivitis, and bleeding on probing. Additionally, DioxiBrite demonstrated statistically significant reduction in dental plaque accumulation when compared with Colgate Total®. Data generated from this preliminary investigation supports further research to determine the continued effects of DioxiBrite toothpaste on oral disease with prolonged use.

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